Marcelo Caetano Parreira da Silva

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Orientador: Prof. Dr. Luiz Renato Paranhos

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DEDICATÓRIA

Este trabalho é dedicado ao meu Avô RONAN GERVASIO PARREIRA.

Eu tinha 11 anos de idade, e na porta de sua casa, ele conversando com dois amigos, disse me abraçando: - esse menino terá um "Doutor" na frente do nome e eu tenho muito orgulho dele!

Não basta ensinar ao homem uma especialidade porque se tornará assim uma máquina utilizável e não uma personalidade. É necessário que adquira um sentimento, um senso prático daquilo que é belo, de que é moralmente correto.

Albert Einstein

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Iniciando os trabalhos o(a) presidente da mesa, Dr(a). Luiz Renato Paranhos apresentou a Comissão Examinadora e o candidato(a), agradeceu a presença do público, e concedeu ao Discente a palavra para a exposição do seu trabalho. A duração da apresentação do Discente e o tempo de arguição e resposta foram conforme as normas do Programa.

A seguir o senhor(a) presidente concedeu a palavra, pela ordem sucessivamente, aos(às) examinadores(as), que passaram a arguir o(a) candidato(a). Ultimada a arguição, que se desenvolveu dentro dos termos regimentais, a Banca, em sessão secreta, atribuiu o resultado final, considerando o(a) candidato(a):

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O competente diploma será expedido após cumprimento dos demais requisitos, conforme as normas do Programa, a legislação pertinente e a regulamentação interna da UFU.

Nada mais havendo a tratar foram encerrados os trabalhos. Foi lavrada a presente ata que após lida e achada conforme foi assinada pela Banca Examinadora.

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SUMÁRIO

RESUMO

Introdução: O bruxismo é definido como uma atividade mastigatória parafuncional, caracterizado pelo apertamento e/ou ranger de dentes, que ocorre tanto durante o sono como em momentos de vigília. A toxina botulínica tipo A apresenta-se como coadjuvante terapêutico para atenuar alguns sintomas causados pelo bruxismo, devido ao fato de ser um miorrelaxante potente e específico, pois promove o relaxamento dos músculos mastigatórios. **Método:** Foram selecionados trinta pacientes do sexo feminino, com idade entre 18 e 40 anos, que apresentavam bruxismo e dores orofaciais. Após criteriosa anamnese, as pacientes responderam `a uma Escala Visual Analógica EVA) para mensurar a dor orofacial e outra para a qualidade de vida. Uma randomização em dois grupos foi realizada: um grupo controle (n=15), onde foram aplicados 0,05ml de soro fisiológico estéril no feixe anterior do músculo Temporal e 0,2ml em cada músculo masseter; e um grupo experimental (n=15), onde foram aplicadas 20 Unidades de Toxina Botulínica A (Botox®) em cada músculo Masseter e 05 Unidades em cada músculo Temporal, no seu feixe mais anterior. Todas as aplicações foram realizadas no mesmo dia por um operador previamente calibrado. As pacientes retornaram para reavaliação após 30, 60, 90, 120, 150 e 180 dias. Nesses tempos, as pacientes foram novamente submetidas à aplicação de EVA para dor e qualidade de vida; avaliação da força de carga e eletromiografia. **Resultados:** Nos períodos 30, 60 e 90 dias observou-se uma diminuição da atividade eletromiografica no grupo Botox ($p<0.001$). Na equiparação de dor e qualidade de vida foi observada uma diferença estatisticamente significativa ($p<0.001$). Com relação `a qualidade de vida foi observada diferença significativa no intervalo analisado ($p=0.021$). No grupo Botox considerando o mesmo intervalo avaliativo no que tange a comparação de dor e qualidade de vida, houve uma diferença significativa respectivamente ($p<0.001$) e ($p<0.001$). Quando avaliado o critério qualidade de vida entre os grupos ao longo do tempo, foi observada no tempo 90 uma diferença significativa

(p=0.041), observando melhora da qualidade de vida no grupo Botox. **Conclusão:** A aplicação de Toxina Botulínica tipo A intramuscular nos pacientes com bruxismo e dor orofacial, mostrou-se um método eficaz, no que se refere à hiperatividade do músculo masseter, um pacientes com bruxismo, melhorando a qualidade da vida dos pacientes.

Palavras-Chave: Toxina Botulínica Tipo A, Dor Orofacial, Odontologia, Bruxismo, Articulação Temporo-mandibular, Qualidade de Vida, Transtorno da Articulação Temporo-mandibular

ABSTRACT

Introduction: Bruxism is defined as a parafunctional chewing activity, characterized by the clenching and / or grinding of teeth, which occurs both during sleep and during waking moments. Botulinum toxin type A presents itself as a therapeutic adjuvant to mitigate some symptoms caused by bruxism, due to the fact that it is a potent and specific myorelaxant, as it promotes the relaxation of the masticatory muscles. **Method**: Thirty female patients, aged between 18 and 40 years, who had bruxism and orofacial pain were selected. After careful anamnesis, the patients answered `a Visual Analogue Scale (VAS) to measure orofacial pain and another for quality of life. A randomization in two groups was performed: a control group (n = 15), where 0.05 ml of sterile saline solution were applied to the anterior bundle of the Temporal muscle and 0.2 ml to each masseter muscle; and an experimental group (n = 15), where 20 Units of Botulinum Toxin A (Botox®) were applied to each Masseter muscle and 05 Units to each Temporal muscle, in its most anterior bundle. All applications were performed on the same day by a previously calibrated operator. The patients returned for reevaluation after 30, 60, 90, 120, 150 and 180 days. In those times, patients. **Results:** In periods of 30, 60 and 90 days, a decrease in electromyographic activity was observed in the Botox group ($p < 0.001$). When comparing pain and quality of life, a statistically significant difference was observed ($p < 0.001$). Regarding quality of life, a significant difference was observed in the analyzed interval ($p = 0.021$). In the Botox group, considering the same evaluation interval regarding the comparison of pain and quality of life, there was a significant difference, respectively ($p < 0.001$) and ($p < 0.001$). When assessing the quality of life criterion between groups over time, a significant difference was observed in time 90 ($p = 0.041$), observing an improvement in quality of life in the Botox group. **Conclusion:** The application of intramuscular Botulinum Toxin type A in patients with bruxism and orofacial pain, proved to be an effective method, with regard to masseter muscle hyperactivity, in patients with bruxism, improving the quality of life of patients.

Keywords: Botulinum Toxin Type A, Orofacial Pain, Dentistry, Bruxism, Temporo-mandibular Joint, Quality of Life, Temporo-mandibular Joint Disorder

1. INTRODUÇÃO E REFERENCIAL TEÓRICO

O bruxismo é definido como uma atividade mastigatória parafuncional, caracterizado pelo apertamento e/ou ranger de dentes, que pode ocorrer tanto durante o sono ou em momentos de vigilía (Teixeira SAF, Sposito MMM. 2013). Quando a manifestação ocorre no período diurno, é chamado Bruxismo Cêntrico, e quando durante o sono, de Bruxismo Excêntrico; e está relacionado com fatores emocionais, interferências oclusais e distúrbios neurológicos[1]. Em média 90% da população é diagnosticada com bruxismo em alguma época da vida (Goldstein LB. 2000).

A causa do bruxismo depende de uma série de fatores, o que dificulta a descoberta exata de sua etiologia. Portanto, estabelecer um plano de tratamento para todos portadores dessa parafunção é um desafio. Como ainda não há um tratamento específico, cada paciente deve ser individualmente avaliado e controlado (Ferrario et. al. 2002; Guarda-Nardini et. al. 2008). Os estudos sobre o bruxismo mostram uma associação com alguns fatores como ansiedade, estresse, depressão, tipos de personalidade, deficiências nutricionais (magnésio, cálcio, iodo e complexos vitamínicos), má oclusão dentária, disfunção e/ou transtornos do sistema nervoso central, uso de drogas com ação neuroquímica e fatores genéticos (Goldstein LB. 2000; Guarda-Nardini et. al. 2008; Madjid OW. 2010).

Distúrbios no Sistema Nervoso Central (SNC) são diretamente relacionados ao bruxismo de modo que, na neurofisiologia temos que os núcleos da base, que são estruturas anatômicas do cérebro responsáveis pela modulação dos movimentos, sendo as catecolaminas as substâncias reguladoras da ação dos mesmos. As disfunções na concentração das catecolaminas estão associadas a determinadas patologias como doença de Parkinson, doença de Huntington, síndrome de Shy-Drager, distonia orofacial, discinesia oral tardia, síndrome de Gilles de laTourette, espasmos hemifaciais, acatisia e distonia tardia (Lund, JP, Lavigne, GJ. 2003).

A dor é um sintoma frequente em quadros clínicos de bruxismo. Dentre as manifestações clínicas mais comumente observadas estão: a hipersensibilidade dentinária, desgastes dentários excessivos, fraturas de

dentes e restaurações, hipertrofia e mialgia dos músculos mastigatórios, principalmente masseter e temporal, dor de cabeça e dores na Articulação Têmporo-Mandibular (Bahils A et. al. 1999; Sposito MMM. 2000).

O plano controle desenvolvido para o bruxismo deve atender aos seguintes objetivos: redução da tensão física e psicológica, tratamento dos sinais e sintomas, minimização de interferências oclusais e rompimento do padrão neuromuscular habitual. A terapia oclusal é feita com ajuste oclusal. Para o controle do comprometimento muscular e oclusal pode ser indicado placas mio-relaxantes. O uso de medicamentos (relaxantes musculares) para diminuir e melhorar os quadros álgicos do paciente é um tratamento de eficácia temporária (Ferrario et. al. 2002; Guarda-Nardini et. al. 2008; Bahils A et. al. 1999).

A Toxina Botulínica tipo A tem sido objeto de estudos no controle das dores miofasciais, nevralgias e hiperestesias, estando relacionada com o mecanismo de alívio da dor, não somente nos receptores da junção neuromuscular, mas também nos receptores nociceptivos (Sposito, MMM. 2009; Aoki, KR. 2004; Silberstein, S. 2004).

A Toxina Botulínica é produzida por uma bactéria anaeróbica Gram positiva chamada *Clostridium botulinium.* Essa bactéria produz neurotoxinas que são divididas de sete formas distintas, que vai do Tipo A ao Tipo G (Ferrario et. al. 2002; Madjid OW. 2010; Sposito, MMM. 2009; Aoki, KR. 2004). Essas neurotoxinas causam dessensibilização temporária nos músculos esqueléticos, através da inibição da liberação de acetilcolina nas terminações nervosas dos neurônios motores alfa e gama, diminuindo a contração muscular. Esta propriedade a torna útil em regiões onde há excesso de contração muscular (Silverstein, s. 2004; Litham, WJ. 2004; Carruters, L, Carruthers A. 2007).

A Toxina Botulínica tipo A apresenta-se como coadjuvante terapêutico para o bruxismo, devido a sua ação miorrelaxante potente e específica, promovendo o relaxamento dos músculos mastigatórios e, consequentemente, diminuindo a dor orofacial. Os efeitos colaterais são raros e, mesmo que existam,

são transitórios, não acarretando maiores problemas aos pacientes (Zhang, LD et. al. 2016; Chung-Chih, et. al. 2007; Awan, KH, et. al. 2019).

Devido ao amplo conhecimento da anatomia da cabeça e do pescoço e oclusão é importante salientar que o Cirurgião-Dentista é o profissional mais capacitado para auxílio de diagnóstico e de tratamento dos sinais e sintomas dos pacientes portadores de Bruxismo e Dores Orofaciais.

Diante do exposto, percebendo a escassez de estudos específicos, o presente trabalho tem o objetivo de avaliar os efeitos da Toxina Botulínica A em pacientes do sexo feminino, diagnosticadas com bruxismo e dor orofacial, através de um estudo clínico randomizado duplo cego.

2. PROPOSIÇÃO

Este estudo tem o objetivo analisar a ação da Toxina Botulínica em pacientes do sexo feminino, portadores de Bruxismo e dores orofaciais, através de um estudo clínico randomizado duplo-cego.

2.1. Objetivos Específicos

- Analisar a ação da Toxina Botulínica A nos músculos da mastigação, através de célula de carga e eletromiografia em pacientes com Bruxismo e dores orofaciais.
- Avaliar a duração da efetividade de ação da Toxina Botulínica A nos pacientes com Bruxismo e dores orofaciais.
- Analisar a sintomatologia dolorosa nos pacientes portadores de Bruxismo e dores orofaciais, após a aplicação da Toxina Botulínica A nos músculos Masséter e Temporal.
- Avaliar se houve melhora na qualidade de vida após a aplicação da Toxina Botulínica A nos pacientes com Bruxismo e dores orofaciais.

Capítulo 1

Effect of botulinum toxin treatment on quality of life of patients with bruxism and orofacial pain – Randomized double-blind clinical trial.

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Abstract

Bruxism is defined as a parafunctional chewing activity characterized by clenching and/or grinding of teeth that occurs both during sleep and vigilance periods. Type A-botulinum toxin is a therapeutic adjunct to bruxism because it is a powerful and specific myorelaxant. Thirty female patients between 18 and 40 years-old who presented bruxism and orofacial pain were selected, and randomized into two groups: control group (n ■ 15), where the individuals received 0.05ml of sterile saline solution which was applied to the anterior bundle of the temporal muscles and 0.2ml to each masseter muscle, and an experimental group (n ■ 15), individuals received 20 units of A-botulinum toxin (Botox®) applied to each masseter muscle and 5 units of A-botulinum toxin applied to the anterior bundle of each temporal muscle. All applications were performed in the same day by a previously calibrated operator. Patients were recalled for reevaluation after 30, 60, 90, 120, 150, and 180 days. At these times they were again submitted to VAS application for pain and quality of life, as well as loading force evaluation and electromyography. At 30, 60 90 and 120 days, a decrease in electromyographic activity was observed in the A-botulinum toxin group (p <0.001). A statistically significant difference was observed (p<.001) in the pain versus quality of life comparison, as well as for quality of life in the analyzed range (p■.021). In the A-botulinum toxin group, considering the same interval and the comparison between pain and quality of life, there was a significant difference (p <.001 and p <.001, respectively). The comparison of the quality of life between groups over time revealed a significant difference at time 90 (p■.041), being observed an improvement of quality of life in the A-botulinum toxin group. Intramuscular application of A-type botulinum toxin for bruxism and orofacial pain patients proved to be an effective method for hyperactivity of the masseter muscle in patients with bruxism, improving the quality of life of patients.

Keywords	A-type botulinum toxin; Facial pain; Bruxism; Quality of life; Temporomandibular joint disorder

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Abstract

Introduction: Bruxism is defined as a parafunctional chewing activity characterized by clenching and/or grinding of teeth that occurs both during sleep and vigilance periods. Type A-botulinum toxin is a therapeutic adjunct to bruxism because it is a powerful and specific myorelaxant.

Methods: Thirty female patients between 18 and 40 years-old who presented bruxism and orofacial pain were selected, and randomized into two groups: control group (n = 15), where the individuals received 0.05ml of sterile saline solution which was applied to the anterior bundle of the temporal muscles and 0.2ml to each masseter muscle, and an experimental group (n = 15), individuals received 20 units of A-botulinum toxin (Botox®) applied to each masseter muscle and 5 units of A-botulinum toxin applied to the anterior bundle of each temporal muscle. All applications were performed in the same day by a previously calibrated operator. Patients were recalled for reevaluation after 30, 60, 90, 120, 150, and 180 days. At these times they were again submitted to VAS application for pain and quality of life, as well as loading force evaluation and electromyography.

Results: At 30, 60 90 and 120 days, a decrease in electromyographic activity was observed in the A-botulinum toxin group ($p < 0.001$). A statistically significant difference was observed ($p < .001$) in the pain versus quality of life comparison, as well as for quality of life in the analyzed range ($p = .021$). In the A-botulinum toxin group, considering the same interval and the comparison between pain and quality of life, there was a significant difference ($p < .001$ and $p < .001$, respectively). The comparison of the quality of life between groups over time revealed a significant difference at time 90 ($p = .041$), being observed an improvement of quality of life in the A-botulinum toxin group.

Conclusion: Intramuscular application of A-type botulinum toxin for bruxism and orofacial pain patients proved to be an effective method for hyperactivity of the masseter muscle in patients with bruxism, improving the quality of life of patients.

Keywords: A-type botulinum toxin, Facial pain, Dentistry, Bruxism, Temporomandibular joint, Quality of life, Temporomandibular joint disorder

Introduction

Bruxism is defined as a parafunctional chewing activity characterized by clenching and/or grinding of teeth, which occurs during both sleep and vigilance[1]. It is related to emotional factors, occlusal interference and neurological disorders[1]. On average 90% of the population is diagnosed with bruxism at some time in their life[2].

Bruxism is caused by several factors, which makes it difficult to accurately discover its etiology, making it complex to establish a treatment plan for all patients with this parafunction. Therefore, there is no specific treatment, and each patient should be individually evaluated and controlled[3,4]. Studies on bruxism show an association of the syndrome with anxiety, stress, depression, personality types, nutritional deficiencies (magnesium, calcium, iodine and vitamin complexes), dental malocclusion, central nervous system dysfunction and/or disorders, neurochemical drugs and genetic factors[2,4,5].

Central Nervous System (CNS) disorders are directly related to bruxism. According to the neurophysiology, the nuclei of the base are anatomical structures of the brain responsible for the modulation of the movements, and catecholamines are the regulatory substances of their action[6]. Dysfunctions in catecholamine concentration are associated with certain conditions such as Parkinson's disease, Huntington's disease, Shy-Drager syndrome, oral mandibular dystonia, late oral dyskinesia, Gilles de laTourette syndrome, hemifacial spasms, akathisia, late dystonia (all of these conditions are movement-associated disorders)[6,7].

Pain is a frequent symptom in clinical signs of bruxism. Dentin hypersensitivity, excessive tooth wear, fractures of teeth and restorations, hypertrophy and myalgia of the masticatory muscles (mainly temporal and masseter), headache and TMJ pain are among the most commonly observed clinical manifestations[8,9].

The control plan developed for bruxism should meet the following objectives: reduction of physical and psychological tension, treatment of signs and symptoms, minimization of occlusal interference and disruption of habitual neuromuscular pattern. Occlusal therapy is performed with occlusal adjustment. Occlusal splints may be indicated for controlling the muscle activity and occlusal commitment. The use of medication (such as muscle relaxants) to subside and eliminate patient's pain and consequently bruxism is a temporary treatment[3,4,8,10].

Botulinum toxin is produced by gram-positive anaerobic bacteria called *Clostridium botulinium*, which form a protease of neurotoxins that are divided into seven distinct forms ranging from type A to G, where each subtype produces a different neurotoxin[3,5,9,11]. Its protease activity causes temporary chemical desensitization of skeletal muscles by blocking the Ca^{+2}-mediated release of acetylcholine from nerve endings in alpha and gamma motor neurons that inhibits acetylcholine release in motor nerve terminals, causing a decrease in muscle contraction. This property makes it useful in regions where there is excess contraction[12,13,14].

Type-A botulinum toxin has been employed to control several chronic pain conditions, including myofascial pain, neuralgia and hyperesthesia, and is related to the pain relief mechanism, not only in neuromuscular junction receptors, but also in the nociceptive receptor system[9,11,12]. Side effects are rare and, even if they exist, are transient, causing no major problems for patients[15,16,17]. The use of botulinum toxin to control bruxism is increasing, but there is no consensus regarding the effectiveness of this method[18]. Given the above and realizing the scarcity of specific studies, the present study aimed to evaluate the effect of botulinum toxin type A in the control of pain, quality of life and masticatory force in female patients with sleep bruxism, by means of a double blind randomized clinical trial.

Material and methods

Ethical Criteria

This study was approved by the Institutional Human Research Ethics Committee (register: CAEE64309416.1.0000.5152). All participants signed an informed consent form.

Patient Selection

This is a randomized, double-blind controlled clinical study carried out according to the CONSORT (Consolidated Standards of Reporting Trials) standards and registered in the National Clinical Trial Registry under number U1111-1217-7400. The patients were recruited by digital media and appointment of dental surgeons in the city of Uberlândia, Minas Gerais, Brazil, and were accomplished at the School of Dentistry of the Federal University of Uberlândia, Minas Gerais, Brazil from April to November of 2017.

Inclusion criteria were individuals between 18 and 40 years-old, female, with self-reported sleep bruxism and associated orofacial pain reported in the last 3 months. The exclusion criteria were patients with active psychosis, other active psychiatric illness or cognitive impairment; serious comorbid diseases; individuals exposed to botulinum toxin in the last 6 months; participation in another experimental therapeutic protocol; patients with myasthenia gravis, amyotrophic lateral sclerosis and other acute diseases; history of dysphagia and/or botulism; impairment of intellectual capacity, pregnancy, making use of myorelaxant plaques, and egg allergies.

Experimental Protocol

Patients were randomized into two groups: (1) Experimental, with 15 individuals received 20 units of A- Botulinum Toxin (Botox®, Allergan Pharmaceuticals LTDA, Dublin, Ireland) applied to each masseter muscle and 5 Units to the most anterior bundle of each temporal muscle, and (2) Control, with 15 individuals received 0.2ml of sterile saline to each masseter muscle and 0.05ml applied to the anterior temporal muscle bundle.

a) Patients were allocated according to a list created at the website *www.sealedenvelope.com* by the operator 1 (A.C.M), which also placed saline or botox syringes inside the envelopes with corresponding patient's identification (4 syringes per envelope, one for each muscle), without group identification, in order to keep the operator 2 blinded. The latter (M.C.P.S.), an experienced professional in charge of all of the interventions, only opened the envelope when was to perform the procedure.

A third researcher (C. E. F.), without knowledge of the group allocation, was responsible to assess the response of the patients to the intervention. In the first session, previous to any procedure (baseline), and in follow-up after 30, 60, 90, 120, 150 and 180 days, orofacial pain was registered according to a visual analogue scale (VAS) with values from zero to 10, where zero represents no pain and 10 the worst pain imaginable. Another VAS for quality of life in relation to bruxism was applied, where zero was the worst quality of life and 10 the best quality of life. Electromyography and chewing force test (Load Cell) at maximum contraction with a dynamometer were also obtained in each of these periods[2].

Load Cell Test and Electromyography

For Load CEll Test, a calibrated dynamometer (Model IDDK V4, Kratos Industrial Equipment, Cotia, SP, Brazil) was inserted at the region of the first molar on right side then at the left side. The patient was asked to bite three times with maximum force, and the value was recorded in Newtons (N). The average was considered the final value, for each side.

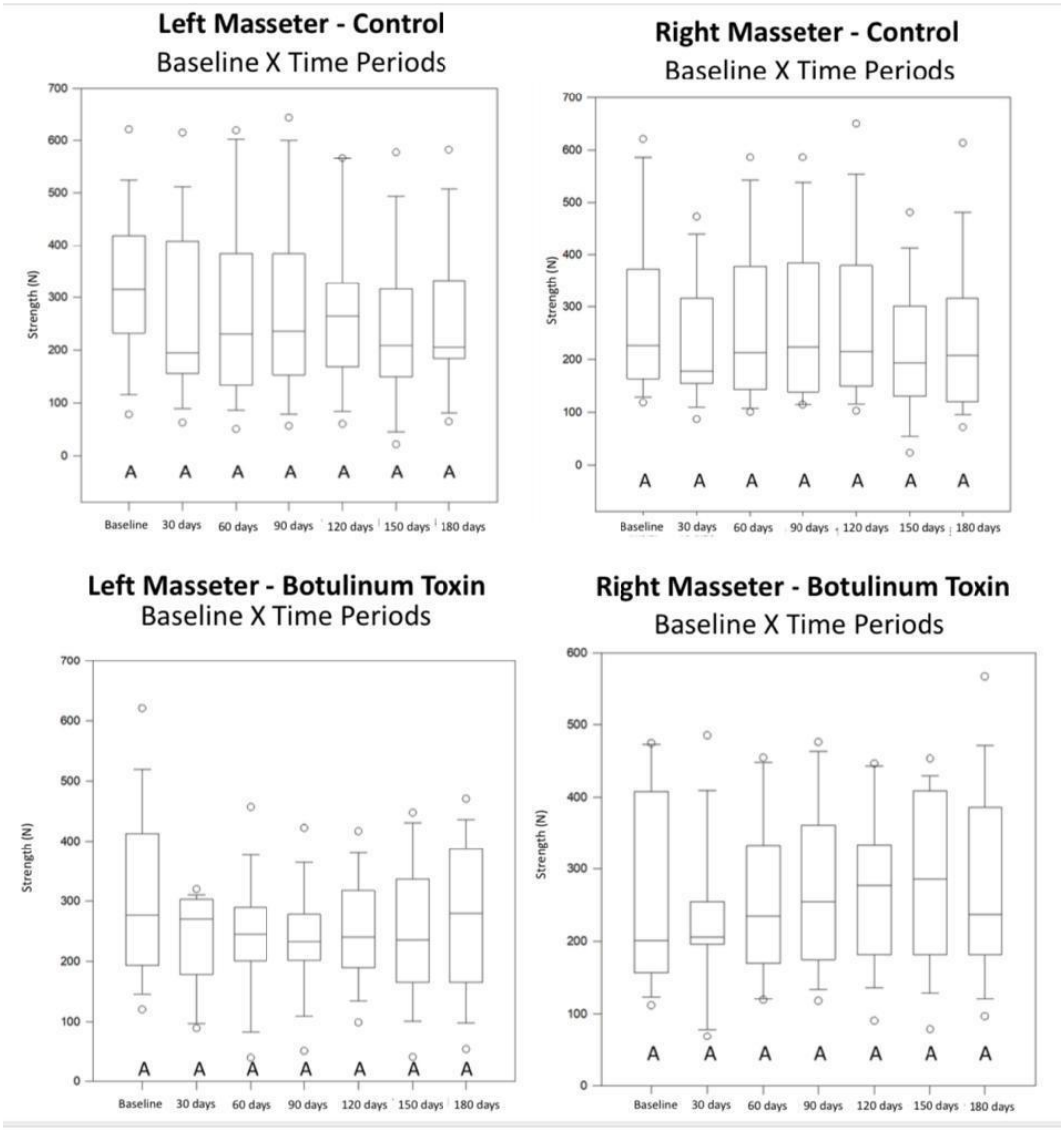
For electromyography, records were obtained using a computerized electromyograph (830 C model, EMG System of Brazil LTDA, Sao Jose dos Campos, SP, Brazil) designed in accordance with the International Society of Electrophysiology and Kinesiology standards (ISEK). The device had the following characteristics: eight input channels for EMG signals from passive or active electrodes; two input channels for auxiliary signals such as load cells, electrogoniometers and isokinetic equipment. During collection, the skin was prepared with alcohol friction to remove dead epithelial cells. During the electromyographic record the patient was kept sitting with the Frankfurt horizontal plane parallel to the ground. Electrode positioning in the masseter muscle was performed through muscle palpation, and the patient was instructed to keep the teeth in occlusal contact. In the masseter muscle, an electrode was positioned in the center of the equidistant point of the upper and lower insertions. Patients were instructed to keep the maximum usual intercuspal position with maximum force, for 10 seconds, for analysis of muscle contraction. Each one made the collection 3 times to avoid possible external interference of electrical signals, being the final value the average between the three collections.

Results

Load Cell Evaluation (dynamometer)

The values of total masticatory force of the masseter muscle were for the Control group were compared between the baseline and the other periods after application of A-Botulinum Toxin. The mean chewing force in the Control group masseter at the baseline was (518N), at 30 days (355N), at 60 days (430N), at 90 days (458N), at 120 days (449N), at 150 days (429N) and at 180 days (408N). There was only a significant difference in the comparison between baseline versus 150 days ($p < 0.05$) (Figure 1A and 1B). The measurement of total masticatory force of the masseter muscle in the Botox group at baseline was (468), at 30 days (479), at 60 days (480), at 90 days (435), at 120 days (481), at 150 days (465) and 180 days (522), with no significant difference between the baseline and the other time intervals ($p <0.05$) (Figure 1).

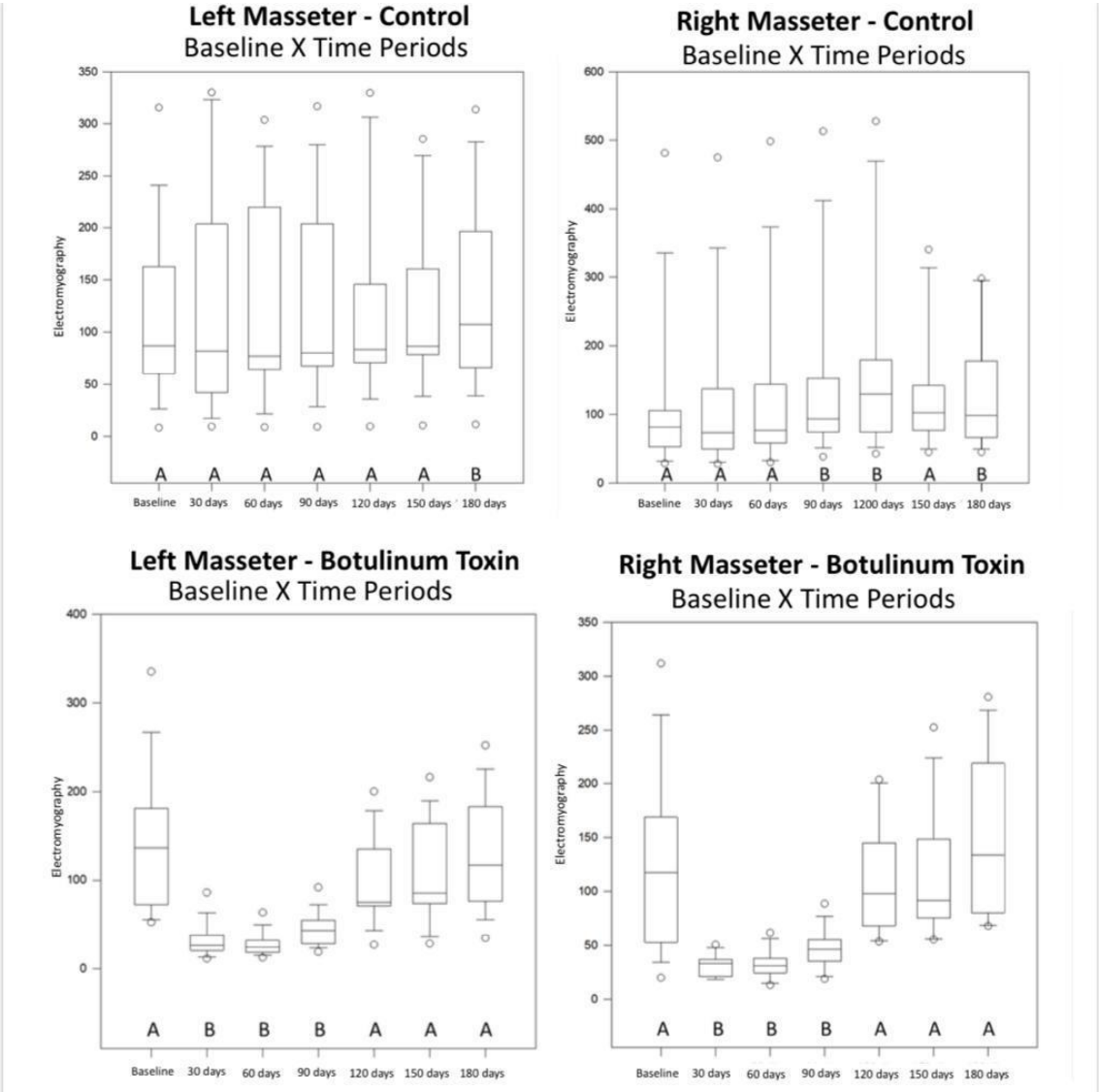
Figure 1


Left Masseter - Control
Baseline X Time Periods
Strength (N)
0
100
200
300
400
500
600
700
A A A A A A A
Baseline 30 days 60 days 90 days 120 days 150 days 180 days
Right Masseter - Control
Baseline X Time Periods
Strength (N)
0
100
200
300
400
500
600
700
A A A A A A A
Baseline 30 days 60 days 90 days 120 days 150 days 180 days
Left Masseter - Botulinum Toxin
Baseline X Time Periods
Strength (N)
0
100
200
300
400
500
600
700
A A A A A A A
Baseline 30 days 60 days 90 days 120 days 150 days 180 days
Right Masseter - Botulinum Toxin
Baseline X Time Periods
Strength (N)
0
100
200
300
400
500
600
A A A A A A A
Baseline 30 days 60 days 90 days 120 days 150 days 180 days

Evaluation of electromyography of the masseter muscle

Measurements were performed only on the masseter muscle because of the risk of results being altered by the hair during the temporal muscle measurement. The analysis of the electromyographic activity of the right masseter muscle in the Control group revealed that when the baseline was compared to the other time intervals, the average values at baseline (81.6mV), at 30 days (73.8 mV), at 60 days (76.6 mV), at 90 days (93 mV), at 120 days (129 mV), at 150 days (102 mV) and 180 days (98 mV), difference was found to significant only between 90, 120 and 180 days ($p < 0,05$) (Figure 2)

Figure 2



The mean values of electromyographic activity of the left masseter muscle in the botulinum toxin group was found to be at baseline (140.33mV), at 30 days (31.46 mV), at 60 days (27.52 mV), at 90 days (44.18 mV), at 120 days (98.17 mV) at 150 days

(101.74 mV) and 180 days (127.53 mV), and statistically significant differences were observed only between 15, 30, and 90 days ($p < 0.05$) (Figure 3C).

The mean values of electromyographic activity of the right masseter muscle in the Botox group was found to be at baseline (117 mV), at 30 days (33 mV), at 60 days (30 mV), at 90 days (46 mV), at 120 days (97 mV) at 150 days (91 mV) and 180 days (133 mV), and statistically significant differences were observed only between 15, 30, and 90 days ($p < 0.05$).

The comparison between the Control and Paired Botox groups revealed that there was no statistical difference ($p = 0.254$) at baseline for both groups. It was observed a statistically significant difference between groups at 30, 60 and 90 days ($P < 0.05$). Decrease of electromyographic activity of the right masseter muscle was observed in the Botox group for the aforementioned periods (Table-1).

The analysis of the electromyographic activity of the left masseter muscle in the Control group, at different time intervals resulted in the following mean values at baseline (86.6 mV), at 30 days (81.4 mV), at 60 days (76.5 mV), at 90 days (79.7 mV), at 120 days (83 mV), at 150 days (86 mV), and at 180 days periods (107 mV). It was noted significant difference only at 180 days ($p < 0.05$). The mean values of the electromyographic activity of the left masseter muscle in the Botox group were at baseline (136 mV), at 30 days (26 mV), at 60 days (24 mV), at 90 days (42.4 mV), at 120 days (74.8 mV), at 150 days (85.5 mV) and at 180 days (116.5 mV). Statistically significant differences were observed at 15, 30 and 90-day periods ($p < 0.05$) (Table-1).

The comparison between the Control and Paired Botox groups for the left masseter muscle revealed no statistically significant difference ($p > 0.05$) at baseline for both groups. Statistically significant difference occured between groups at 30, 60 and 90 days ($P < 0.05$). Decreased electromyographic activity of the left masseter muscle was observed in the Botox group for the aforementioned periods (Table-1).

Tables:
Electromyography:
Mean (standard deviation) and median (25%; 75%) values for the groups

		Controle	Botox	Valor de p
Left	Baseline	109,55 (77,88) 86,60 (60,50; 162,80)	140,33 (76,80) 136,50 (71,90; 181,00)	0.237
	30 days	118,45 (104,88) 81,40 (41,70; 203,70)	31,46 (18,30) 26,20 (20,80; 38,10)	0.002*
	60 days	114,84 (90,92) 76,51 (64,30; 219,90)	27,52 (12,49) 24,09 (18,30; 32,00)	<0.001*
	90 days	120,03 (87,82) 79,80 (67,41; 203,95)	44,18 (17,82) 42,42 (28,45; 54,81)	<0.001*
	120 days	125,22 (89,53) 83,08 (70,24; 146,08)	98,17 (46,93) 74,83 (70,70; 135,14)	0.590
	150 days	116,88 (76,31) 86,07 (78,24; 160,68)	101,74 (53,64) 85,55 (73,50; 163,80)	0.709
	180 days	130,81 (87,81) 107,16 (65,67; 196,63)	127,53 (60,66) 116,57 (75,88; 182,72)	0.740
Right	Baseline	113,31 (113,64) 81,60 (52,80; 105,90)	128,24 (79,05) 117,40 (52,80; 169,00)	0.254
	30 days	120,07 (115,05) 73,80 (49,30; 137,30)	32,02 (10,07) 33,20 (20,70; 36,70)	<0.001*
	60 days	134,58 (126,11) 76,65 (58,57; 143,80)	32,39 (12,57) 30,94 (24,26; 37,95)	<0.001*
	90 days	148,16 (128,56) 93,44 (74,33; 153,23)	46,87 (17,18) 46,40 (35,17; 55,02)	<0.001*
	120 days	161,74 (136,92) 129,43 (74,33; 179,41)	111,32 (48,52) 91,82 (68,04; 144,98)	0.455
	150 days	129,40 (85,07) 102,26 (77,04; 142,29)	113,96 (59,54) 91,72 (75,17; 148,40)	0.803
	180 days	131,98 (87,75) 98,67 (66,02; 177,61)	144,46 (72,22) 133,53 (79,81; 219,00)	0.455

Load Cell Correlation, Electromyography and Time in the Masseter Muscle

When load cell, electromyography and period of time for the masseter muscle were correlated, Control and Botox groups showed a statistically significant difference in the right masseter control group (coef = 0.407; p <0.001) between the electromyography and load cell values. However, there was no significant difference between the variables "period of time" and "electromyography" (p = 0.081) and the load cell (p = 0.297). In the experimental group, the right masseter muscle showed a statistically significant difference between the electromyography and load cell variables (coef = 0.195; p <0.004) and between time and electromyography (coef = 0.431; p <0.001). However, no statistically significant difference was observed in the time versus load correlation (p = 0.254). In the control group, in the left masseter muscle, no significant difference was observed in the correlation between time versus load (p = 0.399) for between time versus electromyography (p = 0.233), and only a difference in the correlation between load cell and electromyography was observed (cef = 0.358; p <0.001). In the experimental group, the left masseter muscle showed no significant difference between the load cell variable and time (p = 0.968), nor between the electromyography versus load (p = 0.072), and a statistically significant difference was observed between time and electromyography (coef = 0.322; p <0.001).

Comparison between time, pain and quality of life

When comparing time versus pain with quality of life in the control group, there was no statistically significant difference respectively (p = 0.127) and (p = 0.806) (Figure 3). However, the correlation in the experimental group between time and pain decreased pain over time with a statistical difference of (p = 0.013) at intervals of 30, 60 90 and 120 days (Figure 4). Regarding the relationship between time and quality of life, there was an improvement of quality of life, as measured by time after application of the botulinum toxin, with statistically significant difference (p = 0.014)

Comparative analysis between two groups with a 95% confidence interval. T test for when the data were considered parametric and Mann-Whitney Rank Sum Test for non-parametric data. * It means difference between the control and botox groups for the same time of comparison (p <0.05).

Figure 3

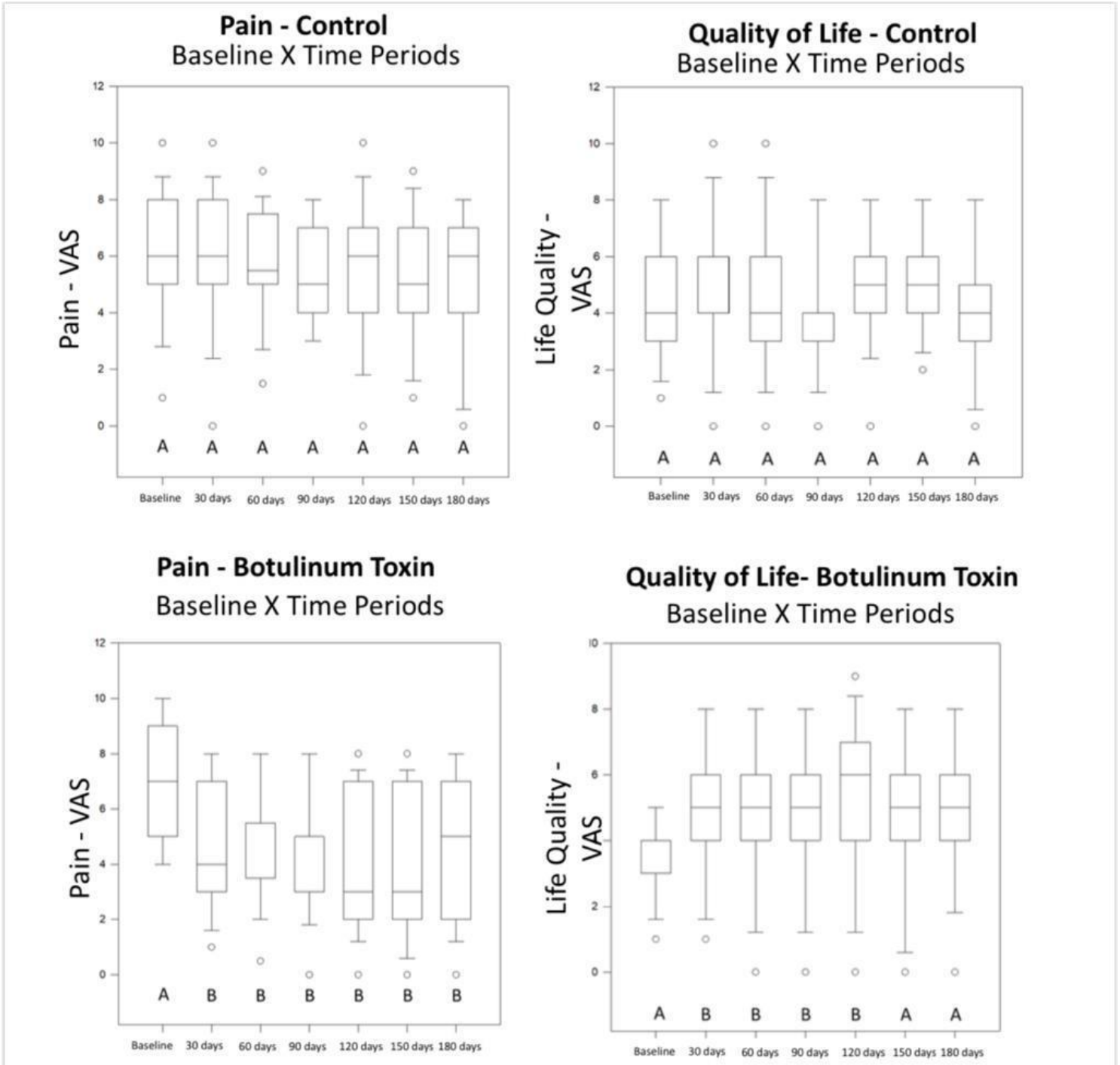
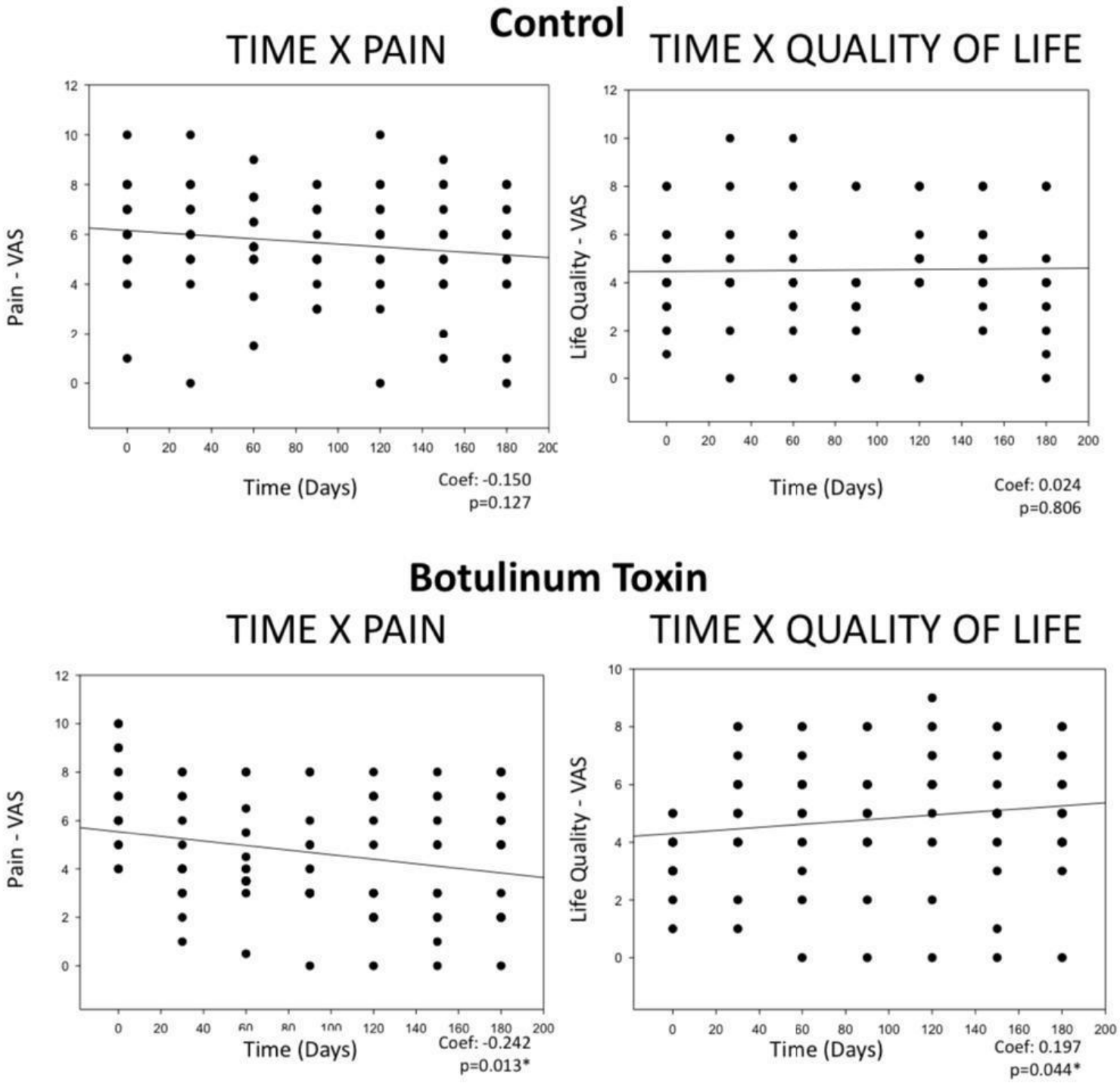

Pain - Control
Baseline X Time Periods
Pain - VAS
A A A A A A A
Baseline 30 days 60 days 90 days 120 days 150 days 180 days
Quality of Life - Control
Baseline X Time Periods
Life Quality - VAS
A A A A A A A
Baseline 30 days 60 days 90 days 120 days 150 days 180 days
Pain - Botulinum Toxin
Baseline X Time Periods
Pain - VAS
A B B B B B B
Baseline 30 days 60 days 90 days 120 days 150 days 180 days
Quality of Life- Botulinum Toxin
Baseline X Time Periods
Life Quality - VAS
A B B B B A A
Baseline 30 days 60 days 90 days 120 days 150 days 180 days

Figure 4


Control
TIME X PAIN
Pain - VAS
Time (Days)
Coef: -0.150
p=0.127
TIME X QUALITY OF LIFE
Life Quality - VAS
Time (Days)
Coef: 0.024
p=0.806
Botulinum Toxin
TIME X PAIN
Pain - VAS
Time (Days)
Coef: -0.242
p=0.013*
TIME X QUALITY OF LIFE
Life Quality - VAS
Time (Days)
Coef: 0.197
p=0.044*

Discussion

Botulinum toxin was firstly described in 1817 by Justinus Kerner, a German physicist, who began its use on animals. In 1897, microbiologist Emile Van Ermengem related the botulism epidemic to the bacteria found in food, thus isolating it and producing it in the laboratory[2,4,5]. Botulinum toxin A has been used in recent years to help treat temporomandibular dysfunction[18], to reduce musculoskeletal pain[19] and myofascial pain associated with bruxism[4].

Regarding the treatment of TMJ dysfunction, there is still no therapy that permanently heals bruxism. Several issues regarding the subject are proposed and detailed in the literature.

Santos[20] and collaborators conducted a review on the treatment of orofacial pain through acupuncture in patients with bruxism in order to prove the effectiveness of acupuncture in analgesia in patients with bruxism. They found that acupuncture causes endogenous release of chemical mediators such as opioids, cortisone and acetylcholine, improving pain. Thus, this therapy may be an alternative in the treatment of chronic and myofacial facial pain, such as those arising from bruxism.

Saletu[21] et al. studied the pharmacotherapy of sleep bruxism to investigate the acute effects of clonazepam on bruxism. Their study included 10 patients who received previous treatment with bruxism splint. The authors found that clonazepan may reduce the symptoms of sleep bruxism by presenting good patient tolerability.

Another use of botulinum toxin is with occlusal appliances. Bruxism splint is the most commonly used therapy for the treatment of bruxism, although its mechanism of action is not well understood[22]. According to Harada[23] et al. (2006), the use of occlusal splint, with or without occlusal coverage, was effective in the treatment of bruxism.

Literature reports confirm that cognitive behavioral therapy can be used in both types of bruxism, but its long-term application has no significant effect. Actually, it is possible that this therapy have more effect on wake bruxism due to the fact that factors psychological issues prove to be more important in this type of bruxism[24].

The use of catecholamine modulating neurochemical drugs, such as Diazepam and Methocarbamol, via dopaminergic route, have been effective as an auxiliary treatment for bruxism, but at the risk of drug dependence over time[3,6]. The prescription of propranolol, a beta-adrenergic agent was effective in the treatment of bruxism with its action related to direct sedative action due to its inhibition of trigeminal motoneurons [6,7]. The use of buspirone would cause a decrease in the number or sensitivity of presynaptic receptors, thus increasing the synapse for dopamine release, restoring motor modulation and disrupting muscle parafunctional activities[2,6,7].

Botulinum toxin A is a presynaptic neuromuscular blocking agent[25], which inhibits the release of acetylcholine in neuromuscular junctions, thus reducing muscle contractions[26].

Studies evaluating the efficacy of botulinum toxin A have yielded mixed results. Three studies reported that the use of the substance produced no benefit[32,33], while four reported that the use was beneficial[4,29,30,31]. In the studies that reported a positive result for the use of botulinum toxin, some criticisms were observed, since most studies presented smaller sample size.[34,35,36] A short follow-up with a maximum of four months after drug application and verification of its action[33,34,36]; except that in our study the follow-up of patients was maintained over 6 months after application, presenting a relevant sample number for work to be developed.

Studies reported the reduction of myofascial pain in patients with bruxism with reduced occlusion force in the masseter and temporal muscle after botulinum toxin A application[35]. The maximum occlusal force was reduced after three months of botulinum toxin A application[15]. In the present study it was not possible to verify difference between the masseter muscle load cell intergroups nor between groups over time.

In the evaluation of the electromyographic activity (EMG) of the masseter muscle, there was a reduction of EMG activity in the experimental group at intervals of 15, 30 and 90 days after the single application of botulinum toxin A. These findings are compatible with the study of Lee et al.[36], who showed a reduction in EMG activity in the masseter muscle after injection of botulinum toxin, and the number of muscle contraction events was reduced from the fourth week and maintained for twelve weeks. According to a randomized study, with twenty-four patients treated with injection of botulinum toxin into the masseter muscle, a reduction in EMG activity from the 14th day onwards with a return of the increase from the 28th day onwards was observed, as well as decreased pain scores[32].

In the present study, an improvement in quality of life was found in the experimental group around 90 days after botulinum toxin injection. It was also possible to verify the correlation between the pain and time variables in the group that received the botulinum toxin, as well as the improvement of the quality of life over the follow-up time. In the study by Guarda-Nardinie et al.[4], pain during chewing was reduced after 6 months, when patients with bruxism received botulinum toxin application compared to those who received placebo. This corroborates our results, regarding the improvement of pain in patients submitted to A-botulinum toxin (Botox®).

In a study by Ernberg et al.[29], pain intensity was reduced at 30 and 90 days after application of A-botulinum toxin. Thus, one can stress out that the improvement of pain over time has a significant effect on improving the quality of life of the experimental group within 30, 60 90 and 120 days, after this period the effect of botulinum toxin begins to have its effect diminished and therefore new applications are necessary. These results are corroborated by Jadhao et al.[35], who showed improvement in subjective resting and chewing pain parameters in the group treated with botulinum toxin A. In a prospective study of patients with chronic pain treated with injection of botulinum toxin in the temporal muscles and bilateral masseter masses, which were followed for 12 months, a reduction in pain measured by visual analog scale (VAS) and Physician Global Assessment (PGA) was reached[37]. When reviewing the scientific data available in the

literature and the data obtained in this work, we suggest that A-botulinum toxin (Botox) may be indicated as an important aid for patients diagnosed with bruxism and orofacial pain, with periodic applications in the interval 4/4 months shown in this randomized trial.

Conclusion

The use of A-botulinum toxin, applied to the masseter and temporal muscles bilaterally, in patients with bruxism and orofacial pain, proved to be an effective method to control masseter muscle hyperactivity in patients with bruxism, with its maximum peak of action until the ninetieth day after infiltration, with decreased muscle tension, improvement of painful symptoms and, consequently, significant improvement in the quality of life of these patients.

The study shows that the effects produced by botulinum toxin A are temporary, with reversible effectiveness, requiring periodic applications to maintain long-term benefits, such as decreased muscle hyperactivity, decreased pain symptoms and improved quality of life of patients with bruxism and orofacial pain. Thus, it is a multifactorial chronic parafunctional condition that is difficult to control. Nevertheless, further studies are needed to refine the available knowledge on the subject.

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CAPÍTULO 2

Tratamento de Hipertrofia do Masseter com Toxina Botulínica

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Tratamento de Hipertrofia do Masseter com Toxina Botulínica

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Introdução

A hipertrofia masseteriana (HM) é uma condição incomum de etiologia incerta[1]. É reconhecida como ampliação assintomática de um ou de ambos músculos masseter[2]. No geral a HM ocorre de forma bilateral e simétrica, porém podemos encontrar casos de assimetria e de unilateralidade, principalmente, em pacientes que mastigam ou apertam apenas um dos lados[2]. O tratamento tradicional da HM, consiste na excisão parcial cirúrgica do músculo masseter o que pode gerar algumas complicações como formação de hematomas, paralisa do nervo facial, infecções, limitação da abertura bucal e sequelas de anestesia geral[3]. Smyth, Moore e Wood (1994) geraram uma forma menos invasiva para o tratamento da HM ao introduzirem, pela primeira vez, a injeção de toxina botulínica tipo A no músculo masseter[4,5]. O organismo anaeróbico *Clostridium Butolinum* produz a Toxina Botulinica (BOTOX®) e essa consiste em uma neurotoxina potente que quando injetada provoca paralisia e subsequente atrofia do músculo[6,7].

O objetivo desse trabalho é relatar o caso de aplicação de toxina botulínica para tratamento de Hipertrofia Masseter.

Palavra-chave: Hipertrofia; Masseter; Toxina botulinica.

Relato de Caso

Paciente gênero feminino, 25 anos, procurou o serviço de Cirurgia e Traumatologia Buco-Maxilo-Facial do Hospital de Clínicas da UFU com queixa estética de volume excessivo em

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Tabela 1: Aferição da força mastigatória com dinamômetro

Lado/Aferição	Pré-aplicação	30 dias pós-aplicação	120 dias pós-aplicação
Lado Direito	175N	170N	162N
Lado Esquerdo	207N	186N	171N

Com isso foi observada a diminuição da força mastigatória, aferida em dinamômetro (Tabela 1), assim como achados clínicos que demonstram a diminuição da hipertrofia massetérica após um mês de aplicação.

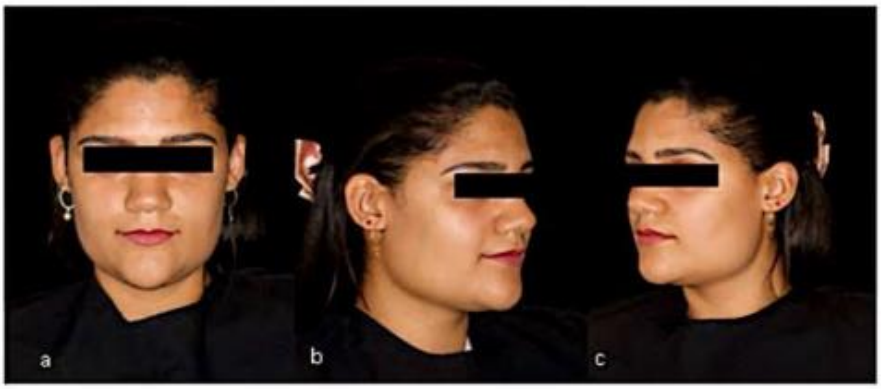

Figura 3. Avaliação da paciente após 1 mês de tratamento

Discussão

A hipertrofia muscular do masseter é definida como o crescimento excessivo de sua massa muscular[8] no sentido medial a lateral. No que diz respeito à toxina botulínica, é composta de uma cadeia pesada 100kDa e que existem 7 sorotipos (tipos A, B,C1, D, E, F e G) sendo que cada um tem seu sítio específico de ação. O tipo A da toxina Botulinum (BTA) é usada também, extensivamente, para endereçar interesses cosméticos, principalmente, para o rejuvenescimento da face superior e inferior. O uso da toxina butolínica no terço inferior tornou-se rapidamente uma das formas mais populares de rejuvenescer o rosto, devido à sua eficácia nesta área e à falta de efeitos colaterais importantes se devidamente aplicada.

Jae-Hong Kim e col.[9] observaram que após a aplicação da toxina botulínica, a atrofia do músculo masseter é estabelecida em um período de 2 a 4 semanas. Para aplicação correta na região massetérica, Nam-Ho Kim[10] descreveu uma zona de segurança que é delimitada por traçar uma linha horizontal a partir do canto direito do lábio para a base do lobo da orelha, outra linha horizontal pela flange inferior da mandíbula em direção ao ângulo e duas linhas verticais; uma pela borda ante-

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rios do músculo masseter e a outra pela borda posterior do músculo masseter.

Neste relato de caso, 30 dias após a aplicação de toxina botulínica, foi observada uma diminuição do volume dos músculos masseter e temporal, bilateralmente, o que corrobora com os autores supracitados. Adicionalmente, a diminuição da força de mastigação até 120 dias traz benefícios estéticos e funcionais à paciente, uma vez que isso contribui para a manutenção da atrofia muscular, bem como protege as estruturas mastigatórias. Apesar do baixo risco do procedimento e previsibilidade, o efeito desta toxina é passageiro, durando em torno de 2 a 6 meses[11,12] o que leva à possível necessidade de nova aplicação para manutenção a longo prazo da atrofia muscular. Entretanto, os benefícios se sobrepõem aos riscos e desvantagens, tornando esta modalidade de tratamento para a Hipertrofia de Masseter muito vantajosa para o paciente.

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CAPÍTULO 3

Surgical correction of Ankylosed TMJ in a child: Case report

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Surgical Correction of Ankylosed TMJ in a Child: Case Report

Surgical Correction of Ankylosed TMJ in a Child: Case Report

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ABSTRACT

The temporomandibular joint (TMJ) ankylosis describes the bone or fibrous adhesion of the TMJ components, with functional impairment. The present report shows the surgical correction the TMJ ankylosis due to a condyle fracture in a child. A 12 years old patient, female, attended to the Oral and Maxillofacial Surgery Department of the Clinical Hospital/Federal University of Uberlandia, showing severe mouth oppening limitation (9mm) and history of bilateral condyle fracture and symphysis fracture. The right TMJ ankylosis was diagnosed, removed, reshaped and repositioned to form the reshaped condyle, by the sliding reconstruction of the condyle using posterior border of mandibular ramus and myofascial interposition of the temporal fascia. A 5 months of follow up showed mouth opening of 44 mm maintained after 2 years, without complaints. The surgical treatment of the TMJ ankylosis is needed for the reestablishment of the immediate function, however the patient must be watched until the end of development.

KEY WORDS: Trauma, Temporomandibular joint ankylosis, Child.

INTRODUCTION

The temporomandibular joint (TMJ) ankylosis is the result of the fibrous or bone fusion between the condylar head and the glenoid fossa [1]. The ankylosis can be related to facial trauma, local or systemic infection, and to systemic conditions, such as ankylosing spondylitis and rheumatoid arthritis [2].The trauma is the prevalent factor in the TMJ ankylosis, especially in children, due to falls, traffic-accidents and forceps delivery [3].

The condylar fractures in the pediatric and teenager population pose a serious challenge, once the condyle is an important growing center in the developing mandible. The traumatic fracture includes as complications: facial asymmetry, restrict mandible movements and TMJ derangements and/or ankylosis [4].When in children, the ankylosis plays a serious and disabling condition, resulting in impairment of speech and chewing, lack of oral hygiene, caries, facial and mandibular growing disturbances, malocclusion and acute airway involvement [5,6].

The ankylosis of the TMJ can be classified as true ankylosis, result of any condition that may induce fibrous or bone adhesions and pseudo ankylosis, that presents mandible movements restriction due to pathologies from outside the TMJ, such as muscle, bone and neurological disorders [7].It was first classified by Shawney, in four types (I-IV), based in anatomical data and tomographic joint changes [8]. In type I, the condyle head is present without distortion and the fibrous union makes the movement impossible; the type II shows the fusion the condylar deformed head and the articular surface; the type III shows a bone fusion that involves the mandible ramus and the zygomatic arch. And medially is found a dislocated fragment of the anterior condyle; and in type IV the normal TMJ anatomy is completely destroyed by the mass newly formed between the mandible ramus and cranial base [9].

Ankylosis management includes aggressive resection, ipsilateral coronoidectomy, contralateral choronoidectomy, gap arthroplasty, fascia interposition or temporal cartilage arthroplasty, and low osteotomy of the mandibular ramus, reconstruction of the ramus with a cochlear-grafted reconstruction, alloplastic reconstruction with stock or custom prostheses, all associated with early mobilization and physiotherapy [5,10].

The aim of the present study is to report the surgical correction of TMJ ankylosis, result of bilateral condyle fracture associated with symphysis fracture in a child, treated by the bone segment slip technique from the partial vertical osteotomy of the mandibular branch and interposition of myofascial flap.

CASE REPORT

Patient, female, 12 years old, melanoderma, was referred to the Oral and Maxillofacial Surgery Department at the Federal University of Uberlândia, Uberlândia, Minas Gerais, Brazil in 2017, victim of a bicycle accident, who developed a bilateral condyle and symphysis fracture 6 years earlier (Fig.1). At the time, it was opted for conservative treatment of condyles and rigid internal fixation of the symphysis fracture. On clinical examination, the patient denied allergies, comorbidities and medication use. Extra-oral clinical examination showed no signs of facial asymmetry, but the presence of mandibular retrognathism (Fig. 2A and 2B). On intra-oral clinical examination, the patient complained of pain, severe trismus (9 mm), chewing difficulties, malocclusion and phonetic disorder (Fig.3).

Computed Tomography (CT), it was possible to verify the presence of a dense radiopaque image in the right condyle in close contact with the zygomatic arch and a 4-hole miniplate in the symphysis region (Fig. 4A). CT scan revealed an ankylotic mass involving the right temporomandibular joint, type 4 of the Shawney classification (Fig. 4B).

Surgical removal of the ankylotic block was performed in the operating room under general anesthesia and nasotracheal intubation. The surgical access chosen was the Al Kayat, with preauricular extension. The incision site was marked with methylene blue (Fig.5A) and infiltrated with diluted epinephrine at 1: 100,000. Subsequent to the total mucoperiosteal dissection of the planes (Fig. 5B) with ankylotic mass exposure (Fig. 5C), the osteotomy site was previously demarcated and later osteotomized by means of drills (Fig. D), osteotomy with sawing (Fig. 5E) and block cleavage using the Wagner chisel. (Fig. 5F). Subsequently, vertical mandibular ramus osteotomy was performed (Fig. 5G and Fig. 5H), stump removal, and condylar remodeling, based on the osteotomy proposed by Liu et al. (2011) (Fig. 5I - Fig. 5K). Then it was fixed by means of 2 L 2.0 miniplates of the system 2.0 with 4 screws of 7 mm each (Fig. 5L). The myofascial temporalis fascia flap was finally interposed (Fig. 5M and 5N). The site was thoroughly washed with 0.9% saline solution and sutured with Monocryl® 4-0 and 5-0 nylon sutures.

In panoramic X-ray after five months of surgery it is possible to observe the miniplates in position and condylar remodeling (Fig. 6A). In CT scanner it is possible to verify the absence of the ankylotic mass (Fig. 6B). There were no complications during the follow-up period. After 5 months a mouth opening of 44mm was observed and maintained occlusion (Fig. 7A-7C). The patient was followed up for 2 years, without mouth opening limitations or pain complaints, where orthodontic treatment was started, for future reevaluation of the need for surgical reintervention at the end of its growth (Fig. 8A-8C), through bilateral TMJ prosthesis and orthognathic surgery.

DISCUSSION

TMJ ankylosis describes the bone or fibrous adherence of the TMJ components (condyle and skull base), with functional limitations [11]. Clinical characteristics of TMJ ankylosis in childhood include mouth opening limitation, facial asymmetry, mandibular micrognathia, Class II posterior crossbite malocclusion (unilateral ankylosis) / anterior open bite (bilateral ankylosis) [6].

In a case series conducted in Nigeria by Bello *et al*. (2011) [12] with 23 patients, it was observed that the age of the patient when exposed to injury appears to be an important factor in the assessment of maxillofacial deformities resulting from TMJ ankylosis. Ankylosis in children is worrisome and may cause jaw growth disorders, resulting in gross deformity and limited mouth opening [13].

Imaging used to diagnose TMJ ankylosis requires a three-dimensional view of the joint that is provided by computed tomography, especially in the coronal section, which helps in assessing the nature and severity of ankylosis [8].

TMJ ankylosis should be surgically treated as early as possible [14]. The surgical procedure is performed under general anesthesia. Fiber-optic intubation is the technique of choice in children with trismus that cannot be intubated orally due to limited mouth opening [6]. Limitation on mouth opening and mandible protrusion are independent predictors of difficult airway in pediatric patients with TMJ ankylosis [15].

Al-kayat & Bramley access gives wide access to the TMJ, temporal region, and zygomatic arch, which has the advantage of protecting the facial nerve branches and access to the temporal myofascial flap used in interposition arthroplasty [16]. Kaban *et al*., (2009) [17] describe a protocol for the treatment of ankylosis in children, which involves aggressive surgical removal of the ankylotic mass and ipsilateral coronoidectomy. The contralateral coronoidectomy is performed if incisal opening is less than 35mm after ipsilateral side, temporal myofascial flap or articular disc interposition when it can be recovered, condyle reconstruction by osteogenic distraction or rib bone graft, early jaw mobilization and aggressive physiotherapy.It was chosen for maintaining bilaterally jaw choronous processes, as transcirurgical manipulation revealed immediate reestablishment of the full mouth opening. It was performed a remodeling of the ankylosis mass and its refixation, once rib bone graft presents high morbidity, unpredictablegrowth and possibility of re-ankylosis. Moreover, the current public health system does not provide stock neither customized TMJ prostheses and the patient could not afford, neither had health insurance to finance it, limiting the case.

Arthroplasty with interposition with the myofascial temporalis flap, according to the Kaban protocol, was considered the most successful treatment for ankylosis treatment [16]. In a prospective randomized clinical study conducted between 2005 and 2015 in 60 patients with TMJ ankylosis,in which the patients were treated with gap arthroplasty or interpositional arthroplasty, he observed that interpositional arthroplasty is better than gap arthroplasty in terms of mouth opening and prevention of re-ankylosis [18].

In the present case, the technique chosen was the one proposed by Liu *et al*. (2011) [19] with the bone segment slip from the partial vertical osteotomy ofthe mandibular ramus and myofascial flap interposition, with modifications. The vertical osteotomy of the mandibular ramus involves the sigmoid notch to the lower edge of the mandible by distal lingula [20]. Despite the suggestion to maintain a musculoskeletal pedicle for survival of the osteotomy, it was not possible, due to the extension of the ankylotic mass and the need for evaluation of the medial condyle structures, with necessity of removing the bone stump for drill remodeling and its internal fixation.

In a retrospective cohort study conducted by Chen *et al*., (2019) [21], he reviewed data on TMJ ankylosis patients between 2006 and 2015, totaling 130 patients aged 3 to 67 years. It was observed that the rate of joint re-ankylosis among children was 19.1% and while in adults it was 7.3%. In a study by Al-Kamali *et al*., (2018) [22] of 77 patients with TMJ ankylosis between 2001 and 2013 was observed that radical removal of ankylosis is essential to prevent re-ankylosis. In a systematic review by Rozanski *et al*., (2019) [23], including reports or case series published from 1990 to 2017, where children under 18 years old had TMJ surgically treated in a total of 176 patients, it was observed that 2.27% of patients reported development of re-ankylosis without correlation with different types of intervention. To date, despite the short follow-up, the patient has no clinical or radiographic signs

CONCLUSION

Surgical treatment of TMJ ankylosis is necessary to restore immediate function. Interpositional myofascial flap arthroplasty shows the lower re-ankylosis indexes. Early physiotherapy should be stimulated for optimizing muscular movements and resetting the maximum mouth opening, as patients must be followed until finalization of mandibular growth for necessary current assessment.

CONFLICT OF INTEREST

The authors declare that they have no conflict of interest.

ETHICAL APPROVAL

For this type of case report, formal consent is not required.

INFORMED CONSENT

The authors certify that they have obtained all appropriate patient consent forms, as a protocol for treatment in the Clinical Hospital of the Federal University of Uberlândia. In the form the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal.

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Figure 1

Click here to download Figure FIGURE-1.tiff

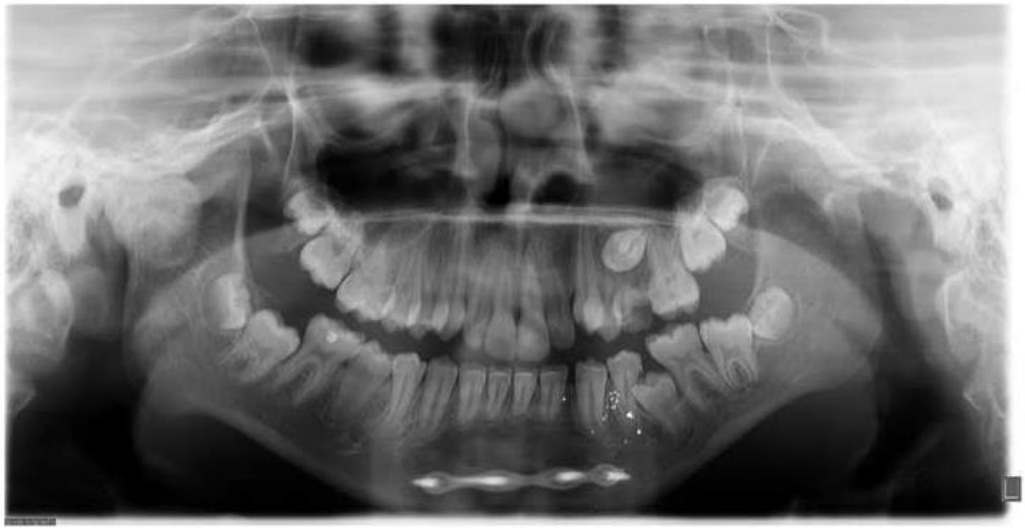

Figure1: Panoramic radiography showing bilateral condyle and symphysis fracture 6 years earlier.

Figure 2

Click here to download Figure FIGURE-2.tiff

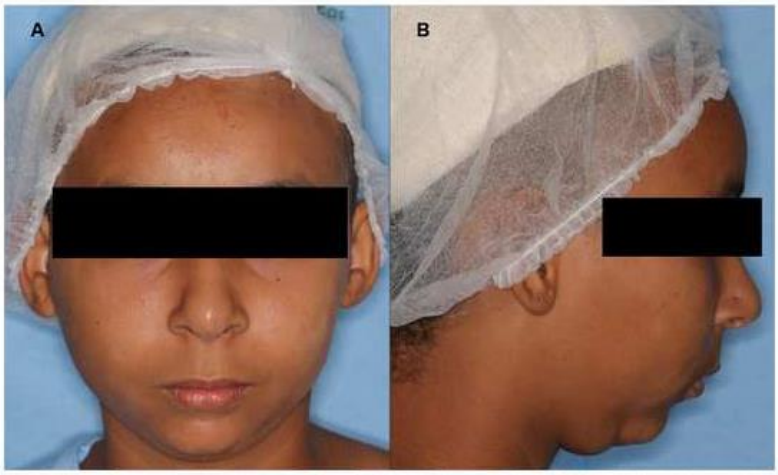

Figure 2: Extra-oral clinical examination showed no signs of facial asymmetry (Fig. 2A), but the presence of mandibular retrognathism (Fig. 2B).

Figure 3

Click here to download Figure FIGURE-3.tiff

Figure 3: Intra-oral clinical examination, the patient complained of pain, severe trismus (9 mm).

Figure 4

Click here to download Figure FIGURE-4.tiff

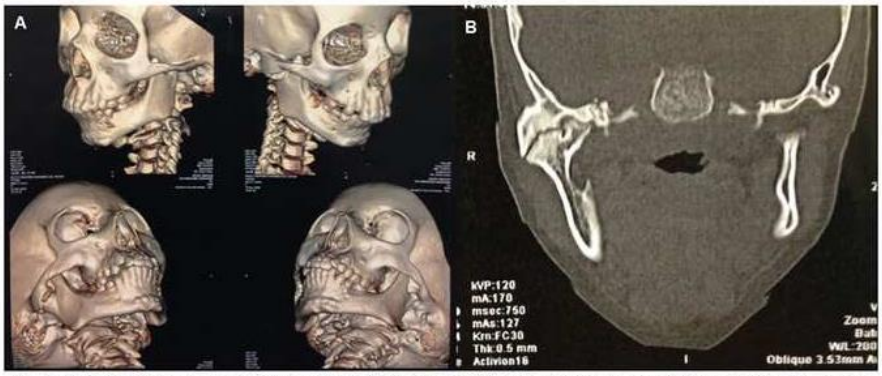

Figure 4: Computed Tomography (CT), it was possible to verify the presence of a dense radiopaque image in the right condyle and a 4-hole miniplate in the symphysis region (Fig. 4A). CT scan revealed an ankylotic mass involving the right temporomandibular joint, type 4 of the Shawney classification (Fig. 4B).

Figure 5

Click here to download Figure FIGURE-5.tiff

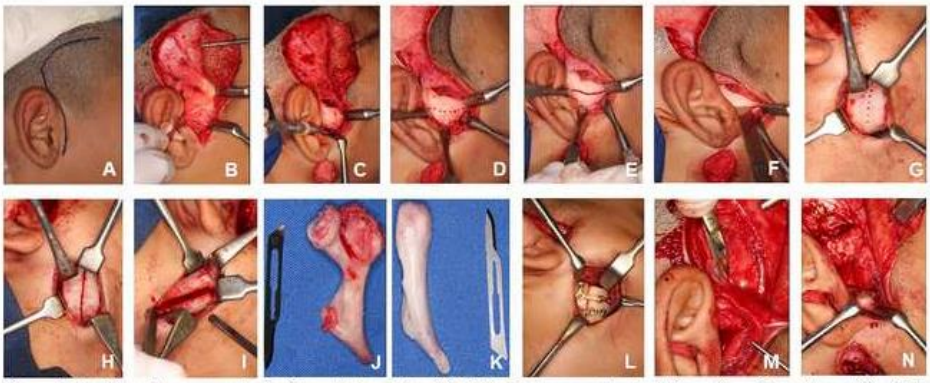

Figure 5: Incision site was marked with methylene blue (Fig.5A); total mucoperiosteal dissection of the planes (Fig. 5B); with ankylotic mass exposure (Fig. 5C); the osteotomy site was previously demarcated and later osteotomized by means of drills (Fig. D); osteotomy with sawing (Fig. 5E); block cleavage using the Wagner chisel (Fig. 5F); subsequently, vertical mandibular ramus osteotomy was performed (Fig. 5G and Fig. 5H); stump removal, and condylar remodeling (Fig. 5I - Fig. 5K); then it was fixed by means of 2 L 2.0 miniplates of the system 2.0 with 4 screws of 7 mm each (Fig. 5L); the myofascial temporalis fascia flap was finally interposed (Fig. 5M and 5N).

Figure 6

Click here to download Figure FIGURE-6.tiff

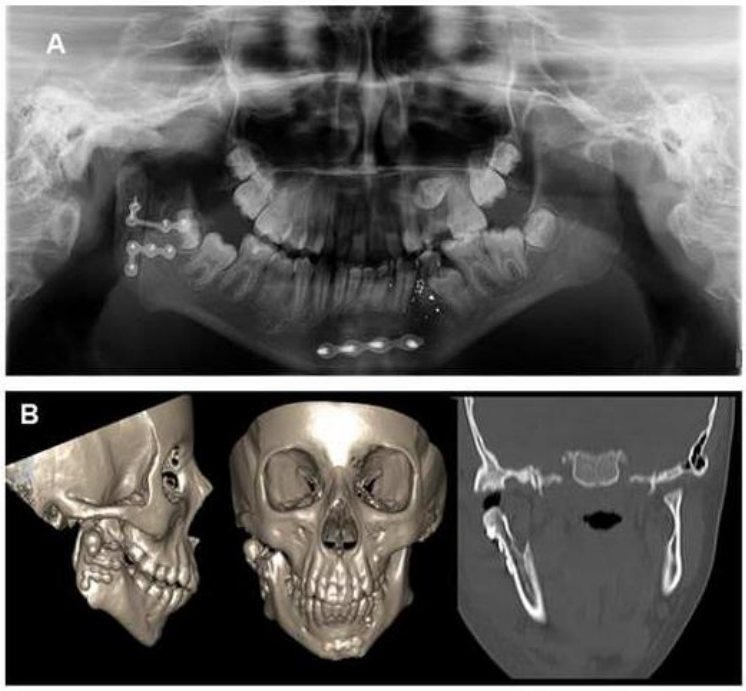

Figure 6: Panoramic radiography after five months of surgery (Fig. 6A). In CT scan it is possible to verify the abscence of the ankylotic mass (Fig. 6B).

Figure 7

Click here to download Figure FIGURE-7.tiff

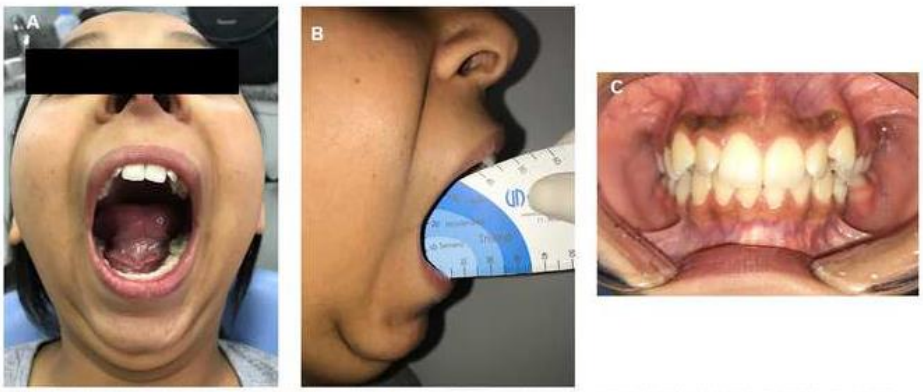

Figure 7: After 5 months a mouth opening of 44mm was observed (Fig. 7A and 7B) and maintained occlusion (Fig.7C).

CONSIDERACÕES FINAIS

A aplicação da Toxina Botulínica Tipo A nos músculos Masséter e Temporal nas pacientes com bruxismo e dor orofacial, mostrou-se um método eficaz para o controle da hiperatividade muscular, tendo seu pico máximo de ação até nonagésimo dia pós infiltração. Observou-se diminuição da tensão muscular, melhora da sintomatologia dolorosa e consequente ganho de qualidade de vida.

Este trabalho mostra que os efeitos produzidos pela Toxina Botulínica Tipo A, são temporários, de efetividade reversível, necessitando de aplicações periódicas para manutenção à longo prazo dos benefícios, tais quais, diminuição da hiperatividade muscular, da sintomatologia dolorosa e uma evolução positiva da qualidade de vida dos pacientes com bruxismo, pois trata-se de condição parafuncional crônica e multifatorial de difícil controle. Não obstante, mais estudos são necessários para refinar o conhecimento disponível sobre o tema.

Este trabalho é o primeiro de uma vasta linha de pesquisa. Para obtenção de mais resultados e conclusões, sugerimos os seguintes temas para novas pesquisas:

1. Aplicação de Toxina Botulínica Tipo A nos músculos Masséter e Temporal, em pacientes do gênero feminino, portadoras de Bruxismo e dores orofaciais em associação com o uso de placas miorrelaxantes.
2. Aplicação de doses maiores da Toxina Botulínica Tipo A nos músculos Masséter e Temporal, em pacientes do gênero feminino, portadoras de Bruxismo e dores orofaciais.
3. Aplicação de Toxina Botulínica Tipo A nos músculos Masséter e Temporal, em pacientes do gênero masculino, portadores de Bruxismo e dores orofaciais.

4. Aplicação de Toxina Botulínica Tipo A nos músculos Masséter e Temporal, em pacientes do gênero masculino, portadores de Bruxismo e dores orofaciais em associação com o uso de placas miorrelaxantes.

5. Aplicação de doses maiores da Toxina Botulínica Tipo A nos músculos Masséter e Temporal, em pacientes do gênero masculino, portadores de Bruxismo e dores orofaciais.

6. Aplicação de Toxina Botulínica Tipo A nos músculos Masséter e Temporal, em pacientes especiais.

7. Aplicação de outras formas de Toxina Botulínica, nos diversos pacientes portadores de Bruxismo e dores orofaciais.

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ANEXOS

• O sujeito da pesquisa tem a liberdade de recusar-se a participar ou de retirar seu consentimento em qualquer fase da pesquisa, sem penalização alguma e sem prejuízo ao seu cuidado (Res. CNS 466/12) e deve receber uma via original do Termo de Consentimento Livre e Esclarecido, na íntegra, por ele assinado.
• O pesquisador deve desenvolver a pesquisa conforme delineada no protocolo aprovado e descontinuar o estudo somente após análise das razões da descontinuidade pelo CEP que o aprovou (Res. CNS 466/12), aguardando seu parecer, exceto quando perceber risco ou dano não previsto ao sujeito participante ou quando constatar a superioridade de regime oferecido a um dos grupos da pesquisa que requeiram ação imediata.
• O CEP deve ser informado de todos os efeitos adversos ou fatos relevantes que alterem o curso normal do estudo (Res. CNS 466/12). É papel de o pesquisador assegurar medidas imediatas adequadas frente a evento adverso grave ocorrido (mesmo que tenha sido em outro centro) e enviar notificação ao CEP e à Agência Nacional de Vigilância Sanitária – ANVISA – junto com seu posicionamento.
• Eventuais modificações ou emendas ao protocolo devem ser apresentadas ao CEP de forma clara e sucinta, identificando a parte do protocolo a ser modificada e suas justificativas. Em caso de projetos do Grupo I ou II apresentados anteriormente à ANVISA, o pesquisador ou patrocinador deve enviá-las também à mesma, junto com o parecer aprobatório do CEP, para serem juntadas ao protocolo inicial (Res.251/97, item III.2.e).

Este parecer foi elaborado baseado nos documentos abaixo relacionados:

Tipo Documento	Arquivo	Postagem	Autor	Situação
Informações Básicas do Projeto	PB_INFORMAÇÕES_BÁSICAS_DO_PROJETO_794357.pdf	22/04/2017 18:11:36		Aceito
Outros	respostaaoparecer.docx	22/04/2017 18:05:12	Marcelo Caetano Parreira da Silva	Aceito
TCLE / Termos de Assentimento / Justificativa de Ausência	termo.doc	22/04/2017 18:04:36	Marcelo Caetano Parreira da Silva	Aceito
Projeto Detalhado / Brochura Investigador	projeto.docx	22/04/2017 18:04:17	Marcelo Caetano Parreira da Silva	Aceito
Outros	fichafinal.docx	30/03/2017 17:20:02	Marcelo Caetano Parreira da Silva	Aceito
Outros	fichadeacompanhamento.docx	30/03/2017	Marcelo Caetano	Aceito

Comentários e Considerações sobre a Pesquisa:
PENDÊNCIAS ANTERIORMENTE APONTADAS:

a) Embora o projeto tenha sido encaminhado para apreciação no início de fevereiro, seu cronograma prevê a etapa de recrutamento iniciado em janeiro. Readequar o cronograma a fim de que sua execução só tenha início após parecer do CEP. PENDÊNCIA ATENDIDA.

b) O projeto prevê como riscos da pesquisa apenas a questão da identificação do participante, no entanto, o TCLE informa acerca de eventual não remissão dos sintomas e diminuição da força da mastigação. Uniformizar a informação, inserindo-a na Plataforma. PENDÊNCIA ATENDIDA.

c) Esclarecer no TCLE: a quantas aplicações da toxina o participante será submetido;
durante quantos meses ele será acompanhado mensalmente (de acordo com o projeto, 6 meses); realização de eletromiografias e preenchimento de fichas mensais; para que o participante tenha plena ciência de todas as etapas e procedimentos. PENDÊNCIA ATENDIDA

d) Esclarecer melhor local e forma de abordagem/recrutamento, bem como a faixa etária dos participantes (maiores de 18 anos?). PENDÊNCIA ATENDIDA.

e) Deve-se contemplar todos os riscos aos quais todos os participantes da pesquisa estarão sujeitos e as atitudes que os pesquisadores tomarão para minimizar os riscos. (desde hematomas, dor causada pela agulha, risco de paralisias tanto pela toxina quanto por possível lesão causada pelo contato da agulha com nervos etc..) PENDÊNCIA ATENDIDA.

f) Descrever no TCLE todos os procedimentos aos quais os participantes que receberão o Botox serão submetidos e todos os riscos (já informados no projeto) aos quais os participantes estarão sujeitos e os procedimentos que os pesquisadores tomarão para prestar atendimento adequado aos participantes que possivelmente sofrerem algum efeito adverso com a pesquisa. (lembrando que não se pode onerar o SUS). Da mesma forma descrever para os participantes que receberão o soro fisiológico. PENDÊNCIA ATENDIDA.

existência de doenças graves co-mórbidas, indivíduos que tiveram exposição a qualquer preparação de toxina botulínica nos últimos 6 meses, participação em outro protocolo terapêutico experimental, qualquer condição médica na qual a administração da toxina botulínica é contra-indicada, incluindo miastenia grave, esclerose lateral amiotrófica e outras doenças agudas, história da disfagia, história de botulismo, uma condição ou a situação em que os investigadores detectem confusão na capacidade do sujeito para participação no estudo, incapacidade de compreender e assinar o consentimento informado, gravidez, indivíduos que não satisfazem os critérios de inclusão e indivíduos que possuam hipersensibilidade a qualquer componente da pesquisa.

Objetivo da Pesquisa:

Objetivo Primário:

Analisar a influência da Toxina Botulínica nos pacientes com Bruxismo.

Objetivo Secundário:

Analisar a ação da Toxina Botulínica em dois músculos da mastigação através de célula de carga e eletromiografia em pacientes com Bruxismo. Avaliar a duração da efetividade de ação da Toxina Botulínica nos paci-entes com Bruxismo. Analisar a sintomatologia dos pacientes com Bruxismo após a aplicação da Toxina Botulínica em dois músculos da mastigação.Avaliar se houve melhora na qualidade de vida após a aplicaçãoda Toxina Botulínica nos pacientes com Bruxismo.

Avaliação dos Riscos e Benefícios:

Segundo os pesquisadores:

Riscos: Por se tratar de procedimentos seguros, o único risco apresentado quanto à inclusão na pesquisa é a quebra de sigilo quanto à identificação dos participantes, que será minimizado pela codificação dos prontuários. projeto completo e TCLE também esclarecem que há também a possibilidade de não remissão dos sintomas e diminuição da força mastigatória.

Benefícios:

O benefício direto da pesquisa é que o tratamento realizado terá condições de avaliar um terapia alternativa para os pacientes com bruxismo com possibilidade na melhoria da sintomatologia dolorosa em algumas ocasiões e ganho de qualidade de vida.

uma qualidade de vida ruim por conta da sintomatologia, além de poderem apresentar alterações bucais, comprometendo a efetividade mastigatória.

METODOLOGIA: O estudo será composto por dois grupos; um grupo controle, onde será aplicado soro fisiológico estéril e um grupo experimental, onde será aplicada 20 Unidades de Toxina Botulínica A (Botox)em cada músculo Masséter e 10 Unidades em cada Músculo Temporal. Após cálculo amostral, encontrou-se amostra de xx sujeitos por grupo (OBS: não foi especificado na PB, mas o projeto completo indica cálculo e necessidade de 42 participantes no total). Cada paciente selecionado preencherá um questionário específico relacionados aos problemas causados pelo bruxismo e preencherá duas escalas visuais analógicas; sendo uma relacionada com a sintomatologia dolorosa da Articulação Têmporo Mandibular e outra relacionada com a qualidade de vida relacionada com o problema. O fatores em estudo serão distribuídos aleatoriamente por sorteios em envelopes opacos e escuros.
Para definição dos grupos, a lista de randomização será criada na página www.sealedenvelope.com. O operador encarregado da intervenção apenas irá abrir o envelope no momento de executar o procedimento. Todas as aplicações serão realizadas no mesmo dia por operadores previamente calibrados. Nem os operadores, nem os sujeitos saberão que substância estará sendo aplicada. Apenas um operador irá manipular as substâncias, prepara-las para a aplicação e realizar os devidos arquivamentos de informações. A análise inicial (baseline) será realizada mensalmente após as aplicações durante 6 meses. Em cada acompanhamento mensal novamente serão realizadas eletromiografias, mensurações em célula de carga e avaliações nas escalas visuais analógicas de dor e qualidade de vida de cada sujeito.Qualquer informação e dados adicionais serão anotados e devidamente arquivados. Após as conclusões do trabalho, caso sejam identificados benefícios da técnica sobre os sujeitos do grupo experimental, os sujeitos do grupo controle passaram pela mesma terapia para sejam também beneficiados.

Critério de Inclusão:
Indivíduos portadores de bruxismo; Estar de acordo em participar e assinar o termo de consentimento livre e esclarecido (TCLE) (Pesquisadores informaram posteriormente que serão pacientes maiores de 18 anos).

Critério de Exclusão:
Existência de psicose ativa, outra doença psiquiátrica ativa ou comprometimento cognitivo,

PARECER CONSUBSTANCIADO DO CEP

DADOS DO PROJETO DE PESQUISA

Título da Pesquisa: Efeito do Tratamento com Toxina Botulínica na qualidade de vida de pacientes com bruxismo e dores na Articulação Têmporo-Mandibular

Pesquisador: Marcelo Caetano Parreira da Silva

Área Temática:

Versão: 2

CAAE: 64309416.1.0000.5152

Instituição Proponente: FACULDADE DE ODONTOLOGIA

Patrocinador Principal: Financiamento Próprio

DADOS DO PARECER

Número do Parecer: 2.088.851

Apresentação do Projeto:

Trata-se de resposta às pendências apontadas no parecer consubstanciado número 2.060.482, de 12 de Maio de 2017.

Conforme apresenta:

O protocolo de pesquisa intitulado "Efeito do Tratamento com Toxina Botulínica na qualidade de vida de pacientes com bruxismo e dores na Articulação Têmporo-Mandibular", a ser desenvolvido em sede de pós-graduação,pretende analisar, através de um estudo clínico randomiza-do, os efeitos da aplicação de Toxina Botulínica (Botox) na musculatura mastigatória nos pacientes com bruxismo diagnosticado, buscando a melhora na qualidade de vida dos sujeitos da pesquisa. De acordo com os pesquisadores, aplicações clínicas deste agente tem se tornado comum nos últimos 30 anos, obtendo resultados previsíveis. A toxina botulínica bloqueia a liberação de acetilcolina na junção neuromuscular, e como resultado, o músculo não recebe a ordem de contração. O bruxismo é um hábito parafuncional que leva o paciente a ranger os dentes de forma rítmica, principalmente durante o sono. Além de poder causar desgastes nos dentes, pode ser um dos fatores causais da cefaléia e distúrbios da articulação temporomandibular e na musculatura da mastigação, principalmente dor. Sendo assim, as pessoas que portadoras de bruxismo podem ter