

DAVISSON ALVES PEREIRA

Fotobiomodulação em duplo comprimento de onda como manejo pós-operatório de exodontias de terceiros molares

Dual wavelength photobiomodulation as post-operative management of third molar
extractions

Tese apresentada ao Programa de Pós-Graduação em Odontologia da Faculdade de Odontologia da Universidade Federal de Uberlândia, como requisito de defesa de tese para obtenção do título de doutor em Odontologia – Processo de Reparo.

Uberlândia, 15 de março de 2024

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Orientadora: Prof^o. Dr^o. Guilherme José Pimentel Lopes de Oliveira

Banca Examinadora

Prof. Dr. Guilherme José Pimentel Lopes de Oliveira

Prof. Dr. Sérgio Vitorino Cardoso - UFU

Prof. Dr. Roberto Sales e Pessoa -UNITRI

Prof^a. Dr^a Leticia Helena Theodoro - Araçatuba

Prof^a. Dr^a. Rosemary Adriana Chiéríci Marcantonio UNESP - Araraquara

Uberlândia, 15 de março de 2024

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Coordenação do Programa de Pós-Graduação em Odontologia
Av. Pará, 1720, Bloco 4L, Anexo B, Sala 35 - Bairro Umuarama, Uberlândia-MG, CEP
38400-902
Telefone: (34) 3225-8115/8108 - www.ppgoufu.com - copod@umuarama.ufu.br



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DEDICATÓRIA

Dedico este trabalho a Deus e a toda minha família, meus pais, meus irmãos, minha esposa e sobretudo a meus filhos, espero que em algum momento se for da vontade deles, que eles possam ler este trabalho e que lhes sirva de inspiração para algo...

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Como se pode observar não seria fácil para min considerar-me como um profissional de excelência, basta avaliar a competência daqueles que me orientaram. Verdadeiramente, não é tão simples, porque ao observar cada um desses nomes que eu acabei de citar tomará nota de que estamos diante de um time com competências extraordinárias, o que dificultou um pouco para min, mas tentei fazer o meu melhor. Não gostaria de ser injusto com outros professores que não estão expressamente citados aqui, claro que todos os professores são importantes, mas não caberia todos aqui, então por este motivo foi necessário fazer essa pequena seleção.

Não poderia finalizar esses agradecimentos sem mencionar minha família meus pais, irmãos, esposa e filhos. Gostaria de destacar a minha mãe, meu maior e melhor exemplo de persistência. Minha mãe não tem curso superior, concluiu o ensino médio após os seus três filhos já “criados” e ato contínuo fez curso de auxiliar e técnico de enfermagem. Honestamente, não me importo com títulos, por isso minha mãe é, e sempre será, minha maior professora. Por fim gostaria de registrar a minha esposa, mãe dos meus filhos, penso que deus a colocou na minha vida para por luz à penumbra. Ela me deu três filhos, Enzo Gabriel, Maria Júlia e João Lucas. “ Amor obrigado por tudo, por apoiar a minha carreira e por cuidar das crianças na minha ausência, no paraíso, Deus tem um lugar especial para você, espero algum dia poder retribuir tudo que você fez e faz por min. Te amo.

“Se você pode sonhar, você pode realizar”

Walt Disney

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Lista de abreviaturas

PBMT - Fotobiomodulação

ATB - Antibiótico

R-PBMT – Fotobiomodulação com laser no comprimento de onda vermelho

RL-PBMT - Fotobiomodulação com laser no comprimento de onda infravermelho

IRL-R-PBMT - Fotobiomodulação com laser no comprimento de onda vermelho e infravermelho

EVA - Escala Visual analógica

CTR- Controle

DF – Dimensão fractal

Resumo

O objetivo deste trabalho foi avaliar os efeitos de diferentes protocolos de fotobiomodulação (PBMT) em mono vermelho ou infra-vermelho ou duplo comprimento de onda (vermelho e infravermelho) e da antibiotiterapia no manejo pós-operatório de exodontias de terceiros molares. Este trabalho foi dividido em 5 capítulos contemplando os objetivos específicos desse estudo. No estudo 1 foi comparado a evolução processo de reparo de alvéolos pós-extração de terceiros molares em pacientes tratados com PBMT em duplo comprimento de onda ou antibioticoterapia. No estudo 2, 3 e 4, foram comparados os diferentes protocolos de PBMT (duplo comprimento de onda intraoral ou de aplicação intra e extraoral, aplicação isolada de laser vermelho ou de laser infravermelho) no manejo pós-operatório de exodontia de terceiros molares por meio de estudos clínicos controlados, randomizados em modelo de boca dividida. No estudo 5 foi avaliado prospectivamente o reparo de alvéolos pós-extração de terceiros molares tratados com PBMT em duplo comprimento de onda aplicado somente de forma intraoral. A PBMT foi aplicada imediatamente no 3 e 7 dias após a cirurgia. Análises clínicas envolvendo os parâmetros (edema, variação de abertura bucal e cicatrização de tecidos moles); e análises centradas no paciente (escala visual analógica (EVA) para avaliação de dor, inflamação, sangramento, dificuldade de abertura da boca e mastigação) foram realizadas no período de 3, 7, 14, 30 e 90 dias após o procedimento cirúrgico. Análises radiográficas foram realizadas para avaliar o reparo ósseo mensurando a densidade radiográfica e a dimensão fractal nos períodos de 7 e 90 dias após a extração dentária. A PBMT em duplo comprimento de onda apresentou redução de edema e maior conforto pós-operatório, devido a redução da dor e menor perda de amplitude de abertura de boca quando comparada a aplicação de ATB. A PBMT com luz infravermelha e diferentes protocolos de aplicação de PBMT em duplo comprimento de onda foram igualmente efetivos no curso pós-operatório de exodontias de terceiros molares. Pode-se concluir que o PBMT reduz o processo inflamatório após extrações de terceiros molares e o ATB não tem efeito benéfico no controle pós-operatório dessas cirurgias.

Palavras-chave: Fototerapia de Baixa Intensidade; Terceiro Molar; Cicatrização de Feridas; Edema.

Abstract

The objective of this study was to evaluate the effects of different photobiomodulation protocols (PBMT) in mono or dual-wavelength (red and infrared), and the antibiotic therapy in the postoperative management of third molar extractions. This PhD thesis was divided into 5 chapters carried out as follows according to the specific objectives of this study. In the study 1, a parallel randomized trial assessed the evolution of the alveolar repair process after third molar extraction compared the patients treated with dual-wavelength PBMT or antibiotic therapy. In study 2, 3 and 4, the different PBMT protocols (dual-wavelength with intraoral - or association of intra and extraoral application, isolated application of red laser or infrared laser) in the post-operative management after extraction of third molars through of split-mouth randomized trial. In study 5, the repair of post-extraction alveoli of third molars treated with dual-wavelength PBMT applied only intraorally was prospectively evaluated. PBMT was applied immediately at 3 and 7 days after oral surgery. Clinical analyzes, involving the (edema, variation in mouth opening and soft tissue healing); and the patient-centered analyzes (application of visual analog scale (VAS) to assess pain, inflammation, bleeding, difficulty opening the mouth and chewing) were performed at 3, 7, 14, 30 and 90 days after the oral surgical procedure. Radiographic analyzes were performed to evaluate bone repair by measuring the radiodensity and fractal dimension at periods of 7 and 90 days after tooth extraction. Dual wavelength PBMT reduced the edema and generated greater postoperative comfort due to reduced pain and less loss of mouth opening range than the application of ATB. PBMT with infrared light and different dual-wavelength PBMT application protocols were equally effective in improving the postoperative course of third molar extractions. It can be concluded that PBMT reduces the inflammatory process after third molar extractions and ATB has no beneficial effect on the postoperative control of these surgeries.

Keywords: Low Intensity Light Therapy; Third Molar; Wound Healing; Edema.

Introdução

A irrupção dos terceiros molares ocorre frequentemente entre 17-20 anos (Mahanta et al., 2022), sendo, portanto, os últimos dentes a irromperem na cavidade oral. Por vezes essa irrupção pode ocorrer de forma incompleta ou até mesmo não ocorrer, podendo levar a complicações, como reabsorções ósseas (Hermann et al., 2019), reabsorções das raízes dos segundos molares (Claudia et al., 2018), osteítes (Øyri H et al., 2020; Santos et al., 2020 Mohanty R., 2022), pericoronarite, lesões císticas e ou tumorais (Adeyemo et al., 2006; Patil et al., 2014). Esses são alguns dos motivos pelos quais este tipo de cirurgia oral está entre as mais realizadas no mundo, com objetivo de se evitar tais ocorrências (Hermann et al., 2019; Santos et al., 2020). Todavia, o tempo necessário para a realização, a necessidade de realização de manobras, tais como osteotomias e odontosecções (Sánchez-Torres et al., 2020), podem levar a alta morbidade no local gerando reações inflamatórias potencialmente desagradáveis aos pacientes (Eshghpour et al., 2016). Esses efeitos envolvem a ocorrência de dor (Xu & Xia, 2020), edema (Daugela et al., 2018), trismo (Zhu et al., 2021), lesões neurais (Abdelkarim Elafifi et al., 2021), alveolites (Blondeau & Daniel, 2007). Somando-se a essas repercussões existem as complicações inerente a realização de qualquer procedimento cirúrgico, como ocorrência de processos infecciosos (Pasupathy et al., 2011).

Diferentes protocolos de terapias são encontrados na literatura objetivando minimizar as repercussões pós-operatórias nas cirurgias de terceiros molares (Pereira et al., 2022; Singh et al., 2023). Assim como, na tentativa de evitar a instalação de processos infecciosos. A utilização de protocolos farmacológicos, termoterápicos, bem como, protocolos físicos, como a fotobiomodulação (PBMT) mediada por laser de baixa intensidade estão entre os mais citados (Cervino et al., 2019; Elmowitz et al., 2021;). A antibióticoterapia é quase unanimidade nos protocolos atuais nas cirurgias de terceiros molares, sobretudo as penicilinas, essa droga tem sido usada de modo profilático de diferentes maneiras objetivando proteger o paciente de uma possível instalação de processo infeccioso local (Rabi et al., 2018; Kimbauer et al., 2022).

A PBMT tem sido proposta como ferramenta no manejo do processo de reparo em diversas condições clínicas, como, por exemplo, na redução de edema em lesões musculares

(Jawko et al., 2019), e controle da dor no tratamento de distúrbios da articulação temporomandibular (Madani et al., 2020). Especificamente em tecido ósseo, estudos clínicos e pré-clínicos demonstraram acelerar a consolidação de fraturas (Chang et al., 2014), melhorar a osseointegração em implantes osseointegráveis (Oliveira et al., 2020) bem como o reparo ósseo em áreas enxertadas com diferentes substitutos ósseos osteocondutores (Oliveira et al., 2018). Levando em consideração os casos citados e as repercussões no reparo em diferentes condições, essa terapia pode ser valiosa no manejo pós-operatório das cirurgias de terceiros molares. Para a aplicação da PBMT, dois grupos de lasers têm sido utilizados de acordo com o comprimento de luz: vermelho e infravermelho (Freddo et al., 2009; Cunha et al., 2012). Lasers com comprimento de onda dentro da faixa da luz infravermelha apresentam maior penetrabilidade dentro dos tecidos e por isso são preferíveis na aceleração da cicatrização óssea (Freddo et al., 2009; Oliveira et al., 2021). Porém, o seu protocolo de irradiação requer pelo menos 7 sessões de irradiação, o que pode ser clinicamente crítico. Lasers dentro do comprimento de onda vermelho também têm demonstrado serem efetivos no processo de regeneração óssea em estudos pré-clínicos em animais imunossuprimidos (Garcia et al., 2014; Garcia et al., 2018). Evidencia-se, a vantagem de que apenas uma aplicação trans-cirúrgica seja efetiva na promoção de efeitos benéficos na cicatrização óssea (Garcia et al., 2014; Garcia et al., 2018). Entretanto, esse laser tem poder de penetrabilidade tecidual menor o que pode limitar seu potencial na cicatrização de tecidos em profundidade (Batista et al., 2021).

Estudos clínicos prévios têm apresentado diferentes protocolos de irradiação, que dificultam o estabelecimento da evidência da utilidade da PBMT em reduzir morbidade pós-exodontia de terceiros molares (Domah et al., 2021). A associação das luzes de laser com comprimento de onda vermelho e infra-vermelho demonstraram que a utilização do laser vermelho intraoral e do laser infravermelho extraoral foram efetivos na redução de dor e do edema pós-operatório de exodontia de terceiros molares impactados (Eshghpour et al., 2016). O uso da PBMT em duplo comprimento de onda, quando utilizada de maneira simultânea e combinada neste tipo de cirurgia comparada ao reparo natural, foi mais efetiva do que a ausência de

tratamento adjunto (Pereira et al., 2022). Em contrapartida, outro estudo clínico demonstrou que a aplicação do laser vermelho e infra-vermelho, intraoral e extraoral, não foi efetiva no controle da dor após exodontia dos terceiros molares (Sierra et al., 2015). Em uma revisão sistemática foi demonstrado que a PBMT demonstrou efetividade na redução do edema após exodontia dos terceiros molares, no entanto, os resultados quanto ao controle da dor são contraditórios, sendo necessário mais estudos clínicos controlados e randomizados para avaliar o efeito da PBMT nessas condições pois os achados não são suficientes (Domah et al., 2021).

Diante do exposto, devido ao processo de cicatrização dos alvéolos pós-extração de terceiros molares envolverem diferentes níveis de complexidade biológica, a indicação de tratamentos adjuntos para melhorar o processo de reparo parece ser benéfica (Caputo et al., 2023). A antibioticoterapia tem sido aplicada de forma extensiva, a despeito do conhecimento que boa parte dos efeitos mórbidos iniciais associados a exodontia são de caráter inflamatório (Cervino et al., 2019). No entanto, a ausência de contaminação pode beneficiar processos de reparo, e o estímulo local nas feridas do hospedeiro pode acelerar eventos cicatriciais como a angiogênese, migração, divisão e diferenciação celular (Cai et al., 2022). Dessa forma, a proposta de tratamento adjunto com PBMT parece ser mais interessante dentro desse contexto, e por isso, a avaliação de diferentes protocolos com essa terapia sobre a cicatrização de alvéolos pós-extração de terceiros molares foi o foco dessa tese.

Objetivos

Objetivo Geral

O objetivo dessa tese foi avaliar o efeito de diferentes protocolos de PBMT e antibióticoterapia sobre o reparo de alvéolos pós-extração de terceiros molares humanos.

Objetivo Específicos

1. Comparar a evolução processo de reparo de alvéolos pós-extração de terceiros molares em pacientes que foram tratados com PBMT em duplo comprimento de onda e com cura espontânea.
2. Comparar a evolução do reparo de alvéolos pós-extração de terceiros molares tratados com PBMT em duplo comprimento de onda ao reparo de alvéolos pós-extração tratados com PBMT com laser vermelho, por meio de análise clínica e radiográfica.
3. Comparar a evolução do reparo de alvéolos pós-extração de terceiros molares tratados com PBMT em duplo comprimento de onda ao reparo de alvéolos pós-extração tratados com PBMT com protocolo infra-vermelho, por meio de análise clínica e radiográfica.
4. Comparar a evolução do reparo de alvéolos pós extração de terceiros molares tratados com PBMT em duplo comprimento de onda intraoral ao reparo de alvéolos pós-extração tratados com PBMT com protocolo misto (intra e extraoral), por meio de análise clínica e radiográfica.
5. Analisar prospectivamente o reparo de alvéolos pós-extração de terceiros molares tratados com PBMT em duplo comprimento de onda.

Hipóteses

Hipóteses Objetivo Específico 1

Hipótese Nula: Não haverá diferença no reparo tecidual pós-exodontia de terceiros molares em pacientes submetidos a antibióticoterapia, PBMT em duplo comprimento de onda e com ausência de tratamento adjunto.

Hipótese Alternativa: Haverá diferença no reparo tecidual pós-exodontia de terceiros molares em pacientes submetidos a antitoxicoterapia, PBMT em duplo comprimento de onda e com ausência de tratamento adjunto.

Hipóteses Objetivo Específico 2

Hipótese Nula: Não hávera diferenças no reparo tecidual pós-exodontia de terceiros molares em sítios tratados com PBMT em duplo comprimento de onda e com PBMT com laser vermelho.

Hipótese Alternativa: Haverá diferenças no reparo tecidual pós-exodontia de terceiros molares em sítios tratados com PBMT em duplo comprimento de onda e com PBMT com laser vermelho.

Hipóteses Objetivo Específico 3

Hipótese Nula: Não haverá diferenças no reparo tecidual pós-exodontia de terceiros molares em sítios tratados com PBMT em duplo comprimento de onda e com PBMT com laser infravermelho.

Hipótese Alternativa: Hávera diferenças no reparo tecidual pós-exodontia de terceiros molares em sítios tratados com PBMT em duplo comprimento de onda e com PBMT com laser infravermelho.

Hipóteses Objetivo Específico 4

Hipótese Nula: Não háavera diferenças no reparo tecidual pós-exodontia de terceiros molares em sítios tratados com diferentes protocolos de PBMT em duplo comprimento de onda.

Hipótese Alternativa: Hávera diferenças no reparo tecidual pós-exodontia de terceiros molares em sítios tratados com diferentes protocolos de PBMT em duplo comprimento de onda.

Hipóteses Objetivo Específico 5

Hipótese Nula: Não haverá interferência de fatores demográficos e clínicos sobre o reparo tecidual pós-exodontia de terceiros molares tratados com PBMT em duplo comprimento de onda.

Hipótese Alternativa: Haverá interferência de fatores demográficos e clínicos sobre o reparo tecidual pós-exodontia de terceiros molares tratados com PBMT em duplo comprimento de onda.

1. CAPÍTULO 1

ARTIGO 1

Comparação da antibioticoterapia e da fotobiomodulação com laser vermelho e infravermelho na cicatrização dos alvéolos pós-extrações de terceiros molares. Um ensaio clínico randomizado.

Comparison of antibiotic therapy and photobiomodulation with red and infrared laser on healing of the post-extraction sockets of third molars. A randomized controlled trial.

***Artigo em revisão no periódico Clinical Oral Investigations**

Original Article: Comparison of antibiotic therapy and photobiomodulation with red and infrared laser on healing of the post-extraction sockets of third molars. A randomized controlled trial.

Davisson Alves Pereira¹, Mariana Silva Bonatto¹, Samara de Souza Santos¹, Pedro Gomes Junqueira Mendes¹, Roberto Sales e Pessoa², Guilherme José Pimentel Lopes de Oliveira¹

¹ Department of Periodontology, School of Dentistry, Universidade Federal de Uberlândia - UFU, Uberlândia, MG, Brazil

² School of Dentistry, Universidade do Triangulo -UNITRI, Uberlândia, MG, Brazil

Conflict of interesting

The authors declare no conflicts of interest

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Trial registration Brazilian Registry of Clinical Trials (REBEC - RBR-4bct2km - Date of registration: 12/06/2021) under number U1111-1263-9675

Author for Correspondence

Guilherme José Pimentel Lopes de Oliveira

Pará, Av., 1760-1844 - Umuarama, Uberlândia - MG, Zip-code: 38405-320

E-mail: guilherme.lopesoliveira@ufu.br

Abstract

Objectives The aim of this study was to evaluate the effect of dual-wavelength photobiomodulation (PBMT) on the post-operative symptoms after third molar extraction compared to antibiotic therapy with amoxicillin. **Material and methods** Sixty patients were randomly allocated in a parallel model according to the protocol of care after extraction of the 4 third molars (n = 15): CTR: No adjunctive therapy; ATB3: Amoxicillin for 3 days; ATB7: Amoxicillin for 7 days; PBMT: PBMT in dual-wavelength. Clinical analyses (assessment of edema, mouth opening variation, and soft tissue healing) and patient-centered analyses (application of visual analogue scale (VAS) to assess pain, inflammation, bleeding, difficulty during opening the mouth, and chewing) were performed at 3, 7, 14, 30, and 90 days after the surgical procedure. Radiographic analysis was performed to evaluate the bone repair by observing the radiographic density and fractal dimension in the periods of 7 and 90 days after tooth extraction. **Results** It was observed that PBMT reduced the loss of mouth opening amplitude and the sensation of pain and edema. There were no differences between the ATB and CTR groups. **Conclusion** PBMT modulates the inflammatory process accelerating the patients recovered after third molar extractions. The ATB had no benefit on the postoperative control after these oral surgeries.

Clinical Relevance PBMT reduced the morbidity after the third molar extraction, while the antibiotic therapy had no beneficial effect.

Keywords: Antibiotic therapy. Healing. Photobiomodulation. Tooth extraction.

Introduction

Third molar extraction surgery is one of the most commonly performed surgeries in the oral cavity [1]. This procedure is usually indicated because these teeth are not functional in some patients [2]. This indication occurs due to the frequent incomplete eruption of these teeth, serving as a niche for the initiation of infectious processes [3], by hindering oral hygiene [1], and providing an adequate means for the emergence of caries lesions [4], as well as promoting bone destruction associated with the distal surface of the second molar [5]. Postoperative repercussions are critical in third molar extraction surgeries. These occurrences are related to inflammatory processes that result in edema, trismus, dysphagia, and pain [1, 2]. Furthermore, the patient's age, position of the tooth in the bone and mouth opening can be factors that predict the difficulty of the surgery [6]. Additionally, the professional skill should be considered, as well as the duration of the oral surgery [7]. Clinical procedures that require more tissue damage, as well as longer procedures, can lead to the emergence of local infections and inflammation [8].

Although the negative repercussions after third molar extraction are basically related to inflammatory processes, the prescription of antibiotics for postoperative control is common [9, 10]. However, the real necessity to administer antibiotics in the postoperative procedures still generates discussions. The occurrence of complications after third molar extraction has not been related to the absence or presence of antibiotic consumption in the post-operative period, since it seems clear that this type of medication is indicated for the treatment or prevention of complications related to infection and not repercussions related to inflammation [11]. The advantages of this therapy, it was necessary to operate on at least 40 patients for one to obtain any benefit [12-14].

The application of photobiomodulation therapy with low-intensity laser (PBMT) has been shown to be an alternative in postoperative inflammatory control in patients undergoing third molar extraction surgery [15, 16]. The application of PBMT can reduce the pain, edema, and inflammation on the treatment of muscle injuries [17], postoperative period of oral surgeries, such as tooth extractions and implant installation [18, 19]. The anti-inflammatory effects of PBMT could make this therapy an effective alternative to the use of antibiotics during the postoperative phase of third molar extraction surgeries.

The bacterial resistance increasing to antibiotics generates the need for more precise indications of these medications. It is necessary to evaluate whether antibiotic therapy medication protocols add advantages when associated with analgesics and anti-inflammatories. Furthermore, it is also important to evaluate whether PBMT could be a good alternative to replace the use of antibiotics in the post-operative care after third molar extraction. Therefore, the aim of this study was to evaluate the effect of dual-wavelength photobiomodulation (PBMT) on the repair of

sockets after third molar extraction compared to antibiotic therapy with amoxicillin. The null hypothesis of this study was that the PBMT and ATB would not influence the post-operative symptoms after the third molars extraction

Material and methods

Study design

This is a single-blinded parallel randomized controlled clinical trial was carried out following the CONSORT (Consolidated Standards of Reporting Trials) protocol. The patient was considered as a sampling unit. The sample size consisted of 60 patients treated at the clinic of the postgraduate School of the Instituto de Pesquisa e Ensino em Saúde Clínica (INPES, Uberlândia, Brazil). The patients underwent tooth extraction procedures for third molars and were randomly allocated into 4 groups, depending on the postoperative care protocol indicated for the patients (n = 15): CTR: use of analgesics and anti-inflammatories; ATB3: Use of analgesics, anti-inflammatories, and antibiotics (Amoxicillin EMS pharm®) for 3 days postoperatively; ATB7: of analgesics, anti-inflammatories, and antibiotics (Amoxicillin EMS pharm®) for 7 days postoperatively; PBMT: use of analgesics, anti-inflammatories, and PBMT at low intensity with light in red and infrared wavelengths used simultaneously and combined in 3 sessions for 7 days. The randomization process to select the treatment for each patient was obtained using an online randomization table (random.org) (GJO). This study was conducted in accordance with the Declaration of Helsinki, and was approved by the human research ethics committee of the Federal University of Uberlândia, under protocol number CAAE: 37924720.3.0000.5152, and was registered with the Brazilian Registry of Clinical Trials (REBEC - RBR-4bct2km - Date of registration: 12/06/2021) under number U1111-1263-9675.

Sample size calculation

The sample calculation was performed based on the study by Eshghpour et al., 2016 [20], which evaluated the effect of PBMT on controlling of pain and edema in the postoperative period after third molar extraction. The primary outcome considered to perform the sample calculation was the level of pain assessed by the VAS scale applied 3 days postoperatively. Considering that a clinically significant difference in patient pain sensation was determined as 2 points on the VAS scale and the standard deviation expected for this analysis over a period of 3 days, as found in the aforementioned article was 1.4, establishing a β power of 0.85 and an α power of 0.05, a minimum sample of 13 patients per group. Therefore, 15 patients per group were recruited to prevent any reduction in the statistical power of the study through patient withdrawals.

Eligibility criteria

To be included in this study, patients were required to present the following characteristics: being over 18 years of age; having good oral hygiene (<20% visible oral biofilm); and having four third molars that were suitable for extraction.

Patients who presented the following characteristics were excluded from the study: those with periodontal disease; allergic to the drugs chosen for use in the study; patients with systemic diseases or conditions or users of medications that alter bone metabolism; decompensated diabetics (glycated hemoglobin above 7%); pregnant or lactating women; heavy smokers (more than 10 cigarettes daily); and the presence of acute periapical and pericoronal lesions.

PBMT Protocol

The GaAlAs laser (Therapy EC, λ 660nm and λ 808nm, 100mW, ϕ ~0.600 μ m, tip divergence = 0.37rad, CW, spot area of 0.0283 cm², DMC Equipamentos, São Carlos, SP, Brazil) was used to carry out the irradiations. This laser radiates light energy in red and infrared wavelengths simultaneously. Two irradiations were carried out at the central point of each extraction socket covering the entire area (vestibular and palatal/lingual portion). The laser was irradiated immediately after the surgical procedure and at the 3rd and 7th postoperative days. Each patient in the group underwent PBMT in all 4 alveoli. Each alveolus was treated with two applications of 4J at red and infrared wavelengths simultaneously and combined, totaling 8J of energy and 40 seconds of irradiation. The energy applied in each session per patient was 32 J. The irradiation energy density used per session was approximately 1.130,74 J/cm²/session and 3.392,22J/cm² throughout the treatment.

Surgical Procedure

All patients referred to the study presented a previous panoramic x-ray, on which it was possible to detect the presence of four third molars. The patients underwent anamnesis and clinical examination. The third molars were classified according to the Pell & Gregory and Winter classifications. All patients received the administration orally 8 mg of dexamethasone (EMS pharm®) one hour before the procedure. For the surgical procedure, patients underwent extraoral and intraoral asepsis and antisepsis with chlorhexidine digluconate at concentrations of 2% and 0.12% respectively, then sterilized surgical drapes were positioned and local anaesthesia using nerve block techniques. The teeth were accessed through a total flap when necessary, and were extracted through the use of various instruments, depending on the necessity, such as levers and the use of high and low rotation drills. After the surgical procedure the sutures were performed.

The medication protocol adopted post-surgery for all patients was as follows: diclofenac sodium (50 mg) for 3 days every 8 hours, and dipyrone sodium (500 mg) for 3 days every 6 hours, in

addition of the use of ATB according to the operated group. Additionally, a mouthwash based on 0.12% chlorhexidine digluconate was prescribed for 7 consecutive days. The sutures were removed after 7 days. All the surgeries were performed by two experienced surgeons that were blinded about the allocation of the patients (DAP, MSB).

Clinical analysis

Patients were clinically evaluated 3, 7, 14, 30, and 90 days after the surgical procedure. The analyses in this study were divided into qualitative (centered on the patient's report and centered on the evaluators' analysis) and quantitative analyses. For patient-centered qualitative analyses, a VAS scale was applied, graduated from 0-10, with 0 being considered the best result. Patients were asked about their perceptions regarding edema, pain, bleeding, opening of the mouth, and chewing quality.

Regarding the qualitative analyses, focused on professional perceptions, 4 aspects were evaluated, graded from 1-3 [21]: I) bleeding: 1) no bleeding, 2) induced by palpation, 3) spontaneous; II) tissue color: 1) 100% pink gum; 2) < 50% of hyperemic and mobile gingiva; 3) >50% of hyperemic and mobile gingiva; III) Exudate: 1) absent, 2) present associated with the presence of pronounced plaque around the alveolus, 3) suppuration; IV) consistency of the healing tissue: 1) resilient and pink, 2) flabby and red, 3) fragile and green or grayish. The overall score can range from 4-12.

Regarding quantitative analyses, mouth opening were measured on the interincisal distance at the midline, with the patient at maximum mouth opening in a comfortable situation. Vertical and horizontal dimensions of the face were measured aiming to assess the post-surgical edema, vertical measurement lateral extremity of the external palpebral commissure to the angle of the mandible, horizontal measurement, ear tragus to ipsilateral external labial commissure [21]. The facial distances and opening of the mouth were expressed as the variation of the values measured at the experimental period compared to the measurements performed before the surgical procedures. All the clinical analyses were performed by one calibrated evaluator blinded regarding the allocation of the patients (SSS).

Fractal and bone density analysis

Panoramic exams were obtained immediately and 90 days after the surgical procedure, aiming to evaluate the alveolar bone density into the remnants defects and the trabecular arrangement, using bone density end fractal dimension analyses. To perform the density analysis, ImageJ software (version 1.3; National Institutes of Health, Bethesda, MD, USA) was used, with the "histometry" tool in a region of interest (ROI) of 32 x 32 pixels in the center of each alveolus, making it possible to obtain the values of gray tones present in the x-ray and to compare the two moments.

To carry out the fractal dimension, the same software and ROI as described above were used. After treatments, an image of the trabecular arrangement of the alveolus was obtained, which in turn can be measured using the “Box-counting” function, which performs the count squares of 2, 3, 4, 6, 8, 12, 16, and 32 pixels in size within the ROI. The number of squares surrounding these trabeculae and the total square count were measured for each different sized pixel. From this count, a logarithmic scale graph of the values was formed, and the fractal dimension value was then calculated by measuring the slope of the line formed aligned with the points plotted on the graph. Alveolar density and fractal dimension analyses were performed for each alveolus. After 30 days, 30% of the samples were reevaluated by the examiner to assess the intra-examiner reproducibility ($r > 95\%$). The radiographic analyses were performed by one calibrated evaluator that were blinded regarding the allocation of the patients (PGLM).

Statistical analysis

Data of fractal analysis, bone density, the VAS scale, and measurements of edema and mouth opening were tested to normality (shapiro-wilk test). Data associating the factors under study (treatment and evaluation time), were performed using the two-way ANOVA test followed by the Tukey test. Repair score data were compared between groups using the non-parametric Kruskal-Wallis test complemented by the Dunn test, The analysis of this intra-group parameter varying between the experimental periods was performed using the non-parametric Friedman test complemented by the Dunn test. GraphPad Prism 8 software (San Diego, CA, USA) was used to perform the statistical analysis. All statistical tests used in this project were applied at a significance level of $\alpha = 0,05 \%$.

Results

Of the 60 patients enrolled in this study, 57 completed the study (23 males and 34 females) with the mean age of 28 years (20 - 48). Two patients in the CTR group and 1 patient in the ATB7 group missed follow-up appointments after suture removal and were excluded of the study. Therefore, 13 patients were included in this study in the CTR group (52 teeth), 14 patients in the ATB7 group (56 teeth), and 15 patients in each of the ATB3 and PBMT groups (60 teeth) (Figure 1). The patients were included and followed-up in this study between August/2021 to August/2022. At the baseline period, it was found that patients of the PBMT and ATB7 groups had a greater number of angulated upper teeth than patients in the CTR group ($p < 0.05$) according to Winter's classification (Table 1). However there were no differences between the groups regarding the position of the lower teeth. The Pell & Gregory classification showed no differences between the groups regarding to the distribution of the extracted teeth (Table 2).

Regarding the baseline data, no differences was found between the groups regarding surgery time, amount of anesthetics used, in relation to osteotomy and odontosection procedures,

mouth opening, and facial dimensions (Table 3). Osteotomy was performed on 10 patients in the CTR group (22 teeth, 18 lower and 4 upper), 8 patients in the ATB3 group (17 teeth, 15 lower and 2 upper), 11 patients in the ATB7 (23 teeth, 22 lower and 1 upper), and 12 patients in the PBMT group (22 teeth, 21 lower and 1 upper). An odontosection was performed in 9 patients in the CTR group (15 lower teeth), 7 patients in the ATB3 group (12 lower teeth), 10 patients in the ATB7 group (19 teeth, 17 lower and 2 upper), and 10 patients in the PBMT group (13 lower teeth). The need for odontosection and osteotomy procedures was not different between groups.

Regarding the facial measurements and mouth opening, at 7 days the patients in the PBMT group showed less loss of mouth opening amplitude than all the other groups (Table 4) ($p < 0.05$). It was also noted that patients of the PBMT group presented less pain than patients of the ATB7 and CTR groups at the 3-day period ($p < 0.05$), and lower edema values than patients in the ATB3 and ATB7 groups at the 3- and 7-day periods ($p < 0.05$) (Table 5). The healing of soft tissues presented progressive improvement in clinical appearance over the longer periods of evaluation (Table 6). This finding was also noted in the radiographic analysis, since a progressive increase in radiographic bone density was observed, with an increase in the evaluation period ($p < 0.05$), without influence from the type of treatment the patient received (Table 7).

Discussion

In general, in the current study it was observed that PBMT reduced the symptoms related to the inflammatory process. There was less reduction in mouth opening range and the patients noticed less sensation of swelling and pain. Additionally, no postoperative interference was observed in patients of the CTR and ATB groups. Therefore, the null hypothesis was rejected.

The effects of PBMT to control the inflammatory process, expressed by the reduction of the edema, was expressed by the reduction on the limitation of mouth opening. Although data of facial dimensions were not influenced by PBMT, these measurements were performed extraorally, and it is possible that the intraoral component suffered greater interference from PBMT. [16]. Previous studies have demonstrated that PBMT reduce the expression of pro-inflammatory biological mediators, which may explain the findings of this study [22, 23]. As the inflammatory process was better controlled in the PBMT group, the classic signs of inflammation were less widely noticed by patients (e.g., pain and edema).

The PBMT protocol used in this study consists in the application of the laser in dual wavelength since the red laser presented higher rates of superficial absorption while the infrared laser penetrates deeper in the tissues [24]. So the use of both wavelength may present additional effect of the tissue healing and also on the inflammatory response modulation [16, 25]. Previous studies have shown that the association of the red and infrared laser improves the healing and reduces the inflammations associated with the molars extractions [16, 24, 25]. However, the

protocols applied were different. One study used the same protocol applied in this study present similar findings [16], while other clinical study demonstrated superiority in the application of PBMT with red laser intraorally and of PBMT with extraoral infrared laser in reducing edema compared to other forms of PBMT application at dual wavelengths [24]. More studies are necessary to check if different protocols of dual-wavelength PBMT presents potential on the inflammation control and tissue healing after then third molar extraction.

Another important finding observed in the current study was the lack of beneficial effects in patients who used ATBs during the postoperative phase. The results of this study confirm that most of the possible postoperative complications after third molar extraction are related to inflammatory processes resulting from the surgical procedure [8, 10, 26], being the complications related to infectious processes are minimal [14, 27]. Therefore, modulation of the inflammatory process is a more beneficial approach to the clinical course after third molar extraction than the application of ATBs, especially in immunocompetent patients, such as those included in this study.

In addition, no significant differences was found regarding to the bone formation within the post-extraction alveoli between the groups. These findings confirm the results of the a previous study which show that despite the good clinical results observed with PBMT in reducing edema and pain and improving soft tissue healing, these results were not observed at the same level in bone tissue [16]. Although PBMT has been shown in preclinical studies to accelerate the bone formation process in defects [28], and the osseointegration process [29], as well as improve bone repair in grafted areas [30] This effect was not observed in the current study. It is possible that the 3-month evaluation time, and also the more favorable healing process associated with the type of defect involved with the post-extraction socket may have influenced the lack of effects of PBMT.

This study presents has an intrinsic limitation the fact that it was not possible to blind the patients due to the obvious differences in therapies between the groups. However, the analyses were performed by blind examiners, and the data obtained clinically, especially the assessment of the inflammatory process, were consistent with what was reported by the patients. The loss of 3 patients during the experimental period was also observed, two of whom were from the CTR group. Although it is not possible to state with certainty, the lack of adherence to the follow-up may have occurred due to dissatisfaction with the recovery process. The PBMT protocol used in this study needs to be compared with other protocols using isolated red or infrared light, in order to evaluate whether the association of these lights is indeed important to obtain the effects of PBMT in third molar extraction surgeries.

Conclusion

PBMT with dual wavelengths benefited the postoperative clinical course after third molar extraction surgeries. The ATBs used for 3 and 7 days did not demonstrate clinical benefits.

Declarations

Author Contribution

Conceptualization, GJO, DAP, RSP; methodology, DAP, SSS, PGJM, MSB, ECS; formal analysis, pgjm, GJO; investigation, MSB, DAP, SSS, PJM, ECS; data curation, RSP, GJO.; writing—original draft preparation, DAP, MSB, GJO; writing—review and editing, DAP, MSB, GJO; visualization, all the authors; supervision, RSP, GJO.; project administration, RSP, GJO.; funding acquisition, GJO. All authors have read and agreed to the published version of the manuscript.

Ethics Approval

This study was conducted in accordance with the Declaration of Helsinki, and was approved by the human research ethics committee of the Federal University of Uberlândia, under protocol number CAAE: 37924720.3.0000.5152, and was registered with the Brazilian Registry of Clinical Trials (REBEC - RBR-4bct2km - Date of registration: 12/06/2021) under number U1111-1263-9675.

Informed consent

Informed consent was obtained from each individual participant in this study. All the participants signed and informed consent that was previously approved by the ethics committee of the Federal University of Uberlândia

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Conflict of interesting

All the authors have no conflict of interesting to declare.

Data availability

The datasets generated and/or analysed during the current study is available from corresponding author on request.

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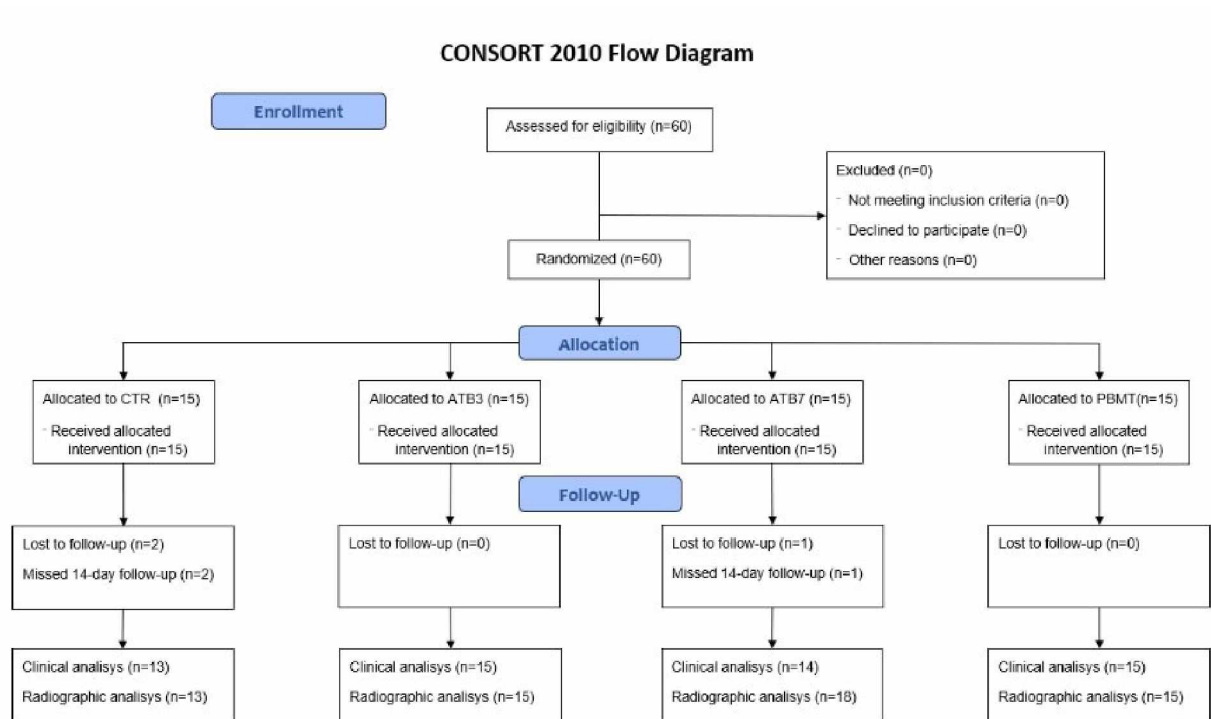
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Figure

Figure 1. Flow diagram of the study



Tables

Original Article: Comparison of antibiotic therapy and photobiomodulation with red and infrared laser on healing of the post-extraction sockets of third molars. A randomized controlled trial.

Table 1: Distribution of the position of extracted teeth in each group according to Winter's classification.

Classification/Group	CTR		ATB3		ATB7		PBMT	
	Upper	Lower	Upper	Lower	Upper	Lower	Upper	Lower
Vertical	22	10	24	16	18	17	18	13
Mesio angled	-	9	1	9	4	9	8	11
Disto angled	4	1	5	1	6	-	4	2
Horizontal	-	6	-	4	-	2	-	4
Total	26	26	30	30	28	28	30	30

Table 2: Distribution of the position of extracted teeth in each group according to the Pell & Gregory classification.

Classification/Group	CTR		ATB3		ATB7		LLLT	
	Upper	Lower	Upper	Lower	Upper	Lower	Upper	Lower
A	18	10	14	14	14	10	11	15
B	6	13	8	13	4	12	8	13
C	2	3	8	3	10	6	11	2
Total	26	26	30	30	28	28	30	30

Table 3: Clinical data on the surgery time, mouth opening, facial measurements, number of tubes applied, and need for anesthetic supplementation.

Parameter	CTR	ATB3	ATB7	PBMT
Surgery time (min)	69.4 ± 23.4	54.0 ± 17.3	71.2 ± 27.5	66.3 ± 34.9
Anesthetic (Tubes p/ patient)	6.5 ± 1.1	6.5 ± 1.3	6.8 ± 1.4	6.8 ± 1.4
Osteotomy (Teeth p/ patient)	1.6 ± 1.3	1.1 ± 1.2	1.5 ± 1.0	1.6 ± 0.7
Odontosection (Teeth p/ patient)	1.1 ± 0.9	0.8 ± 0.9	1.3 ± 1.1	1.0 ± 0.8
Opening of the mouth (mm)	45.3 ± 7.4	41.2 ± 9.6	43.4 ± 6.4	40.5 ± 9.1
Vertical dimension (mm)	10.8 ± 0.6	10.7 ± 0.9	10.1 ± 0.8	10.6 ± 0.8
Horizontal dimension (mm)	11.8 ± 1.3	11.3 ± 1.2	11.4 ± 0.7	11.6 ± 1.0

Table 4: Longitudinal clinical data on the variation in mouth opening and facial dimensions.

*p<0.05- Lower loss of mouth opening amplitude than all other groups – Two-way ANOVA complemented by the Tukey test.

Parameters	Groups	3 days	7 days	15 days	30 days	90 days
Δ Opening of the mouth (mm)	CTR	19.0 $\pm$ 6.8	11.3 $\pm$ 4.8	3.6 $\pm$ 9.7	2.1 $\pm$ 6.2	-0.6 $\pm$ 4.0
	ATB3	14.1 $\pm$ 8.9	12.4 $\pm$ 8.6	1.3 $\pm$ 7.4	-0.3 $\pm$ 4.9	1.1 $\pm$ 6.0
	ATB7	19.2 $\pm$ 8.5	15.7 $\pm$ 9.1	6.3 $\pm$ 7.2	1.4 $\pm$ 7.1	-2.6 $\pm$ 5.3
	PBMT	15.5 $\pm$ 8.4	4.0 $\pm$ 5.8*	-0.4 $\pm$ 6.8	-0.6 $\pm$ 8.5	-2.9 $\pm$ 4.9
Δ Vertical dimension (mm)	CTR	0.1 $\pm$ 0.7	0.1 $\pm$ 0.7	0.0 $\pm$ 1.4	0.2 $\pm$ 0.9	0.8 $\pm$ 3.6
	ATB3	0.1 $\pm$ 0.9	0.1 $\pm$ 0.8	0.2 $\pm$ 0.7	0.1 $\pm$ 0.8	0.2 $\pm$ 0.9
	ATB7	0.7 $\pm$ 1.1	0.7 $\pm$ 1.0	0.9 $\pm$ 0.8	0.6 $\pm$ 1.0	0.5 $\pm$ 0.6
	PBMT	0.6 $\pm$ 0.8	0.4 $\pm$ 1.1	0.2 $\pm$ 1.0	0.2 $\pm$ 1.0	0.3 $\pm$ 0.9
Δ Horizontal dimension (mm)	CTR	0.3 $\pm$ 1.1	0.3 $\pm$ 1.1	0.4 $\pm$ 1.7	0.2 $\pm$ 0.7	0.1 $\pm$ 0.9
	ATB3	0.3 $\pm$ 0.7	0.2 $\pm$ 0.9	0.3 $\pm$ 1.0	0.3 $\pm$ 0.7	0.1 $\pm$ 1.0
	ATB7	0.26 $\pm$ 0.65	0.1 $\pm$ 0.6	-0.1 $\pm$ 0.7	0.1 $\pm$ 0.8	0.1 $\pm$ 0.5
	PBMT	0.47 $\pm$ 1.03	-0.1 $\pm$ 1.0	-0.1 $\pm$ 1.4	-0.1 $\pm$ 0.8	-0.1 $\pm$ 0.8

Table 5: Longitudinal clinical data from the VAS scale that was applied to the patients. *Lower values than the ATB7 group.

Parameters	Groups	3 days	7 days	15 days	30 days	90 days
Pain	CTR	4.5 ± 1.9	2.6 ± 2.2	0.6 ± 0.9	0.2 ± 0.6	0.2 ± 0.8
	ATB3	4.1 ± 1.6	3.2 ± 2.3	0.73 ± 1.2	0.2 ± 0.5	0.1 ± 0.1
	ATB7	4.6 ± 1.6	2.4 ± 1.3	0.5 ± 0.9	0.2 ± 0.5	0.3 ± 1.3
	PBMT	2.7 ± 1.8* ^δ	2.2 ± 1.9	0.4 ± 0.8	0.2 ± 0.4	0.3 ± 1.1
Bleeding	CTR	2.8 ± 3.0	0.8 ± 0.9	0.0 ± 0.0	0.03 ± 0.1	0.1 ± 0.6
	ATB3	2.3 ± 2.1	0.7 ± 1.5	0.3 ± 0.9	0.03 ± 0.1	0.03 ± 0.1
	ATB7	1.5 ± 1.7	0.4 ± 1.1	0.1 ± 0.1	0.0 ± 0.0	0.0 ± 0.0
	PBMT	2.4 ± 2.0	1.5 ± 1.6	0.1 ± 0.1	0.1 ± 0.4	0.0 ± 0.0
Edema	CTR	4.0 ± 1.8	2.1 ± 1.5	0.2 ± 0.6	0.1 ± 0.3	0.4 ± 1.2
	ATB3	5.2 ± 2.6	2.5 ± 1.4	0.4 ± 0.7	0.1 ± 0.2	0.0 ± 0.0
	ATB7	5.6 ± 2.3	2.9 ± 1.7	0.3 ± 0.8	0.0 ± 0.0	0.4 ± 1.6
	PBMT	3.2 ± 1.0* [#]	1.1 ± 0.8* [#]	0.4 ± 0.7	0.3 ± 0.5	0.2 ± 1.0
Chewing	CTR	5.7 ± 2.1	2.8 ± 2.4	0.4 ± 0.6	0.1 ± 0.3	0.3 ± 0.8
	ATB3	6.0 ± 2.2	2.8 ± 2.1	1.2 ± 1.9	0.1 ± 0.4	0.0 ± 0.0
	ATB7	5.9 ± 1.5	3.7 ± 2.8	1.0 ± 1.4	0.2 ± 0.6	0.4 ± 1.6
	PBMT	5.0 ± 2.6	3.0 ± 1.9	0.7 ± 1.1	0.4 ± 1.2	0.4 ± 1.4
Opening of the mouth	CTR	5.0 ± 2.7	1.8 ± 2.5	1.0 ± 1.5	0.1 ± 0.4	0.3 ± 0.7
	ATB3	5.1 ± 2.9	2.2 ± 1.7	1.1 ± 1.5	0.2 ± 0.5	0.0 ± 0.0
	ATB7	6.1 ± 2.1	3.1 ± 2.4	0.9 ± 1.8	0.2 ± 0.7	0.5 ± 1.9
	PBMT	5.3 ± 2.6	3.0 ± 2.6	0.7 ± 1.1	0.3 ± 0.6	0.4 ± 1.4

Lower values than the ATB3 group; ^δLower values than the CTR group. P < 0.05 – Two-way

ANOVA complemented by the Tukey test.

Table 6: Distribution of scores from analyses of the clinical appearance of alveoli after extraction of upper molars.

Region	Upper					Lower				
Group/Period	3d.	7d.	15d.	30d.	90d.	3d.	7d.	15d.	30d.	90d.
CTR	4.5 (3.5;5.2)	5.0 (4.0; 6.0)	4.0 (4.0; 5.0)	4.0(4.0; 4.0)	4.0(4.0; 4.0)	6.0 (4.0; 7.0)	5.0(4.2; 6.0)	5.0 (4.0; 5.0)	4.0(4.0; 4.0)	4.0(4.0; 4.0)
ATB3	5.0 (4.0; 6.0)	5.0 (4.0;5.0)	4.5 (4.0; 5.0)	4.0(4.0; 4.0)	4.0(4.0; 4.0)	5.0 (4.0; 6.0)	5.0 (5.0; 6.0)	4.0(4.0; 5.0)	4.0(4.0; 5.0)	4.0(4.0; 4.0)
ATB7	7.0 (5.0;7.0)	5.0 (4.0;6.0)	4.0 (4.0;5.0)	4.0(4.0; 4.0)	4.0(4.0; 4.0)	6.0(5.2;7.0)	5.0(4.0;5.0)	4.0(4.0; 5.0)	4.0(4.0;4.7)	4.0(4.0; 4.0)
PBMT	6.0 (4.0;7.0)	5.0 (5.0;6.2)	4.5 (4.0;6.0)	4.0(4.0; 4.0)	4.0(4.0; 4.0)	6.0(4.7;7.0)	5.0(5.0;6.0)	5.0(4.0;5.0)	4.0(4.0; 4.0)	4.0(4.0; 4.0)

Table 7: Mean and standard deviation of values obtained in the analyses of radiographic density and fractal dimension in all groups and experimental periods.

Period	Group	Radiographic density		Fractal dimension	
		Upper	Lower	Upper	Lower
Immediate	CTR	113.0 ± 28.4	128.2 ± 15.8	1.3 ± 0.1	1.3 ± 0.1
	ATB3	118.3 ± 19.3	119.9 ± 20.0	1.2 ± 0.1	1.3 ± 0.1
	ATB7	120.5 ± 24.3	118.2 ± 20.7	1.2 ± 0.1	1.3 ± 0.1
	PBMT	117.6 ± 21.8	118.4 ± 19.2	1.3 ± 0.1	1.3 ± 0.1
90 days	CTR	146.8 ± 13.1	145.3 ± 15.1	1.3 ± 0.1	1.2 ± 0.1
	ATB3	134.4 ± 13.3	135.9 ± 12.0	1.2 ± 0.1	1.3 ± 0.1
	ATB7	137.5 ± 22.4	140.3 ± 13.6	1.3 ± 0.1	1.3 ± 0.1
	PBMT	140.4 ± 16.6	137.1 ± 17.9	1.3 ± 0.1	1.3 ± 0.1

Cover Letter

Dear Prof. Dr. Matthias Hannig and Prof. Dr. Stefan Ruhl

We are submitting the paper entitled: Comparison of antibiotic therapy and photobiomodulation with red and infrared laser on healing of the post-extraction sockets of third molars. A randomized controlled trial.” to the Clinical Oral Investigations. The aim of this clinical trial was to evaluate the effect of dual-wavelength photobiomodulation (PBMT) on the repair of sockets after third molar extraction compared to antibiotic therapy with amoxicillin. The extraction of third molars is related with high morbidity level. These occurrences are related to inflammatory processes that result in edema, trismus, dysphagia, and pain. Although the negative repercussions after third molar extraction are basically related to inflammatory processes, the prescription of antibiotics for postoperative control is common. However, the real necessity to administer antibiotics in the postoperative period after these surgeries still generates discussions. The application of photobiomodulation therapy with low-intensity laser (PBMT) has been shown to be an alternative in postoperative inflammatory control in patients undergoing third molar extraction surgery, and our hypothesis was that this adjunctive therapy may be more beneficial in the post-operative phase regarding the soft and hard tissues healing, pain and edema control, and reduction of complications compared with the antibiotic therapy.

The main finding of this study was that the PBMT reduced the loss of mouth opening amplitude and the sensation of pain and edema while the antibiotic therapy presented no beneficial effect.

In addition, we declare that all the authors listed in this study meet the criteria for authorship giving: 1) substantial contributions to conception and design of, or acquisition of data or analysis and interpretation of data, 2) drafting the article or revising it critically for important intellectual content and 3) final approval of the version to be published.

This study was supported by grants from CNPq, National Council for Scientific and Technological Development and FAPEMIG, Fundação de amparo a pesquisa de Minas Gerais (Grants INCT Saúde Oral e Odontologia 406840/2022-9, FAPEMIG APQ-02211-21, and CNPq – Financial code 001). Furthermore, the authors declare to have no conflict of interest regarding this paper.

All my best regards

Guilherme José Pimentel Lopes de Oliveira

Pará, Av., 1760-1844 - Umarama, Uberlândia - MG, Zip-code: 38405-320

email: guilherme.lopesoliveira@ufu.br

2. CAPÍTULO 2

ARTIGO 2

**Comparação da fotobiomodulação em duplo comprimento de onda e
com luz vermelha no reparo associado a exodontias de terceiros
molares: Ensaio clínico controlado e randomizado em modelo de boca**

dívida. Comparison of dual-wavelength photobiomodulation and red light in repair
associated with third molar extractions: Controlled and randomized clinical trial in a debt
mouth model.

***Artigo em revisão no periódico Lasers in medical science**

Original Research: Comparison of photobiomodulation with dual-wavelength and red laser on the post extraction repair associated with third molar extraction. A split-mouth double blinded randomized clinical trial

Davisson Alves Pereira (0000-0001-5422-6927)¹, Mariana Silva Bonatto (0000-0002-7280-103X)¹, Eduvaldo Campos Soares Junior (0000-0003-1206-8005)¹, Samara de Souza Santos (0000-0002-9799-4739)¹, Roberto Sales e Pessoa (0000-0003-1763-3691)², Guilherme José Pimentel Lopes de Oliveira (0000-0001-8778-0115)¹

¹ Federal University of Uberlândia - UFU, School of Dentistry, Department of Periodontology, Uberlândia, MG, Brazil

² School of Dentistry, Universidade do Triangulo -UNITRI, Uberlândia, MG, Brazil

Declarations

Author Contribution

Conceptualization, GJO, DAP, RSP; methodology, DAP, SSS, MSB, ECS; formal analysis, DAP, SSS, GJO; investigation, MSB, DAP, SSS, ECS; data curation, RSP, GJO.; writing—original draft preparation, DAP, MSB, GJO; writing—review and editing, DAP, MSB, GJO; visualization, all the authors; supervision, RSP, GJO.; project administration, RSP, GJO.; funding acquisition, GJO. All authors have read and agreed to the published version of the manuscript.

Ethics Approval

This study was conducted in accordance with the Declaration of Helsinki, and was approved by the human research ethics committee of the Federal University of Uberlândia, under protocol number CAAE: 72834023.3.0000.5152, and was registered with the Brazilian Registry of Clinical Trials (REBEC - RBR-103g7j28- Date of registration: 12/07/2023) under number U1111-1297-6962.

Informed consent

Informed consent was obtained from each individual participant in this study.

Conflict of interesting

The authors declare no conflicts of interest.

Acknowledgments

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Data availability

The datasets generated and/or analysed during the current study is available from corresponding author on request. The data will be included in the repository of the Universidade Federal de Uberlândia after pHD thesis finalization of Davisson Alves Pereira.

Author for Correspondence

Guilherme José Pimentel Lopes de Oliveira

Pará, Av., 1760-1844 - Umuarama, Uberlândia - MG, Zip-code: 38405-320

Email: guilherme.lopesoliveira@ufu.br

Original Research: Comparison of photobiomodulation with dual-wavelength and red laser on the post extraction repair associated with third molar extraction. A split-mouth double blinded randomized clinical trial

Abstract

Purpose: The aim of this split-mouth double blinded randomized clinical trial was to compare the effect of photobiomodulation (PBMT) using red and infrared wavelengths combined and PBMT with only red wavelength on the healing of post-extraction alveoli of third molars.

Material and methods: Twenty patients underwent third molar extraction. The alveoli were treated randomly in a split mouth model with: PBMT with red laser (R-PBMT) or PBMT with red and infrared laser combined (IR-R-PBMT). PBMT was applied immediately, and 3 and 7 days after surgery. Patients were clinically evaluated in relation to repair (bleeding, exudate, color, and consistency of the tissues), degree of the edema, and through the application of a VAS scale (Pain, edema, bleeding, chewing, mouth opening) in the baseline period, and 3, 7, 14, 30, and 90 days after the surgical procedure. In addition, bone tissue density and structure were measured by radiographic analysis at 7 and 90 days postoperatively. **Results:** Clinical analysis showed that dual-wavelength PBMT induce more reduction of the edema 7 days after surgery compared with the PBMT performed with red laser, however, no significant differences were noted between groups in other parameters. **Conclusion:** Dual-wavelength PBMT improved the postoperative clinical parameters by reducing edema 7 days postoperatively.

Keywords: Bone. Healing. Photobiomodulation. Soft tissue. Third molar.

Introduction

A range of surgical procedures are routinely performed in clinical dental practice [1-6], with great variations in techniques and approaches. However, in general, invasive procedures can cause patients a certain degree of postoperative discomfort [7]. Postoperative morbidity is related to inflammatory processes, which are the result of surgical interventions. These interventions lead to the local release of biological mediators of inflammation (i.e., pro-inflammatory cytokines, arachidonic acid metabolites, bradykinin, histamine) [8, 9].

The use of low intensity laser photobiomodulation has been used to treat the wounds resulting from oral surgical procedures (PBMT) [10]. PBMT has shown promise for reducing the painful symptoms associated with temporomandibular disorders [11], as well as for reducing muscle pain [12], and edema associated with third molar extractions [13, 14]. In addition, PBMT has been showed to improve the recover after neural lesions of the inferior alveolar nerve [15]. An enhance in the osseointegration of dental implants has also been reported [16]. These effects may indicate the ability of PBMT to modulate the inflammatory response [17]. However, factors inherent to the physical properties of lasers can influence the success of PBMT [18]. Among these factors, the wavelength has been highlighted, as it presents different properties regarding to the tissue penetrability, even in cases with the application of a similar amount of energy and number of therapy sessions [19, 20]. Lasers with wavelengths within the infrared light range have greater tissue penetrability, which makes them preferable when a deep tissue approach is indicated (i.e., osseointegration of implants, treatment of paresthesias) [21]. On the other hand lasers that emit red wavelength light have less tissue penetration [22]. However, there is a concentration of energy at wound superficial regions, which makes this type of PBMT more indicated for treating the superficial tissue approaches (i.e., treatment of mucositis or periodontal disease) [18, 19].

As a way of simplifying the therapeutic protocol, PBMT can be applied with the association of lasers with red and infrared wavelengths combined, which could be beneficial in situations where there is a need to stimulate both superficial and deep tissue repair. An example of a clinical condition that could benefit from this type of approach is the post-extraction sockets especially after third molar extraction. This type of surgery involves the need for extensive tissue detachment and wear of surrounding bone tissue, generating a considerable inflammatory process [23].

Due to the varied therapeutic possibilities of PBMT, it is necessary to improve outcomes and obtain more predictable results by establishing more precise protocols and indications for this treatment modality. For this purpose, the objective of this study was to compare, using a split-mouth randomized, controlled clinical trial study design, the effect of PBMT in third molar extraction surgeries using a red wavelength laser or multiwave laser (red and infrared) used simultaneously. The null hypothesis was that the protocols would have similar clinical results during the postoperative analyses of third molar extractions.

Material and methods

Study design

This split-mouth randomized, controlled clinical trial was carried out following the CONSORT (Consolidated Standards of Reporting Trials) protocol. For statistical purposes, each post-extraction alveolus was considered as an individual case and each patient underwent the split-mouth model, whereby they were subjected to both test and control treatments. The sample consisted of 20 patients who were approached at the clinic of XXXXX. These patients underwent procedures for dental extraction of the third molars and a subsequent stimulation procedure for healing of the post-extraction alveoli with PBMT with dual-wavelength of 4J on one side, twice, and on the contralateral side 2 further irradiations of 4J at red wavelength. The randomization process to select treatments was based on an online randomization table (random.org). The researcher responsible for the treatment allocation did not participate on the surgeries and evaluations. The patients were blinded regarding the protocols of PBMT applied. This study was conducted in accordance with the Declaration of Helsinki, and was approved for conduction by the human research ethics committee of the XXXX under protocol number XXXXX and was registered with the XXXXX under number XXXXX.

Sample size calculation

The sample calculation was performed based on the study by Heo et al., 2002 [20], which carried out fractal analysis of bone in the regeneration phase after orthognathic surgery. A fixed mean difference of 0.10 points was established as being clinically relevant, and with an expected mean standard deviation of 0.05, a sample size of 15 patients was calculated to be sufficient to determine this level of difference, with a β power of 0.90 and an α power of 0.05. Then 20 patients were allocated per group to replace any patients who withdrew during the project.

Inclusion and exclusion criteria

To be included in this study, the patients need to present the following characteristics: be over 18 years of age, have good oral hygiene, have 4 third molars, and be indicated for all third molars extractions.

Patients who presented the following characteristics were excluded from the study: with periodontal disease, or with allergies to the drugs chosen for use in the study with systemic diseases or conditions or have taking medications that alter bone metabolism (except diabetics), decompensated diabetics (glycated hemoglobin above 7%); pregnant or lactating women; heavy smokers (more than 10 cigarettes a day); the presence of metallic artifacts that make tomographic analysis difficult; and the presence of periapical lesions.

Laser therapy Protocol

The GaAlA laser (XTherapy EC, λ 660nm and λ 808nm, 100mW, $\phi \sim 0.600 \mu\text{m}$, tip divergence = 0.37rad, CW, spot area of 0.0283 cm², DMC Equipamentos, São Carlos, SP, Brazil) was used to carry out the irradiations. The laser emits light energy on the red and infrared wavelengths

simultaneously. In the area where the third molars were extracted, two irradiation points were used at the central location of each extraction socket. The emitted light covered the entire area. The laser irradiation was performed immediately after the sutures and at the 3rd and 7th postoperative days. The side was treated using dual-wavelength PBMT simultaneously and combined. Two irradiations were performed per alveolus, with 4 J of energy emitted in each irradiation, which totaled 8 J per alveolus, and 16 J per side treated, per session. On the side treated with red wavelength PBMT, the irradiation protocol followed the same pattern as on the previous side, with the only change being in the use of the emitted wavelength, therefore, 4J of energy was used per application, with two applications for each alveolus. The irradiation energy density used per session was approximately 859.9 J/cm²/session and 2,579.7cm² throughout the treatment for each protocol.

Surgical procedure and study groups

All patients referred to the study underwent a panoramic x-ray, on which it was possible to detect the presence of the lower and upper third molars. Subsequently, the patients underwent an anamnesis and clinical examination. The third molars were classified according to the Pell & Gregory and Winter classifications and all data necessary for the surgery were collected. On the day of the surgical procedure, all patients took 8mg of dexamethasone (EMS pharm®) one hour before the procedure, administered orally. Furthermore, the patients underwent extraoral and intraoral asepsis and antisepsis with chlorhexidine digluconate, at concentrations of 2% and 0.12% respectively. Following positioning of sterilized surgical drapes, the local anesthesia was performed and the teeth were accessed through a full flap when necessary and extracted using various instruments, depending on the need, such as levers and the use of high and low rotation handpieces associated with cutting or abrasion drills. The procedure was finished with tissue synthesis techniques. The patients were allocated on the two groups according to the protocol of PBMT applied after the extraction of the 4 third molars, in a split-mouth model: the control side was treated with irradiation from a low intensity laser with red wavelength (660 nm red laser) (R-PBMT), and the test side with irradiation from a low intensity laser with dual-wavelength, used simultaneously and combined (660 nm red wavelength and 808 nm infrared laser) (IR-R-PBMT), both applications performed intraorally.

The medication protocol adopted post-surgery administrated via oral for all patients was as follows: diclofenac sodium 50 mg ((EMS pharm®) for 3 days every 8h and dipyron sodium 500 mg (EMS pharm®) for 3 days every 6. Additionally, mouthwash was prescribed 30 minutes after meals using 0.12% chlorhexidine digluconate was prescribed for 7 days at intervals of 12. The sutures were removed 7 days after the surgical procedure. The surgical procedures were executed by two experienced operators XXXX.

Clinical analysis

Patients were clinically evaluated 3, 7, 14, 30, and 90 days after the surgical procedure. The analyses were divided into qualitative (centered on the patient's report and on the evaluators' analysis) and quantitative analyses. For patient-centered qualitative analyses, a VAS scale graduated from 0-10 was applied, with 0 being considered the best result, where the patients were asked about their perceptions regarding edema, pain, bleeding, opening of the mouth, and limitations on the chewing.

Regarding qualitative analyses focused on professionals' perceptions, 4 aspects were evaluated, graded from 1-3 [14]: i) bleeding: 1) no bleeding, 2) induced by palpation, 3) spontaneous; ii) tissue color: 1) 100% pink gum; 2) < 50% of hyperemic and mobile gingiva; 3) >50% of hyperemic and mobile gingiva; iii) exudate: 1) absent, 2) present associated with the presence of pronounced plaque around the alveolus, 3) suppuration; iv) consistency of the healing tissue: 1) resilient and pink, 2) flabby and red, 3) fragile and green or grayish, with the overall score being graded from 4-12.

Regarding quantitative analyses, mouth opening was measured with digital caliper considering the interincisal distance at the midline with the patient at maximum mouth opening in a comfortable position. In addition, vertical and horizontal dimensions of the face were measured with the aim of establishing post-surgical edema: vertical measurement: lateral extremity of the external palpebral commissure to the angle of the mandible; horizontal measurement: ear tragus to ipsilateral external labial commissure [14] The facial distances and mouth opening were expressed as the variation values analyzed in each experimental period compared to the values recorded before the surgical procedure. All the clinical analysis were performed by a single, calibrated and blinded evaluator XXXX.

Panoramic x-ray analysis

Panoramic exams were obtained at 7 and 90 days after the surgical procedure. To perform the density analysis, ImageJ software (version 1.3; National Institutes of Health, Bethesda, MD, USA) was used, with the "histometry" tool in a region of interest (ROI) of 32 x 32 pixels in the center of each alveolus, making it possible to obtain the values of gray tones present in the x-ray and to compare the two moments.

To carry out the fractal dimension, the same software and ROI as described above were used, and after a series of treatments, an image of the trabecular arrangement of the alveolus was obtained, which in turn can be measured using the "Box-counting" function, which performs the count squares of 2, 3, 4, 6, 8, 12, 16, and 32 pixels in size within the ROI. The number of squares surrounding these trabeculae and the total square count were measured for each different sized pixel. From this count, a logarithmic scale graph of the values was created, and the fractal dimension value was calculated by measuring the slope of the line formed aligned with the points plotted on the graph. Alveolar density and DF analyses was performed for each alveolus. After 30 days, 30% of the samples were reevaluated by the examiner to assess the intra-examiner

reproducibility ($r > 90\%$). All the radiographic analysis were performed by a single, calibrated and blinded evaluator XXXXX.

Statistical analysis

The classification of teeth was compared between groups using Fisher's exact test. The evaluation of the effects of the independent treatment variables (IR-R-PBMT vs. R-PBMT) with the evaluation period for facial dimensions and VAS scale and with the location of the teeth in the oral cavity (upper and lower) was performed through the application of linear mixed models. Jamovi software was used to perform the statistical analysis. All statistical tests used in this project were applied at a significance level of 5%.

Results

Level of difficulty of the extraction procedure and the occurrence of complications were similar between the different PBMT protocols

A total of 80 teeth were extracted from the 20 patients in this study, 40 lower teeth and 40 upper teeth, half of which were treated with IR-R-PBMT and the other half with R-PBMT. The patients were treated and follow-up between July to November 2023. There were no patient withdrawals from this study (Fig. 1). In total, 24 osteotomies (1 upper and 12 lower teeth whose alveoli were treated by R-PBMT and 11 lower teeth whose alveoli were treated by IR-R-PBMT) and 17 odontosections (8 lower teeth treated by R-PBMT and 9 lower teeth treated by IR-R-PBMT) were performed during the dental extraction surgical procedure, with no statistically significant differences between the groups. The average surgery time was 60.1 ± 25.9 min, and there were no differences in relation to the positioning of the teeth between the experimental groups according to Winter's (Table 1) and Pell & Gregory's classifications (Table 2). There were also no differences between the groups in relation to the frequency of unpleasant repercussions related to surgical procedures. The main negative repercussions were trismus (1 case at 3 days and 3 cases at 7 days), the presence of bone spicules within a 7-day period in a patient associated with the alveoli of both upper molars, and the need for irrigation with chlorhexidine and saline solution in two lower molar alveoli in one patient within a 7-day period.

Degree of healing and symptoms noted during the postoperative phase of third molar extraction by professionals and patients were not different between the different PBMT protocols

No differences were noted between the groups in relation to the healing assessed by the researchers involved in this study (Table 3). There were also no differences observed among patients between the different PBMT protocols in the assessment of pain, edema, bleeding, mouth opening, and chewing obtained by the VAS scale in any of the evaluated periods (Table 4).

There was a reduction in the inflammatory process in both groups, however the IR-R-PBMT protocol was associated with greater reductions in edema over a 7-day period than the R-PBMT protocol

After tooth extraction surgery a reduction was observed in mouth opening and an increase in facial dimensions bilaterally, with the peak of these measurements occurring between 3-7 days after the surgical procedure. From this moment on, a substantial improvement was observed in mouth opening and a return of facial dimensions to values recorded before the surgical procedure. Over the 7-day period, both the variation in horizontal and vertical facial dimensions was smaller in the IR-R-PBMT group, which indicates less edema associated with this PBMT protocol than in the R-PBMT group (Table 5).

IR-R-PBMT and R-PBMT showed similar potential for bone tissue healing

No differences were observed between the groups in relation to bone density and fractal dimension, however, in both groups there was an increase in bone density in the 90-day period compared to the baseline period ($p < 0.05$) (Table 6).

Discussion

The dual-wavelength PBMT protocol used simultaneously in this study modulates the postoperative clinical course after third molar surgery, as it reduced edema over a 7-day period. However, no other differences were observed in the postoperative clinical course in relation to the use of PBMT with red laser. Therefore, the alternative hypothesis of this study was partially accepted.

This reduction in edema promoted by dual-wavelength PBMT corroborates data from a previous study that observed a reduction in edema and pain, and improvement in soft tissue repair after extraction of lower third molars compared to sockets that were not subjected to PBMT [24]. In the current study, the observation of differences only in edema parameters may be linked to the PBMT treatment with red laser used in the other alveoli. The anti-inflammatory effects observed with dual-wavelength PBMT may be due to the modulatory effects of this therapy observed in cell culture studies. PBMT accelerated the proliferation and migration of fibroblasts and increased their ability to synthesize collagen and produce angiogenic factors even when these cells were challenged with pro-inflammatory cytokines (TNF- α , IL-1 β , IL-6, and IL-8) [21]. In a study with macrophage cultures, it was observed that PBMT accelerated the differentiation of undifferentiated mesenchymal cells into macrophages, and increased the conversion of M1 to M2 macrophages; this event was associated with a reduction in pro-inflammatory cytokines TNF α and IL6 [22]. A preclinical study demonstrated that PBMT reduced edema formation in the paws of mice that were injected with phlogistic agents [23].

The mechanism of action of PBMT with red and infrared light is similar and targets the action of light energy on cellular mitochondrial chromophores, accelerating metabolism by stimulating the process of cellular respiration [24]. In this way, PBMT can stimulate the proliferation, migration, differentiation, and action of different cell types [25, 26]. The difference between red and infrared lasers is due to their tissue penetrability power, as the red laser is more absorbed superficially, while the infrared laser has greater penetrability power [27]. Post-

extraction alveoli are clinical conditions that can benefit from the interaction of PBMT with the dual-wavelength laser since these types of lesions have superficial and deep components that can be affected differently by red and infrared light. Interestingly, the clinical analyses of superficial tissues were not different between the groups, while differences between the protocols tested in this study were observed in the analysis of edema, which included the assessment of deep tissues. Therefore, the findings of this study are in agreement with the applicability of red light in the healing of superficial tissues and of infrared light in deep tissues [27].

In the current study, patients noticed no differences between the treated and untreated sides. This absence may have occurred due to the study design using a split-mouth model, which makes it difficult for the patient to distinguish differences between therapies, as well as to the fact that the procedure was performed in a single surgical procedure by experienced professionals, which may have reduced the postoperative morbidity. The fact that it was not possible to observe postoperative clinical differences related to the level of surgical complexity and the different protocols used, treatment with PBMT at red wavelength and with PBMT at red and infrared dual-wavelength seems to make it clear that the postoperative repercussions are not related to the position of the teeth and the protocols used. It is possible that in more difficult surgical conditions, which require longer procedure execution times, dual-wavelength PBMT may prove superior in controlling postoperative morbidity, and may be better distinguished by patients. This hypothesis should be tested in the future.

There were no differences between the PBMT protocols regarding the formation and structure of bone tissue in the post-extraction sockets. These findings may have occurred because both protocols act in a similar way on bone tissue. However, it is worth noting that studies that demonstrate the effects of PBMT on bone formation present a greater number of PBMT sessions than the protocols tested in the current study. A previous clinical study did not demonstrate differences in the tomographic appearance of post-extraction alveoli of third molars treated or not with dual-wavelength PBMT [23], therefore, the protocol tested in this study is not realistically intended to accelerate bone formation in post-extraction sockets.

The current study presents some limitations that should be taken into account when evaluating the results. The split mouth model is a good way to evaluate tissue regeneration processes, preventing differences between patients from interfering with the results; however, the fact that the surgeries were performed on the same day can generate confusion in patient reports regarding VAS scale values, especially in the case of pain description. There is also the possibility that the drugs used pre- and postoperatively in both groups masked the patients' response to the use of the laser (for example, dexamethasone and diclofenac sodium). Furthermore, pain perception is subjective and presents considerable variability in the threshold between patients, which in turn can be influenced by psychological factors. Testing the PBMT protocol in more challenging clinical conditions could be important to identify patients who could really benefit

from the application of this therapy and its different variations and whether the consumption of anti-inflammatories and analgesics could be reduced in the future if PBMT proves to be sufficiently effective to predictably control inflammation and its pain-inducing components associated with third molar extraction.

It can be concluded that dual-wavelength PBMT improved the postoperative clinical course by reducing edema 7 days postoperatively.

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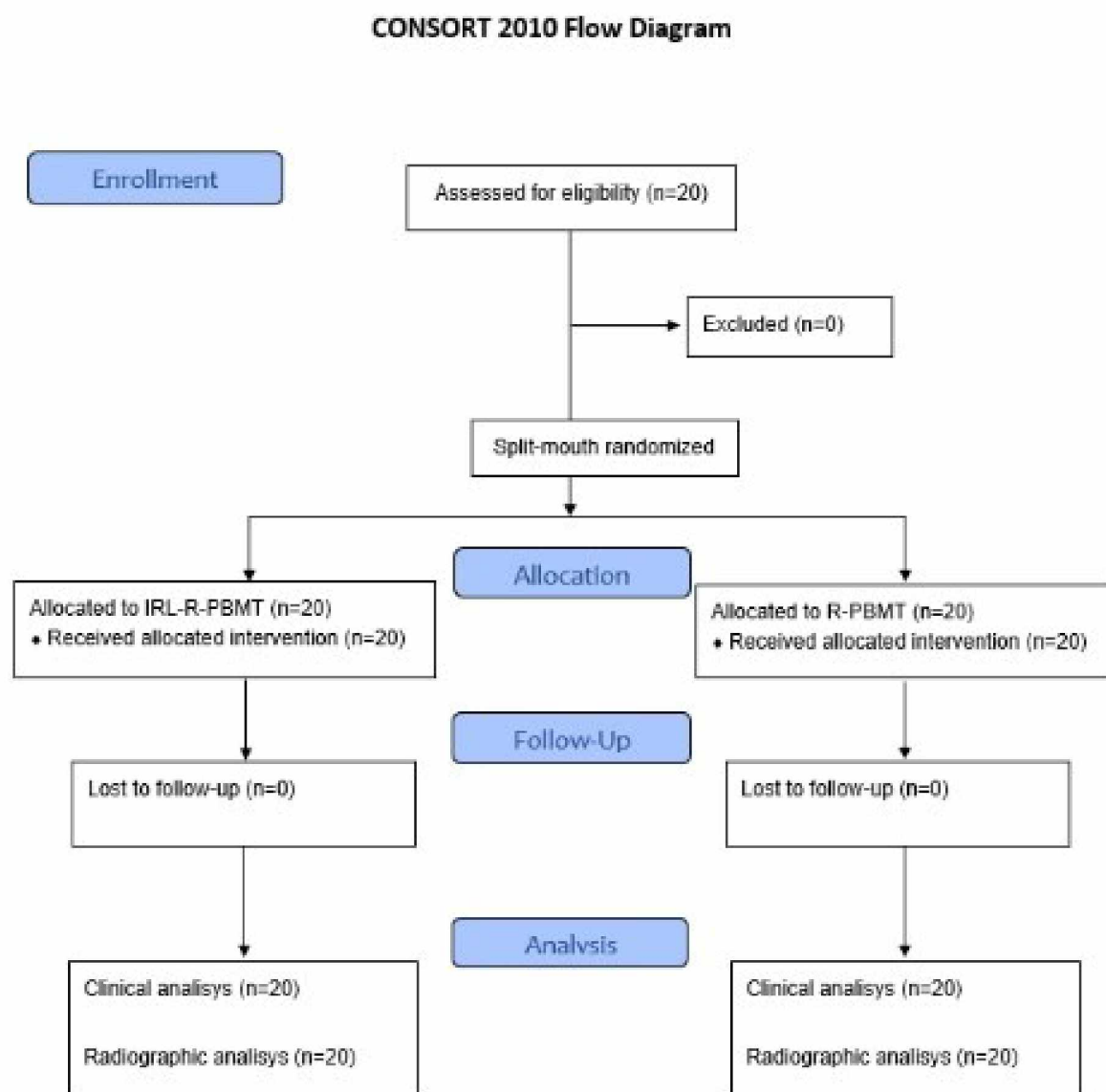
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Figure

Fig. 1. Flow diagram of the study



Tables

Original Research: Comparison of photobiomodulation with dual-wavelength and red laser on the post extraction repair associated with third molar extraction. A split-mouth double blinded randomized clinical trial

Table 1: Classification of tooth positioning according to Winter.

Classification/Group	IR-R-PBMT		R-PBMT	
	Upper	Lower	Upper	Lower
Vertical	18	14	16	11
Disto-angled	1	0	4	0
Mesio-Angulated	1	5	0	4
Horizontal	0	1	0	5
Total	20	20	20	20

Table 2: Classification of tooth positioning according to Pell & Gregory.

Classification/Group	IR-R-PBMT		R-PBMT	
	Upper	Lower	Upper	Lower
A	13	14	13	10
B	3	2	6	8
C	7	4	1	2
Total	20	20	20	20

Table 3: Median and interquartile range values of healing index.

Position	Period/Group	IR-R-PBMT	R-PBMT
Upper	3 days	5.5 (5.0 – 7.0)	5.0 (4.0 – 7.0)
	7 days	6.0 (4.7 – 7.0)	6.0 (4.0 – 7.0)
	15 days	4.0 (4.0 – 5.0)	4.0 (4.0 – 4.2)
	30 days	4.0 (4.0 – 5.0)	4.0 (4.0 – 4.0)
	90 days	4.0 (4.0 – 4.0)	4.0 (4.0 – 4.0)
Lower	3 days	5.5 (5.0 – 6.0)	5.0 (4.7 – 6.2)
	7 days	6.0 (4.7 – 7.0)	5.0 (4.0 – 7.0)
	15 days	5.0 (4.0 – 5.0)	5.0 (4.0 – 5.0)
	30 days	4.0 (4.0 – 5.0)	4.0 (4.0 – 4.2)

90 days	4.0 (4.0 – 4.0)	4.0 (4.0 – 4.0)
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Table 4: Median and interquartile range values of VAS scale for pain, edema, bleeding, mouth opening, and chewing.

Parameter	Period/Group	IR-R-PBMT	R-PBMT
Pain	3 days	3.0 (1.0 – 6.0)	3.0 (1.0 – 5.0)
	7 days	2.0 (0.0 – 6.5)	2.5 (0.0 – 7.0)
	15 days	0.0 (0.0 – 2.0)	0.0 (0.0 – 1.2)
	30 days	0.0 (0.0 – 0.0)	0.0 (0.0 – 0.0)
	90 days	0.0 (0.0 – 0.0)	0.0 (0.0 – 0.0)
Edema	3 days	5.0 (1.5 – 8.0)	3.0 (1.5 – 8.0)
	7 days	2.0 (0.0 – 5.7)	2.0 (0.0 – 5.0)
	15 days	0.0 (0.0 – 1.2)	0.0 (0.0 – 2.0)
	30 days	0.0 (0.0 – 0.0)	0.0 (0.0 – 0.0)
	90 days	0.0 (0.0 – 0.0)	0.0 (0.0 – 0.0)
Bleeding	3 days	2.0 (0.0 – 5.0)	2.0 (0.0 – 6.0)
	7 days	1.0 (0.0 – 2.0)	0.5 (0.0 – 2.0)
	15 days	0.0 (0.0 – 0.0)	0.0 (0.0 – 0.0)
	30 days	0.0 (0.0 – 0.0)	0.0 (0.0 – 0.0)
	90 days	0.0 (0.0 – 0.0)	0.0 (0.0 – 0.0)
Chewing	3 days	7.0 (3.5 – 9.0)	5.0 (3.5 – 8.0)
	7 days	4.0 (1.0 – 6.2)	4.0 (1.7 – 7.0)
	15 days	1.0 (0.0 – 1.2)	0.5 (0.0 – 2.0)
	30 days	0.0 (0.0 – 0.0)	0.0 (0.0 – 0.0)
	90 days	0.0 (0.0 – 0.0)	0.0 (0.0 – 0.0)
Mouth opening	3 days	5.0 (4.5 – 8.0)	6.0 (4.5 – 8.0)
	7 days	2.5 (0.7 – 7.0)	2.5 (0.0 – 5.2)
	15 days	0.0 (0.0 – 1.2)	0.0 (0.0 – 1.2)
	30 days	0.0 (0.0 – 0.0)	0.0 (0.0 – 0.0)
	90 days	0.0 (0.0 – 0.0)	0.0 (0.0 – 0.0)

Table 5: Mean and standard deviation values for variation in facial dimensions and mouth opening. *p<0.05 – Lower values of facial dimension variation than observed in the R-PBMT group – Linear mixed models.

Parameter	Period/Group	IR-R-PBMT	R-PBMT
Mouth opening	Baseline	40.9 ± 8.3	
	ΔBas – 3d	17.7 ± 8.2	
	ΔBas – 7d	9.3 ± 8.0	
	ΔBas – 15d	2.7 ± 7.9	
	ΔBas – 30d	-0.7 ± 6.7	
	ΔBas – 90d	-3.3 ± 6.4	
Vertical Dimension	Baseline	10.9 ± 0.9	$10.8 \pm 0.$
	ΔBas – 3d	0.2 ± 1.1	0.2 ± 1.0
	ΔBas – 7d	$-0.3 \pm 1.1^*$	0.3 ± 0.9
	ΔBas – 15d	-0.1 ± 1.0	-0.0 ± 0.8
	ΔBas – 30d	-0.1 ± 0.8	-0.0 ± 0.8
	ΔBas – 90d	-0.0 ± 0.6	0.0 ± 0.6
Horizontal dimension	Baseline	11.6 ± 0.8	11.6 ± 0.8
	ΔBas – 3d	0.1 ± 0.7	0.1 ± 0.6
	ΔBas – 7d	$-0.2 \pm 0.6^*$	0.2 ± 0.6
	ΔBas – 15d	-0.0 ± 0.6	0.0 ± 0.5
	ΔBas – 30d	-0.1 ± 0.5	-0.0 ± 0.4
	ΔBas – 90d	0.0 ± 0.6	-0.1 ± 0.6

Table 6: Mean and standard deviation values of radiographic density and fractal dimension through radiographic analysis.

Position	Parameter	Period/Group	IR-R-PBMT	R-PBMT
Upper	Radiographic density	Baseline	106.1 ± 20.7	105.9 ± 19.3
		90 days	134.6 ± 20.1	132.6 ± 19.1
	Fractal dimension	Baseline	1.21 ± 0.1	1.3 ± 0.1
		90 days	1.29 ± 0.1	1.3 ± 0.1
Lower	Radiographic density	Baseline	119.5 ± 15.7	117.1 ± 17.0
		90 days	131.3 ± 18.1	128.1 ± 18.7
	Fractal dimension	Baseline	1.3 ± 0.1	1.3 ± 0.1
		90 days	1.3 ± 0.2	1.3 ± 0.1

Cover Letter

Dear Prof. Dr. Keyvan Nouri

We are submitting the paper entitled: Comparison of photobiomodulation with dual-wavelength and red laser on the post extraction repair associated with third molar extraction. A split-mouth double blinded randomized clinical trial.” to the Lasers in Medical Science. The aim of this clinical trial was to compare the effect of photobiomodulation (PBMT) with red and infrared wavelengths combined and PBMT with only red wavelength on the healing of post-extraction alveoli of third molars. The PBMT has been showed beneficial effects of the healing and control of inflammation associated with a myriad of oral surgeries. Regarding the extraction of the third molars, the PBMT with red and infrared lasers have been showed these effects. The association of these two lasers have been recently proposed and showed good outcomes in maneuver of the third molars extraction. However, the comparison of the association of red and infrared laser compared with the PBMT with the red laser isolated lacks information. The main finding of this study was that the PBMT with red and infrared laser reduces the edema after the 7-day period. So, the dual-wavelength PBMT may be more beneficial to control de post-operative morbidity associated with the third molars extraction compared with the PBMT only with red laser.

In addition, we declare that all the authors listed in this study meet the criteria for authorship giving: 1) substantial contributions to conception and design of, or acquisition of data or analysis and interpretation of data, 2) drafting the article or revising it critically for important intellectual content and 3) final approval of the version to be published.

This study was supported by grants from CNPq, National Council for Scientific and Technological Development and FAPEMIG, Fundação de amparo a pesquisa de Minas Gerais (Grants INCT Saúde Oral e Odontologia 406840/2022-9, FAPEMIG APQ-02211-21, and CNPq – Financial code 001). Furthermore, the authors declare to have no conflict of interesting regarding this paper.

All my best regards

Guilherme José Pimentel Lopes de Oliveira
Pará, Av., 1760-1844 - Umuarama, Uberlândia - MG, Zip-code: 38405-320
email: guilherme.lopesoliveira@ufu.br

3.CAPÍTULO 3

ARTIGO 3

Comparação dos efeitos da fotobiomodulação da luz infravermelha e em duplo comprimento de onda sobre o reparo após exodontia de terceiros molares: Ensaio clínico controlado e randomizado em modelo de boca d vida.

Comparison of the effects of photobiomodulation of infrared and dual wavelength light on repair after extraction of third molars: Controlled and randomized clinical trial in a debt mouth model.

***Artigo em revis o no per dico Journal of Oral and maxillofacial surgery**

Original Research: Photobiomodulation with infrared and dual-wavelength laser induces similar repair and control of inflammation after third molar extraction. A double-blinded split-mouth randomized controlled trial

Davisson Alves Pereira (0000-0001-5422-6927)¹, Mariana Silva Bonatto (0000-0002-7280-103X)¹, Eduvaldo Campos Soares Junior (0000-0003-1206-8005)¹, Pedro Gomes Junqueira Mendes (0000-0002-0599-7802)¹, Roberto Sales e Pessoa (0000-0003-1763-3691)², Guilherme José Pimentel Lopes de Oliveira (0000-0001-8778-0115)¹

¹ Federal University of Uberlândia - UFU, School of Dentistry, Department of Periodontology, Uberlândia, MG, Brazil

² School of Dentistry, Universidade do Triangulo -UNITRI, Uberlândia, MG, Brazil

Declarations

Author Contribution

Conceptualization, GJO, DAP, RSP; methodology, DAP, PGJM, MSB, ECS; formal analysis, DAP, PGJM, GJO; investigation, MSB, DAP, PGJM, ECS; data curation, RSP, GJO.; writing—original draft preparation, DAP, MSB, GJO; writing—review and editing, DAP, MSB, GJO; visualization, all the authors; supervision, RSP, GJO.; project administration, RSP, GJO.; funding acquisition, GJO. All authors have read and agreed to the published version of the manuscript.

Ethics Approval

This study was conducted in accordance with the Declaration of Helsinki, and was approved by the human research ethics committee of the Federal University of Uberlândia, under protocol number CAAE: 72834023.3.0000.5152, and was registered with the Brazilian Registry of Clinical Trials (REBEC - RBR-103g7j28- Date of registration: 12/07/2023) under number U1111-1297-6962.

Informed consent

Informed consent was obtained from each individual participant in this study.

Conflict of interesting

The authors declare no conflicts of interest.

Acknowledgments

This study was supported by grants from CNPq, National Council for Scientific and Technological Development and FAPEMIG, Fundação de amparo a pesquisa de Minas Gerais (Grants INCT Saúde Oral e Odontologia 406840/2022-9, FAPEMIG APQ-02211-21, and CNPq – Financial code 001).

Data availability

The datasets generated and/or analysed during the current study is available from corresponding author on request. The data will be included in the repository of the Universidade Federal de Uberlândia after pHD thesis finalization of Davisson Alves Pereira.

Author for Correspondence

Guilherme José Pimentel Lopes de Oliveira

Pará, Av., 1760-1844 - Umuarama, Uberlândia - MG, Zip-code: 38405-320

Email: guilherme.lopesoliveira@ufu.br

Abstract

Objectives: The aim of this study was to compare the repair of post-extraction alveoli of third molars treated with dual-wavelength PBMT (red and infrared) compared with PBMT with infrared laser alone on the contralateral side. **Material and methods:** This double-blinded split mouth randomized controlled trial enrolled 20 patients, who were submitted to the extraction of the 4 third molars. The patients were allocated to two groups according to the PBMT protocol applied on the post-extraction sockets: IRL-PBMT: irradiation with PBMT with an infrared laser (808 nm); IRL-RL-PBMT: irradiation with dual-wavelength PBMT (660 nm and 808 nm). Patients were clinically evaluated at 3, 7, 14, 30, and 90 days after the surgical procedure. The analyses in this study were divided into qualitative (centered on the patient's report and on the evaluators' analysis) and quantitative analyses. The analyses centered on the patients' perceptions were performed by the application of a VAS scale to assess pain, bleeding, edema, difficulty in chewing, and mouth opening conditions. Healing was assessed by the evaluation of the tissue consistence, color, exudation, and bleeding, while the edema was clinically assessed by mouth opening, and vertical and horizontal dimensions of the face. In addition, the bone tissue density and structure were measured by radiographic analysis, performed at 7 and 90 days postoperatively. **Results:** No significant differences were found between the groups irrespected of the tested parameters. **Conclusion:** It can be concluded that PBMT with dual wavelengths (red and infrared) and an infrared laser alone induced similar postoperative clinical results after third molar extraction surgeries. **Clinical Relevance:** PBMT with dual wavelengths (red and infrared) and an infrared laser alone induced good outcomes in post-operative clinical results after third molar extraction surgeries.

Keywords: Bone. Photobiomodulation. Soft tissue. Third molar.

Introduction

Third molar surgery is one of the most frequently performed procedures in the dental clinic, and often causes undesirable inflammatory repercussions for patients, including the occurrence of pain, edema, trismus, and difficulty in chewing and swallowing in the acute post-operative period [1]. These repercussions occur due to the surgical manipulation required to extract these teeth, which often involves extensive surgical access as well as wear and tear on the surrounding bone tissue, generating overexpression of biological mediators of inflammation [2].

Stimulating the soft tissue and bone tissue repair processes can mitigate, shorten, or eliminate discomfort related to surgical procedures [3, 4]. In general, pharmacological therapies are used to modulate the effects of inflammation resulting from surgery, with administration of steroidal and non-steroidal anti-inflammatory drugs associated with analgesics for systemic use [5]. Another non-pharmacological alternative that aims to modulate postoperative symptoms is photobiomodulation (PBMT). Light therapy consists of applying a low-power laser, with the aim of modulating the inflammatory process, by suppressing the release of derivatives from the breakdown of arachidonic acid and consequently reducing its effects [6]. Two light wavelengths are widely used for this purpose, red and infrared wavelengths, both used at low power [7, 8].

Lasers with wavelengths within the infrared light range have greater penetrability within tissues and are therefore preferable for accelerating the repair of deep tissues, such as bone tissue [9, 10]. In fact, studies using PBMT with an infrared laser have demonstrated improved healing of bone fractures [11], osseointegration of implants [10], and repair in grafted areas [12]. Another clinical study demonstrated that PBMT with an infrared laser reduced the sensation of pain in patients undergoing third molar extraction surgeries [13].

Red lasers showed better results when used in superficial tissues, and therefore, PBMT with a red laser demonstrated good results in the treatment of wounds, such as mucositis lesions or in wounds on the palate after gingival graft removal [14]. PBMT with red and infrared lasers when used simultaneously have been showed to reduce pain and edema, and improve healing of post extraction sockets after the third molars extraction compared to non-irradiated post-extraction sockets [15]. Another study demonstrated that the combination of red and infrared lasers was beneficial in the healing of hard and soft tissues around dental implants [16]. Thus, the dual-wavelength PBMT protocol can beneficially intervene in different tissues and can improve post-extraction socket repair compared to other PBMT protocols which use a laser with a specific wavelength.

Therefore, the objective of the current study was to compare the repair of post-extraction sockets of third molars treated with dual-wavelength PBMT (red and infrared) used simultaneously, compared to PBMT with an infrared laser on the contralateral side. The null hypothesis of this study was that there would be no differences between these therapies in the repair of hard and soft tissues and in patients' perception after third molar extraction.

Material and methods

Study design

This double-blinded split-mouth randomized controlled trial was carried out following the CONSORT statement (Consolidated Standards of Reporting Trails) where, for statistical purposes, each post-extraction alveolus was considered as an individual case and each patient was subjected to the split-mouth model. The sample consisted of 20 patients approached at the clinic of the INPES postgraduate school (Institute for Clinical Health Research), and at the Federal University of Uberlândia (UFU). These patients underwent procedures for tooth extraction of the third molars and a subsequent stimulation procedure to repair the post-extraction alveoli photobiomodulation therapy (PBMT). The randomization process to select treatments in each alveolus was based on the use of an online randomization table (random.org) (GJO). The researcher involved in the randomization process was not the same involved in the other parts of this study. The patients were blinded regarding the type of PBMT applied. Furthermore, This study was conducted in accordance with the Declaration of Helsinki, and was approved for conduction by the human research ethics committee of the Federal University of Uberlândia, under protocol number CAAE: 72834023.3.0000.5152 and was registered with the Brazilian Registry of Clinical Trials (REBEC) under number U1111-1297-6962 (RBR-103g7j28)

Sample size calculation

The sample calculation was performed based on the study by Heo et al., 2002[17], which carried out fractal analysis of bone in the regeneration phase after orthognathic surgery. The authors found a fixed mean difference of 0.10 points as being clinically relevant, with an expected mean standard deviation of 0.05, a sample size of 15 patients would be sufficient to determine this level of difference, with a β power of 0.90 and an α power of 0.05. In this way, 20 patients were treated per group to replace any patients who withdrew during the project.

Inclusion and exclusion criteria

To be included in this study, patients were required to present the following characteristics: 1) be over 18 years of age; 2) Presents good oral hygiene; 3) Presents the four third molars indicated for tooth extraction. The patients were excluded if presented the following characteristics: 1) patients with periodontal disease. 2) patients with allergies to the drugs chosen for use in the study; 3) patients with systemic diseases or conditions which interfere with soft and hard tissues healing; 4) user of medications that alter bone metabolism; 5) pregnant or lactating women; 6) heavy smokers (more than 10 cigarettes daily); and 7) presence of teeth with periapical or pericoronal lesions.

Laser therapy Protocol

The GaAlA laser (XTherapy EC, λ 660 nm and λ 808 nm, 100mW, $\phi \sim 0.600$ μ m, tip divergence = 0.37 rad, CW, spot area of 0.0283 cm², DMC Equipamentos, São Carlos, SP, Brazil) was used to carry out irradiations. This laser radiates light energy with red and infrared wavelengths,

simultaneously or separately. The test side was treated with dual-wavelength PBMT, emitted simultaneously the red and infrared laser, by two irradiations performed per alveolus, with 4 J of energy emitted in each irradiation, totaling 8 J per alveolus and 16 J per side treated in a session. On the control side, PBMT was emitted at the infrared wavelength isolated and the irradiation protocol consisted of the application of 2 points of irradiation per alveolus, with 4 J of energy emitted in each irradiation, which totaled 8 J per alveolus, and 16 J per side. Both protocols were performed intraorally, immediately after the sutures at baseline, and 3 and 7 days after surgery. Therefore, 8J was administered to each alveolus, totaling 32 J per session, 16 J on the control side and 16J on the test side, which resulted in a total energy applied in the 3 sessions of 96J. The irradiation energy density used per session was approximately 859.9 J/cm²/session and 2,579.8 /cm² throughout the treatment.

Surgical procedure and study groups

All patients referred to the study underwent a panoramic x-ray, on which it was possible to detect the presence of the third molars. Subsequently, the patients underwent an anamnesis and clinical examination. The third molars were classified according to the Pell & Gregory and Winter classifications, and all the data necessary for surgery were collected. On the day of the surgical procedure, all patients took 8mg of dexamethasone one hour before the procedure, administered orally. For the surgical procedure, patients underwent extraoral and intraoral asepsis and antisepsis with chlorhexidine digluconate, at concentrations of 2% and 0.12% respectively. Following positioning of sterilized surgical drapes, the patients were anesthetized (articaine 4% with epinephrine 1:100,000). The teeth were then accessed through a total flap when necessary and extracted using various instruments, such as levers and the use of high and low rotation handpieces associated with cutting or abrasion drill. The procedure was finished using tissue synthesis techniques. The patients were distributed between the two groups according to the type of PBMT applied on the post-extraction sockets, in a split mouth model: IRL-PBMT: the post-extraction sockets were irradiated with PBMT with infrared laser (808 nm); IRL-RL-PBMT: the post-extraction sockets were treated with dual-wavelength PBMT (660 nm red wavelength and 808 nm infrared laser), performed intraorally.

The medication protocol adopted post-surgery for all patients was as follows; diclofenac sodium (50 mg) for 3 days every 8 hours and dipyron sodium (500 mg) for 3 days every 6 hours, all for oral consumption. Additionally, a mouthwash based on 0.12% chlorhexidine digluconate was prescribed for 7 consecutive days every 12h, 30min after meals. The sutures were removed 7 days after the surgical procedure. The surgeries were performed by two experienced surgeons (DAP and MSB).

Clinical analysis

Patients were clinically evaluated at 3, 7, 14, 30, and 90 days after the surgical procedure. The analyses in this study were divided into qualitative (centered on the patient's report and on the

evaluators' analysis) and quantitative analyses. For patient-centered qualitative analyses, a VAS scale graduated from 0-10 was applied, with 0 being considered the best result, where patients were asked about their perceptions regarding edema, pain, bleeding, and soft tissue repair.

Regarding the qualitative analyses, focused on professionals' perceptions, 4 aspects were evaluated, graded from 1-3 [18]: i) bleeding: 1) no bleeding, 2) induced by palpation, 3) spontaneous; ii) tissue color: 1) 100% pink; 2) < 50% of hyperemic and mobile soft tissue; 3) >50% of hyperemic and mobile soft tissue; iii) exudate: 1) absent, 2) present associated with the presence of pronounced plaque around the alveolus, 3) suppuration; iv) consistency of the healing tissue: 1) resilient and pink, 2) flabby and red, 3) fragile and green or grayish. the overall score being graded from 4-12.

Regarding the quantitative analyses, mouth opening assessments were carried out and recorded by measuring the interincisal distance at the midline of the upper incisors with the lower incisors with the patient in maximum mouth opening in a comfortable position. In addition, vertical and horizontal dimensions of the face were measured with the aim of establishing post-surgical edema: Vertical measurement: lateral extremity of the external palpebral commissure to the angle of the mandible; Horizontal measurement: ear tragus to the ipsilateral external labial commissure [18]. Comparisons of the results of the facial measurements and mouth opening were performed by subtracting the pre -surgical data values from the data measured at 3, 7, 14, 30, and 90 days after surgery. The analysis were performed by a blinded examiner (ECS)

Panoramic x-ray analysis

Panoramic images were obtained immediately and 90 days after the surgical procedure, with the aim of evaluating the alveolar density in the remnants of bone defects and the trabecular arrangement of the region, using bone density analysis and fractal dimension analysis. To perform the density analysis, ImageJ software (version 1.3; National Institutes of Health, Bethesda, MD, USA) was used, with the "histometry" tool, in a region of interest (ROI) of 32 x 32 pixels in the center of each alveolus, making it possible to obtain the values of gray tones present in the x-ray and comparing the two moments.

To carry out the fractal dimension, the same software and ROI described above were used, and after a series of treatments, an image of the trabecular arrangement of the alveolus was obtained, which in turn can be measured using the "Box-counting" function, that performed the counting of squares of 2, 3, 4, 6, 8, 12, 16, and 32 pixels in size within the ROI. The number of squares surrounding these trabeculae and the total square count were measured for each different sized pixel. From this count, a logarithmic scale graph of the values was formed, and the fractal dimension value was then calculated by measuring the slope of the line formed aligned with the points plotted on the graph. Alveolar density and DF analyses were performed for each alveolus. After 30 days, 30% of the samples were re-evaluated by the examiner to analyze intra-examiner reproducibility. A blinded examiner perform the radiographic analysis (PGJM)

Statistical analysis

The classification of teeth was compared between groups using Fisher's exact test. The evaluation of the effects of the independent treatment variables (IR-R-PBMT vs. IR-PBMT) with the evaluation period for facial dimensions and VAS scale and with the location of the teeth in the oral cavity (Upper and Lower) was performed through the application of linear mixed models. Jamovi software was used to perform the statistical analysis. All statistical tests used in this project were applied at a significance level of 5%.

Results

Pre-surgery tooth position and post-surgery complications were similar between IR-PBMT and IR-R-PBMT

The patients were treated and follow-up between July to December 2023. Of the 20 patients operated, two were excluded due to not attend follow-up appointments (Figure 1). Therefore, data from 18 patients who underwent extraction of 72 teeth were included in this study (36 lower teeth and 36 upper teeth). Half of the teeth were treated with IR-R-PBMT and the other half with IR-PBMT. In total, 34 osteotomies were performed (1 upper tooth and 33 lower teeth) with 16 lower alveoli and 1 upper alveolus being treated with IR-R-PBMT and 17 lower alveoli being treated with IR-PBMT. In addition, 31 odontosections were performed (all on lower teeth), with 15 alveoli treated with IR-R-PBMT and 16 alveoli treated with IR-PBMT. There were no statistically significant differences between the groups regarding the complexity of the surgical procedure. The average surgery time was 66.04 ± 24.12 min, and there were no differences in relation to the positioning of the teeth between the experimental groups according to the Winter (Table 1) and Pell & Gregory classifications (Table 2). There were also no differences between the groups in relation to the frequency of complications. The main complications were the presence of local pain in the post-extraction sockets, with this symptom being noted in one lower alveoli within 3 days (IR-PBMT Group), and 3 lower alveoli within 7 days (2 alveoli treated with IR-R-PBMT and 1 treated with IR-PBMT). The presence of bone spicules was noted in two post-extraction alveoli, 1 upper alveolus and 1 lower alveolus, both treated with IR-PBMT. Patients presented local pain were treated with local irrigation with 0.12% chlorhexidine without the need for adjustments in systemic medication. The bone spicules resolved spontaneously.

Patients and professionals did not notice differences in healing and morbidity between different PBMT protocols during the postoperative period.

The treatment parameters (IR-R-PBMT and IR-PBMT) and position of the tooth in the arch (upper and lower) did not interfere with the healing of the evaluated tissues (Table 3). Additionally, the independent variable treatment (IR-R-PBMT and IR-PBMT) did not influence the patient's perception regarding the parameters evaluated on the VAS scale (Table 4). The independent variable evaluation period impacted the healing data and all VAS scale parameters,

where reductions in the values of all these parameters were noted with the increase in the evaluation period ($p < 0.05$) (Tables 3-4).

The inflammatory process reduced with increasing follow-up time without distinguishing between the IR-R-PBMT and IR-PBMT protocols

After tooth extraction surgery, a reduction in mouth opening and an increase in facial dimensions bilaterally were observed, with the peak of these measurements occurring between 3-7 days after the surgical procedure. From this moment, a substantial improvement was observed in mouth opening and a return of facial dimensions to values recorded before the surgical procedure. Over the 7-day period, the variations in both horizontal and vertical facial dimensions were smaller in the IR-R-PBMT group, indicating less edema associated with this PBMT protocol than in the R-PBMT group (Table 5).

IR-R-PBMT and IR-PBMT showed similar potential for bone tissue healing

No differences were observed between the groups in relation to bone density and fractal dimension, however, in both groups there was an increase in bone density in the 90-day period compared to the baseline period (Table 6) ($p < 0.05$).

Discussion

Photobiomodulation in infrared wavelengths (IR-PBMT), and in red and infrared wavelengths (IR-R-PBMT) simultaneously, presented similar results in all periods evaluated, and in all variables measured. Therefore, the null hypothesis of this study was accepted.

The data obtained from qualitative and quantitative variables demonstrated that both protocols adopted in this study presented similar effects in the analyses of pain, edema, trismus, soft tissue repair, bleeding, and chewing. It was also noted that patients in this study had a low incidence of reports of postoperative morbidity, which demonstrates that PBMT increases the comfort of patients during the postoperative period [15]. Positive results in reducing edema and improving soft tissue repair induced by the application of IR-R-PBMT compared to alveoli that were not subjected to PBMT. However, the absence of differences between irradiation protocols may have occurred due to the fact that infrared light alone has the potential to modulate inflammatory processes associated with third molar extractions [19]. Furthermore, Sierra et al., 2016[20] demonstrated that PBMT with infrared light reduced inflammation and trismus compared to sites treated with PBMT with red light. Therefore, the dual-wavelength infrared component may be more useful PBMT protocol for managing the clinical condition tested.

The mechanisms of action of PBMT with red and infrared light are similar and have shown satisfactory effects in the management of different clinical conditions. Both types of laser demonstrated effects in reducing postoperative pain and inflammation [20, 21]. In fact, the reduction in inflammation associated with PBMT may occur due to its effects in suppressing the kinin pathway and the production of arachidonic acid metabolites [22], and reversing the effects of pro-inflammatory cytokines [23, 24], that are activated after surgical trauma. For this reason,

the reduction in postoperative edema in third molar extractions has been described as a common repercussion inherent to PBMT [19, 20, 25]. Therefore, regardless of the wavelength used in this study, the anti-inflammatory effect is expected for both types of protocol.

Another important point in this study was the reduced occurrence of complications, which was associated with the good healing observed in soft and bone tissues. The previous effects demonstrated with PBMT explain the good clinical findings observed in this study. PBMT with infrared and red light increased the proliferation and migration of fibroblasts, as well as increasing their ability to form collagen [24, 26]. In cultured keratinocytes, PBMT with infrared and red light was associated with increased proliferation and metabolism of these cells [23, 26]. In osteoblasts, it was found that PBMT with red and infrared lasers stimulates cell differentiation and the formation of mineralized matrix [27]. These modulatory effects on the tissues covered in dental extractions may justify the healing benefits found in this study.

One factor that differentiates the properties of PBMT with an infrared laser compared to with a red laser is its tissue penetration capacity. Infrared light has greater penetrability power than red light and this indicates that PBMT with infrared light has greater action potential in deeper tissues [9, 28]. The inflammatory process in third molar extraction surgeries is related to more invasive surgeries, in impacted teeth, with large flaps and the need for osteotomies and odontosection [29, 30]. Thus, within the dual-wavelength PBMT protocol, infrared light has the ability to modulate the inflammatory process in such a way that, in the clinical conditions analyzed, it makes the application of the red light component of the protocol unnecessary. However, in situations where there are problems related to flap closure or superficial tissue healing, it is possible that the red laser may present additional benefits to the use of the infrared laser. This hypothesis needs to be tested in the future.

It is important to highlight that most of the patients operated on in this study are young and without comorbidities and that these conditions are positive factors for the rapid repair of any wound. Thus, these combined conditions may have influenced the findings of this study, since post-extraction alveoli not subjected to major osteotomy, with at least 3 bone walls remaining, represent a defect that favors the development of a good clot mesh and that, with the progression of the inflammatory process, naturally benefits bone regeneration [15, 31]. These conditions may have favored the course of both bone and soft tissue repair, and masked possible differences between protocols. The current study has other limitations that must be considered when interpreting the findings. Although the split mouth model is a good way to evaluate bone regeneration processes and soft tissue assessment, preventing individual differences between patients from interfering with the results, subjective patient-centered assessments, for example of edema and pain represent a difficult factor, since the fact that the extractions were performed at the same surgical time could generate confusion in the patients' reports in relation to the VAS scale values. There is also the possibility that the drugs used in the pre- and postoperative periods

in both groups may have masked the patients' response to the use of PBMT. Further studies with different PBMT protocols, in more challenging clinical conditions, should be carried out, as this is of utmost importance to identify patients who could really benefit from the application of this therapy. In addition, new investigations are needed to confirm whether the consumption of anti-inflammatory and analgesic medications could be reduced in the future, if PBMT proves to be effective enough to predictably control the inflammation generated in third molar surgeries.

Conclusion

It can be concluded that PBMT with dual wavelengths (red and infrared) and an infrared laser isolated induced similar postoperative clinical results in third molar extraction surgeries.

Declarations

Ethics Approval and Consent to Participate

This study was conducted in accordance with the Declaration of Helsinki, and was approved by the human research ethics committee of the Federal University of Uberlândia, under protocol number CAAE: 72834023.3.0000.5152, and was registered with the Brazilian Registry of Clinical Trials (REBEC - RBR-103g7j28- Date of registration: 12/07/2023) under number U1111-1297-6962. Informed consent was obtained from each individual participant in this study.

Funding

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Author Contribution

Conceptualization, GJO, DAP, RSP; methodology, DAP, PGJM, MSB, ECS; formal analysis, DAP, PGJM, GJO; investigation, MSB, DAP, PGJM, ECS; data curation, RSP, GJO.; writing—original draft preparation, DAP, MSB, GJO; writing—review and editing, DAP, MSB, GJO; visualization, all the authors; supervision, RSP, GJO.; project administration, RSP, GJO.; funding acquisition, GJO. All authors have read and agreed to the published version of the manuscript.

Conflict of interesting

The authors declare no conflicts of interest.

Data availability

The datasets generated and/or analysed during the current study is available from corresponding author on request. The data will be included in the repository of the Universidade Federal de Uberlândia after PhD thesis finalization of Davisson Alves Pereira.

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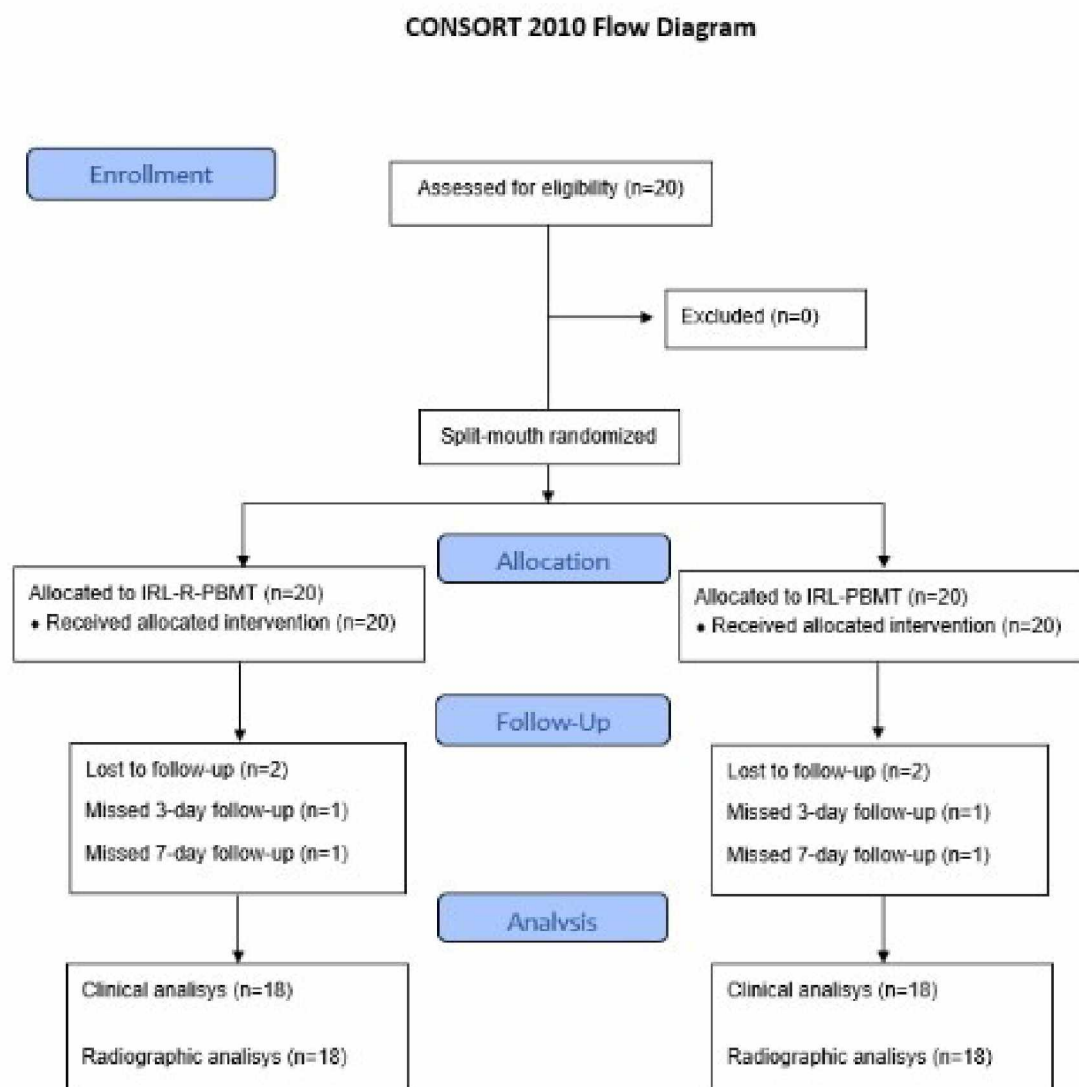
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Figure

Fig. 1. Flow diagram of the study.



Tables

Original Research: Photobiomodulation with infrared and dual-wavelength laser induces similar repair and control of inflammation after third molar extraction. A double-blinded split-mouth randomized controlled clinical trial

Table 1: Classification of tooth positioning according to Winter

Classification/Group	IR-R-PBMT		IR-PBMT	
	Upper	Lower	Upper	Lower
Vertical	13	11	11	12
Disto-angled	5	0	6	0
Mesio -Angulated	0	5	1	2
Horizontal	0	2	0	4
Total	18	18	18	18

Table 2: Classification of tooth positioning according to Pell & Gregory

Classification/Group	IR-R-PBMT		IR-PBMT	
	Upper	Lower	Upper	Lower
A	13	9	10	6
B	2	9	6	12
C	3	0	2	0
Total	18	18	18	18

Table 3: Median and interquartile range values of healing index

Position	Period/Group	IR-R-PBMT	IR-PBMT
Upper	3 days	5.0 (4.0 - 6.0)	5.0 (4.0 - 5.0)
	7 days	5.0 (4.0 - 6.0)	5.0 (4.2 - 7.0)
	15 days	4.0 (4.0 - 5.0)	4.0 (4.0 - 5.0)
	30 days	4.0 (4.0 - 4.0)	4.0 (4.0 - 4.0)
	90 days	4.0 (4.0 - 4.0)	4.0 (4.0 - 4.0)
Lower	3 days	6.0 (5.0 - 6.0)	6.0 (5.0 - 7.0)
	7 days	5.0 (5.0 - 6.0)	5.0 (5.0 - 6.0)
	15 days	4.5 (4.0 - 5.0)	4.5 (4.0 - 5.0)
	30 days	4.0 (4.0 - 4.0)	4.0 (4.0 - 4.0)
	90 days	4.0 (4.0 - 4.0)	4.0 (4.0 - 4.0)

Table 4: Median and interquartile range values of VAS scale for pain, edema, bleeding, mouth opening, and chewing.

Parameter	Period/Group	IR-R-PBMT	IR-PBMT
Pain	3 days	3.0 (2.0 - 6.5)	4.5 (3.0 - 7.0)
	7 days	3.0 (2.0 - 6.5)	3.0 (1.0 - 6.0)
	15 days	0.0 (0.0 - 1.0)	0.0 (0.0 - 0.0)
	30 days	0.0 (0.0 - 0.0)	0.0 (0.0 - 0.0)
	90 days	0.0 (0.0 - 0.0)	0.0 (0.0 - 0.0)
Edema	3 days	4.5 (2.0 - 7.5)	3.5 (3.0 - 6.0)
	7 days	2.5 (1.5 - 4.7)	2.0 (0.2 - 3.0)
	15 days	0.0 (0.0 - 0.7)	0.0 (0.0 - 0.7)
	30 days	0.0 (0.0 - 0.0)	0.0 (0.0 - 0.0)
	90 days	0.0 (0.0 - 0.0)	0.0 (0.0 - 0.0)
Bleeding	3 days	2.0 (0.0 - 3.7)	2.0 (0.0 - 4.7)
	7 days	0.0 (0.0 - 2.7)	0.0 (0.0 - 3.7)
	15 days	0.0 (0.0 - 1.0)	0.0 (0.0 - 0.0)
	30 days	0.0 (0.0 - 0.0)	0.0 (0.0 - 0.0)
	90 days	0.0 (0.0 - 0.0)	0.0 (0.0 - 0.0)
Chewing	3 days	5.0 (3.2 - 7.7)	5.5 (4.0 - 7.0)
	7 days	3.5 (2.0 - 5.7)	4.0 (2.0 - 6.0)
	15 days	0.0 (0.0 - 1.0)	0.5 (0.0 - 0.0)
	30 days	0.0 (0.0 - 0.0)	0.0 (0.0 - 0.0)
	90 days	0.0 (0.0 - 0.0)	0.0 (0.0 - 0.0)
Mouth opening	3 days	5.0 (4.2 - 8.0)	5.0 (4.0 - 6.0)
	7 days	2.0 (1.0 - 5.0)	2.5 (1.2 - 5.0)
	15 days	0.0 (0.0 - 1.5)	0.0 (0.0 - 0.0)
	30 days	0.0 (0.0 - 0.0)	0.0 (0.0 - 0.0)
	90 days	0.0 (0.0 - 0.0)	0.0 (0.0 - 0.0)

Table 5: Mean and standard deviation values for variations in facial dimensions and mouth opening.

Parameter	Period/Group	IR-R-PBMT	IR-PBMT
Mouth opening	Baseline	41.3 ± 6.5	
	ΔBas – 3d	15.0 ± 8.7	
	ΔBas – 7d	6.2 ± 9.7	
	ΔBas – 15d	2.9 ± 6.7	
	ΔBas – 30d	-0.1 ± 5.6	
	ΔBas – 90d	0.2 ± 5.6	
Vertical Dimension	Baseline	10.8 ± 1.1	10.8 ± 0.9
	ΔBas – 3d	0.2 ± 0.8	0.1 ± 0.6
	ΔBas – 7d	-0.0 ± 0.9	0.0 ± 0.9
	ΔBas – 15d	0.0 ± 0.6	-0.0 ± 0.6
	ΔBas – 30d	-0.1 ± 0.7	-0.0 ± 0.6
	ΔBas – 90d	0.1 ± 1.0	0.0 ± 0.9
Horizontal dimension	Baseline	11.3 ± 0.8	11.2 ± 0.7
	ΔBas – 3d	-0.2 ± 0.4	-0.3 ± 0.6
	ΔBas – 7d	-0.1 ± 0.6	-0.1 ± 0.7
	ΔBas – 15d	-0.0 ± 0.4	0.0 ± 0.5
	ΔBas – 30d	0.1 ± 0.5	0.0 ± 0.3
	ΔBas – 90d	0.0 ± 0.5	0.0 ± 0.5

Table 6: Mean and standard deviation values of radiographic density and fractal dimension through radiographic analysis.

Position	Parameter	Period/Group	IR-R-PBMT	IR-PBMT
Upper	Radiographic density	Baseline	112.4 ± 15.7	112.8 ± 23.0
		90 days	135.0 ± 21.8	133.1 ± 22.2
	Fractal dimension	Baseline	1.1 ± 0.3	1.1 ± 0.3
		90 days	1.3 ± 0.0	1.2 ± 0.3
Lower	Radiographic density	Baseline	107.1 ± 20.1	110.3 ± 20.1
		90 days	122.3 ± 27.8	124.8 ± 24.4
	Fractal dimension	Baseline	1.3 ± 0.1	1.3 ± 0.1
		90 days	1.2 ± 0.4	1.3 ± 0.3

Cover Letter

Dear Prof. Dr. Matthias Hannig and Prof. Dr. Stefan Ruhl

We are submitting the paper entitled: Photobiomodulation with infrared and dual-wavelength laser induces similar repair and control of inflammation after third molar extraction. A double-blinded split-mouth randomized controlled trial.” to the Clinical Oral Investigations. The aim of this clinical trial was to compare the effect of photobiomodulation (PBMT) with red and infrared wavelengths combined and PBMT with only infrared wavelength on the healing of post-extraction alveoli of third molars. The PBMT has been showed beneficial effects of the healing and control of inflammation associated with a myriad of oral surgeries. However, some factors can interfere with PBMT therapy. The wavelength of the laser deserves highlight since these parameters interferes with the deepness of the energy dispersion which can indicates that laser with different wavelengths can be used in different clinical situation. The red and infrared laser have been used commonly to treat oral wounds in an isolated way. However, the association of the both wavelengths have been showed promising outcomes since the PBMT with red and infrared lasers have been showed these good effects on the soft tissue, reduction of pain and edema associated with third molars extraction. However, the comparison of the association of red and infrared laser compared with the PBMT with the infrared laser isolated lacks information. The main finding of this study was that the PBMT with dual wavelengths (red and infrared) and an infrared laser alone induced similar postoperative clinical results after third molar extraction surgeries. So, the red laser may be not necessary to be applied in usual third molars extraction. However, in situations where there are problems related to flap closure or superficial tissue healing, it is possible that the red laser may present additional benefits to the use of the infrared laser. This hypothesis needs to be tested in the future.

In addition, we declare that all the authors listed in this study meet the criteria for authorship giving: 1) substantial contributions to conception and design of, or acquisition of data or analysis and interpretation of data, 2) drafting the article or revising it critically for important intellectual content and 3) final approval of the version to be published. This study was supported by grants from CNPq, National Council for Scientific and Technological Development and FAPEMIG, Fundação de amparo a pesquisa de Minas Gerais (Grants INCT Saúde Oral e Odontologia 406840/2022-9, FAPEMIG APQ-02211-21, and CNPq – Financial code 001). Furthermore, the authors declare to have no conflict of interesting regarding this paper.

All my best regards

Guilherme José Pimentel Lopes de Oliveira, Pará, Av., 1760-1844 - Umuarama, Uberlândia - MG, Zip-code: 38405-320 email: guilherme.lopesoliveira@ufu.br

4. CAPÍTULO 4

ARTIGO 4

Comparação da aplicação de diferentes protocolos de fotobiomodulação de duplo comprimento de onda em extrações de terceiros molares. Um ensaio clínico randomizado e controlado.

Comparison of different dual-wavelength photobiomodulation protocols application in third molar extractions. A split-mouth randomized controlled trial.

Minor revision respondido no periódico Photodiagnosis and Photodynamic Therapy

Original Research: Comparison of different dual-wavelength photobiomodulation protocols application in third molar extractions. A split-mouth randomized controlled trial.

Running title: photobiomodulation and oral surgery

Davisson Alves Pereira email: davisoncaneda@hotmail.com (0000-0001-5422-6927)¹, Mariana Silva Bonatto email: mariana.bonatto@hotmail.com (0000-0002-7280-103X)¹, Samara de Souza Santos email: samarasmsantos@gmail.com (0000-0002-9799-4739)¹, Pedro Gomes Junqueira Mendes email: pedrogomesjm@ufu.br (0000-0002-0599-7802)¹, Roberto Sales e Pessoa email: rp@inpes.com.br (0000-0003-1763-3691)², Guilherme José Pimentel Lopes de Oliveira email: guilherme.lopesoliveira@ufu.br (0000-0001-8778-0115)¹

¹ Federal University of Uberlândia - UFU, School of Dentistry, Department of Periodontology, Uberlândia, MG, Brazil

² School of Dentistry, Universidade do Triangulo -UNITRI, Uberlândia, MG, Brazil

Declarations

Data availability

The datasets generated and/or analysed during the current study is available from corresponding author on request. The data will be included in the repository of the Universidade Federal de Uberlândia after PhD thesis finalization of Davisson Alves Pereira.

Funding

This study was supported by grants from CNPq, National Council for Scientific and Technological Development and FAPEMIG, Fundação de amparo a pesquisa de Minas Gerais (Grants INCT Saúde Oral e Odontologia 406840/2022-9, FAPEMIG APQ-02211-21, and CNPq – Financial code 001).

Conflict of interesting

The authors declare no conflicts of interest.

Ethics Approval and clinical trial registration

This study was conducted in accordance with the Declaration of Helsinki, and was approved by the human research ethics committee of the Federal University of Uberlândia, under protocol number CAAE: 72834023.3.0000.5152, and was registered with the Brazilian Registry of Clinical Trials (REBEC - RBR-103g7j28- Date of registration: 12/07/2023) under number U1111-1297-6962.

Informed consent

Informed consent was obtained from each individual participant in this study.

Author Contribution

Conceptualization, GJO, DAP, RSP; methodology, DAP, PGJM, MSB, SSS; formal analysis, DAP, PGJM, SSS, GJO; investigation, MSB, DAP, PGJM, SSS; data curation, RSP, GJO.; writing—original draft preparation, DAP, MSB, GJO; writing—review and editing, DAP, MSB, GJO; visualization, all the authors; supervision, RSP, GJO.; project administration, RSP, GJO.; funding acquisition, GJO. All authors have read and agreed to the published version of the manuscript.

Author for Correspondence

Guilherme José Pimentel Lopes de Oliveira

Pará, Av., 1760-1844 - Umuarama, Uberlândia - MG, Zip-code: 38405-320

Email: guilherme.lopesoliveira@ufu.br

Abstract

Objective: To compare the use of PBMT in the soft tissue and bone healing after third molar extraction using the dual-wavelength laser directly into the post-extraction alveoli (PBMT-I), or PBMT with a red laser directly into the alveoli and with an infrared laser externally on the patient's face (PBMT-IE). **Methods:** Twenty patients underwent extraction of four third molars were involved in this split-mouth double-blind randomized controlled trial. The Post-extraction alveoli were treated with the following protocols: PBMT-IE: Application of a red laser directly into the alveolus, and infrared laser irradiation transcutaneously and PBMT-I: Application of dual-wavelength laser intraorally. Patients were clinically evaluated 3, 7, 14, 30, and 90 days after the surgical procedure. The analyses in this study were divided into qualitative (centered on the patient's report and on the evaluators' analysis), and quantitative analyses (measurement of the vertical and horizontal dimensions of the face with the objective of measuring post-surgical edema and radiographic analyses for evaluation of the density and structure of the newly formed bone). **Results:** A progressive improvement was observed in all parameters evaluated in this study, however, this improvement was time dependent, with no distinct effect observed between the PBMT treatments applied. **Conclusion:** The different dual-wavelength PBMT protocols induced a similar postoperative clinical course in third molar extraction surgeries, with a reduced occurrence of complications and a good healing pattern of hard and soft tissues.

Keywords: Bone. Oral surgery. Photobiomodulation. Soft tissue healing. Third molar.

Highlights

Different dual-wavelength PBMT protocols induced a similar postoperative clinical course in third molar extraction surgeries.

The occurrence of complications was low and a good healing pattern of hard and soft tissues was observed in the both dual-wavelength PBMT protocols;

The fact that the current study did not obtain different results when comparing the different protocols mentioned is not due to a lack of effect of PBMT, but rather to the similarity in the effectiveness of the protocols.

Introduction

Extraction of thirds molar is one of the most frequent procedures performed in oral and maxillofacial surgery and can cause immediate postoperative pain, swelling, and restricted mouth opening,^{1, 2} which can impact the patient's quality of life. One of the difficulties encountered in these surgical procedures is access, as these teeth are often positioned in an unfavorable position, which can lead to the need for extensive tissue detachment, as well as significant wear of the surrounding bone tissue³. Surgeries that involve greater wear and tear may be related to postoperative complications, such as late hemorrhages, dry sockets, and infections.^{4, 5}

To contain the exacerbated release of pro-inflammatory mediators associated with third molar extractions, pharmacological and non-pharmacological therapies have been indicated. The former are composed of the use of steroidal and non-steroidal anti-inflammatory drugs associated with the use of analgesics before and after the surgery^{6, 7}. Among non-pharmacological therapies it can mention therapies mediated by local temperature conditioning⁸, and physical methods, such as photobiomodulation (PBMT)⁹. PBMT has demonstrated promising results in improving the osseointegration of dental implants^{10, 11}, reducing pain and edema, and improving soft tissue repair in third molar surgery¹², reducing pain in temporomandibular disorders (TMD)¹³, improving the sleep quality¹⁴. With the aim of promoting repair in oral tissues, PBMT has been applied with lasers at infrared (830nm) and red (660nm) wavelengths^{12, 15, 16}. Lasers with a wavelength within the range of infrared light present greater penetrability in tissues and are therefore used more frequently for the purpose of repairing deeper injuries, such as in bone defects¹⁷, while lasers with a red wavelength present lower tissue penetrability and are indicated for the treatment of superficial lesions, such as mucositis¹⁸.

The lack of standardization in PBMT protocols in the literature makes it difficult to understand the real effects of this therapy after third molar extractions^{16, 19}. In this sense, there is a clear need to carry out clinical studies comparing different PBMT protocols, in order to assess whether there is a more appropriate form of management¹⁹. Recently, the association of red and infrared laser for PBMT in the treatment of surgical lesions in the oral cavity has been proposed, and clinical studies have demonstrated a positive effect from this type of approach^{12, 20}. However, the PBMT has been applied differently between studies. In the study by Pereira et al., 2022¹², PBMT was applied intraorally, and the results demonstrated that dual-wavelength PBMT applied intraorally reduced pain and edema in alveoli post-extraction of third molars. In the study by Gururaj et al., 2022²⁰, which also presented similar findings in third molar extraction surgeries, PBMT was applied with an infrared laser directly to the post-extraction socket and with a red laser transcutaneously. Finally, Sierra et al., 2016²¹ demonstrated a reduction in edema and trismus associated with third molar extractions when PBMT was applied with a red laser directly to the post-extraction socket and with an infrared laser extraorally.

Due to these inconsistencies in dual-wavelength PBMT protocols, the objective of the current study was to compare the use of PBMT in third molar extraction surgeries using the dual-wavelength laser directly in the post-extraction alveoli and PBMT with a red laser directly into the alveoli and with an infrared laser externally on the patient's face. The null hypothesis of this study was that there will be no differences between the dual-wavelength PBMT protocols on the tissue healing after the third molar extractions.

Material and methods

Study design

This split-mouth double-blinded randomized controlled trial was carried out following the CONSORT (Consolidated Standards of Reporting Trials) guidelines, where, for statistical purposes, each post-extraction alveolus was considered as an individual case and each patient received both PBMT protocols. The sample consisted of 20 patients approached at the undergraduate clinic of the Faculty of Dentistry of the Federal University of Uberlândia (FOUFU). The randomization process to select treatments in each alveolus was based on the use of an online randomization table (random.org) (GJO). The researcher involved in the randomization process was not the same involved in the other parts of this study. Furthermore, this study was conducted in accordance with the Declaration of Helsinki, and was approved for conduction by the human research ethics committee of the Federal University of Uberlândia, under protocol number CAAE: 72834023.3.0000.5152 and was registered with the Brazilian Registry of Clinical Trials (REBEC) under number U1111-1297-6962 (RBR-103g7j28)

Sample size calculation

The sample size calculation was carried out based on the study by Eshghpour et al., 2016²², which evaluated the effect of PBMT in controlling pain and edema in the postoperative period of third molar extraction. The primary outcome considered for the sample calculation was the level of pain assessed by the VAS scale applied on the third postoperative day. Based on a clinically significant difference in patients' pain sensation of 1 point on the VAS scale and considering that the expected standard deviation for this analysis over a period of 3 days was 1.4, establishing a β power of 0.85, and an α power of 0.05, a minimum sample of 17 patients was determined to receive the treatments. Thus, 20 patients were recruited in order to avoid patient dropouts during the project reducing the statistical power of the study.

Eligibility criteria

To be included in this study, patients were required to present the following characteristics: I) be over 18 years of age; II) present good oral hygiene, III) Presents the four third molars indicated for tooth extraction.

Patients who presented the following characteristics were excluded from the study: I) Patients with periodontitis; II) Allergies to the drugs chosen for use in the study; III) Patients

with systemic diseases or conditions or who were taking medications that alter bone metabolism; IV) pregnant or lactating women; V) heavy smokers (more than 10 cigarettes daily); VI) Patients with third molar with periapical or pericoronal lesions.

Photobiomodulation Protocol

The GaAlAs laser (Therapy EC, λ 660nm and λ 808nm, 100mW, $\phi \sim 0.600\mu\text{m}$, tip divergence = 0.37rad, CW, spot area of 0.0283 cm², DMC Equipamentos, São Carlos, SP, Brazil) was used to carry out the irradiations. This laser radiates light energy with red and infrared wavelengths simultaneously. PBMT was performed immediately after the sutures and on the 3rd and 7th postoperative days. In the PBMT-IE the intra-oral and extra-oral application at red and infrared wavelengths was performed individually, 4J of energy at red wavelength (660 nm red laser) was irradiated in the region of the center of each alveolus, while the infrared laser was irradiated by extra-oral applications that were carried out in the region of the corresponding intraoral alveolus as follows: 1) In the upper alveolus, using as a reference an imaginary line drawn from the tragus of the ear to the lateral part of the nose wing, 4 different points were irradiated sequentially in the masseter muscle, with 1J administered 1J at each point in its anteroposterior extension, adjacent to the dental socket, totaling 4J, 2) In the lower alveolus region, the same procedure was performed but the reference was the lower insertion of the masseter muscle (Figure 1). Therefore, on the test side, adding intra- and extraoral irradiations, 8J of energy was administered per quadrant and 16J per treated side in each session. In the intraoral PBMT (PBMT-I), the irradiation protocol consisted of applying 4J of energy twice in the center of each alveolus, with the laser with red and infrared wavelengths being administered simultaneously, which totaled 8J per alveolus and 16J of energy in total. Thus, the same amount of energy was emitted on both the sides treated with the different protocols. The energy applied in each session per patient was 32 J, which resulted in a total energy application in the 3 sessions of 96 J. The irradiation energy density used was approximately 1,130.74 J/cm²/session and 3,392.22J/cm² throughout the treatment. The patients were blinded regarding the type of dual-wavelength PBMT protocol applied. The researcher that applied the PBMT was not the same that evaluates the patients. (GJO)

Surgical procedure and study groups

All patients referred to the study had a panoramic x-ray to detect the presence of the third molars. Subsequently, the patients underwent anamnesis and clinical examination. The third molars were classified according to the Pell & Gregory and Winter classifications, and all data necessary for the surgery were collected. In the day of the surgical procedure, all patients took 8mg of dexamethasone (EMS pharm®) one hour before the procedure, administered orally. For the surgical procedure, patients were initially anesthetized (4% articaine with 1:100,000 epinephrine) and then the teeth were accessed through a total flap and extracted using various instruments, depending on the necessity, such as levers, and drills mounted on high and low rotation motors to promote osteotomy and odontosections, followed by sutures. The medication protocol adopted

post-surgery for all patients was as follows; diclofenac sodium 50 mg (EMS pharm®) for 3 days every 8 hours and dipyron sodium 500 mg (EMS pharm®) for 3 days every 6 hours, all via oral consumption. Additionally, a mouthwash based on 0.12% chlorhexidine digluconate was prescribed for 7 consecutive days every 12 hours. The sutures were removed 7 days after the surgical procedure.

Patients were distributed between groups according to the type of PBMT applied. After extraction of the 4 third molars, the post-extraction sockets were randomly allocated to receive in a split-mouth model: PBMT-IE: photobiomodulation performed at red wavelength (660 nm red laser) directly into the alveolus, and at infrared wavelength (808 nm Infrared laser) transcutaneously. PBMT-I: photobiomodulation with dual wavelength used simultaneously (660 nm red wavelength, 808 nm infrared laser) irradiated intraorally. The PBMT was applied just after the sutures, and after 3, and 7 days the surgical procedure. The surgeries were performed by two experienced surgeons (MSB and DAP).

Clinical analysis

Patients were clinically evaluated 3, 7, 14, 30, and 90 days after the surgical procedure. The analyses in this study were divided into qualitative (centered on the patient's report and the evaluators' analysis) and quantitative analyses. For patient-centered qualitative analyses, a visual analogic scale (VAS) graduated from 0 -10 was applied, with 0 being considered the best comfort, where patients were asked about their perceptions regarding edema, pain, bleeding, and discomfort when chewing and opening their mouth.

Regarding qualitative analyses focused on the professionals' perceptions, 4 aspects were evaluated, graded from 1-3²³: I) Bleeding: 1) No bleeding, 2) Induced by palpation, 3) Spontaneous; II) Tissue color: 1) 100% pink; 2) < 50% of hyperemic and mobile tissue; 3) >50% of hyperemic and mobile tissue; III) Exudate: 1) Absent, 2) Present associated with the presence of pronounced plaque around the alveolus, 3) Suppuration; IV) Consistency of the healing tissue: 1) Resilient and pink, 2) Flabby and red, 3) Fragile and green or grayish, with the overall score being graded from 4-12.

Regarding quantitative analyses, mouth opening assessments were carried out, recorded by measuring the interincisal distance at the midline of the upper incisors with the lower incisors, with the patient in maximum comfortable mouth opening. In addition, vertical and horizontal dimensions of the face were measured, with the aim of establishing post-surgical edema: 1) Vertical measurement: lateral extremity of the external palpebral commissure to the angle of the mandible; 2) Horizontal measurement: ear tragus to ipsilateral external labial commissure²³. The results of the facial measurements and mouth opening were expressed by subtracting the initial value obtained at the baseline from the values measured on the 3, 7, 14, 30, and 90 days of the postoperative period. A blinded and calibrated evaluator performed the clinical analysis (SSS).

Image analysis - Remnants of bone defects and fractal analysis

For radiographic analysis, postoperative and 90-day panoramic radiographs were used, with the aim of evaluating alveolar density in the remnants of bone defects and the trabecular complexity of the region. Histometric analysis and fractal dimension (FD) analysis, respectively, were used for each analysis. To perform the density analysis, ImageJ software (version 1.3; National Institutes of Health, Bethesda, MD, USA) was used, with the “*histometry*” tool in a region of interest (ROI) of 32x32 pixels in the center of each alveolus, making it possible to obtain the gray tone values present on the radiograph and comparing the two moments, immediately postoperative and 3 months. To carry out the FD, the methodology proposed by Coşgunarslan et al. 2020²⁴, was used. This involves a mathematical equation that enables quantification of complex structures and assessment of their level of shape irregularities, making it possible to identify changes in bone microarchitecture. For the FD analysis, the same software and ROI described above were used, and after a series of treatments, an image of the trabecular complexity of the alveolus was obtained, which in turn can be measured using the “*Box-counting*” function, which performs the count of squares of 2, 3, 4, 6, 8, 12, 16, and 32 pixels in size within the ROI. The number of squares surrounding these trabeculae and the total square count were measured for each different sized pixel. From this count, a logarithmic scale graph of the values was formed and the FD value was then calculated by measuring the slope of the line formed aligned with the points plotted on the graph, providing a final FD value. A blinded and calibrated evaluator performed the radiographic analysis (PGJM).

Statistical analysis

The classification of teeth position was compared between groups using Fisher's exact test. The evaluation took into account the independent variables, treatment (different PBMT protocols), evaluation period and teeth location (Upper vs. Lower) influence on dependent variables (Clinical and radiographic analysis) was performed by applying linear mixed models. Jamovi software was used to perform the statistical analysis. All statistical tests used in this project were applied at a significance level of 5%.

Results

The position of the dental elements was similar between the PBMT groups and did not influence postoperative repercussions

The patients were treated and follow-up between July to December 2023. Of the 20 patients operated on in this study (10 male and 10 females with age of 26.13 ± 6.43), 3 did not attend all follow-ups and were excluded from the study (Figure 2). A total of 68 teeth were extracted from the 17 patients in this study (34 lower and 34 upper molars). Half of these teeth were treated with PBMT-I and the other half with PBMT-IE. In total, 28 osteotomies were performed (1 upper tooth and 27 lower teeth) with 13 lower alveoli treated with PBMT-I and 14 lower alveoli and 1 upper alveolus treated with PBMT-IE. In addition, 16 odontosections were performed (all on lower

teeth). Half of these alveoli were treated with each type of PBMT protocol. The average surgery time was 42.67 ± 14.76 min. There were no statistically significant differences between the groups regarding the position of the teeth (Table 1-2), and the level of difficult of the teeth extraction.

There were also no differences between the groups in relation to the frequency of complications. The main complications observed in this study were the occurrence of bone spicules; Five of these structures were verified in 4 patients, in 3 sites treated with PBMT-I, and 2 treated with PBMT-IE. At the end of the follow-up, it was necessary to remove the spicule from one of these patients, as the patient reported discomfort. The other 4 spicules remodeled alone and a second surgical intervention was not necessary. One case of severe trismus (mouth opening < 10 mm), one case of hyperalgesia at a site treated with PBMT- I, and one case of lingual nerve paresthesia at a site which received PBMT-IE were also observed over a 3-day period. In the patient reporting trismus, this condition resolved spontaneously between 3 and 7 days postoperatively. In the patient with hyperalgesia, post-extraction socket irrigation was performed with saline solution on the third postoperative day and within 7 days the patient no longer reported discomfort at the surgical site. The patient with reported lingual nerve paresthesia underwent 5 sessions of PBMT with infrared laser with application of 4J per session on alternate days between the 15th and 25th postoperative days at the lingual mucosa associated with the surgical site. At the 90-day clinical analysis, the patient reported progressive improvement in the sensation of paresthesia, but still with some points of altered sensitivity associated with the lingual mucosa.

Patients and professionals did not notice differences in healing and morbidity between different PBMT protocols during the postoperative period.

The treatment parameters (PBMT) and position of the tooth in the arch (upper and lower) did not influence the healing course of the evaluated tissues (Table 3). Additionally, the independent variable treatment (PBMT-I and PBMT-IE) did not influence the patients' perception regarding the parameters evaluated on the VAS scale (Table 4). The independent variable evaluation period impacted the healing data and all parameters of the VAS scale, where reductions in values were noted with the increase in the evaluation period, especially when comparing periods of 3 and 7 days in relation to periods of 15, 30, and 90 days ($p < 0.05$) (Tables 3-4).

The different PBMT protocols showed similar potential in controlling inflammation and healing bone tissue

After tooth extraction surgery, a reduction in mouth opening and an increase in facial dimensions bilaterally were observed, with the peak of these findings occurring between 3-7 days after the surgical procedure. From this moment on, there was improvement in mouth opening and a return of facial dimensions to values observed before the surgical procedure (Table 5). No differences were observed between the groups in relation to bone density and fractal dimension, however, in both groups there was an increase in bone density in the 90-day period compared to the baseline period (Table 6) ($p < 0.05$).

Discussion

In general, the different dual-wavelength PBMT protocols used in the current research behaved in a similar way, with no superiority between one and the other. Therefore, the null hypothesis of this study was accepted.

The evaluators and patients not notice differences in any of the variables assessed in this study in the sites treated with PBMT-I and PBMT-IE. It is important to highlight that a previous study by Pereira et al., 2022¹² presented positive outcomes when comparing PBMT-I with no use of photobiomodulation on the control side in reduced edema and improved repair of soft tissues associated with lower molar extraction. Therefore, despite the previously demonstrated effects, the effects of the PBMT protocol are not distinct when comparing different PBMT protocols. The mechanism described for the effects of PBMT on tissue healing includes stimulation of the proliferation and migration of fibroblasts, associated with an increase in the capacity of these cells to synthesize collagen and produce angiogenic factors (e.g., VEGF; EGF) even after a previous challenge from pro-inflammatory cytokines (e.g., TNF- α , IL-1 β , IL-6, and IL-8)²⁵. In keratinocyte culture, PBMT was associated with increased proliferation of these cells and increased expression of genes related to the production of epidermal growth factors (hEGF) and keratinocyte growth factors (hKGF)²⁶. Preclinical studies demonstrated that PBMT accelerated the healing of soft tissue wounds on the dorsum of rats²⁷, and in the oral mucosa of rabbits²⁸. In this sense, the findings of the current study demonstrate that the application of irradiation is more important than the PBMT protocol used, regardless of the form of application.

Due to the different penetrability characteristics of red and infrared lasers, the application of these different wavelengths in specific regions of the wound has been proposed to improve the surface healing through PBMT with red light and healing in deep tissues with the application of PBMT with an infrared laser²⁰. However, in this study the applications of the lasers with different wavelength in different regions after third molar extraction did not demonstrate different effects between the groups. This finding is partially in line with the findings of Sierra et al., 2016²¹, which demonstrated superiority in the application of PBMT with red laser intraorally and of PBMT infrared laser extra orally in reducing edema compared to other forms of PBMT application at dual wavelengths, but without statistical significance. Another study demonstrated a positive effect of dual-wavelength PBMT applied in an inverted manner from that proposed in the current study, with the application of a red laser extraorally and an infrared laser intraorally, with patients presenting reduced pain and improved healing in third molar post-extraction sites²⁰.

Indeed, the above-mentioned effects of the dual-wavelength PBMT may be associated with the suppression on the kinin pathway and in the production of arachidonic acid metabolites²⁹, and reversing the effects of pro-inflammatory cytokines^{25, 26} that are activated after surgical trauma. The reduction in postoperative edema in third molar extractions has been described as a common repercussion inherent to PBMT^{12, 30}. The fact that the current study did not obtain

different results when comparing the different protocols mentioned is not due to a lack of effect of PBMT, but rather to the similarity in the effectiveness of the protocols^{21, 30}.

It was also not possible to observe a difference in bone repair in the different protocols, which may be related to the type of defect evaluated, since post-extraction alveoli of third molars present favorable conditions for the formation of bone tissue^{12, 31}. In fact, although PBMT has demonstrated effects on the formation of bone tissue in more challenging situations, such as in grafted areas^{10, 32} and in animals with systemic involvement³³, this effect was not confirmed in post-extraction alveoli of third molars¹².

The current study has some limitations that may have interfered with the findings presented. The patients selected for this study had third molars in different conditions, so, different levels of surgical complexity was necessary to extract the teeth, and, it is possible that more difficult surgeries may induce more morbidity which consequently may increase the differences between the PBMT protocols. Furthermore, most patients were young, which naturally benefits the repair process. The split-mouth model study is an effective study model to evaluate bone and soft tissues regeneration processes, while preventing differences between patients from interfering with the results. However, for the assessment of edema, pain, and trismus, the split-mouth model can present difficulties, since the fact that the extractions were performed at the same surgical time could generate confusion in the description of patients' reports in relation to the VAS scale values, especially in the case of describing pain. There is also the possibility that the drugs used in the pre- and postoperative periods in both groups masked the patients' response to the use of the PBMT, as well as the fact that pain perception is subjective and the pain threshold varies considerably between patients, which in turn can be influenced by psychological factors. Further research with different PBMT protocols in more challenging clinical conditions should be carried out, as it is of utmost importance to identify patients that could really benefit from the application of this therapy and whether the consumption of anti-inflammatory and analgesic medications could be reduced in the future, if PBMT proves to be effective enough to predictably control inflammation in third molar surgeries.

Conclusion

It can be concluded that the different PBMT protocols with dual wavelengths induced similar postoperative clinical courses in third molar extraction surgeries, with reduced occurrence of complications and a good healing pattern of hard and soft tissues.

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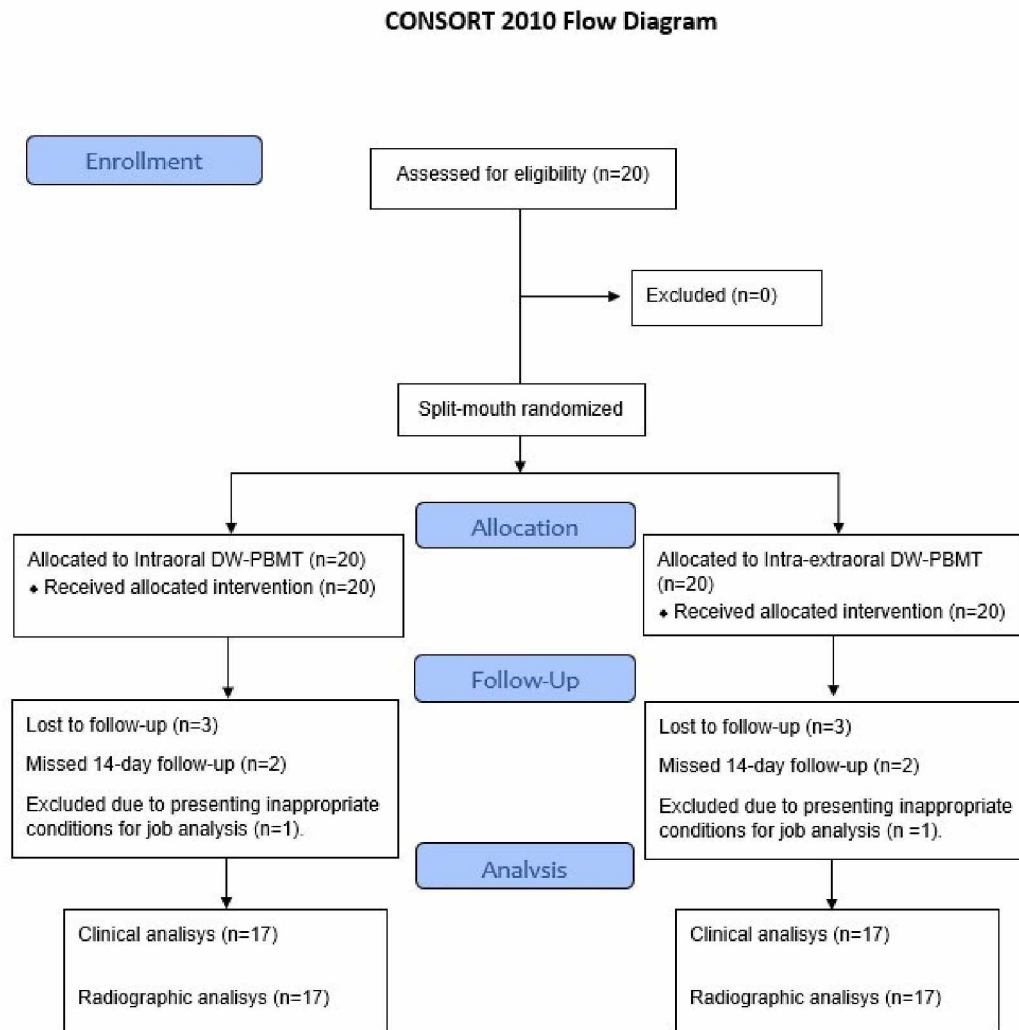
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Figure

Figure 1: Scheme for extraoral PBMT. A) In the upper alveolus, using as a reference an imaginary line drawn from the tragus of the ear to the lateral part of the nose wing, 4 different points were irradiated sequentially in the masseter muscle; In the lower alveolus region, the same procedure was performed but the reference was the lower insertion of the masseter muscle; B) PBMT with the infrared laser.



Figure 2: Flow diagram of this study.

Tables

Table 1: Classification of tooth positioning according to Winter

Classification/Group	PBMT I		PBMT IE	
	Upper	Lower	Upper	Lower
Vertical	12	11	13	10
Disto-angled	4	0	3	0
Mesio-angled	1	4	1	5
Horizontal	0	2	0	2
Total	17	17	17	17

Table 2: Classification of tooth positioning according to Pell & Gregory

Classification/Group	PBMT I		PBMT IE	
	Upper	Lower	Upper	Lower
A	10	11	11	9
B	6	6	3	7
C	1	0	3	1
Total	17	17	17	17

Table 3: Median and interquartile range of healing index values.

Position	Period/Group	PBMT I	PBMT IE
Upper	3 days	5.0 (5.0 - 7.0)	5.0 (5.0 - 7.0)
	7 days	6.0 (5.0 - 8.0)	6.0 (5.0 - 7.0)
	15 days	4.0 (4.0 - 5.0)	4.0 (4.0 - 5.0)
	30 days	4.0 (4.0 - 4.0)	4.0 (4.0 - 4.0)
	90 days	4.0 (4.0 - 4.0)	4.0 (4.0 - 4.0)
Lower	3 days	5.0 (5.00 - 6.00)	5.00 (5.00 - 7.00)
	7 days	5.0 (5.00 - 7.00)	5.00 (5.00 - 8.00)
	15 days	4.0 (4.0 - 4.0)	4.0 (4.0 - 5.0)
	30 days	4.0 (4.0 - 4.0)	4.00 (4.0 - 4.0)
	90 days	4.0 (4.0 - 4.0)	4.00 (4.0 - 4.0)

Table 4: Median and interquartile range of VAS scale values for pain, edema, bleeding, mouth opening, and chewing.

Parameter	Period/Group	PBMT I	PBMT IE
Pain	3 days	4.0 (2.0 - 6.0)	3.0 (2.0 - 8.0)
	7 days	3.0 (1.0 - 4.0)	2.0 (2.0 - 6.0)
	15 days	1.0 (0.0 - 2.0)	0.0 (0.0 - 1.0)
	30 days	0.0 (0.0 - 0.0)	0.0 (0.0 - 0.0)
	90 days	0.0 (0.0 - 0.0)	0.0 (0.0 - 0.0)
Edema	3 days	5.0 (2.0 - 6.0)	5.0 (2.0 - 7.0)
	7 days	3.0 (2.0 - 4.0)	2.0 (1.0 - 4.0)
	15 days	0.0 (0.0 - 2.0)	0.0 (0.0 - 1.0)
	30 days	0.0 (0.0 - 0.0)	0.0 (0.0 - 0.0)
	90 days	0.0 (0.0 - 0.0)	0.0 (0.0 - 0.0)
Bleeding	3 days	3.0 (1.0 - 4.0)	2.0 (1.0 - 5.0)
	7 days	0.0 (0.0 - 1.0)	0.0 (0.0 - 1.0)

	15 days	0.0 (0.0 - 0.0)	0.0 (0.0 - 0.0)
	30 days	0.0 (0.0 - 0.0)	0.0 (0.0 - 0.0)
	90 days	0.0 (0.0 - 0.0)	0.0 (0.0 - 0.0)
Chewing	3 days	6.0 (4.0 - 8.0)	6.0 (5.0 - 8.0)
	7 days	4.0 (2.0 - 6.0)	4.0 (2.0 - 5.0)
	15 days	1.0 (0.0 - 2.0)	0.0 (0.0 - 1.0)
	30 days	0.0 (0.0 - 0.0)	0.0 (0.0 - 0.0)
	90 days	0.0 (0.0 - 0.0)	0.0 (0.0 - 0.0)
Mouth opening	3 days	7.0 (5.0 - 8.0)	7.0 (5.0 - 8.0)
	7 days	5.0 (2.0 - 5.0)	5.0 (2.0 - 5.0)
	15 days	1.0 (0.0 - 3.0)	1.0 (0.0 - 2.0)
	30 days	0.0 (0.0 - 1.0)	0.0 (0.0 - 0.0)
	90 days	0.0 (0.0 - 0.0)	0.0 (0.0 - 0.0)

Table 5: Mean and standard deviation of variation in facial dimensions and mouth opening.

Parameter	Period/Group	PBMT I	PBMT IE
Mouth opening	Baseline	42.1 ± 10.5	
	ΔBass – 3d	18.6 ± 7.7	
	ΔBass – 7d	12.6 ± 10.7	
	ΔBass – 15d	3.2 ± 8.6	
	ΔBass – 30d	0.1 ± 7.4	
	ΔBass – 90d	-4.1 ± 8.2	
Vertical dimension	Baseline	10.4 ± 1.0	10.3 ± 0.8
	ΔBass – 3d	-0.3 ± 0.6	0.0 ± 0.7
	ΔBass – 7d	-0.1 ± 0.7	-0.1 ± 0.7
	ΔBass – 15d	0.2 ± 0.5	0.1 ± 0.6
	ΔBass – 30d	0.1 ± 0.6	0.1 ± 0.6
	ΔBass – 90d	0.0 ± 0.7	0.00 ± 0.7
Horizontal dimension	Baseline	11.7 ± 0.8	11.6 ± 0.7
	ΔBass – 3d	-0.2 ± 1.1	-0.2 ± 0.7
	ΔBass – 7d	-0.3 ± 0.8	-0.2 ± 0.9
	ΔBass – 15d	-0.5 ± 0.9	-0.6 ± 0.7
	ΔBass – 30d	-0.3 ± 1.3	-0.1 ± 1.0
	ΔBass – 90d	-0.1 ± 0.8	-0.3 ± 0.8

Table 6: Mean and standard deviation of radio density and fractal dimension measured by digital radiographic analysis.

Place	Parameter	Period/Group	PBMT I	PBMT IE
Upper	Radio density	Baseline	121.6 ± 18.5	116.3 ± 22.2
		90 days	144.2 ± 15.8	143.1 ± 17.2
	Fractal dimension	Baseline	1.2 ± 0.1	1.2 ± 0.1
		90 days	1.2 ± 0.1	1.3 ± 0.1
Lower	Radiodensity	Baseline	120.4 ± 16.2	115.8 ± 16.4
		90 days	138.0 ± 21.0	135.1 ± 22.2
	Fractal dimension	Baseline	1.3 ± 0.1	1.3 ± 0.1
		90 days	1.3 ± 0.1	1.3 ± 0.1

Cover Letter

Dear Prof. Dr. Brian Wong

We are submitting the paper entitled: “Comparison of different dual-wavelength photobiomodulation protocols application in third molar extractions. A split-mouth randomized controlled trial” to the *Laser in Surgery and Medicine*. The aim of this clinical trial was to compare the effect of photobiomodulation (PBMT) in the soft tissue and bone healing after third molar extraction using the dual-wavelength laser directly into the post-extraction alveoli (PBMT-I), or PBMT with a red laser directly into the alveoli and with an infrared laser externally on the patient's face (PBMT-IE). The PBMT has been showed beneficial effects of the healing and control of inflammation associated with a myriad of oral surgeries. However, some factors can interfere with PBMT therapy. The wavelength of the laser deserves highlight since these parameters interferes with the deepness of the energy dispersion which can indicates that laser with different wavelengths can be used in different clinical situation. The red and infrared laser have been used commonly to treat oral wounds in an isolated way. However, the association of both wavelengths have been showed promising outcomes since the PBMT with red and infrared lasers have been showed these good effects on the soft tissue, reduction of pain and edema associated with third molars extraction. Different protocols of dual-wavelength have been tested before, however, the comparison of these protocols of PBMT with the infrared and red laser associated lacks information. The main finding of this study was that the different dual-wavelength PBMT protocols induced a similar postoperative clinical course in third molar extraction surgeries, with a reduced occurrence of complications and a good healing pattern of hard and soft tissues. So, the fact that the current study did not obtain different results when comparing the different protocols mentioned is not due to a lack of effect of PBMT, but rather to the similarity in the effectiveness of the protocols

In addition, we declare that all the authors listed in this study meet the criteria for authorship giving: 1) substantial contributions to conception and design of, or acquisition of data or analysis and interpretation of data, 2) drafting the article or revising it critically for important intellectual content and 3) final approval of the version to be published. This study was supported by grants from CNPq, National Council for Scientific and Technological Development and FAPEMIG, Fundação de amparo a pesquisa de Minas Gerais (Grants INCT Saúde Oral e Odontologia 406840/2022-9, FAPEMIG APQ-02211-21, and CNPq – Financial code 001). Furthermore, the authors declare to have no conflict of interesting regarding this paper.

All my best regards

Guilherme José Pimentel Lopes de Oliveira, Pará, Av., 1760-1844 - Umuarama, Uberlândia - MG, Zip-code: 38405-320 email: guilherme.lopesoliveira@ufu.br

5. CAPÍTULO 5

ARTIGO 5

Ensaio clínico prospectivo sobre a cicatrização de alvéolos pós-exodontia de terceiros molares tratados com fotobiomodulação de duplo comprimento de onda.

Prospective clinical trial on the healing of post-extraction alveoli of third molars treated with dual-wavelength photobiomodulation.

Artigo a ser enviado no periódico Oral and Maxillofacial Surgery

Original Research: Prospective clinical trial on the healing of post-extraction alveoli of third molars treated with dual-wavelength photobiomodulation.

Davisson Alves Pereira ¹, Mariana Silva Bonatto ¹, Henrique Alves Barros Assunção ¹, Samara de Souza Santos ¹, Pedro Gomes Junqueira Mendes ¹, Guilherme José Pimentel Lopes de Oliveira¹

¹ Federal University of Uberlândia - UFU, School of Dentistry, Department of Periodontology, Uberlândia, MG, Brazil

Author for Correspondence

Guilherme José Pimentel Lopes de Oliveira

Pará, Av., 1760-1844 - Umuarama, Uberlândia - MG, Zip- code: 38405-320

Email: guilherme.lopesoliveira@ufu.br

SUMMARY

Objective: This study evaluates the effect of Photobiomodulation therapy (PBMT) with red and infrared wavelength lasers in the postoperative management of third molar extraction surgeries.

Methods: This cohort prospective study involved the participation of 65 patients who underwent third molar extractions and received PBMT with a combination of red (λ 660 nm) and infrared (λ 808 nm) lasers. The PBMT protocol was applied in 3 sessions, immediately and 3 and 7 days after the surgical procedure. Clinical analyses were performed 3, 7, 14, 30, and 90 days after the extraction surgery. Each socket was subsequently clinically evaluated and classified in relation to bleeding, tissue color in the region of the surgery, presence of suppuration or plaque, and color and texture of the healing tissue. Using a visual analogue scale, patients assessed the parameters of pain, inflammation, bleeding, difficulty chewing, and difficulty opening the mouth. Furthermore, post-extraction alveolar healing was assessed using x-rays, bone density, and fractal dimension analysis at the baseline period and 90 days after the surgical procedure. **Results:** Clinical analyses demonstrated that PBMT promoted an improvement in postoperative morbidity, reducing edema 15 days after surgery and accelerating the healing of soft tissues, while the analysis of bone tissue revealed an increase in radiographic density and the fractal dimension in the 90-day period compared to the postoperative period. The bilateral application of PBMT was associated with a lower incidence of VAS values greater than 5 over a 3-day period. **Conclusion:** Dual-wavelength PBMT (λ 660nm/808nm) was beneficial for postoperative management after third molar extraction.

Keywords: Low Intensity Light Therapy; Third Molar; Wound Healing; Edema.

INTRODUCTION

Third molar extraction surgery is one of the most common surgical procedures in Dentistry, (BAILEY et al., 2020; CAMPS-FONT et al., 2023), and involves several factors that must be taken into consideration during planning (RIZQIAWAN et al., 2022). Incorrect planning can lead to significant trans- and/or post-operative problems for the patient. Therefore, in addition to a thorough assessment of the patient's systemic condition, it is necessary to carry out a careful analysis of local conditions. Among the most important aspects are the position of the tooth, the patient's age, the ability to open the mouth, and the presence of pre-existing lesions (HERRERA-BARRAZA et al., 2022). However, even with good planning, it is expected that after the surgical procedure patients will present some repercussions resulting from the inflammatory reaction to the surgical manipulation, such as edema (YANINE et al., 2021), limitation of mouth opening (YAMADA et al., 2022), and a transient decrease in masticatory functions (XIE et al., 2021) .

These repercussions are traditionally treated with pharmacological therapies, generally with the use of analgesics, and non-steroidal and steroidal anti-inflammatory drugs (ISOLAN et al., 2021), with the aim of controlling the exacerbated release of inflammatory mediators (MOMESSO et al., 2021). Although these drugs are essential in controlling postoperative repercussions (ALTAWHEEL et al., 2022), it is necessary to use it with caution due to possible side effects inherent to their systemic administration (SINGH et al., 2023). In this sense, local therapies to control inflammation can be useful for postoperative management after surgical extraction of third molars, among which photobiomodulation (PBMT) with a low-power laser stands out (KAHRAMAN et al., 2017). PBMT has demonstrated promising results, improving the osseointegration of dental implants (VANDE; et al., 2022), reducing pain and edema, improving soft tissue repair in third molar surgery (FERREIRA et al., 2022; MADANI et al., 2020), and reducing pain in temporomandibular disorders (TMD) (LANGELLA et al., 2018) and muscle pain in various regions of the body (DE OLIVEIRA et al., 2022).

Two laser groups are most commonly used, according to the wavelength of the emitted light: red (660nm) and infrared (830nm) in the PBMT (CUNHA et al., 2012; GONÇALVES et

al., 2023). Lasers with wavelengths within the infrared light range have greater penetrability within tissues and are therefore preferable in accelerating bone healing (FREDDO et al., 2009; GONÇALVES et al., 2023). Lasers within the red wavelength have also been shown to be effective in the bone regeneration process in pre-clinical studies in immunosuppressed animals (GARCIA et al., 2014, 2018). However, the greater superficial absorption of oral tissues with light emitted at the red wavelength indicates that this type of PBMT is more beneficial for soft tissue healing (DE VASCONCELOS CATÃO et al., 2015).

A spit-mouth randomized trial that evaluated 20 patients treated with dual-wavelength PBMT after lower molar extraction, reported that this therapy reduced pain and edema in treated areas compared to areas where PBMT was not performed (PEREIRA et al., 2022). Despite the satisfactory results found in this study, the small sample size limits the external validity of the study, making it necessary to expand the application of this protocol by increasing the number of cases, in order to evaluate the effectiveness of dual-wavelength PBMT at in postoperative management after third molar extractions.

The aim of this study was to evaluate the effect of using PBMT with red and infrared wavelengths, used simultaneously, in the postoperative management of third molar extraction surgeries.

MATERIAL AND METHODS

Ethical considerations

This study was carried out in accordance with resolution 466 of 12/12/2012 of the National Health Council of the Brazilian Ministry of Health. The study was previously approved by the Human Research Ethics Committee of the Federal University of Uberlândia under protocol number CAAE: 49164821.0.0000.5152.

Study design

This prospective cohort study involved the participation of 65 patients from the Federal University of Uberlândia. The patients included in the study underwent third molar extractions and received photobiomodulation therapy (PBMT) with red (λ 660 nm) and infrared (λ 808 nm) laser therapy.

Sample size calculation

The sample calculation was performed based on the study by Eshghpour *et al.*, 2016 that evaluated the effect of low-intensity laser therapy on controlling pain and edema in the postoperative period after third molar extraction. The primary outcome considered for the sample calculation was the variation in the VAS pain scale applied on the 3rd and 7th postoperative days. The size of the expected outcome considering a clinical improvement for the VAS scale was 0.5, with an expected mean standard deviation for this analysis of 1.01. Setting the type I error at 5% and β power at 90 %, a minimum sample size of 45 patients was established.

Eligibility Criteria

Patients over 18 years of age, with good oral hygiene (plaque index < 20%), and presenting the third molars requiring extraction were included in this study. Individuals were excluded from this study if the cases of history of periodontal disease, diseases or systemic conditions that contraindicated the surgical procedure, used medications that alter bone metabolism, presented decompensated diabetes (glycated hemoglobin above 7%), pregnancy or lactation, heavy smoking (above 10 cigarettes per day), and the presence of periapical or pericoronal lesions.

Surgical procedures and study groups

Initially, all patients underwent screening, which included a clinical and panoramic radiographic examination to confirm the presence of third molars with an indication for extraction. The patients then attended an initial clinical examination, at which a thorough anamnesis was collected with systemic health data, as well as facial measurements. Third molars were classified according to the Pell & Gregory and Winter classifications.

On the day of the surgical procedure, all patients took 8mg of dexamethasone one hour before the procedure, administered orally. For the surgical procedure, patients underwent extraoral and intraoral asepsis and antisepsis with chlorhexidine digluconate, at concentrations of 2% and 0.12% respectively. Following positioning of the sterilized surgical drapes, all nerve endings involved in the sensitization of the four third molars were anesthetized. Then, the teeth were accessed through a full flap when necessary and were extracted using various instruments depending on the necessity, such as extractors and high and low rotation handpieces associated with cutting or abrasion drills and finished through tissue synthesis techniques. Post-extraction, the alveoli were treated with dual-wavelength PBMT (660 nm red laser and 808 nm infrared laser), just after and 3- and 7-days after the surgical procedure. After the surgeries, the patients were prescribed; diclofenac sodium (50mg) every 8 hours for 3 days and dipyrone sodium (500mg) every 6 hours for 3 days, all taken orally. Additionally, a mouthwash based on 0.12% chlorhexidine digluconate was prescribed for 7 days. The sutures were removed 7 days after the surgical procedure.

Outcomes

The primary outcome of the current study was the assessment of pain using the VAS scale. The secondary outcomes were clinical analyses, patient-centered analyses, radiographic analysis, the incidence of complications, and analysis of facial measurements and mouth opening.

Photobiomodulation protocol

Patients in this study were treated using PBMT with red and infrared light in 3 sessions over 7 days. PBMT was performed by applying dual-wavelength laser energy. The GaAlAs laser

(XTherapy EC, λ 660nm and λ 808nm, 100mW, $\phi \sim 0.600\mu\text{m}$, tip divergence = 0.37rad, CW, spot area of 0.0283 cm², DMC Equipamentos, São Carlos, SP, Brazil). The application of the laser was carried out in each of the extraction sockets for 40 seconds, immediately after tooth extraction, and 3 and 7 days after, which resulted in an applied energy of 8J per session, totaling a total energy application of 24J, in the three sessions. The irradiation energy density used was approximately 35.33 J/cm²/point and 282.64 J/cm² in total.

Clinical analysis

Patients were evaluated 3, 7, 14, 30 and 90 days after the surgical procedure. Each socket was subsequently clinically evaluated and classified in relation to bleeding, tissue color in the region of surgery, presence of suppuration or plaque, and color and texture of the healing tissue (Mozzati, 2014). A score on a scale of 1-3 was applied to each of these items, where the highest number depicted a poorer condition of the parameter evaluated, with the overall score ranging from 4 to 12 per alveolus. A value of four was characterized as complete healing. A continuous VAS scale from 0-10 was also applied to the patients, where the lowest value characterized a better clinical condition related to the assessment of the parameters of pain, inflammation, bleeding, difficulty chewing, and difficulty opening the mouth.

Finally, the patients' mouth opening and possible facial dimension changes were measured to evaluate the inflammatory process. The measurement of horizontal dimensions (distance from the tragus to the labial commissure) and vertical dimensions (gonium of the mandible to the palpebral commissure) was performed using dental floss associated with a digital caliper (DAUGELA et al., 2018; ESHGHPOUR; AHRARI; TAKALLU, 2016). Regarding mouth opening, the caliper was used to evaluate the distance between the upper and lower central incisors, with patients opening the mouth to a comfortable position (DAUGELA et al., 2018; ESHGHPOUR; AHRARI; TAKALLU, 2016). Data from the evaluation periods were expressed in relation to the variation in measurements obtained in the baseline period. Any clinical complications that were observed by the evaluators or reported by the patients were also noted (presence of infections, need for irrigation of the surgical bed, trismus).

Image analysis - Remnants of bone defects and fractal analysis

For radiographic analysis, immediate and 90-day postoperative panoramic radiographs were used, with the aim of evaluating alveolar density in the remnants of bone defects and the trabecular complexity of the region, using the histometric analysis and fractal dimension (FD) analysis respectively. To perform the density analysis, ImageJ software (version 1.3; National Institutes of Health, Bethesda, MD, USA) was utilized, with the “*histometry*” tool in a region of interest (ROI) of 32x32 pixels in the center of each alveolus, making it possible to obtain the gray tone values present in the radiograph and compare the two moments, postoperative and 3 months.

For the FD analysis, the same software and ROI described above were used, and after a series of treatments, an image of the trabecular complexity of the alveolus was obtained, which in turn can be measured using the “Box-counting” *function*, which allowed counting of squares of 2, 3, 4, 6, 8, 12, 16, and 32 pixels in size within the ROI. The number of squares surrounding these trabeculae and the total square count were measured for each different sized pixel. From this count, a logarithmic scale graph of the values was formed and the FD value was then calculated by measuring the slope of the line formed aligned with the points plotted on the graph, providing a final FD value.

Statistical analysis

The data obtained in this study were subjected to the Shapiro-Wilk normality test, confirming the normal distribution of data on facial dimensions, mouth opening, fractal dimension, and radiographic density, while non-normal distribution of data was observed for the VAS scale and soft tissue healing analyzes. The comparison between the evaluation periods was performed using the paired t-test for radiographic analyses. The repeated measurements ANOVA complemented by the Tukey test was used for analyses of facial dimensions and mouth opening, while the Friedman test complemented by the Dunn was used for VAS scale and soft tissue healing analyses. Patients with less favorable clinical recovery were also considered to be those presented any item on the VAS scale equal to or above 5 in the experimental period. The factors that influenced the patient's recovery were evaluated using multivariate logistic regression, observing

the effect of surgery time, tooth position, initial mouth opening, patient age, soft tissue healing, and PBMT, carried out unilaterally or bilaterally. Jamovi software was used for inferential data analysis and all tests were applied at a significance level of 5%.

RESULTS

The surgical sockets treated with PBMT presented teeth with different levels of difficulty for the extraction procedure

In this study, 65 patients underwent surgery, and a total of 154 teeth were extracted, including 77 lower teeth and 77 upper teeth. In 53 patients, dual-wavelength PBMT was applied to one upper and one lower alveoli, while in 12 patients, dual-wavelength PBMT was applied to 2 upper alveoli and 2 lower alveoli. The distribution of the position of teeth extracted and treated with dual-wavelength PBMT according to the Winter and Pell & Gregory classifications is shown in table 1. Most of the upper teeth were in a vertical position or in position A, while the lower teeth were found to be more vertical or in position B.

Table 1: Distribution of extracted teeth in relation to Winter and Pell & Gregory classifications.

Winter	Upper	Lower	Pell & Gregory	Upper	Lower
Vertical	57	38	A	43	31
Disto-angled	13	1	B	19	40
Mesio--angled	7	28	C	15	6
Horizontal	0	10	-	-	-
Total	77	77	Total	77	77

Regarding surgical procedure maneuvers, osteotomies were performed for extraction of 1 upper tooth and 55 lower teeth. Odontosections were performed associated with extraction surgeries of 44 lower teeth, and in 43 cases, these odontosections were accompanied by osteotomies, and in 1 case the odontosection was performed alone. In 12 cases of lower tooth extraction, osteotomy was performed in isolation.

The perception of improvement in postoperative morbidity by patients was dependent on the evaluation period and was associated with a reduction in edema and improvements in the healing of soft tissue and bone tissue.

Patients presented greater postoperative morbidity in periods of 3 and 7 days than in periods from 15 days onwards in all events assessed by the VAS scale (Table 2). Of the parameters evaluated, only bleeding was found to be reduced from 7 days onwards, while pain, edema, and difficulties chewing, and opening the mouth presented moderate measurements, with a median above or equal to 3 (Table 2).

Table 2: Median and interquartile range of the VAS scale values reported by patients in relation to postoperative morbidity.

Parameter	3 days	7 days	15 days	30 days	90 days
Pain	4.50(2.00-6.00)	3.00(1.00-7.00)	0.00(0.00-2.00)	0.00(0.00-0.00)	0.00(0.00-0.00)
Edema	5.00(2.00-7.25)	3.00(1.00-5.00)	0.00(0.00-0.00)	0.00(0.00-0.00)	0.00(0.00-0.00)
Bleeding	3.00(0.00-5.00)	1.00(0.00-4.00)	0.00(0.00-0.00)	0.00(0.00-0.00)	0.00(0.00-0.00)
Mouth opening	7.00(5.00-8.00)	5.00(1.00-6.00)	0.00(0.00-2.00)	0.00(0.00-0.00)	0.00(0.00-0.00)
Chewing	6.00(4.00-8.00)	5.00(2.00-7.00)	0.00(0.00-1.00)	0.00(0.00-0.00)	0.00(0.00-0.00)

Although facial dimensions were not changed during the postoperative period, a considerable limitation in mouth opening was observed in the 3 and 7 days, with this limitation being practically non-existent after the 15 days period. These findings confirm the data observed on the VAS scale (Table 3).

Table 3: Mean and standard deviation values of changes in facial dimensions and mouth opening during the postoperative period.

Parameter	3 days	7 days	15 days	30 days	90 days
Δ Vertical dimension	-0.22 ± 0.98	-0.08 ± 0.97	-0.19 ± 0.95	-0.22 ± 1.41	-0.14 ± 0.87

Δ Horizontal dimension	-0.26 ± 0.87	-0.09 ± 0.81	0.11 ± 1.04	0.13 ± 0.72	0.00 ± 0.72
Δ Mouth opening	16.80 ± 8.82	8.65 ± 10.15	1.67 ± 8.74	-0.61 ± 6.97	-2.42 ± 6.98

Soft tissue healing occurred quickly, as a median of at least 5 was observed in all experimental periods (Table 4). In the analysis of the bone tissue, an increase in radiographic density and fractal dimension was observed over time until the analysis at 90 days (Table 5), except for the sites of the lower molars, in relation to the fractal dimension, which remained constant over the 90-day period compared to the baseline period (Table 5).

Table 4: Median and interquartile range values of the assessment of the quality of soft tissue healing during the postoperative period.

Tooth	3 days	7 days	15 days	30 days	90 days
Upper	5.00(4.00-7.00)	5.00(4.00-7.00)	4.00(4.00-5.00)	4.00(4.00-4.00)	4.00(4.00-4.00)
Lower	5.00(5.00-7.00)	5.00(5.00-6.00)	4.00(4.00-5.00)	4.00(4.00-4.00)	4.00(4.00-4.00)

Table 5: Mean and standard deviation values from the assessment of bone healing during the postoperative period.

Analysis	Tooth	Baseline	90 days
Fractal Dimension	Upper	1.2 ± 0.3	1.3 ± 0.1
	Lower	1.3 ± 0.2	1.2 ± 0.4
Radiographic density	Upper	107.8 ± 29.4	129.3 ± 38.4
	Lower	110.8 ± 28.4	131.4 ± 21.4

The factors that influenced patient comfort in the postoperative period were related to the difficulty of the surgical procedure and the application of PBMT.

At 3 days, it was observed that 53 patients had a value on the VAS scale above 5, and at 7 days, 39 patients had values on the VAS scale above 5. The factors that significantly interfered with the VAS scale above 5 in the period of 3 days were the position of the teeth according to the Pell & Gregory and Winter classifications, the execution of osteotomies and odontosection, and the execution of PBMT bilaterally. Teeth with a more complex position, which required osteotomy and odontosection, and unilateral application of PBMT were more likely to present a VAS scale score above 5. Factors such as mouth opening, age, surgery time, and soft tissue healing rate did not significantly influence the occurrence of values above 5 on the VAS scale (Table 6). At 7 days, none of the factors tested influenced the occurrence of values above 5 on the VAS scale.

Table 6: The p values of the relationship of variables that influenced the occurrence of VAS scale ≥ 5 , obtained by multivariate logistic regression 3 days after surgery

VAS Scale ≥ 5	p
Winter classification	<0.01
Pell & Gregory classification	<0.01
Osteotomy	<0.01
Odontosection	<0.01
Soft tissue healing	0.80
Age	0.80
Surgery time	0.93
PBMT protocol	<0.01
Baseline opening of the mouth	0.91

DISCUSSION

In general, the dual-wavelength PBMT protocol tested in this study promoted a good clinical course in the postoperative period of third molar surgery, as there was a reduction in edema and improvements in the healing of soft tissue and bone tissue. However, there were no significant changes in facial dimensions, other than the fractal dimension when observed in the lower alveoli. Therefore, the alternative hypothesis of this study was partially accepted.

The alveoli treated with PBMT showed an uneventful course of soft tissue healing, with progressive improvement in color and texture, and the absence of bleeding and purulent secretions throughout the healing phase. The good healing presented in the alveoli may have been influenced by the PBMT protocol applied. PBMT can stimulate the proliferation and migration of different types of cells, including fibroblasts (MOKOEMA et al., 2020 LAYERGH et al., 2020) and osteoblasts (DA FONSECA et al., 2022), and these cells are involved in the formation of soft and bone tissues, modulating the healing process. A previous clinical study demonstrated that the application of red laser to ulcers in patients admitted to hospitals led to improved healing and this finding was related to a reduction in the expression of TNF- α and an increase in the expression of VEGF and TGF β (TARADAJ et al., 2018). PBMT has also been associated with an increase in the expression of proteins related to epithelial proliferation and maturation, which may induce faster closure of wounds treated with PBMT (SPERANDIO et al., 2015). Pre-clinical studies have also demonstrated effects of PBMT on the healing of hard and soft tissue, such as accelerating the production of bone matrix and consequently bone repair around implants installed in rat femurs (DA FONSECA et al., 2022), in post extraction alveoli in rabbits (HAMAD; NAIF; ABDULLAH, 2016), and in the oral mucosa of rats (CHOUNG et al., 2019). Therefore, the positive outcomes related to bone and soft tissue healing in the previously mentioned studies related to PBMT may explain the satisfactory results observed in the current study related to bone and soft tissue healing.

The positive course of soft and bone tissue healing after PBMT treatment can be attributed to several factors and mechanisms related to this therapy, as already described in the literature,

such as; stimulation of cell proliferation and migration (PIVA et al., 2011), growth and angiogenic factors (RUH et al., 2018), and reduction in inflammation and improvement in cellular energy metabolism (RYU et al., 2023), in addition to induced activation of lymphatic flow (SMOOT et al., 2015; TOMAZ DE MAGALHÃES et al., 2016). These mechanisms can explain two results of this study, where there was a significant reduction in postoperative morbidity in the 15-day period measured by the visual analogue scale, mainly in the parameters of pain and edema. Furthermore, there were no significant changes in facial measurements in the postoperative period, which may be due to the reduction in acute vascular events promoted by PBMT. Previous clinical studies have also demonstrated a reduction in edema after application of PBMT (ESHGHPOUR; AHRARI; TAKALLU, 2016; HADAD et al., 2022).

Another finding of this study was that the reduction in mouth opening had an influence on the comfort of patients measured by the VAS scale, especially on the 3rd and 7th postoperative days. In fact, the period of 03 and 07 days after tooth extraction is a critical period in which patients generally experience peaks of pain and discomfort. In addition, post-operative edema peaks within 48 hours (DARAWADE et al., 2014), and tends to gradually regress 7 days after extraction (JEONG et al., 2021). These factors explain the findings of the current study for the decrease in mouth opening in the first days after extraction, concomitant with greater postoperative morbidity in the period of 3 and 7 days measured by the VAS scale, given that edema is directly associated with limited mouth opening, and its remission along with resolution of the inflammatory process is expected within 7 days, a fact confirmed in the current study in which at the 15-day period there was practically no difficulty opening the mouth related by the patients.

The bleeding rate was the only variable totally reduced after 7 days in this study. This observation in relation to PBMT can be elucidated by several factors. As previously mentioned, PBMT is known for its potential to stimulate the healing of soft and bone tissues, promoting cell proliferation, collagen synthesis, and angiogenesis (YAKOUT et al., 2023). Although these mechanisms may also be related to reducing bleeding, the direct effect of PBMT on blood clotting

may not be as pronounced as on other aspects of healing (SPERANDIO et al., 2015; TARADAJ et al., 2018). Another aspect likely to elucidate this finding is the hemostasis performed during the surgical procedure, given that, in surgical procedures such as third molar extractions, surgeons often adopt measures to minimize intraoperative bleeding, such as the application of hemostasis techniques. This may reduce the impact of bleeding as an important index to be modulated by PBMT.

Regarding fractal analysis of bone healing, the current study demonstrated no variations in the fractal dimension in the lower alveoli between the baseline period and the 90-day postoperative period. A likely explanation for this finding is that the biostimulatory effects of PBMT (HANNA et al., 2021; WAN et al., 2020) were not sufficient to induce changes in the structure of the bone tissue. The present study selected only healthy patients with third molars in different impaction conditions. As the majority of these patients are young, they do not fit into what is defined as risk factors for the extraction of third molars, since most of the extracted teeth were not in bone impaction. Thus, clot formation is more efficient in this scenario than in alveoli that have undergone large osteotomies. The conditions mentioned above, may have favored bone maturation, avoiding the perception of the modulated effects promoted by PBMT in the bone consolidation process as demonstrated in other studies in compromised health situations (PENG et al., 2020) , in animals with systemic diseases (GARCIA et al., 2018), and in grafted areas (HUANG et al., 2023). Therefore, more studies on dual-wavelength PBMT are needed, regarding the extraction of third molars, to elucidate which protocol is effective and which patient could benefit from this therapy.

However, it is worth highlighting that when considering patient-focused outcomes, the bilateral application of PBMT in teeth that underwent simpler surgical procedures, without the need for osteotomies or odontosections, provided greater comfort for patients during the postoperative period of 3 days. These findings highlight that despite the limited findings on clinical effects, especially in bone tissue, PBMT has a modulating effect on the inflammatory

process, which was noted with greater effect in patients undergoing bilateral application of PBMT.

The present study had some limitations that must be considered when analyzing the results. Firstly, in this study there was no control group, all patients underwent PBMT. The absence of a control group makes it more difficult to determine whether the observed results are in fact due to the experimental treatment or to other factors, such as the placebo effect or progression of natural bone and tissue healing. Furthermore, there is also the possibility that the drugs used by all patients pre- and post-operatively (for example, dexamethasone, dipyrone sodium), hide the response to the use of PBMT. Another aspect is in relation to pain measurement, given that pain is subjective and presents a level of variability in the threshold between patients, which could be influenced by environmental and, mainly, psychological factors. It can be concluded that the post-extraction alveoli of third molars treated with dual-wavelength PBMT (λ 660nm/808nm) showed good healing of bone and soft tissues.

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Considerações finais

De maneira geral esta tese teve como objetivo avaliar o processo de reparo nas cirurgias de terceiros molares mediante a utilização de diferentes protocolos de fotobiomodulação e com protocolos diversos de antibioticoterapia profilática. Para essa finalidade, foram executados 5 estudos clínicos (1 estudo clínico controlado e randomizado em modelo paralelo; 3 estudos clínicos controlados e randomizados em modelo de boca dividida e 1 estudo de coorte prospectivo) com diferentes abordagens.

Os achados dessa tese demonstraram que a PBMT beneficia o curso clínico pós-operatório após exodontia de terceiros molares, sobretudo nos primeiros 7 dias de acompanhamento, que é o momento mais crítico em relação a morbidade do paciente inerente ao processo inflamatório que ocorre nesse tipo de tratamento. Um fato importante demonstrado nesse conjunto de estudos é que o componente de laser infravermelho da PBMT foi mais impactante clinicamente, pois demonstrou não ser inferior ao tratamento com PBMT em duplo comprimento de onda (Estudo 3), enquanto a PBMT com laser vermelho não foi tão eficiente no controle do edema aos 7 dias em comparação a PBMT em duplo comprimento de onda (Estudo 2). É provável que o fato do laser infravermelho alcançar maior penetrabilidade tecidual promova maiores benefícios, visto que a maior morbidade associada a exodontia de terceiros molares ocorre devido ao maior grau de manipulação nas intervenções, pois retalhos mais amplos, maiores osteotomias, e dentes impactados tem relação com eventos mórbidos mais pronunciados durante a fase de recuperação pós-cirúrgica. É importante frisar que o melhor resultado apresentado pela PBMT com laser infravermelho não desabona o uso da PBMT com laser vermelho, uma vez que, está amplamente verificado na literatura resultados positivos com esse tipo de irradiação.

Em relação aos antibióticos entendemos ter sido importante a condução do estudo 1, visto que esse grupo de fármacos é amplamente utilizado em cirurgias de terceiros molares objetivando evitar infecções posteriores no sítio cirúrgico. Entendemos que a possibilidade de haver esse tipo de contaminação poderia de alguma forma atrapalhar o processo de reparo em seu curso normal, então, justifica-se a análise dessa variável. Os resultados do estudo 1 demonstraram que a

utilização de antibioticoterapia não mudou o curso do processo de reparo, tampouco diminuiu o índice de infecção, simplesmente porque não houve nenhuma infecção dentre todos os pacientes operados. Diante do exposto, entendemos que a PBMT é uma boa terapia não farmacológica, enquanto a indicação rotineira de antibioticoterapia profilática deve ser repensada.

Por fim, os protocolos de PBMT com duplo comprimento de onda, independentemente de sua forma de aplicação (Estudo 4), foi efetiva no manejo pós-operatório após exodontia de terceiros molares. De fato, o índice de complicações, e o curso de reparo de tecidos moles e duros após esses procedimentos foi previsível (Estudo 5). Dessa forma, sugerimos que futuramente avalie-se o impacto desse protocolo de PBMT na redução da carga medicamentosa de analgésicos e anti-inflamatórios, pode ser que essa análise traga benefícios sem precedentes para pacientes que necessitam dessas drogas, mas não podem consumi-las por problemas sistêmicos. Ato contínuo em havendo comprovação de efetividade similar entre PBMT e anti-inflamatório e analgésicos poderia ser observado ganho notável no custo-benefício dessa terapia adjunta dentro do contexto do sistema único de saúde.

Conclusão

De maneira geral, pode-se concluir que a PBMT beneficiou a evolução clínica pós-operatória na extração de terceiros molares, sobretudo, quando comparada a não aplicação da terapia de luz e quando associada a antibioticoterapia. Parece claro que à antibióticoterapia quando usada em pacientes saudáveis não contribui para melhora clínica no curso pós-operatório deste tipo de cirurgia, tampouco diminui a incidência de infecção. Quanto aos diferentes protocolos de PBMT, as associações dos comprimentos de onda ou a utilização isolada do laser infravermelho apresentam benefícios clínicos no reparo após extração de terceiros molares.

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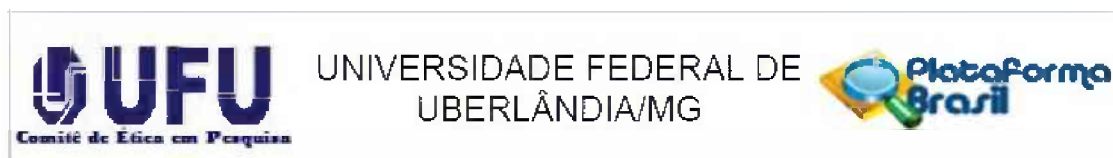
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Anexos

CEP: Parecer consubstanciado do CEP, capítulo 1



PARECER CONSUBSTANCIADO DO CEP

DADOS DO PROJETO DE PESQUISA

Título da Pesquisa: Avaliação de diferentes protocolos trans-operatórios de anestesia local e pós-operatórios de antibioticoterapia e laserterapia em cirurgias de exodontia de terceiros molares. Estudo Clínico, controlado e randomizado.

Pesquisador: Guilherme José Pimentel Lopes de Oliveira

Área Temática:

Versão: 2

CAAE: 49164821.0.0000.5152

Instituição Proponente: FACULDADE DE ODONTOLOGIA

Patrocinador Principal: Financiamento Próprio

DADOS DO PARECER

Número do Parecer: 4.944.835

CEP: Parecer consubstanciado do CEP, capítulo 2,3,4,5



PARECER CONSUBSTANCIADO DO CEP

DADOS DO PROJETO DE PESQUISA

Título da Pesquisa: Avaliação de diferentes protocolos de anestesia local e fotobiomodulação em cirurgias de exodontia de terceiros molares.

Pesquisador: Guilherme José Pimentel Lopes de Oliveira

Área Temática:

Versão: 1

CAAE: 72834023.3.0000.5152

Instituição Proponente: FACULDADE DE ODONTOLOGIA

Patrocinador Principal: Financiamento Próprio

DADOS DO PARECER

Número do Parecer: 6.249.217

Apendices

TCLE: Termo de consentimento livre e esclarecido capítulo 1

TERMO DE CONSENTIMENTO LIVRE E ESCLARECIDO

Você está sendo convidado(a) a participar da pesquisa intitulada **Avaliação de diferentes protocolos trans-operatórios de anestesia local e pós-operatórios de antibioticoterapia e laserterapia em cirurgias de exodontia de terceiros molares. Estudo Clínico, controlado e randomizado.**”, sob a responsabilidade dos pesquisadores: **Prof. Dr. Guilherme José Pimentel Lopes de Oliveira e Davisson Alves Pereira.**

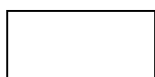
Nesta pesquisa nós estamos buscando avaliar o efeito da aplicação de avaliar a eficiência da laserterapia e da antibioticoterapia no controle da cicatrização e desconforto pós-operatório e na prevenção de infecções bem como será avaliado o efeito de dois diferentes anestésicos no controle da sensibilidade durante as cirurgias de terceiros molares

O Termo de Consentimento Livre e Esclarecido será obtido pelos pesquisadores (**Prof. Dr. Guilherme José Pimentel Lopes de Oliveira e Davisson Alves Pereira**) no momento da entrevista após identificar que sua condição clínica se enquadra nas características do público alvo a ser abordado nessa pesquisa. Para ser incluído nessa pesquisa foi verificado que você apresentar as seguintes características: Ser maior de 18 anos de idade, apresentar boa higiene bucal, apresentar os quatro terceiros molares e ter indicação para extração dentária de todos os terceiros molares. A equipe de pesquisa tem experiência e é habilitada para execução de todos os procedimentos cirúrgico. O aceite de sua participação nessa pesquisa será obtido no momento em que você se sentir confortável para tomar sua decisão. A indicação de extração dos seus terceiros molares está indicada para seu caso independente de sua decisão em participar ou não dessa pesquisa, e poderá ser executada no âmbito da Faculdade de Odontologia da Universidade Federal de Uberlândia caso assim você desejar.

Na sua participação, você será primeiramente entrevistado(a) para obtenção dos seus dados gerais, dentários e médicos. Posteriormente, você será submetido(a) a cirurgia de extração dentária dos terceiros molares e esse procedimento tem como fases a aplicação de anestesia local, acesso ao dente e uso de extratores. Durante a anestesia, um lado da sua boca será anestesiado com articaína e o outro lado será anestesiado com lidocaína e você será consultado em relação ao tempo de início da obtenção da anestesia e o tempo que a mesma se manterá durante e após a cirurgia. A qualquer sinal de desconforto você será submetido a reforço anestésico de tal forma que o procedimento será executado de forma mais confortável para você. A depender do seu caso, pode ser necessário o desgaste de osso ou cortes nos dentes por meio do uso de brocas montadas em motor, sendo que essas ações ocorrem rotineiramente nesse tipo de cirurgia. O que será diferente em relação aos procedimentos normalmente aplicado será a do laser e a aplicação de diferentes protocolos de antibioticoterapia que serão determinados por sorteio. Serão fornecidos aos pacientes capsulas que poderão conter o antibiótico ou não. Caso ocorra complicações durante a fase de cicatrização, você será avaliado e medicado de acordo com a necessidade. Vale ressaltar que o foco desse estudo é reduzir a aplicação indiscriminada de antibióticos em procedimentos de exodontia. Com relação aos exames a serem realizados, você será avaliado antes e após os períodos de 3, 7, 14, 30 e 90 dias do procedimento cirúrgico. Esses exames serão executados para avaliar a cicatrização dos locais

onde os dentes foram extraídos. Nesses períodos também serão executados procedimentos de higienização. Também será executado radiografias panorâmicas antes e após 90 dias do procedimento cirúrgico para analisar a formação de osso onde os dentes foram extraídos.

Em nenhum momento você será identificado. Os resultados da pesquisa serão publicados e ainda assim a sua identidade será preservada. Os pesquisadores se responsabilizam pela guarda e confidencialidade dos dados, bem como a não exposição dos seus dados pessoais e de pesquisa. Os dados serão expostos em congressos e revistas científicas da área, porém, sem expor a sua identificação. Também serão confeccionados materiais informativos que serão expostos as participantes dessa pesquisa e para população em geral informado os resultados desse estudo.



Rubrica do participante



Rubrica do pesquisador

Você não terá nenhum gasto nem ganho financeiro por participar na pesquisa. Esses períodos de retornos é o normalmente indicado para pessoas que passarão pelo menos tipo de cirurgia que você será submetido(a), entretanto, caso exista limitação financeira para fazer todos os retornos fique à vontade para solicitar auxílio para o transporte para as visitas de manutenção pós-operatória.”

Havendo algum dano decorrente da pesquisa, você terá direito a solicitar indenização através das vias judiciais (Código Civil, Lei 10.406/2002, Artigos 927 a 954 e Resolução CNS nº 510 de 2016, Artigo 19).

Por essa pesquisa ter como abordagem um procedimento cirúrgico, põem ocorrer riscos como como inchaço, dor, sangramento, dificuldade de falar nos primeiros dias, hematomas, infecções e alterações na sensibilidade das áreas operadas. Para evitar essas complicações, os pesquisadores irão prescrever medicações que controlarão a dor, a inflamação e prevenirão as infecções. Os pesquisadores responsáveis entregarão um guia com os cuidados que você deverá ter durante a sua recuperação, e fornecerão o contato telefônico para que você possa entrar em contato caso observe alguma complicação após as cirurgias que causem quaisquer tipos de desconforto. A equipe de pesquisadores tem experiência com esse tipo de procedimento cirúrgico e que esse fato deverá também reduzir as chances de as complicações acontecerem. Pode também ocorrer algum desconforto gástrico, devido ao uso do medicamento (anti-inflamatório-antibiótico), o que pode ser controlado com protetores gástricos. Por outro lado, tudo isso que foi relatado refere-se ao procedimento, não havendo nenhum risco a mais para sua saúde associado à pesquisa. Os benefícios serão a extração dos terceiros molares e que isso poderá evitar eventos que estão relacionados com a manutenção desses dentes tais como inflamações na gengiva, cáries nos segundos molares, tumores benignos de origem dentárias, cistos, entre outras. Além disso, os pesquisadores se comprometem a seguir as recomendações dos órgãos sanitários em relação aos cuidados para evitar a contaminação pelo SARS-Cov-2.

Você é livre para deixar de participar da pesquisa a qualquer momento sem qualquer prejuízo ou coação. Até o momento da divulgação dos resultados, você também é livre para solicitar a retirada dos seus dados da pesquisa.

Uma via original deste Termo de Consentimento Livre e Esclarecido ficará com você.

Em caso de qualquer dúvida ou reclamação a respeito da pesquisa, você poderá entrar em contato com: **Prof. Dr. Guilherme José Pimentel Lopes de Oliveira: (16) 98256-2421 e Davisson Alves Pereira: (61) 99855-1664.** Os pesquisadores são associados a Faculdade de Odontologia da Universidade Federal de Uberlândia que está localizada na Av. Pará, 1720, *campus* Umuarama – Uberlândia/MG, Brasil 38400-902, telefone (34) 32258101. Para obter orientações quanto aos direitos dos participantes de pesquisa acesse a cartilha no link: https://conselho.saude.gov.br/images/comissoes/conep/documentos/Cartilha_Direitos_Eticos_2020.pdf.

Você poderá também entrar em contato com o CEP - Comitê de Ética na Pesquisa com Seres Humanos na Universidade Federal de Uberlândia, localizado na Av. João Naves de Ávila, nº 2121, bloco A, sala 224, *campus* Santa Mônica – Uberlândia/MG, 38408-100; telefone: 34-3239-4131. O CEP é um colegiado independente criado para defender os interesses dos participantes das pesquisas em sua integridade e dignidade e para contribuir para o desenvolvimento da pesquisa dentro de padrões éticos conforme resoluções do Conselho Nacional de Saúde.

Uberlândia, ... de de 20.....

Assinatura do(s) pesquisador(es)

Eu aceito participar do projeto citado acima, voluntariamente, após ter sido devidamente esclarecido.

Assinatura do participante da pesquisa

TCLE: Termo de consentimento livre e esclarecido capítulo 2,3,4,5

TERMO DE CONSENTIMENTO LIVRE E ESCLARECIDO

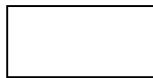
Você está sendo convidado(a) a participar da pesquisa intitulada **Avaliação de diferentes protocolos trans-operatórios de anestesia local e pós-operatórios de fotobiomodulação em cirurgias de exodontia de terceiros molares**, sob a responsabilidade dos pesquisadores: **Prof. Dr. Guilherme José Pimentel Lopes de Oliveira e Davisson Alves Pereira**. Nesta pesquisa nós estamos buscando avaliar a eficiência de diferentes tipos de laser para melhorar a cicatrização após a extração dos dentes. Também será avaliado o efeito de diferentes anestésicos no controle da dor durante as cirurgias de terceiros molares

O Termo de Consentimento Livre e Esclarecido será obtido pelos pesquisadores (**Prof. Dr. Guilherme José Pimentel Lopes de Oliveira e Davisson Alves Pereira**) no momento da entrevista após identificar se você é candidato a pesquisa. Para ser incluído nessa pesquisa foi verificado que você apresenta as seguintes características: Maior de 18 anos de idade, apresenta boa higiene bucal, apresenta os quatro terceiros molares e tem indicação para extração. A equipe de pesquisa tem experiência e é habilitada para execução da cirurgia. O aceite de sua participação nessa pesquisa será obtido quando você se sentir confortável para tomar sua decisão. A indicação de extração dos seus terceiros molares é independente de sua decisão em participar ou não dessa pesquisa, e será executado no âmbito da Faculdade de Odontologia da Universidade Federal de Uberlândia.

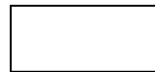
Na sua participação, você será primeiramente entrevistado(a) para obtenção dos seus dados gerais, dentários e médicos. Posteriormente, você será submetido(a) a cirurgia de extração dentária dos terceiros molares e esse procedimento tem como fases a aplicação de anestesia local, acesso ao dente e uso de extratores. Durante a anestesia, um lado da sua boca será anestesiado com um tipo de anestésico e o outro lado será anestesiado outro tipo de anestésico e você será consultado em relação ao tempo de início da obtenção da anestesia e o tempo que a mesma se manterá durante e após a cirurgia. A qualquer sinal de desconforto você será submetido a reforço anestésico para que o procedimento seja executado de forma mais confortável para você. A depender do seu caso, pode ser necessário o desgaste de osso ou cortes nos dentes por meio do uso de brocas, sendo que essas ações ocorrem rotineiramente nesse tipo de cirurgia. O que será diferente em relação aos procedimentos normalmente aplicados é a utilização de diferentes protocolos de laser. Caso ocorra complicações durante a fase de cicatrização, você será avaliado e medicado de acordo com a necessidade. Com relação aos exames a serem realizados, você será avaliado antes e após os períodos de 3, 7, 14, 30 e 90 dias do procedimento cirúrgico. Esses exames serão executados para avaliar a cicatrização dos locais onde os dentes foram extraídos. Nesses períodos também serão executados procedimentos de higienização. Também será executado radiografias panorâmicas antes e após 90 dias do procedimento cirúrgico para analisar a formação de osso onde os dentes foram extraídos. O tempo estimado para execução do exame clínico é de 15 minutos. Nós, pesquisadores, atenderemos as orientações das Resoluções nº 466/2012, Capítulo XI, Item XI.2: f e nº 510/2016, Capítulo VI, Art. 28: IV - manter os dados da pesquisa em arquivo, físico ou digital, sob sua guarda e responsabilidade, por um período mínimo de 5 (cinco) anos após o término da pesquisa

Em nenhum momento você será identificado. Os resultados da pesquisa serão publicados e ainda assim a sua identidade será preservada. Os pesquisadores se responsabilizam pela guarda

e confidencialidade dos dados, bem como a não exposição dos seus dados pessoais e de pesquisa. Os dados serão expostos em congressos e revistas científicas da área, porém, sem expor a sua identificação. Também serão confeccionados materiais informativos que serão expostos as participantes dessa pesquisa e para população em geral informado os resultados desse estudo.



Rubrica do participante



Rubrica do pesquisador

Você não terá nenhum gasto e nem ganho financeiro por participar na pesquisa. Os períodos de avaliação propostos são os comumente indicados para quem se submete aos procedimentos cirúrgicos de exodontia de terceiros molares. O que será executado adicionalmente em relação a pesquisa é a coleta dos dados. Será oferecido pelos pesquisadores ajuda de custo no transporte caso você precise se deslocar exclusivamente por demandas do referido projeto de pesquisa. Caso a coleta de dados ultrapassem 90 minutos, um lanche será oferecido gratuitamente aos participantes da pesquisa. **Havendo algum dano decorrente da pesquisa, você terá direito a solicitar indenização através das vias judiciais (Código Civil, Lei 10.406/2002, Artigos 927 a 954 e Resolução CNS nº 510 de 2016, Artigo 19).**

Por essa pesquisa ter como abordagem um procedimento cirúrgico, pode ocorrer riscos como como inchaço, dor, sangramento, dificuldade de falar nos primeiros dias, hematomas, infecções e alterações na sensibilidade das áreas operadas. Para evitar essas complicações, os pesquisadores irão prescrever medicações que controlarão a dor, a inflamação e prevenirão as infecções. Os pesquisadores responsáveis entregarão um guia com os cuidados que você deverá ter durante a sua recuperação, e fornecerão o contato telefônico para que você possa entrar em contato caso observe alguma complicação após as cirurgias que causem quaisquer tipos de desconforto. A equipe de pesquisadores tem experiência com esse tipo de procedimento cirúrgico e que esse fato deverá também reduzir as chances de as complicações acontecerem. Pode também ocorrer algum desconforto no estômago, o que pode ser controlado com medicamentos que poderemos prescrever caso necessário. Por outro lado, tudo isso que foi relatado refere-se ao procedimento, não havendo nenhum risco a mais para sua saúde associado à pesquisa. Os benefícios desse estudo é o teste de novos protocolos de laser de cuidados pós-operatórios de terceiros molares. O laser comprovadamente tem efeito melhor que utilização de antibióticos no conforto após a extração dos dentes, porém o teste de novos protocolos de laser pode melhorar ainda mais o conforto pós-operatório, e isso pode impactar a comunidade de uma forma geral. Além disso, os pesquisadores se comprometem a seguir as recomendações dos órgãos sanitários em relação aos cuidados para evitar a contaminação pelo SARS-Cov-2. **Você é livre para deixar de participar da pesquisa a qualquer momento sem qualquer prejuízo ou coação. Até o momento da divulgação dos resultados, você também é livre para solicitar a retirada dos seus dados da pesquisa.**

Uma via original deste Termo de Consentimento Livre e Esclarecido ficará com você. Em caso de qualquer dúvida ou reclamação a respeito da pesquisa, você poderá entrar em contato com:

Prof. Dr. Guilherme José Pimentel Lopes de Oliveira: (16) 98256-2421 e Davisson Alves Pereira: (61) 99855-1664. Os pesquisadores são associados a Faculdade de Odontologia da Universidade Federal de Uberlândia que está localizada na Av. Pará, 1720, *campus* Umuarama – Uberlândia/MG, Brasil 38400-902, telefone (34) 32258101. Para obter orientações quanto aos direitos dos participantes de pesquisa acesse a cartilha no link: https://conselho.saude.gov.br/images/comissoes/conep/documentos/Cartilha_Direitos_Eticos_2020.pdf. Você poderá também entrar em contato com o CEP - Comitê de Ética na Pesquisa com Seres Humanos na Universidade Federal de Uberlândia, localizado na Av. João Naves de Ávila, nº 2121, bloco A, sala 224, *campus* Santa Mônica – Uberlândia/MG, 38408-100; telefone: 34-3239-4131. O CEP é um colegiado independente criado para defender os interesses dos participantes das pesquisas em sua integridade e dignidade e para contribuir para o desenvolvimento da pesquisa dentro de padrões éticos conforme resoluções do Conselho Nacional de Saúde.

Uberlândia, ... de de 20.....

Assinatura do(s) pesquisador(es)

Eu aceito participar do projeto citado acima, voluntariamente, após ter sido devidamente esclarecido.

Assinatura do participante da pesquisa

QUESTIONÁRIO DE SAÚDE

Sofre de alguma doença? () Sim () Não. Qual(is)?

Está em tratamento médico atualmente? () Sim () Não.

Gravidez () Sim () Não.

É fumante? () Sim () Não.

Está em uso de alguma medicação? () Sim () Não. Qual(is)? _____

_____. Contato do profissional: _____

Possui alergia? () Sim () Não. Qual(is)? _____

Já foi operado? () Sim () Não. Qual(is)? _____

Teve problemas com cicatrização? () Sim () Não.

Teve problemas com anestesia? () Sim () Não.

Teve problemas com hemorragia? () Sim () Não.

Sofre de alguma das seguintes doenças?

Febre Reumática: Sim () Não ();

Problemas Cardíacos: Sim () Não ()

Problemas Renais: Sim () Não ();

Problemas Gástricos: Sim () Não ()

Problemas Respiratórios: Sim () Não ();

Problemas Alérgicos: Sim () Não ()

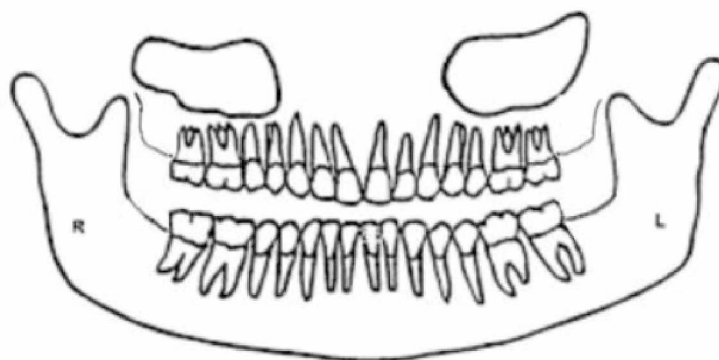
Diabetes: Sim () Não ()

Hipertensão Arterial: Sim () Não ();

Problemas Articulares ou Reumatismo: Sim () Não ().

Antecedentes familiares e outras observações importantes

Local/Data: _____



Classificação de Winter:

18: _____

28: _____

38: _____

48: _____

Classificação de Pell & Gregori:

18: _____

28: _____

38: _____

48: _____

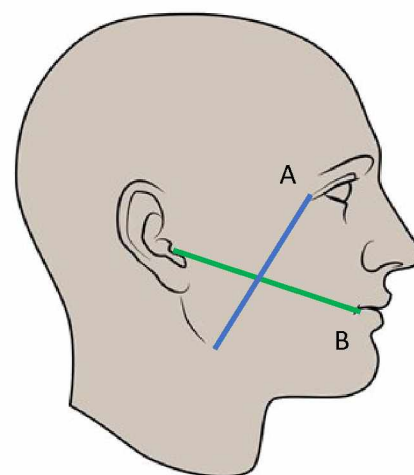
Análise Clínica das Medidas Faciais

Dimensão vertical(A): D: _____ E: _____

(Linha da comissura palpebral até o gônio do paciente)

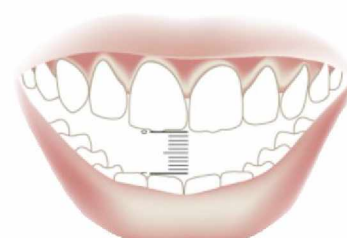
Dimensão Horizontal(B): D: _____ E: _____

(Linha da borda inferior do tragus até a comissura labial inferior do paciente)



Análise Clínica de Abertura de Boca

Valor da Abertura de boca: _____



INFORMAÇÕES GERAIS

Cirurgião responsável: _____.

Prontuário: _____ Data do procedimento: _____

Hora de Início: _____ Hora de término: _____

DADOS RELATIVOS À ANESTESIA**Lado Esquerdo**

Quantidade de tubetes: _____

Complementação anestésica: _____

Tempo de início de analgesia: _____

Tempo de fim da analgesia: _____

Lado Direito

Quantidade de tubetes: _____

Complementação anestésica: _____

Tempo de início de analgesia: _____

Tempo de fim da analgesia: _____

INFORMAÇÕES CIRÚRGICAS

Ordem de Exodontia: _____.

Dentes onde se realizou odontosecção: _____.

Dentes onde se realizou osteostomia: _____.

Presença de complicações

PACIENTE: _____

Como você avalia o desconforto com a Anestesia

Lado Direito:

0	1	2	3	4	5	6	7	8	9	10
Nenhuma	Pouca		Razoável			Média			Excessiva	

Lado Esquerdo:

0	1	2	3	4	5	6	7	8	9	10
Nenhuma	Pouca		Razoável			Média			Excessiva	

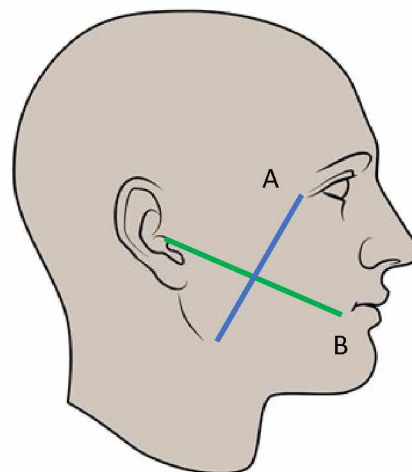
Análise Clínica Edema Facial

Dimensão vertical(A): _____

(Linha da comissura palpebral até o gônio do paciente)

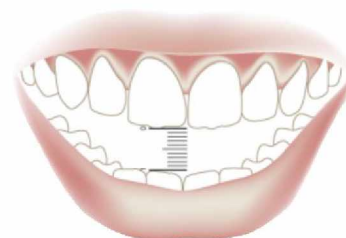
Dimensão Horizontal(B): _____

(Linha da borda inferior do tragus até a comissura I paciente)



Análise Clínica de Abertura de Boca

Valor da Abertura de boca: _____



Análise Clínica da cicatrização do tecido mole pós-exodontia

Parâmetros	Valores	Score
Sangramento	(1) Ausente	
	(2) Induzido por palpação	
	(3) Espontâneo	
Cor tecidual	(1) 100% da gengiva rosa	
	(2) <50% da gengiva hiperêmica e móvel	
	(3) >50% da gengiva hiperêmica e móvel	
Supuração	(1) Ausente	
	(2) Ausente com presença de placa pronunciada ao redor do alvéolo	
	(3) Pronunciada	
Cor e Consistência do tecido de cicatrização	(1) Próximo do normal, Rosa	
	(2) Flácida, vermelha	
	(3) Frágil, esverdeada/acinzentada	
Total	Valor de score varia de 4 a 12.	

Complicações Clínicas

Osteíte alveolar: ☐ SIM ☐ NÃO

Presença de espículas Ósseas: ☐ SIM ☐ NÃO

Presença de outras complicações

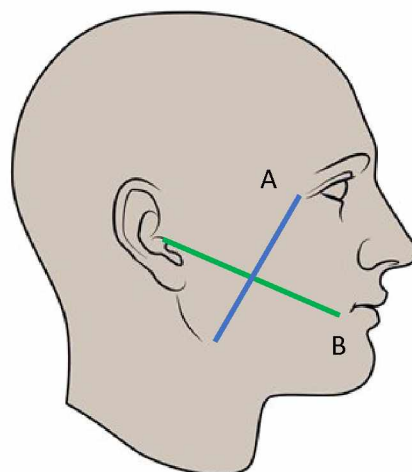
Análise Clínica Edema Facial

Dimensão vertical(A): _____

(Linha da comissura palpebral até o gônio do paciente)

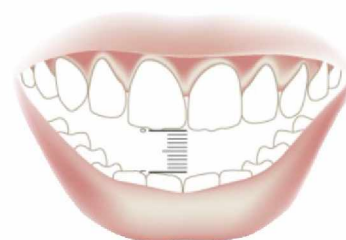
Dimensão Horizontal(B): _____

(Linha da borda inferior do tragus até a comissura l. paciente)



Análise Clínica de Abertura de Boca

Valor da Abertura de boca: _____



Análise Clínica da cicatrização do tecido mole pós-exodontia

Parâmetros	Valores	Score
Sangramento	(1) Ausente	
	(2) Induzido por palpação	
	(3) Espontâneo	
Cor tecidual	(1) 100% da gengiva rosa	
	(2) <50% da gengiva hiperêmica e móvel	
	(3) >50% da gengiva hiperêmica e móvel	
Supuração	(1) Ausente	
	(2) Ausente com presença de placa pronunciada ao redor do alvéolo	
	(3) Pronunciada	
Cor e Consistência do tecido de cicatrização	(1) Próximo do normal, Rosa	
	(2) Flácida, vermelha	
	(3) Frágil, esverdeada/acinzentada	
Total	Valor de score varia de 4 a 12.	

Complicações Clínicas

Osteíte alveolar: ☐ SIM ☐ NÃO

Presença de espículas Ósseas: ☐ SIM ☐ NÃO

Presença de outras complicações

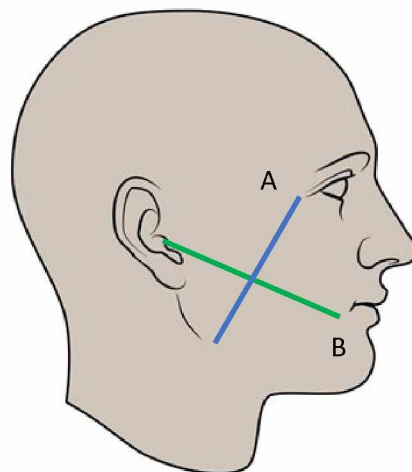
Análise Clínica Edema Facial

Dimensão vertical(A): _____

(Linha da comissura palpebral até o gônio do paciente)

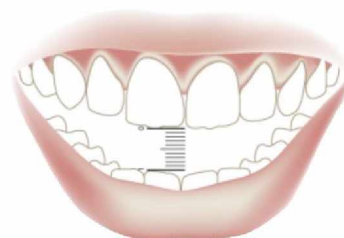
Dimensão Horizontal(B): _____

(Linha da borda inferior do tragus até a comissura l. paciente)



Análise Clínica de Abertura de Boca

Valor da Abertura de boca: _____



Análise Clínica da cicatrização do tecido mole pós-exodontia

Parâmetros	Valores	Score
Sangramento	(1) Ausente	
	(2) Induzido por palpação	
	(3) Espontâneo	
Cor tecidual	(1) 100% da gengiva rosa	
	(2) <50% da gengiva hiperêmica e móvel	
	(3) >50% da gengiva hiperêmica e móvel	
Supuração	(1) Ausente	
	(2) Ausente com presença de placa pronunciada ao redor do alvéolo	
	(3) Pronunciada	
Cor e Consistência do tecido de cicatrização	(1) Próximo do normal, Rosa	
	(2) Flácida, vermelha	
	(3) Frágil, esverdeada/acinzentada	
Total	Valor de score varia de 4 a 12.	

Complicações Clínicas

Osteíte alveolar: ☐ SIM ☐ NÃO

Presença de espículas Ósseas: ☐ SIM ☐ NÃO

Presença de outras complicações

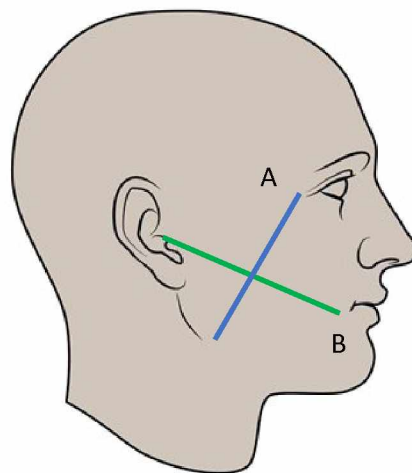
Análise Clínica Edema Facial

Dimensão vertical(A): _____

(Linha da comissura palpebral até o gônio do paciente)

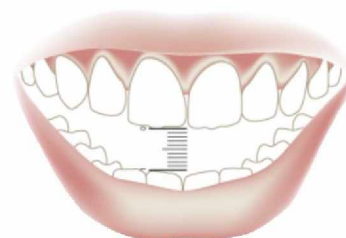
Dimensão Horizontal(B): _____

(Linha da borda inferior do tragus até a comissura 1 paciente)



Análise Clínica de Abertura de Boca

Valor da Abertura de boca: _____



Análise Clínica da cicatrização do tecido mole pós-exodontia

Parâmetros	Valores	Score
Sangramento	(1) Ausente	
	(2) Induzido por palpação	
	(3) Espontâneo	
Cor tecidual	(1) 100% da gengiva rosa	
	(2) <50% da gengiva hiperêmica e móvel	
	(3) >50% da gengiva hiperêmica e móvel	
Supuração	(1) Ausente	
	(2) Ausente com presença de placa pronunciada ao redor do alvéolo	
	(3) Pronunciada	
Cor e Consistência do tecido de cicatrização	(1) Próximo do normal, Rosa	
	(2) Flácida, vermelha	
	(3) Frágil, esverdeada/acinzentada	
Total	Valor de score varia de 4 a 12.	

Complicações Clínicas

Osteíte alveolar: ☐ SIM ☐ NÃO

Presença de espículas Ósseas: ☐ SIM ☐ NÃO

Presença de outras complicações

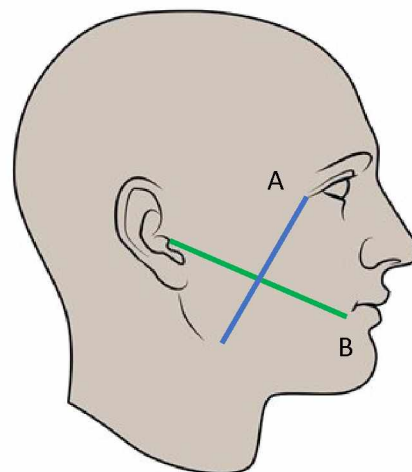
Análise Clínica Edema Facial

Dimensão vertical(A): _____

(Linha da comissura palpebral até o gônio do paciente)

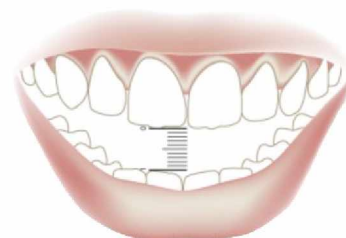
Dimensão Horizontal(B): _____

(Linha da borda inferior do tragus até a comissura I paciente)



Análise Clínica de Abertura de Boca

Valor da Abertura de boca: _____



Análise Clínica da cicatrização do tecido mole pós-exodontia

Parâmetros	Valores	Score
Sangramento	(1) Ausente	
	(2) Induzido por palpação	
	(3) Espontâneo	
Cor tecidual	(1) 100% da gengiva rosa	
	(2) <50% da gengiva hiperêmica e móvel	
	(3) >50% da gengiva hiperêmica e móvel	
Supuração	(1) Ausente	
	(2) Ausente com presença de placa pronunciada ao redor do alvéolo	
	(3) Pronunciada	
Cor e Consistência do tecido de cicatrização	(1) Próximo do normal, Rosa	
	(2) Flácida, vermelha	
	(3) Frágil, esverdeada/acinzentada	
Total	Valor de score varia de 4 a 12.	

Complicações Clínicas

Osteíte alveolar: ☐ SIM ☐ NÃO

Presença de espículas Ósseas: ☐ SIM ☐ NÃO

Presença de outras complicações

Como você avalia a dor pós operatória

Lado Direito:

0	1	2	3	4	5	6	7	8	9	10
Nenhuma	Pouca		Razoável				Média		Excessiva	

Lado Esquerdo:

0	1	2	3	4	5	6	7	8	9	10
Nenhuma	Pouca		Razoável				Média		Excessiva	

1- Inflamação / Inchaço pós operatório

Lado Direito:

0	1	2	3	4	5	6	7	8	9	10
Nenhuma	Pouca		Razoável				Média		Excessiva	

Lado Esquerdo:

0	1	2	3	4	5	6	7	8	9	10
Nenhuma	Pouca		Razoável				Média		Excessiva	

2- Hemorragia / Sangramento pós operatório

Lado Direito:

0	1	2	3	4	5	6	7	8	9	10
Nenhuma	Pouca		Razoável				Média		Excessiva	

Lado Esquerdo:

0	1	2	3	4	5	6	7	8	9	10
Nenhuma	Pouca		Razoável				Média		Excessiva	

3- Dificuldade na mastigação

Lado Direito:

0	1	2	3	4	5	6	7	8	9	10
Nenhuma	Pouca		Razoável				Média		Excessiva	

Lado Esquerdo:

0	1	2	3	4	5	6	7	8	9	10
Nenhuma	Pouca		Razoável				Média		Excessiva	

4- Limitação de Abertura de boca

Lado Direito:

0	1	2	3	4	5	6	7	8	9	10
Nenhuma	Pouca		Razoável				Média		Excessiva	

Lado Esquerdo:

0	1	2	3	4	5	6	7	8	9	10
Nenhuma	Pouca		Razoável				Média		Excessiva	

Como você avalia a dor pós operatória

Lado Direito:

0	1	2	3	4	5	6	7	8	9	10
Nenhuma	Pouca		Razoável				Média		Excessiva	

Lado Esquerdo:

0	1	2	3	4	5	6	7	8	9	10
Nenhuma	Pouca		Razoável				Média		Excessiva	

1- Inflamação / Inchaço pós operatório

Lado Direito:

0	1	2	3	4	5	6	7	8	9	10
Nenhuma	Pouca		Razoável				Média		Excessiva	

Lado Esquerdo:

0	1	2	3	4	5	6	7	8	9	10
Nenhuma	Pouca		Razoável				Média		Excessiva	

2- Hemorragia / Sangramento pós operatório

Lado Direito:

0	1	2	3	4	5	6	7	8	9	10
Nenhuma	Pouca		Razoável				Média		Excessiva	

Lado Esquerdo:

0	1	2	3	4	5	6	7	8	9	10
Nenhuma	Pouca		Razoável				Média		Excessiva	

3- Dificuldade na mastigação

Lado Direito:

0	1	2	3	4	5	6	7	8	9	10
Nenhuma	Pouca		Razoável				Média		Excessiva	

Lado Esquerdo:

0	1	2	3	4	5	6	7	8	9	10
Nenhuma	Pouca		Razoável				Média		Excessiva	

4- Limitação de Abertura de boca

Lado Direito:

0	1	2	3	4	5	6	7	8	9	10
Nenhuma	Pouca		Razoável				Média		Excessiva	

Lado Esquerdo:

0	1	2	3	4	5	6	7	8	9	10
Nenhuma	Pouca		Razoável				Média		Excessiva	

Como você avalia a dor pós operatória

Lado Direito:

0	1	2	3	4	5	6	7	8	9	10
Nenhuma	Pouca		Razoável				Média		Excessiva	

Lado Esquerdo:

0	1	2	3	4	5	6	7	8	9	10
Nenhuma	Pouca		Razoável				Média		Excessiva	

5- Inflamação / Inchaço pós operatório

Lado Direito:

0	1	2	3	4	5	6	7	8	9	10
Nenhuma	Pouca		Razoável				Média		Excessiva	

Lado Esquerdo:

0	1	2	3	4	5	6	7	8	9	10
Nenhuma	Pouca		Razoável				Média		Excessiva	

6- Hemorragia / Sangramento pós operatório

Lado Direito:

0	1	2	3	4	5	6	7	8	9	10
Nenhuma	Pouca		Razoável				Média		Excessiva	

Lado Esquerdo:

0	1	2	3	4	5	6	7	8	9	10
Nenhuma	Pouca		Razoável				Média		Excessiva	

7- Dificuldade na mastigação

Lado Direito:

0	1	2	3	4	5	6	7	8	9	10
Nenhuma	Pouca		Razoável				Média		Excessiva	

Lado Esquerdo:

0	1	2	3	4	5	6	7	8	9	10
Nenhuma	Pouca		Razoável				Média		Excessiva	

8- Limitação de Abertura de boca

Lado Direito:

0	1	2	3	4	5	6	7	8	9	10
Nenhuma	Pouca		Razoável				Média		Excessiva	

Lado Esquerdo:

0	1	2	3	4	5	6	7	8	9	10
Nenhuma	Pouca		Razoável				Média		Excessiva	

Como você avalia a dor pós operatória

Lado Direito:

0	1	2	3	4	5	6	7	8	9	10
Nenhuma	Pouca			Razoável				Média		Excessiva

Lado Esquerdo:

0	1	2	3	4	5	6	7	8	9	10
Nenhuma	Pouca			Razoável				Média		Excessiva

1- Inflamação / Inchaço pós operatório

Lado Direito:

0	1	2	3	4	5	6	7	8	9	10
Nenhuma	Pouca			Razoável				Média		Excessiva

Lado Esquerdo:

0	1	2	3	4	5	6	7	8	9	10
Nenhuma	Pouca			Razoável				Média		Excessiva

2- Hemorragia / Sangramento pós operatório

Lado Direito:

0	1	2	3	4	5	6	7	8	9	10
Nenhuma	Pouca			Razoável				Média		Excessiva

Lado Esquerdo:

0	1	2	3	4	5	6	7	8	9	10
Nenhuma	Pouca			Razoável				Média		Excessiva

3- Dificuldade na mastigação

Lado Direito:

0	1	2	3	4	5	6	7	8	9	10
Nenhuma	Pouca			Razoável				Média		Excessiva

Lado Esquerdo:

0	1	2	3	4	5	6	7	8	9	10
Nenhuma	Pouca			Razoável				Média		Excessiva

4- Limitação de Abertura de boca

Lado Direito:

0	1	2	3	4	5	6	7	8	9	10
Nenhuma	Pouca			Razoável				Média		Excessiva

Lado Esquerdo:

0	1	2	3	4	5	6	7	8	9	10
Nenhuma	Pouca			Razoável				Média		Excessiva

Como você avalia a dor pós operatória

Lado Direito:

0	1	2	3	4	5	6	7	8	9	10
Nenhuma	Pouca		Razoável				Média		Excessiva	

Lado Esquerdo:

0	1	2	3	4	5	6	7	8	9	10
Nenhuma	Pouca		Razoável				Média		Excessiva	

1- Inflamação / Inchaço pós operatório

Lado Direito:

0	1	2	3	4	5	6	7	8	9	10
Nenhuma	Pouca		Razoável				Média		Excessiva	

Lado Esquerdo:

0	1	2	3	4	5	6	7	8	9	10
Nenhuma	Pouca		Razoável				Média		Excessiva	

2- Hemorragia / Sangramento pós operatório

Lado Direito:

0	1	2	3	4	5	6	7	8	9	10
Nenhuma	Pouca		Razoável				Média		Excessiva	

Lado Esquerdo:

0	1	2	3	4	5	6	7	8	9	10
Nenhuma	Pouca		Razoável				Média		Excessiva	

3- Dificuldade na mastigação

Lado Direito:

0	1	2	3	4	5	6	7	8	9	10
Nenhuma	Pouca		Razoável				Média		Excessiva	

Lado Esquerdo:

0	1	2	3	4	5	6	7	8	9	10
Nenhuma	Pouca		Razoável				Média		Excessiva	

4- Limitação de Abertura de boca

Lado Direito:

0	1	2	3	4	5	6	7	8	9	10
Nenhuma	Pouca		Razoável				Média		Excessiva	

Lado Esquerdo: