Allyne Jorcelino Daloia de Carvalho

Cuidados orais e o uso de flúor na prevenção da cárie relacionada à radiação – uma revisão de escopo

Oral care and the use of fluoride in the prevention of radiation-related caries – a scoping review

Dissertação apresentada à Faculdade de Odontologia da Universidade Federal de Uberlândia, para obtenção do título de Mestre em Clínica Odontológica Integrada**.**

Uberlândia MG
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Orientadora: Profa. Dra. Veridiana Resende Novais Simamoto
Coorientador: Prof. Dr. Luiz Renato Paranhos

Banca examinadora:
Profa. Dra. Veridiana Resende Novais Simamoto
Prof. Dr. Paulo César de Freitas Santos Filho
Profa. Dra. Marina Guimarães Roscoe

Uberlândia MG
2022

UNIVERSIDADE FEDERAL DE UBERLÂNDIA
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Data:	Seis de Julho de Dois Mil e Vinte e Dois	Hora de início:	14:00	Hora de encerramento:	[16:50]
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Projeto de Pesquisa de vinculação:	Propriedades Físicas e Biológicas dos materiais Odontológicos e das estruturas dentais				

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“A maior recompensa para o trabalho do homem não é o que ele ganha com isso, mas o que ele se torna com isso.”

John Ruskin

SUMÁRIO

RESUMO

A radioterapia na região de cabeça e pescoço pode causar efeitos adversos à cavidade oral dos pacientes. A cárie relacionada à radiação ionizante é uma complicação grave e apresenta difícil prevenção e tratamento, impactando negativamente a qualidade de vida do paciente. O objetivo desta revisão de escopo foi mapear a literatura sobre protocolos de higiene bucal e o uso do flúor em pacientes que receberam radioterapia. Para isso, foi seguido o protocolo PRISMA-P e a revisão foi registrada no Open Science Framework (OSF). A revisão foi relatada de acordo com a lista de recomendações PRISMA SrC e seguindo as recomendações do JBI Manual de Síntese de Evidência para Revisões de Escopo. As bases MEDLINE (via PubMed), SciELO, Scopus, EMBASE (Ovid), Web of Science, LILACS, LIVIVO e Cochrane Library foram as fontes primárias de busca. Parte da "literatura cinza" foi pesquisada nas bases EASY e ProQuest. Foram incluídos estudos que utilizaram radioterapia na região de cabeça e pescoço e que avaliaram a ocorrência de cárie relacionada à radiação ionizante. Não houve restrições quanto ao idioma do estudo ou data de publicação. Assim, foram incluídos ensaios clínicos (randomizados ou não) e estudos observacionais (prospectivos e retrospectivos). Dois revisores de elegibilidade participaram da seleção dos estudos e da análise dos dados. A síntese qualitativa foi realizada de maneira narrativa/descritiva. Um total de 10.832 registros foram rastreados inicialmente e, após aplicações dos critérios de elegibilidades, resultou em vinte estudos. Em geral, os estudos apresentaram diferentes métodos de cuidados orais e formas de utilização do flúor. O flúor gel foi o método de flúor mais aplicado (70%). Os resultados desta revisão de escopo demonstraram que cuidados orais como instruções de higiene com acompanhamento odontológico regular e flúor diário parecem ser boas estratégias na prevenção de cáries relacionadas à radiação.

Palavras-chave: Cárie Dental; Cuidados Orais; Educação em Saúde; Flúor; Neoplasias de Cabeça e Pescoço; Radioterapia.

ABSTRACT

Radiotherapy in the head and neck region can cause adverse effects to the oral cavity of patients. Radiation-related caries is a serious complication of radiation and presents difficult prevention and treatment, negatively impacting the patient's quality of life. The aim of this scoping review was to map the literature about oral hygiene protocols and the use of fluoride in patients who received radiotherapy. For this, the PRISMA-P protocol was followed and the review was registered in the Open Science Framework (OSF). The review was reported according to the PRISMA SrC list of recommendations and following the recommendations of the JBI Evidence Synthesis Manual for Scope Reviews. MEDLINE (PubMed), SciELO, Scopus, EMBASE (Ovid), Web of Science, LILACS, LIVIVO and Cochrane Library were primary sources. Part of the "gray literature" was searched in EASY and ProQuest databases. Studies that used radiotherapy in the head and neck region and that evaluated the occurrence of radiation-related caries were included. There were no restrictions of study language or publication date. Thus, clinical trials (randomized or not) and observational studies (prospective and retrospective) were included. Two eligibility reviewers participated in study selection and data analysis. The qualitative synthesis was performed in a narrative/descriptive manner. The search was conduct on January 2022. A total of 10,832 studies were initially screened, and after applying the eligibility criteria, resulted in twenty studies. In general, the studies presented different methods of oral care and ways of using fluoride. Fluoride gel was the most applied fluoride method (70%). The results of this scoping review demonstrated that oral care such as hygiene instructions with regular dental follow-up and daily fluoride seem to be good strategies in preventing radiation-related caries.

Keywords: Dental Caries; Fluorides; Head and Neck Neoplams; Health Education; Oral Care; Radiotherapy.

INTRODUÇÃO E REFERENCIAL TEÓRICO

Estimativas globais consideram o câncer bucal, envolvendo lábios e cavidade oral, como o décimo sexto tipo mais comum de neoplasia em todo mundo, sendo o carcinoma de células escamosas responsável por 90% dos casos (Warnakulasuriya et al., 2021). Dentre as diversas formas de tratamento do câncer na região da cabeça e pescoço têm-se a cirurgia, quimioterapia e radioterapia, aplicados isoladamente ou em conjunto (Bhandari et al., 2020).

A radioterapia, embora direcionada às células tumorais, pode gerar danos aos tecidos sadios adjacentes, o que resulta em diversos efeitos colaterais na cavidade oral dos pacientes (Moore et al., 2020). Pacientes submetidos à radiação ionizante na região de cabeça e pescoço podem apresentar sequelas agudas e crônicas nos tecidos orais, gerando deterioração periodontal com risco de osteorradionecrose, além de mucosites, dor, infecções, fibrose tecidual, comprometimento das glândulas salivares e aumento da susceptibilidade à cárie dentária (Sroussi et al., 2017).

A cárie relacionada à radiação é um dos efeitos adversos mais comuns do tratamento radioterápico. A radiação atua de forma direta sobre a estrutura dentária, gerando alterações em suas propriedades químicas, mecânicas e biológicas (Miranda et al., 2018; Rodrigues et al., 2018; Lu et al., 2019). A hipossalivação causada pelos danos às glândulas salivares, associada à dieta altamente cariogênica, são fatores que promovem o ambiente ideal para o surgimento da cárie relacionada à radiação (Mougeout et al., 2019). A radiação também é capaz de causar alterações na microbiota oral, mucosites e trismo que dificultam a higienização (Muller et al., 2019; Moore et al., 2020).

Clinicamente, a cárie relacionada à radiação apresenta-se de maneira diferente da cárie convencional quanto à sua localização e progressão. Afeta principalmente a região cervical, próximo à junção amelodentinária, pontas de cúspides e bordas incisais de dentes anteriores (Jawad et al., 2015; Lu et al., 2019). Inicia-se com alteração da coloração da coroa dental para preto/marrom e trincas no esmalte, seguidas por lascas de esmalte que evoluem para fraturas, expondo a dentina subjacente ao ambiente oral (Palmier et al., 2020). A progressão é rápida e destrutiva, podendo nos casos mais graves levar à amputação das coroas dentais (Moore et al., 2020).

A prevenção da cárie relacionada à radiação ainda é um desafio na prática odontológica. De maneira geral, a prevenção da cárie dentária baseia-se nos cuidados orais regulares, uso de flúor e controle de dieta (Walsh et al., 2019). Portanto, a adoção de protocolos de cuidados orais preventivos e acompanhamento periódico para pacientes de alto risco, submetidos à radiação em região de cabeça e pescoço, é uma alternativa importante na prevenção das sequelas orais da radioterapia, incluindo a cárie relacionada à radiação (Lee et al., 2021). A condição da saúde oral impacta diretamente na saúde geral e na qualidade de vida do indivíduo pós-radioterapia (Ghaffari et al., 2018).

A implementação de protocolos de cuidados orais utilizando métodos de aplicação de flúor mostraram bons resultados na diminuição da incidência da cárie em pacientes pós radioterápicos (Funk et al., 2013; Morais et al., 2016; Sohn et al., 2018). A educação em saúde deve evidenciar a importância do acompanhamento na manutenção da saúde oral e prevenção das sequelas da radioterapia, além de incluir técnicas de escovação, recomendação de escovas macias, uso do flúor tópico pelo paciente e aconselhamento dietético (Lee et al., 2021). Além disso, o acompanhamento periódico mensal dos pacientes sob tratamento de câncer permite diagnosticar alterações orais em estágios inicias, evitando que o problema progrida e o torne o tratamento mais complexo (Bertl et al., 2022).

A eficácia do flúor na prevenção à cárie dentária é consagrada na literatura, devido a sua capacidade de inibir a desmineralização e promover a remineralização da estrutura dental (tenCate, 2013; Marinho et al., 2016). Assim, como forma de aumentar a resistência dos dentes à desmineralização, o uso de flúor tópico é uma importante estratégia (Brook, 2020). Daly, Drane and McComb (1972) realizaram um estudo com a utilização de gel de fluoreto de sódio em pacientes radioterápicos em região de cabeça pescoço e encontraram resultados satisfatórios na diminuição do desenvolvimento de novas lesões de cáries. Este estudo tornou-se referência para a realização de diversos outros estudos, reafirmando a indicação do flúor tópico para este grupo de pacientes (Dreizen et al., 1977; Horiot et al., 1983; Guichard et al., 1983; Bransfield et al.,1987; Meyerowitz & Watson, 1998).

Neste contexto, o objetivo desta revisão de escopo foi mapear a literatura existente sobre protocolos associados ao uso do flúor tópico na prevenção da cárie relacionada à

radiação em pacientes com câncer na região de cabeça e pescoço submetidos à radioterapia.

CAPÍTULO ÚNICO

Este trabalho será submetido à revista Oral Oncology (Qualis CAPES A1; Fator de Impacto: 5.337).

Oral care and the use of fluoride in the prevention of radiation-related caries – a scoping review

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1- Introduction

Radiation-related caries (RRC) is a serious complication of radiotherapy in head and neck region and it is difficult to prevent and treat, negatively affecting the patient's quality of life (Martins et al., 2021; Palmier et al., 2020). The oral environment becomes more cariogenic, due the hyposalivation; in addition, the chemical and mechanical properties of teeth are affected by the radiation, facilitating their destruction (Rodrigues et al., 2018; Lopes et al., 2018; Lu et al., 2019; Miranda et al., 2021). RRC has clinical characteristics, development and progression different from conventional caries, starting with blackish-brown color change in the dental crown and enamel cracks that results in fractures and an aggressive destruction of the subjacent dentin (Martins et al. 2020). When RRC is not treated, it can result in pulpal and periapical pathologies, pain and the need for tooth extraction, which is a risk of osteoradionecrosis development (Bhandari et al. 2021).

Prevention and treatment of RRC are still challenging. It is established in literature that the prevention of dental caries is complex and it must involve regular dental care, fluoride use and dietary advice (Walsh et al., 2019). Highrisk patients need a follow-up with preventive protocols (Epstein et al., 2012; Frydrych et al., 2017). Therefore, there are studies that have evaluated the results of oral care programs and routine follow-up of head and neck cancer patients in the prevention of dental sequelae from radiotherapy (Lee et al., 2021; Sohn et al., 2021). However, the patient's compliance to the oral care follow-up can be a challenge due to socioeconomic and psychological factors, in addition to often the patient's concern with general health, but not with oral health, which can lead to low adherence to follow-up (Morais et al., 2016).

Oral care basically includes brushing instructions, diet explanations and reinforcement of fluoride use (Frydrych et al., 2017; Breslin & Taylor, 2020; Morais et al., 2020). It is known that the use of fluoride can decrease the incidence of RRC (Dreizen et al., 1977; Chambers et al., 2006; Breslin & Taylor, 2020). A recent systematic review showed the effectiveness of various topical fluorides in preventing RRC or changes in bacterial counts, but included studies that evaluated topical fluoride independently or in conjugation with other agents in preventing caries (Agarwal et al., 2022). Due to the possibility of confounding which preventive product was more effective, this scoping review aimed to first analyze the use of topical fluoride alone.

Due to the severity of RRC and the difficulty of its treatment, oral care programs and the use of fluoride can be important strategies in preventing this sequela of radiotherapy. In this context, it was pertinent to undertake a scoping review with the aim of identifying and mapping the evidence on the oral care protocols and fluoride use on preventing RRC.

2- Methods

2.1 Protocol registration

The protocol was reported in accordance with the Preferred Reporting Items for Systematic Review and Meta-Analysis Protocols (PRISMA-P) Statement (Moher et al., 2016) and was registered in Open Science Framework (https://osf.io/jrebd - 10.17605/OSF.IO/JREBD). This scoping review was reported according to the Preferred Reporting Items for Systematic reviews and Meta-Analysis extension for Scoping Reviews (PRISMA-ScR) (Tricco et al., 2018) and followed the Joanna Briggs Institute Critical Appraisal tools (Aromataris et al., 2020). The Arksey and O'Malley methodological framework (Arksey; O'Malley, 2005) was adopted to head this scoping review: a) identify the research question; b) identify relevant studies; c) study selection; d) data charting process and e) summarize and reporting results.

2.2 Research question

The scoping review question was "What is the existing evidences on oral care protocols and fluoride use in preventing radiation-related caries in head and neck radiotherapy patients?".

2.3 Inclusion criteria

a) Population: patients undergoing radiotherapy for head and neck cancer;

b) Concept: oral care and use of fluoride;

c) Context: prevention of radiation-related caries.

d) Study design: randomized and non-randomized clinical trials, observational studies (prospective and retrospective). There was no restrictions of study language or publication date.

2.4 Exclusion criteria

Exclusion criteria were as follows: a) off target studies; b) studies involving different types of cancer and that did not present specific data on radiotherapy; c) studies with overlapping samples (in this case, the most recent study or the one with the most complete information was chosen); d) studies that evaluated other caries prevention methods; e) studies that used biofilm or bacterial counts as an evaluation method.

2.5 Information sources, search and selection of sources of evidence

The search was performed in January 2022. The search strategy was carried out by the researches themselves. MEDLINE (via PubMed), SciELO, Scopus, EMBASE, Web of Science, Cochrane Library, LILACS and LIVIVO databases were used. Part of "gray literature" was researched in EASY and ProQuest. Descriptors were selected using Medical Subject Headings (MeSH), Descriptors in Health Science (DeCS) and Embase Subject Headings (Emtree). Boolean operators (AND and OR) were used to combine descriptors and improve the search strategy through different combinations (Table 1). The MEDLINE search strategy was adapted for the other databases, respecting their rules of syntax. The references found in the primary databases were exported to EndNote Web™ (Clarivate™, Analytics, Philadelphia, USA), excluding duplicates, first automatically and then manually. The references from the "gray literature" were exported to Microsoft Word ™ 2019 software (Microsoft™ Ltd., Washington, USA), and the duplicates were manually excluded.

In cases of not finding the full text of the articles, the Google Scholar, CAPES periodical portal and the Bibliografic Commutation of Federal University of Uberlândia were used. Finally, it was searched on Research Gate and emailed to authors.

Table 1 – Strategies for databases searchers

Database	Search Strategy (January 2022)
MEDLINE (via Pubmed) (http://www.ncbi.nlm.nih.gov/pubmed)	#1 ("Fluorides"[Mesh] OR "Fluoride"[tw] OR "Fluorides, Topical"[Mesh] OR "Topical Fluorides"[tw] OR "Oral Hygiene"[Mesh] OR "Dental Hygiene"[tw] OR "Hygiene, Dental"[tw] OR "Hygiene, Oral"[tw] OR "Oral Health"[Mesh] OR "Dental Care"[Mesh] OR "Care, Dental"[tw] OR "Health Education, Dental"[Mesh] OR "Education, Dental Health"[tw] OR "Dental Health Education"[tw] OR "Health Promotion"[Mesh] OR "Promotion, Health"[tw] OR "Promotion of Health"[tw] OR "Preventive Dentistry"[Mesh] OR "Dentistry, Preventive" OR "Dentifrices"[Mesh] OR "Dentifrice"[tw] OR "Toothpastes"[tw] OR "Toothbrushing"[Mesh]) #2 ("Radiotherapy"[Mesh] OR "Radiotherapies"[tw] OR "Radiation Treatment"[tw] OR "Radiation Treatments"[tw] OR "Radiation Therapy"[tw] OR "Radiation Therapies"[tw] OR "Therapy, Radiation"[tw] OR "Radiation Injuries"[Mesh] OR "Injury, Radiation"[tw] OR "Injuries, Radiation"[tw] OR "Head and Neck Neoplasms"[Mesh] OR "Neoplasms, Head and Neck"[tw] OR "Cancer of Head and Neck"[tw] OR "Head and Neck Cancer"[tw] OR "Head and Neck Neoplasm"[tw] OR "Cancer of the Head and Neck"[tw] OR "Upper Aerodigestive Tract Neoplasms"[tw] OR "Head Neoplasms"[tw]) #3 = #1 AND #2
SciELO (http://www.scielo.org/)	(("Fluorides" OR "Fluoride" OR "Topical Fluorides" OR "Oral Hygiene" OR "Dental Hygiene" OR "Dental Care" OR "Health Education" OR "Preventive Dentistry" OR "Dentifrices" OR "Toothbrushing")) AND (("Radiotherapy" OR "Radiation Treatment" OR "Radiation Therapy" OR "Head and Neck Neoplasms" OR "Head and Neck Cancer" OR "Cancer of Head and Neck"))
Scopus (http://www.scopus.com/)	TITLE-ABS-KEY ("Fluorides" OR "Fluoride" OR "Fluorides, Topical" OR "Topical Fluorides" OR "Oral Hygiene" OR "Dental Hygiene" OR "Hygiene, Dental" OR "Hygiene, Oral" OR "Oral Health" OR "Dental Care" OR "Care, Dental" OR "Health Education, Dental" OR "Education, Dental Health" OR "Dental Health Education" OR "Health Promotion" OR "Promotion, Health" OR "Promotion of Health" OR "Preventive Dentistry" OR "Dentistry, Preventive" OR "Dentifrices" OR "Dentifrice" OR "Toothpastes" OR "Toothbrushing") AND ("Radiotherapy" OR "Radiotherapies" OR "Radiation Treatment" OR "Radiation Treatments" OR "Radiation Therapy" OR "Radiation Therapies" OR "Therapy, Radiation" OR "Radiation Injuries" OR "Injury, Radiation" OR "Injuries, Radiation" OR "Head and Neck Neoplasms" OR "Neoplasms, Head and Neck" OR "Cancer of Head and Neck" OR "Head and Neck Cancer" OR "Head and Neck Neoplasm" OR "Cancer of the Head and Neck" OR "Upper Aerodigestive Tract Neoplasms" OR "Head Neoplasms")
Embase (http://www.embase.com)	('fluorides' OR 'fluoride' OR 'fluorides, topical' OR 'topical fluorides' OR 'oral hygiene' OR 'dental hygiene' OR 'hygiene, dental' OR 'hygiene, oral' OR 'oral health' OR 'dental care' OR 'care, dental' OR 'health education, dental' OR 'education, dental health' OR 'dental health education' OR 'health promotion' OR 'promotion, health' OR 'promotion of health' OR 'preventive dentistry' OR 'dentistry, preventive' OR 'dentifrices' OR 'dentifrice' OR 'toothpastes' OR 'toothbrushing') AND ('radiotherapy' OR 'radiotherapies' OR 'radiation treatment' OR 'radiation treatments' OR 'radiation therapy' OR 'radiation therapies' OR 'therapy, radiation' OR 'radiation injuries' OR 'injury, radiation' OR 'injuries, radiation' OR 'head and neck neoplasms' OR 'neoplasms, head and neck' OR 'cancer of head and neck' OR 'head and neck cancer' OR 'head and neck neoplasm' OR 'cancer of the head and neck' OR 'upper aerodigestive tract neoplasms' OR 'head neoplasms')

Web of Science (http://apps.webofknowledge.com/)	#1 TS=("Fluorides" OR “Fluoride” OR “Fluorides, Topical” OR “Topical Fluorides” OR “Oral Hygiene” OR “Dental Hygiene” OR “Hygiene, Dental” OR “Hygiene, Oral” OR “Oral Health” OR “Dental Care” OR “Care, Dental” OR “Health Education, Dental” OR “Education, Dental Health” OR “Dental Health Education” OR “Health Promotion” OR “Promotion, Health” OR “Promotion of Health” OR “Preventive Dentistry” OR “Dentistry, Preventive” OR “Dentifrices” OR “Dentifrice” OR “Toothpastes” OR “Toothbrushing”) #2 TS=("Radiotherapy" OR “Radiotherapies” OR “Radiation Treatment” OR “Radiation Treatments” OR “Radiation Therapy” OR “Radiation Therapies” OR “Therapy, Radiation” OR “Radiation Injuries” OR “Injury, Radiation” OR “Injuries, Radiation” OR “Head and Neck Neoplasms” OR “Neoplasms, Head and Neck” OR “Cancer of Head and Neck” OR “Head and Neck Cancer” OR “Head and Neck Neoplasm” OR “Cancer of the Head and Neck” OR “Upper Aerodigestive Tract Neoplasms” OR “Head Neoplasms”) #3 = #1 AND #2
LILACS (http://lilacs.bvsalud.org/)	("Fluorides" OR "Fluoride" OR "Topical Fluorides" OR "Oral Hygiene" OR "Dental Hygiene" OR "Dental Care" OR "Health Education" OR "Preventive Dentistry" OR “Dentifrices” OR “Toothbrushing”) AND ("Radiotherapy" OR "Radiation Treatment" OR "Radiation Therapy" OR "Head and Neck Neoplasms" OR "Head and Neck Cancer" OR "Cancer of Head and Neck")
LIVIVO (http://livivo.de)	("Fluorides" OR "Fluoride" OR "Topical Fluorides" OR "Oral Hygiene" OR "Dental Hygiene" OR "Dental Care" OR "Health Education" OR "Preventive Dentistry" OR “Dentifrices” OR “Toothbrushing”) AND ("Radiotherapy" OR "Radiation Treatment" OR "Radiation Therapy" OR "Head and Neck Neoplasms" OR "Head and Neck Cancer" OR "Cancer of Head and Neck")
Cochrane Library (Filter: Trials) (https://www.cochranelibrary.com/)	#1 ("Fluorides" OR “Fluoride” OR “Fluorides, Topical” OR “Topical Fluorides” OR “Oral Hygiene” OR “Dental Hygiene” OR “Hygiene, Dental” OR “Hygiene, Oral” OR “Oral Health” OR “Dental Care” OR “Care, Dental” OR “Health Education, Dental” OR “Education, Dental Health” OR “Dental Health Education” OR “Health Promotion” OR “Promotion, Health” OR “Promotion of Health” OR “Preventive Dentistry” OR “Dentistry, Preventive” OR “Dentifrices” OR “Dentifrice” OR “Toothpastes” OR “Toothbrushing”) #2 "Radiotherapy" OR “Radiotherapies” OR “Radiation Treatment” OR “Radiation Treatments” OR “Radiation Therapy” OR “Radiation Therapies” OR “Therapy, Radiation” OR “Radiation Injuries” OR “Injury, Radiation” OR “Injuries, Radiation” OR “Head and Neck Neoplasms” OR “Neoplasms, Head and Neck” OR “Cancer of Head and Neck” OR “Head and Neck Cancer” OR “Head and Neck Neoplasm” OR “Cancer of the Head and Neck” OR “Upper Aerodigestive Tract Neoplasms” OR “Head Neoplasms”)
Gray literature	
EASY (https://easy.dans.knaw.nl/)	("Fluorides" OR “Fluoride” OR “Fluorides, Topical” OR “Topical Fluorides” OR “Oral Hygiene” OR “Dental Hygiene” OR “Hygiene, Dental” OR “Hygiene, Oral” OR “Oral Health” OR “Dental Care” OR “Care, Dental” OR “Health Education, Dental” OR “Education, Dental Health” OR “Dental Health Education” OR “Health Promotion” OR “Promotion, Health” OR “Promotion of Health” OR “Preventive Dentistry” OR “Dentistry, Preventive” OR “Dentifrices” OR “Dentifrice” OR “Toothpastes” OR “Toothbrushing”) AND ("Radiotherapy" OR “Radiotherapies” OR “Radiation Treatment” OR “Radiation Treatments” OR “Radiation Therapy” OR “Radiation Therapies” OR “Therapy, Radiation” OR “Radiation Injuries” OR “Injury, Radiation” OR “Injuries, Radiation” OR “Head and Neck Neoplasms” OR “Neoplasms, Head and Neck” OR “Cancer of Head and Neck” OR “Head and Neck Cancer” OR “Head and Neck Neoplasm” OR “Cancer of the Head and Neck” OR “Upper Aerodigestive Tract Neoplasms” OR “Head Neoplasms”)
ProQuest (Filter: dissertations and thesis) (https://www.proquest.com/)	("Fluorides" OR "Fluoride" OR "Topical Fluorides" OR "Oral Hygiene" OR "Dental Hygiene" OR "Dental Care" OR "Health Education" OR "Preventive Dentistry" OR “Dentifrices” OR “Toothbrushing”) AND ("Radiotherapy" OR "Radiation Treatment" OR "Radiation Therapy" OR "Head and Neck Neoplasms" OR "Head and Neck Cancer" OR "Cancer of Head and Neck")

The selection process was performed independently by two reviews [AJDC and MBO] and the disagreements were solved by the third reviewer [VRN]. The first stage was the selection by title of the articles, performed by the two reviewers, based on the eligibility criteria and study design. Studies that were out of the review topic were excluded. Then, the reviews read the abstracts of selected studies, according to the inclusion criteria and finally the full texts were read. When the title or abstract did not provide enough information to apply the inclusion and exclusion criteria, the full text was read. The references of eligible studies were evaluated. A recent systematic review was identified thus, their references were also analyzed. This methodological sequence allows minimizing the selection and publication bias.

2.6 Data charting process and data items

After the study selection, reviewers performed a calibration exercise that consisted of selecting and extracting data from three randomly articles. These articles were selected by simple randomization and then an Excel spreadsheet was created in which each reviewer extracted data considered relevant. Then, there was a discussion and standardization of the data by the two reviewers.

The included studies were independently analyzed by each reviewer [AJDC and MBO]. The disagreements were evaluated by the third reviewer [VRN]. The following data were extracted: author, year of publication, country where we study occurred, study design, number of study participants, patient sex and age, method and time of fluoride application, description of oral care, results of caries development and conclusion of the studies. Data were organized in an Excel spreadsheet.

2.7 Synthesis of results

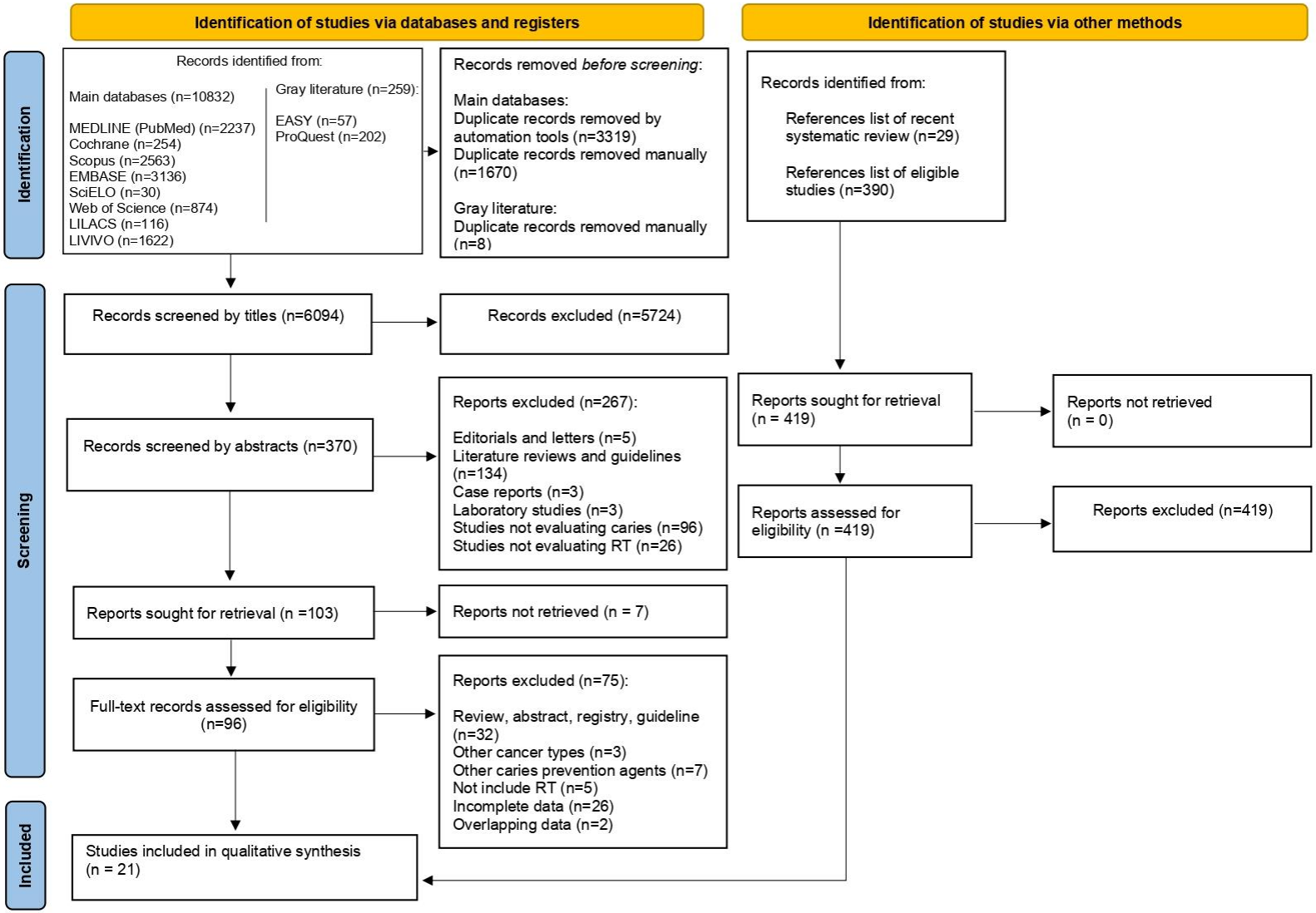
The results of eligible studies were summarized in a descriptive/narrative manner, including study characteristics, oral care methods and fluoride application of relevant to the prevention of RRC.

3 Results

3.1 Selection of evidence sources

The PRISMA flowchart illustrates the process of searching, identifying, inclusion and exclusion of eligible studies (Figure 1). In the initial phase of study selection, 10,832 results were obtained from ten electronic databases, including the gray literature. After excluding the duplicates, 6,094 studies remained for reading titles, of which 5,724 were excluded because they were not related to the research topic. 370 abstracts were read and resulted in 267 exclusions based on eligibility criteria. Of the remaining 103 articles, 7 were not found. So, 96 full texts were read and resulted in 75 exclusions, mainly because the studies had incomplete data on the oral care, on fluoride application and caries or it was congress abstracts, registrations of clinical trials or literature reviews. The 29 references from a recent systematic review were read and 390 references from the eligible studies were carefully evaluated, but none was included. Finally, 21 studies were included in the scoping review.

Figure 1 – FlowChart of the process search



3.2 Characteristics of evidence sources

Overview

The included studies were published between 1972 and 2021. Seven studies were performed in the United States of America (USA) (33%). All studies in a languages other than English were translated using Google Translator (translate.google.com). Thus, one study (Guichard, Combes, Lagarrigue, 1983) was translated from French and it was included in this work. The articles by Horiot et al., (1977; 1981; 1983) presented overlapping data; therefore, the study of 1983 was included (Horiot et al., 1983).

Most of studies (47%) were clinical trials (Daly, Drane, MacComb, 1972; Wescott, Starcke, Shannon, 1975; Dreizen et al., 1977; Bransfield, Horiot, Bône, 1986; Horiot et al., 1983; Pochanugool et al., 1994; Spak, Johnson, Ekstrand, 1994; Meyerowitz, Watson, 1998; Chambers et al., 2006; Soutome et al., 2020), followed by prospective observational studies (24%) (Keys, McCasland, 1976; Regezi, Courtney, Kerr, 1976; Guichard, Combes, Lagarrigue, 1983; Sennhenn-Kirchner et al., 2009; Sohn et al., 2021), retrospective observational studies (23%) (Wang, Chen, Lin, 2008; Jham et al., 2008; Dholam et al., 2013; Bichsel et al., 2016; Frydrych et al., 2017) and a quasi-experimental study (Lee et al., 2021). One article consisted of two separate studies, one prospective observational and one randomized clinical trial, so it was evaluated according to both study designs (Horiot et al., 1983).

The included studies analyzed the effectiveness of oral care and fluoride application after the radiation treatment of head and neck cancer, including different study designs (Table 2). The studies showed that the majority of patients treated with head and neck radiotherapy were male. Among the studies that reported the age of the patients, most have a mean age above 50 years old (81%). All studies presented some method of fluoride use.

Table 2 – Main characteristics of eligible studies

Authors (year)	Country	Study design	Sample			Main results
			n	Gender (Male/ Female)	Average age (years)	
Daly, Drane, MacComb, 1972	USA	Randomized Clinical Trial	134 patients: Fair dentition: control group (n=43); fluoride group (n=38); Good dentition group: control group (n=26); fluoride group (n=27)	N.R	N.R	A good dental follow-up program with conservative thorough dental treatment utilizing fluoride, adequate patient education and good cooperation can minimize the oral complications pos RT
Wescott, Starcke, Shannon, 1975	USA	Non-randomized Clinical Trial	15 patients	N.R	N.R	The results of cooperative patients demonstrate that 0.4% stannous fluoride gel is effective in controlling the development of post irradiation caries if used on a daily basis in conjunction with a program of oral hygiene.
Keys, McCasland, 1976	USA	Observational Prospective	172 patients (with oral management program); 74 patients (without oral management program)	N.R	N.R	The program has been successful in its major objectives by reducing the incidence of radiation caries
Regezi, Courtney, Kerr, 1976	USA	Observational Prospective	130 patients	88 M 42 F	53 M 50 F	Dental caries associated with radiation therapy for oral cancer can be reasonably well controlled using the regimen employed in this study

Dreizen et al., 1977	USA	Randomized Clinical Trial	42 patients: Group 1 (n=15) single protective regimen of red plaque-disclosing dye, nonfluoride gel and unrestricted diet; Group 2 (n=15) double protective regimen of red plaque disclosing dye, 1% sodium fluoride gel, and an unrestricted diet; Group 3 (n=12) triple protective regimen of plaque disclosing dye, 1% sodium fluoride gel, and a sucrose-restricted diet	Group 1: 9 M; 6 F Group 2: 12M; 3 F Group 3: 6 M; 6 F	Group 1: 54.5 ± 9.6; Group 2: 46.5 ± 15.4; Group 3: 53.5 ± 15.5	Caries preventive measures must be instituted as soon as radiation treatment is begun. The program of daily 1% sodium fluoride application and oral hygiene was eminently caries inhibitory both in the presence and absence of dietary sucrose restriction.
Guichard, Combes, Lagarrigue, 1983	France	Observational Prospective	179 patients	N.R	N.R	When the method of fluoridation of teeth of patients undergoing cervicofacial irradiation was well applied, it did not observe failure due caries evolution, on the contrary, coronary destruction is unavoidably done if the attendance is insufficient.
Horiot et al., 1983	France	Study 1: Observational prospective Study 2: Randomized Clinical Trial	Study 1: 935 patients Study 2: 190 patients: Fluor gel group (n=99) Toothpaste group (n=91)	N.R	N.R	Daily topical fluoridation can prevent dental decay in a high-risk population
Bransfield, Horiot, Bône, 1986	France	Randomized Clinical Trial	220 patients: Fluoride gel group (n=110) Toothpaste group (n=110)	N.R	N.R	The program goals were attainable for all the selected patients. The gel and toothpaste instructions paired the desired behavior with preexisting dental practices.

Pochanugool et al., 1994	Thailand	Non-randomized Clinical Trial	73 patients: NaF gel group (n=29); NaF mounthrise group (n=22); NaF gel + mounthrise group (n=22)	47 M 26 F	NaF gel group: 42.62 ±13.5 NaF mounthrise group: 44.36 ±11.58 Mixed group: 44.18 ±13.29	There was no significant difference of the dental status between application of fluoride gel, fluoride solution month rinse and combination of gel and solution. The study concluded that continuing dental care with daily home fluoride month rinse and 3-6 months follow-up by the dentists are the proper way to prevent radiation dental caries.
Spak, Johnson, Ekstrand, 1994	Sweden	Randomized Clinical Trial	55 patients Group A: 0.42% F gel (n=28) Group B: 1.23% F gel + 0.42% F gel (n=27)	Group A: 24 M 4 F Group B: 17 M 10 F	Group A: 58.8 +- 10.6 Group B: 58.5 +- 13.0	Daily 0.42% fluoride gel treatment appears to be sufficient to inhibit caries almost completely and achieve maximal cariostatic prevention in xerostomic patients
Meyerowitz, Watson, 1998	USA	Non-randomized Clinical Trial	23 patients: Fluoride gel group (n=10); Intraoral Fluoride-releasing System – IFRS group (n=13)	Fluoride group: 5 M 4 F IFRS group: 8 M 5 F	Fluoride group: 50.9 +- 4.8 IFRS group: 42.8 +- 3.9	IFRS may be of value in patients who have significant decreases in salivary function and an associated high risk of developing caries, especially if patient compliance with current caries-preventive fluoride regimens is poor.
Chambers et al., 2006	USA	Non-randomized Clinical Trial	22 Patients: Fluoride gel group (n=12) IFRS group (n=10)	Fluoride group: 11 M 1 F IFRS group: 5 M 5 F	Fluoride gel group: 55.4 ± 10.7 IFRS group: 56.0 ± 10.5	When patients follow professional dental care instructions, the IFRS was comparable in efficacy to a fluoride-gel-in-tray treatment when both methods were used together with the daily home use of a 1100-ppm containing fluoride dentifrice

Jham et al., 2008	Brazil	Observational Retrospective	109 patients	86 M 23 F	57.8	The results will be useful as baseline data to determine future measures for prevention and treatment of RT-induced complications and sequelae
Wang, Chen, Lin, 2008	Taiwan	Observational Retrospective	42 patients	N.R	N.R	Fluoride tray fabrication is suggested for dentate patients receiving RT, as it appears to have a positive effect on dental follow-up compliance
Sennhenn-Kirchner et al., 2009	Germany	Observational Prospective	73 patients: 1993 Group (n=37) and 2005 Group (n=36)	1993 Group: 78% M 22% F 2005 Group 92% M 8% F	1993 Group: 54.8 2005 Group: 57	The results show positive changes with cancer patients induced between the observation time points 1993 and 2005
Dholam et al., 2013	India	Observational Retrospective	190 patients	138 M 52 F	46.5	Three months Fluoride Varnish Application helps in decreasing the incidence of radiation caries
Bichsel et al., 2016	Switzerland	Observational Retrospective	70 patients	55 M 15 F	58.7	With the limitations of a retrospective approach, the results showed that patients with high compliance to the prophylaxis protocol showed a reduction of radiation side effects on dental hard tissue. Patients need to be constantly motivated and monitored in a standardized prophylaxis program to reduce avoidable side effects

Frydrych, Slack-Smith, Parsons, 2017	Australia	Observational Retrospective	116 patients	85 M 31 F	57.8 M 53.7 F	Non-compliance with regular dental attendance, oral hygiene instruction, dietary advice and daily fluoride use were all significantly associated with the development of dental caries post completion of cancer treatment, highlighting the importance of a holistic approach to caries prevention in this patient group
Soutome et al., 2020	Japan	Preliminary Clinical Trial	13 patients	10 M 3 F	60.9	Low-concentration fluoride gel in a custom tray during sleep could prevent radiation-related dental caries
Lee et al., 2021	South Korea	Quasi-experimental case-control study	61 patients. Control group (n=30) – oral health education; Experimental group (n=31) – oral health education, fluoride varnish and fluoride month rise	36 M 25 F	N.R	A comprehensive oral care intervention could prevent dental caries and increased quality of life in HNC patients
Sohn et al., 2021	South Korea	Observational prospective	29 patients: Vulnerable group (n=14) - patients with one or more decays, and/or a periodontal pocket depth of at least 4 mm; Healthy group (n=15): patients who did not have any of the above	N.R	N.R	The difference was not statistically significant in either group. The study showed that regular dental visits and periodic professional oral hygiene care using fluoride varnish during and after RT were effective in maintaining oral health among patients with HNC

*N.R = not reported

Most studies carried out oral hygiene instructions, professional teeth cleaning, recommendation for the use of fluoride toothpaste and monthly follow-up as oral care methods. Two studies do not cite whether oral care instructions were given to patients (Sennhenn-Kirchner et al., 2009; Soutome et al., 2020). Most studies showed the need to follow-up patients after radiotherapy (63%).

Fluoride gel was the most applied fluoride method (72%). Most studies used 1% sodium fluoride gel, with the exception of Spak, Johnson, Ekstrand (1994) and Soutome et al. (2020) who used the gel in low concentration and Wescott, Starcke, Shannon (1975), Keys, McCasland (1976) and Chambers et al. (2006) who used stannous fluoride gel. The main recommendation for using fluoride gel was for at least 5 minutes at night, daily. Some studies did not detail how to apply fluoride, but most of them (60%) use custom made trays (Dreizen et al., 1977; Horiot et al., 1983; Guichard, Combes, Lagarrigue, 1983; Bransfield, Horiot, Bône, 1986; Spak, Johnson, Ekstrand, 1994; Meyerowitz, Watson, 1998; Chambers et al., 2006; Wang, Chen, Lin, 2008; Sennhenn-Kirchner et al., 2009; Bichsel et al., 2016; Soutome et al., 2020). Wescott, Starcke, Shannon (1975) instructed that the gel be applied with a toothbrush.

Three studies applied fluoride varnish (Dholam et al., 2013; Lee et al., 2021; Sohn et al., 2021), four studies fluoride month rinses (Regezi, Courtney, Kerr, 1976; Pochanugool et al., 1994; Jham et al., 2008; Lee et al., 2021) and one applied high-fluoride containing toothpaste (Frydrych et al., 2017) (Table 3).

Table 3 – Main results of eligible studies

Authors (year)	Fluoride type	Fluoride method application	Oral care applied	Caries assessment			
				Method	Moment of analysis	Results	Statistical analysis
Daly, Drane, MacComb, 1972	1% sodium fluoride gel	Daily application	Dental hygiene instruction and application of topical fluoride	Number and Percentage of patients with caries	During 6 years	Fair dentition group: control - 30 (69%) / fluoride - 13 (37%) Good dentition group: control - 17 (65%) / fluoride - 7 (25%)	Descriptive
Wescott, Starcke, Shannon, 1975	0.4% stannous fluoride gel	After clean their teeth each night, with the teeth still wet, 0.4% SnF gel was applied to all tooth surfaces with a toothbrush.	The importance of daily cleaning of the teeth and daily application of 0.4% SnF gel was stressed. Each patient was provided with a toothbrush, floss, disclosing tablets and fluoride toothpaste with individual instruction in toothbrushing, oral hygiene technique and follow-up monthly.	Number of crowns amputated due caries and additional carious surfaces	Ranging from 3 years and 3 months to 4 years and 7 months	Noncooperative patients: 57 crowns amputated and 75 additional carious surfaces. Cooperative patients: 0 crowns amputated and 1 additional carious surface.	Descriptive
Keys, McCasland, 1976	Stannous fluoride gel	Daily application	Dental management program divided into 3 phases, with follow-up reinforcement, oral hygiene instructions and daily application of stannous fluoride gel	Percentage of new caries (%)	N.R	12% (with oral management program) 46% (without oral management program)	Descriptive

Regezi, Courtney, Kerr, 1976	3% Sodium fluoride rinse	Held the solution in mouth for 1 minute then expectorated	A basic treatment regimen pre, during and after RT, including oral examination, dental prophylaxis, toothbrush instruction, use of fluoride rinse; reinforcement the oral hygiene regimen after RT	Percentage of patients with caries	Minimum of 1 year to a maximum of 10 years	New carious lesions developed in 20% of the patients	Descriptive
Dreizen et al., 1977	1% sodium fluoride gel (groups 2 and 3)	Use plastic carriers for a minimum of 5 minutes per day throughout the period of RT and continuing everyday indefinitely thereafter	Detailed hygiene instructions and follow-up monthly after RT	DMFT and DMFS index (mean)	3 months during the first-year post RT and at 6 months intervals thereafter. Patients in group 1 evidencing the beginning of a caries was immediately transferred to the group 2 regimen.	Group 1: DMFT 11.00 DMFS 22.21 Group changed from regimen 1 to regimen 2: DMFT 1.22 DMFS 3.67 Group 2: DMFT 1.77 DMFS 3.23 Group 3: DMFT 0.45 DMFS 0.55	N.R
Guichard, Combes, Lagarrigue, 1983	1% sodium fluoride gel (X-Odonte Lab, 3M)	The fluoride gel use started along with the irradiation, every night, in carrier, after the usual oral hygiene, for 10 min daily	Careful monitoring patients, strictly observe oral hygiene and topical fluoride application. Follow-up was performed 2 to 3 months in the first year after RT and longer thereafter.	Number and Percentage of patients with caries	18 months to 6 and a half years	10 patients (5,6%)	Descriptive

Horiot et al., 1983	Study 1: 1% sodium fluoride gel	Study 1: In carrier, after the usual oral hygiene, for a minimum of 5 min daily	Study 1: a multidisciplinary follow up and fluoride use.	Study 1: Percentage of patients with caries	Study 1: 1 to 10 years	Study 1: 4%	Descriptive
	Study 2: Fluoride gel or toothpaste	Study 2: Fluoride gel group: 1% sodium fluoride gel in carrier, after the usual oral hygiene, for a minimum of 5 min daily Toothpaste group: Use a 1350 ppm F- toothpaste for 3 min, twice a day following morning and evening meals.	Study 2: Dental work-up and care prior to radiotherapy, assignment to dental groups and follow-up data were coded.	Study 2: Percentage of patients with caries	Study 2: Minimum 14 months and maximum 3 years after RT	Study 2: Fluoride gel group: 3% Toothpaste group: 11%	
Bransfield, Horiot, Bône, 1986	Fluoride gel or toothpaste (1.350 ppm F)	Fluoride gel group: Custom-fabricated fluoride carrier, after the usual oral hygiene routine, for at least 5 minutes each day. Toothpaste group: brush their teeth for 1 minute and a half with toothpaste and keep the toothpaste in mouth for another 1 minute and a half.	Dental instructions repeated weakly, during the six-to-eight weeks of radiation; follow-up every two-or-three month during the first year after RT	Percentage of patients with caries	Minimum 14 and maximum 36 months after RT	Fluoride gel group: 3% Toothpaste group: 11%	Descriptive

Pochanugool et al., 1994	NaF gel / NaF mounthrise / NaF gel + mounthrise	**NaF gel group:** daily in plastic tray for 1 month then weekly and monthly for 1 year after RT **NaF mounthrise group**: rise the solution for 5 minutes before bedtime **Mixed group:** combine with both procedures as group one and two	Dental work-up including full mouth X-ray. Encouraging to maintain dental care by using a soft brush with non-irritant fluoride toothpaste	Percentage of new caries (%)	7 to 87 months	Extractions due caries: NaF gel: 6.9% NaF sol: 22.7% Mixed: 13.6% Filling: NaF gel: 65.5% NaF sol: 68.5% Mixed: 54.5%	Descriptive
Spak, Johnson, Ekstrand, 1994	**Group A**: 0.42% F gel for 1 year; **Group B:** 0.42% F gel followed by 4-week daily application of a 1.23% F gel. Thereafter they returned to the 0.42% F gel and continued to use it until 1 year	Fluoride gel in trays once a day for 5 min	Dietary advice, oral hygiene instructions and professional tooth cleaning and recommendation to use a fluoride toothpaste.	Number of new caries	Immediately before RT, 6 and 12 months after RT	Mean and SD between the month and baseline: **Group A:** 6 months (n=19): 2.9 +- 7.1 / 12 months (n=18): 4.3 +- 8.6 **Group B:** 6 months (n=22): 2.9 +- 6.7 / 12 months (n=19): 5.3 +- 8.8	Mann-Whitney test with level of significance 0.05
Meyerowitz, Watson, 1998	1.1% fluoride gel or IFRS	**Control group:** fluoride gel in custom-made trays, for 5 minutes once a day at bedtime **IFRS group:** each fluoride pellet contains 35 milligrams of sodium fluoride and is designed to release a mean of 0.12 mg of F- per day for 130 days. The fluoride pellets were changed at the three-month point in this study.	Home care instructions and a fluoridated dentifrice (1.500 ppm F)	Mean of number of carious surfaces. The criteria of Banting, visual-tactile criteria of Radike and radiographs were used to quantify root caries.	6 months after RT	Control group: 0.03 IFRS group: 0.01	Mann Whitney U test

Chambers et al., 2006	0.4% stannous fluoride-gel or IFRS	Fluoride gel: daily use of 0.4% stannous fluoride-gel in custom-made carriers IFRS: intraoral fluoride releasing system following the 3-month post RT	Use of fluoride dentifrice (1100 ppm F), once daily 10-min fluoride gel application in custom-made fluoride carriers, for about 3 months post-RT. After 3 months, the patients were divided in control group or IFRS group. This treatment was continued until about 3 months post-radiation therapy.	Number and of patients with caries. The visual-tactile criteria of Radike, the criteria of Banting et al., and the root caries index (RCI) of Katz were used to quantify root caries.	4, 8, 12, 24, 36, and 48 weeks after RT	Fluoride gel group: 5 weeks (2); 8 weeks (2); 12 weeks (2); 24 weeks (3); 48 weeks (2) IFRS group: 6 weeks (1); 8 weeks (1); 12 weeks (2); 24 weeks (1); 48 weeks (1)	Poisson probability distribution; estimating equations; proportional hazards regression model.
Jham et al., 2008	1% Sodium fluoride rinse	Mouthwash at night for 1 min, concomitant with RT	Oral care instructions by oral hygienists, pre-RT procedures, and use of 1% sodium fluoride mouthwash	Number (n) and percentage of patients with caries	Minimum 6 months, with an average of 120 days	12 (11%)	N.R
Wang, Chen, Lin, 2008	1,23% APF gel or 2% NaF gel	In trays, 4 minutes a day	Treatment before and during RT, improvement in oral hygiene motivation, regular follow-up and fluoridation	Mean of number of carious teeth	N.R	7.18 +- 7.10	Descriptive
Sennhenn-Kirchner et al., 2009	Fluoride gel application	Splints of fluoride gel application	N.R	Percentage of carious teeth	N.R	1993 Group: 20.6% 2005 Group: 10.8%	Descriptive
Dholam et al., 2013	5% sodium fluoride varnish	Before RT and every 3 months after RT	Oral hygiene detailing, professional prophylaxis, topical application of fluoride	DMFT index (mean)	Before RT / 3 / 6 / 9 / 12/ 15 months after RT	Before RT: 4.12 3 months: 4.28 7 months:4.46 9 months: 4.83 12 months: 5.04 15 months: 5.14	Mann-Whitney U test or Kruskal-Wallis test (as appropriate)

Bichsel et al., 2016	Amine-sodium fluoride gel (Paro® Fluor Gelée, Paro, Kilchberg, Switzerland)	In trays, 5 minutes at night	The prophylaxis protocol consisted of two to three sessions during the 6-week IMRT treatment and post-radiotherapy follow-up examinations after 3, 6, and 12 months. Professional oral cleaning, reinstruction, and re-information on the use of the medication tray and the therapeutic agents	Number (n) and Percentage of new caries	1 year after RT	Low compliance group: n=13 (18.6%) caries and n=5 (7.1%) extraction due caries High compliance group: n=5 (7.1%) caries and n=2 (2.9%) extraction due caries	Mann-Whitney U test and Kruskal-Wallis test ($p<0.05$)
Frydrych, Slack-Smith, Parsons, 2017	5000 ppm fluoride-containing toothpaste.	Daily use	The four main facets of caries prevention: (I) a non-cariogenic diet; (II) regular general dental examinations; (III) the provided oral hygiene instruction; and (IV) daily use of a 5000ppm fluoride-containing toothpaste. Patients were monitored at each follow-up visit.	Percentage of patients with caries	12 months to 9 years	38.8% - presented caries before commencing RT / 17.2% - developed caries during the RT follow up period	Univariate analysis ($p< 0.05$)
Soutome et al., 2020	0.145% Sodium fluoride gel	Use of tray during sleep every night after brushing teeth with a toothpaste (1.450 ppm)	N.R	Number (n) of new caries	3 months to 1 year	0 new caries	Descriptive

Lee et al., 2021	Fluoride varnish and 0.05% fluoride rinse (test group)	The fluoride varnish application was done 3x (before, immediate after, 3 months after RT). Sodium fluoride solution was given before and up to 6 months after RT, with 10 to 15ml of the solution once a day for 1 minute.	The contents of the education consisted of the reasons why oral care is important, definition of side effects of radiotherapy, toothbrush selection and tooth brushing method, fluoride mouth-rinsing solution usage, diet, and denture cleaning and storing method caregivers, use of fluoride toothpaste and mouth rinse caregivers	Mean of caries experience	Before and 6 months after RT	Control group: 6.37/8.40 Experimental group: 5.45/5.45	Independent t-test for continuous variable
Sohn et al., 2021	5% sodium fluoride varnish	Every week, for the first month and every 3 months, up to 12 months after RT	Professional oral hygiene care, including education on toothbrushing, at every dental visit, oral prophylaxis, fluoride varnish application. This was performed every week for the first month of radiotherapy and every 3 months until 12 months after radiotherapy	Number of of carious teeth	6 to 12 months	Mean and SD between the month and baseline: 6 months: Healthy group (n=15): 0.07 +- 0.26 / Vulnerable group (n=14): 1.57 +- 2.14 12 months: Healthy group (n=8): 0.13 +- 0.354 / Vulnerable group (n=8): 1.13 +- 1.356	Chi-square test; Mann-Whitney U-test; repeated measures t-test or the one-way repeated measures ($p<0.05$)

*N.R = not reported; IFRS = intraoral fluoride-releasing system; DMFT = decayed, missing, filled teeth; DMFS = decayed, missing, filled surface.

4 Discussion

The incidence and severity of adverse effects of radiotherapy can be attenuated by effective preventive oral care (Frydrych et al., 2017; Morais et al., 2020). It is recommended that head and neck patients undergoing radiotherapy be involved in a multidisciplinary and preventive oral management program at all the stages of treatment, including detailed caries examination, restorations, periodontal therapy and fluoride use (Tolentino et al., 2011; Morais et al., 2016). Furthermore, it is essential to explain to the patient and their family members about the importance of dental follow-up after cancer therapy to avoid the radiation complications and promote quality of life (Bhandari et al. 2021).

Caries preventive protocols must involve oral hygiene, regular dental care, fluoride use and dietary control, but for irradiated patients there is still a limitation in the studies (Frydrych et al., 2017; Lee et al., 2021). In this scoping review, several studies have showed good results of oral care instructions in preventing RRC (Keys, McCasland, 1976; Regezi, Courtney, Kerr, 1976; Bichsel et al., 2016; Frydrych et al., 2017; Lee et al., 2021; Sohn et al., 2021). Oral health education consists of making patients aware of the importance of knowing the side effects caused by radiotherapy, the correct toothbrushing method, recommendations for fluoride use and dietary guidelines (Lee et al., 2021). It is in agreement with others studies that evaluated oral care programs in irradiated patients (Funk et al., 2013; Morais et al., 2016; Sohn et al., 2018).

Periodic follow-up is an important part of maintaining oral health and preventing caries, being a process carried out since the first studies involving oral care in irradiated patients (Daly, Drane, McComb, 1972; Keys, McCasland, 1976; Regezi, Courtney, Kerr, 1976; Dreizen et al., 1977; Bransfield, Horiot, Bône, 1986). Guichard, Combes and Lagarrigue (1983) observed in their study that patients who diligently applied the oral care method did not see the development of any RRC, on the other hand, patients who did not follow the method developed caries over time.

The continued follow-up has to occur with the minimum of three months after radiotherapy and the frequency of visits should variate according to oral health status of each patient (Jham et al., 2008). Monthly intervals after the radiotherapy and then at three months intervals seem to be effective in the oral maintenance (Wescott, Starcke, Shannon,

1975; Lee et al., 2021). The follow-up in the first twelve months is essential for monitoring oral care (Sohn et al., 2021).

Regular monitoring is important because it allows to control any changes that occur immediately, preventing further damage (Wang et al., 2008). In addition, it is an essential strategy to maintaining patient's compliance to the preventive oral care protocol (Frydrych et al., 2017). Thus, a continuous motivation for oral care in these patients is necessary, in order to prevent the patient from giving up their oral care (Sohn et al., 2021). Wescott, Starcke, Shannon (1975) recalled the patients on daily basis to ensure that they understood the instructions. Compliance with preventive protocols must be reinforced frequently by the professional team (Lee et al., 2021).

A systematic review has shown that the reminder therapy is a valuable strategy and can contribute to plaque reduction in orthodontic patients, which presents a plaque increase, drop in oral hygiene and an increased risk of developing caries lesions (Lima et al., 2018). With current technology, it is possible to use smartphones to send messages remaindering patients of hygiene instructions, which can improve outcomes on oral hygiene and plaque control (Lima et al., 2018). Mobile telephone messages reminders can instigate positive behavior and increase the patient's compliance, giving instructions and reinforcing oral hygiene maintenance (Mahmood et al., 2021). Thus, reminder therapy is an interesting suggestion to be applied to patients undergoing cancer therapy.

Toothbrush selection and brushing method should be part of an oral health education to irradiated patients (Lee et al., 2021). Wescott, Starcke, Shannon (1975) and Regezi, Courtney, Kerr (1976) established a basic treatment regimen for these patients including toothbrushing instruction and oral hygiene techniques. The recommendation of using soft toothbrushes should be made to these patients (Regezi, Courtney, Kerr, 1976; Pochanugol et al., 1994; Lee et al., 2021; Sohn et al., 2021). Toothbrushing education can be easily performed by the dental professional and it is an easy strategy to be adhered by patients (Sohn et al., 2021). Reinforcement the oral hygiene regimen is beneficial for increasing patient collaboration in RCC prevention (Bichsel et al, 2015; Lee et al., 2021).

Dietary advice is part of a complete oral care program (Keys, McCasland, 1976; Spak, Johnson and Ekstrand, 1994; Frydrych et al., 2017; Lee et al., 2021). Frydrych et al. (2017) evaluated post-radiotherapy patient's adherence to oral hygiene instructions and dietary advice and concluded that non-compliance was strongly associated with

development of caries (Frydrych et al., 2017). The adherence to a non-cariogenic diet is a difficult caries preventive measure for these patients due to the dry mouth, which makes patients prefer cariogenic foods (Frydrych et al., 2017; Lee et al., 2021). During radiotherapy, patients have frequent small meals with cariogenic foods and often ingest liquids containing carbohydrates, and in association the patient has pain, mucositis and trismus that make oral hygiene difficult, facilitating the development of caries (Deng et al., 2015). Thus, it is essential that the patient undergo multidisciplinary monitoring, such as nutritionists, for the indication of a balanced diet aiming at adequate nutrition and possible reduction in sugar consumption (Frydrych et al., 2017).

The effectiveness of fluoride in the process of preventing dental caries is consecrated in the literature, due to its ability to inhibit demineralization and promote remineralization of the dental structure (ten Cate 1997; ten Cate 2013). Even at low concentrations, fluoride has beneficial effects on the remineralization of enamel and dentin through different treatment methods, such as topical applications, mouth rinses or dentifrices (ten Cate 1997).

The study by Daly, Drane and McComb (1972) applied fluoride to post-radiotherapy caries. The authors observed in previous studies that topical sodium fluoride applied daily was shown to be highly beneficial in preventing caries in children, so they decided to apply the fluoride method in patients irradiated in the head and neck region (Daly, Drane, McComb, 1972). The results were satisfactory, and this methodology served as basis for others studies included in this scoping review (Dreizen et al., 1977; Horiot et al., 1983; Guichard, Combes, Lagarrigue, 1983; Bransfield, Horiot, Bône, 1986; Meyerowitz, Watson, 1998).

Sodium fluoride gel at a concentration of 1% used daily is an efficient methods of caries prevention (Dreizen et al., 1977; Horiot et al., 1983; Guichard, Combes, Lagarrigue, 1983; Jham et al., 2008). But it seems that fluoride even at low concentrations (0.42% and 0.15%) may be able to provide protection against caries (Spak, Johnson and Ekstrand, 1994; Soutome et al., 2020). Most of studies have used fluoride gel in prefabricated or custom-made trays, but it appears that there is a low long-term compliance in the use of trays (Chambers et al., 2006). Although the use of fluoride in trays has shown many benefits (Bichsel et al., 2015), its use seems to be inconvenient, as it is time consuming and oral pain results in poor compliance (Jansma et al., 1988;

Joyston-Bechal et al., 1992; Chambers et al., 2006; Frydrych et al., 2017). Wescott, Starcke, Shannon (1975) recommended the application of stannous fluoride gel with a toothbrush.

Daily home fluoride month rinses are an easy way of fluoride use by the patient (Pochanugool et al., 1994). The recommendation of use consisted in rinse the mouth with the fluoride solution once a day for one minute after brushing, which can be easily adopted in the patient's routine (Lee et al., 2021). This can be a way of optimizing the patient's compliance to fluoride use.

Lee et al. (2021) applied a combination of application of fluoride varnish and fluoride mouthwash for daily use in a comprehensive professional dental care intervention that results in decreased of dental caries in patients undergoing radiotherapy. Fluoride varnish application seems to have an effect on decreasing the incidence of RRC (Dholam et al., 2013; Sohn et al., 2021). Dholam et al. (2013) observed positive results in caries prevention in a three-month application of 5% fluoride varnish, which has better adhesion when compared to fluoride gel in a custom carrier. This fluoride method is easy to apply, creates less patient's discomfort and offers better acceptability (Dholam et al., 2013). Thus, periodic application of fluoride varnish appears to be effective in dental health promotion (Sohn et al.,2021).

There are studies that have evaluated the effectiveness of fluoride in combination with other agents in preventing RRC (Katz et al., 1982; Joyston-Bechal et al., 1992; Meca et al., 2010; Sim et al., 2014). However, this scoping review showed that different topical fluoride methods themselves are able of promoting RRC prevention. Agarwal et al. (2022) performed a systematic review with and meta-analysis that evidenced the effectiveness of several topical fluorides in preventing RRC or changes in bacterial growth, but their investigation included only randomized controlled or uncontrolled trials or quasi randomized trials that evaluated the role of topical fluoride alone or in association with other agents of caries prevention. The main difference from this scoping review was the more embracing selection of the studies, including observational, prospective or retrospective studies, focused on exalting oral care and analyzing topical fluoride independently, so that other preventive agents were not be confounding factors.

As limitation of this scoping review, there were seven articles that were not found and the article translated from French using Google Translator, which may have some

failure in the translation. In addition, the included studies in this review were very heterogeneous in terms of oral care protocols, fluoride application methods and comparison between interventions. It is not possible to make comparisons between the effects of one method and another, but rather to highlight the benefits and results of each one.

This present work addresses the main essential elements of the scoping review: mapping the available literature, summarizing research results, and identifying research gaps. This review does not provide any recommendations on the intervention, but may suggest some preventive alternatives to RRC. Therefore, this scoping review highlights the need for future studies to be performed to assess the effectiveness of oral care programs and fluoride application in prevention RRC.

5 Conclusion

Our findings show that oral care associated with fluoride use should be considered as an effective method to decrease the development of RRC. This scoping review provides direction for conducting randomized clinical trials involving caries preventive methods in head and neck cancer patients and also for the development of preventive protocols for RRC.

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CONSIDERAÇÕES FINAIS

A cárie relacionada à radiação caracteriza um dos efeitos colaterais mais complexos da terapia de radiação na região de cabeça e pescoço. Seu tratamento e prevenção ainda constituem um desafio aos profissionais, sendo de extrema importância buscar alternativas que auxiliem no manejo desta complicação. Esta revisão de escopo permitiu o mapeamento da literatura existente sobre os principais métodos e protocolos utilizados de cuidados orais a este grupo de pacientes, juntamente com a utilização do flúor tópico, de maneira profissional ou uso diário pelo próprio paciente, mostrando bons resultados na prevenção da cárie decorrente do tratamento radioterápico na região de cabeça e pescoço.

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