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Clinical guidance for maintaining oral hygiene in patients undergoing chemotherapy or radiation therapy: a scoping review

KEYWORDS

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Dental prophylaxis
Cancer
Mucositis
Stomatitis

SUMMARY

The aim of this scoping review was to identify clinical guidance for maintaining oral hygiene in patients undergoing chemotherapy, radiation therapy, or both. Electronic searches were conducted in PubMed, Embase, Cochrane Library, and Google Scholar for articles published between January 2000 and May 2020. Systematic reviews, meta-analyses, clinical trials, case series, and expert consensus reports were considered eligible for inclusion. The SIGN Guideline system was used to evaluate the level evidence and the grade of recommendations. A total of 53 studies met the

eligibility criteria. The results showed the presence of recommendation for oral care in three domains: management of oral mucositis, prevention and control of radiation caries, and management of xerostomia. However, most of the included studies had low levels of evidence. The review provides recommendations for healthcare professionals caring for patients undergoing chemotherapy, radiation therapy, or both, but a standard oral care protocol could not be established owing to a paucity of evidence-based data.

Introduction

Patients undergoing chemotherapy, radiation therapy, or both for the treatment of head and neck cancers commonly experience oral side effects, including mucositis, thrush (candidiasis), xerostomia, radiation caries, trismus, tissue damage, and osteo-radiation necrosis. Implementing proactive management of oral problems during and after cancer treatment can decrease the severity of these side effects and enhance the patients' oral health-related quality of life. It has been shown that poor oral hygiene is a significant risk factor for oral complications from chemotherapy and radiation therapy (JOSHI 2010).

Oral mucositis (OM), a widespread side effect experienced by patients undergoing cancer treatment, can hinder proper oral health maintenance. Mucositis is an inflammatory condition that affects the submucosal connective tissues, potentially leading to symptoms in the oral cavity and throughout the digestive tract (EILERS ET AL. 2014). The severity of mucositis can vary greatly, from subtle changes in sensation to the development of painful, ulcerative, bleeding lesions, and infections (EILERS & MILLION 2011). The discomfort associated with mucositis can make maintaining oral hygiene difficult, making oral care protocols essential.

Given the importance of oral hygiene for patients undergoing chemotherapy, radiation therapy, or both, the objective of this scoping review was to collect information on evidence-based oral hygiene instructions, guidance, and tools to effectively manage oral hygiene in these patients. Additionally, the review sought to identify preventive programs and standardized protocols to promote oral hygiene in this patient population.

Material and methods

Four electronic databases, PubMed, Embase, Cochrane Library, and Google Scholar, were searched for studies published from

January 2000 to March 2020 in English and German. The eligible sources included systematic reviews, meta-analyses, clinical studies, case series, expert opinions, and Delphi consensus reports that addressed aspects such as type of toothbrush, tooth brushing technique, frequency and duration of toothbrushing, type of toothpaste, mouthwash use, and interdental cleaning methods. Pamphlets, case reports, posters, and abstract-only reports were excluded.

For the electronic searches, the following keywords and Boolean operators were used:

((("cancer therapy") AND ("stomatitis")) AND ("oral health")) or ((("cancer therapy") AND ("stomatitis") AND ("mucositis")) AND ("oral hygiene")) or (((("cancer therapy") AND ("mouth hygiene")) AND ("stomatitis")) AND ("oral care")) or ("radiation") AND ("caries")) or (((("dental caries") AND ("radiation")) AND ("mouth hygiene")) AND ("xerostomia"))

The electronic search, the removal of duplicates, the title and abstract screening, and the full text assessments were performed by a single investigator. Journals and author names were unblinded during the eligibility assessment. The level of evidence and the grade of recommendations of studies fulfilling the eligibility criteria were assessed according to the SIGN Methodology Checklist (FIFTIETH GUIDELINE DEVELOPER'S HANDBOOK, NHS SCOTTISH INTERCOLLEGIATE GUIDELINES NETWORK SIGN. REVISED EDITION NOVEMBER 2011). Figure 1 and Figure 2 provide detailed information on the levels of evidence and grades of recommendations, respectively.

Results

Of 176 articles included in the full text assessment, 53 fulfilled the eligibility criteria. One article was a meta-analysis, 10 articles were systematic reviews, 12 articles were clinical studies, and 30 articles were narrative reviews. Four of the 10 systematic

Fig. I Levels of evidence by SIGN

1++	High-quality meta-analyses, systematic reviews of RCTs, or RCTs with a very low risk of bias
1+	Well conducted meta-analyses, systematic reviews, or RCTs with a low risk of bias
1-	Meta-analyses, systematic reviews, or RCTs with a high risk of bias
2++	High-quality systematic reviews of case control or cohort studies High-quality case control or cohort studies with a very low risk of confounding or bias
2+	Well conducted case control or cohort studies with a low risk of confounding or bias and a moderate probability that the relationship is causal
2-	Case control or cohort studies with a high risk of confounding or bias and a significant risk that the relationship is not causal
3	Non-analytic studies, e. g. case reports, case series
4	Expert opinion

Fig. II Grades of recommendation by SIGN

A	At least one meta-analysis, systematic review, or RCT rated as 1++, and directly applicable to the target population; or a body of evidence consisting principally of studies rated as 1+, directly applicable to the target population, and demonstrating overall consistency of results
B	A body of evidence including studies rated as 2++, directly applicable to the target population, and demonstrating overall consistency of results; or extrapolated evidence from studies rated as 1++ or 1+
C	A body of evidence including studies rated as 2+, directly applicable to the target population, and demonstrating overall consistency of results; or extrapolated evidence from studies rated as 2++
D	Evidence level 3 or 4; or extrapolated evidence from studies rated as 2+
<i>Note: The grade of recommendation relates to the strength of the evidence on which the recommendation is based. It does not reflect the clinical importance of the recommendation.</i>	

reviews were updates from guidelines of the Mucositis Study Group of the Multinational Association of Supportive Cancer in Cancer / International Society for Oral Oncology (MASCC/ISOO). The 12 clinical studies comprised one cohort study, a case series, and 10 clinical treatment trials (Fig. 3). The results of

the assessment of the level of evidence and the grade of recommendations are reported in detail in Tables I-VI.

The findings revealed that three different guidelines exist for patients undergoing oncological treatment: for the management of oral mucositis, radiation caries (pre-, post and during

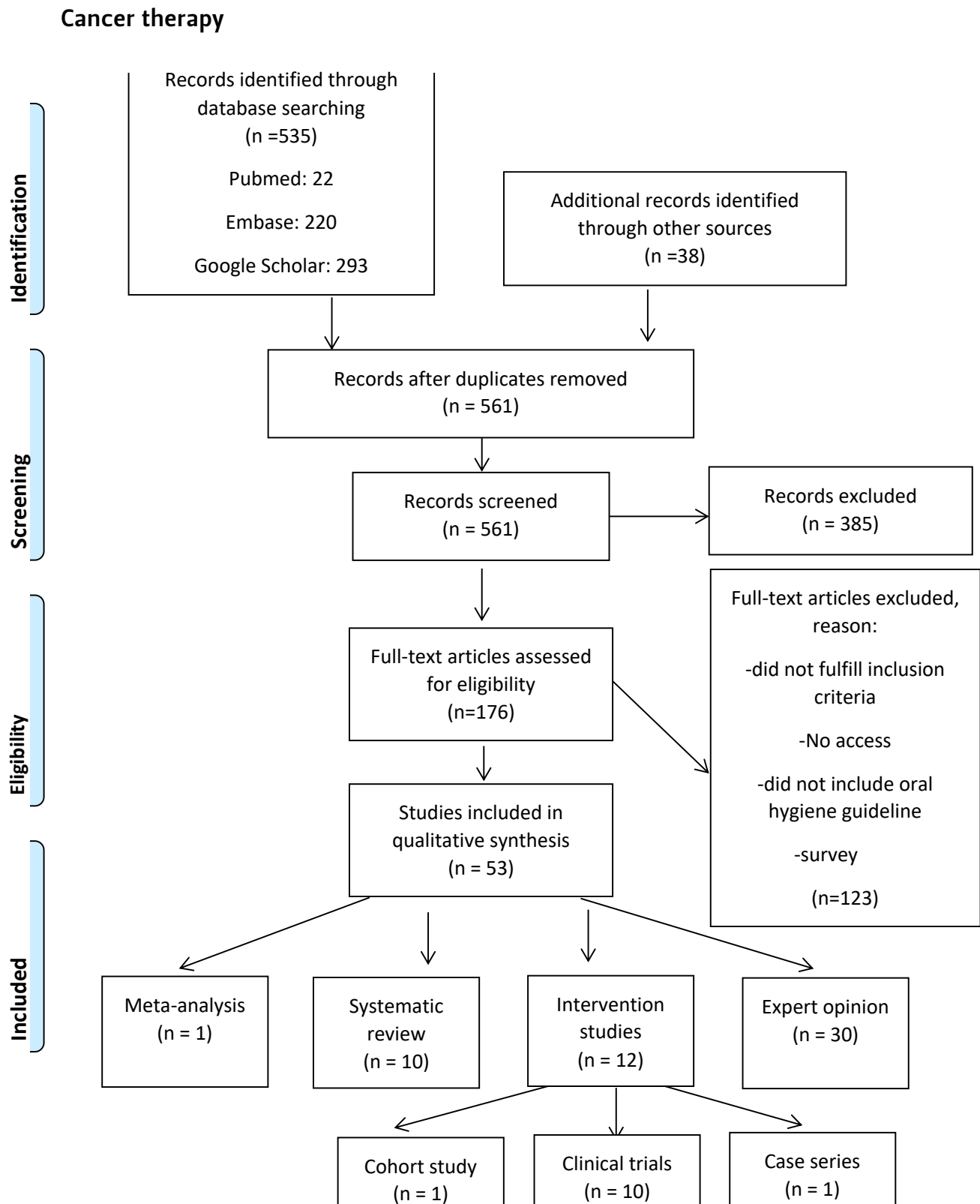


Fig. 3: Flow diagram of study selection

cancer treatment), and xerostomia. The recommendations varied depending on the intended treatment outcome, certain advices were recommended or discouraged by the associations.

The management of oral mucositis

A meta-analysis assessed the impact of nine mouthwashes on the prevention of oral mucositis (YU ET AL. 2020). Basic oral care and clinical guidelines for oral hygiene management were evaluated in a systematic review (HONG ET AL. 2019), a cohort study (CHENG ET AL. 2001), and three clinical treatment trials (DODD ET AL. 2000; KARTIN ET AL. 2014; NIIKURA ET AL. 2020). A clinical treatment trial assessed the effectiveness of three mouthwashes (DODD ET AL. 2000). Another clinical treatment trial evaluated the effectiveness of a saline mouthwash and education program (HUANG ET AL. 2018). One clinical treatment trial investigated the effect of improved dental care to prevent oral mucositis (DJURIC ET AL. 2006). Four of these seven clinical treatment trials had a high risk of bias owing to poor randomization, deficiencies in group allocation concealment, shortcomings in blinding, and a lack of a control group (DODD ET AL. 2000; CHENG ET AL. 2004; DJURIC ET AL. 2006; KARTIN ET AL. 2014). These findings are summarized in Table I and Table II.

Guidelines for the prevention and treatment of oral mucositis

Oral care protocol

B/C A randomized controlled trial (RCT) assessed the impact of professional oral care on preventing everolimus-induced mucositis in 175 patients and was rated as level 1+ (high level of evidence) with a grade B recommendation (NIIKURA ET AL. 2020). The latest update from the MASCC/ISOO association in 2019 showed that an oral care protocol including toothbrushing with a soft toothbrush, flossing, and using more than one mouthwash was effective in preventing oral mucositis. However, there was insufficient evidence to provide a universal oral care protocol recommendation for preventing oral mucositis, with a level of evidence 2+ (moderate) and a grade C recommendation (HONG ET AL. 2019). Despite this, evidence supports the use of a basic oral care protocol. Expert opinions were sought to provide guidance, as no clinical trials showed a clear superiority of one intervention over another (MCGUIRE ET AL. 2013).

Mouthwash

A The effectiveness of different mouthwashes in preventing oral mucositis in patients undergoing chemotherapy and radiation therapy was assessed through a meta-analysis of randomized controlled trials. The results ranked the solutions based on their effectiveness, with curcumin and honey showing the greatest effectiveness, followed by benzydamine, chlorhexidine, allopurinol, sucralfate, granulocyte-macrophage colony-stimulating factor, povidone-iodine, aloe, and placebo in that order (YU ET AL. 2020).

A The study by HUANG ET AL. (2018) found that the combination of a 0.9% saline mouthwash and wet dressing gauze was effective in reducing symptoms of radiation-induced mucositis and improving oral comfort. This intervention was associated with improved physical and social-emotional function.

B The systematic review by MASCC/ISOO concluded that the use of chlorhexidine is not recommended for the prevention of

oral mucositis in patients undergoing head and neck radiation therapy, owing to reported adverse effects such as increased discomfort, taste alteration, and teeth staining. There is limited or conflicting evidence regarding the use of chlorhexidine in cancer patients, hence a recommendation could not be made (HONG ET AL. 2019).

C No significant differences were found in the duration of the signs and symptoms of oral mucositis between chlorhexidine gluconate, magic mouthwash (consisting of Lidocain, Benadryl and Maalox), and a salt and sodium bicarbonate solution (DODD ET AL. 2000).

D The MASCC/ISOO systematic review found limited data on the use of saline or sodium bicarbonate rinses in preventing oral mucositis, making it impossible to establish guidelines. Despite the paucity of data, these rinses were recognized as non-irritating and potentially helpful in maintaining oral hygiene and improving patient comfort (HONG ET AL. 2019).

D Experts recommended rinsing with bland solutions 4 to 6 times daily (HARRIS ET AL. 2008; BECKER-SCHIEBE ET AL. 2012; EILERS ET AL. 2014; PETERSON ET AL. 2015; DE SANCTIS ET AL. 2016).

The management of radiation caries

Three systematic reviews established guidelines for oral care strategies, incorporating RCTs, cohort studies, and case control studies (CARVALHO ET AL. 2018; COHEN ET AL. 2016; HONG ET AL. 2018). The systematic review by COHEN ET AL. (2016) only searched the PubMed database, a major methodological limitation. A randomized controlled trial by PAPAS ET AL. (2008) compared the effects of remineralizing and conventional toothpastes on caries prevention. Tables III and IV illustrate the evaluated studies.

Guidelines for prevention and treatment of radiation caries

Mechanical cleaning

A A systematic review that included only randomized controlled trials with a level 1++ or 1+ evidence recommends brushing at least three times a day with an ultra-soft bristled toothbrush. In cases of open ulcerative lesions in the oral cavity or if the patient cannot tolerate a soft toothbrush or has a low neutrophil and platelet count ($<500/\text{mm}^3$, $<40\,000/\text{mm}^3$, respectively) during oncological treatment, the oral cavity should be cleaned using gauzes moistened with 0.12% chlorhexidine or oral sponges (CARVALHO ET AL. 2018).

A It is recommended to practice dental flossing regularly (CARVALHO ET AL. 2018).

D Alternative methods to clean the oral cavity included using a gloved finger (MILLER & KEARNEY 2001) or cotton Q-tip swabs (JOSHI 2010).

D A single tufted toothbrush or a children's toothbrush may be helpful for plaque control, as suggested by (ELIYAS ET AL. 2013; KUMAR ET AL. 2013).

D It is recommended to brush for at least 90 s (LARSON ET AL. 1998; EPSTEIN & SCHUBERT 1999; RUBENSTEIN ET AL. 2004; HARRIS ET AL. 2008; SIERACKI ET AL. 2009).

D It is recommended to replace the toothbrush every month (PETERSON ET AL. 2015).

D Floss picks may be a useful aid for oral hygiene (CHAI ET AL. 2006).

D Starting interdental cleaning during oncological treatment should be avoided, as it may cause gingival bleeding and damage the epithelial barrier, particularly if it has never been performed prior to therapy (PETERSON 2015).

Toothpaste

A Two phases fluoride toothpastes (≥ 1100 ppm) with calcium and phosphate ions are recommended (PAPAS ET AL. 2008; CARVALHO ET AL. 2018).

D Expert opinions recommended using toothpastes with an increased fluoride concentration of 5000 ppm (KIELBASSA ET AL. 2006; JOSHI 2010; KUMAR ET AL. 2013; RAY-CHAUDHURI ET AL. 2013; JAWAD ET AL. 2015).

D For patients with ulcers and xerostomia, the preferred toothpastes are those without detergents (MOSLEMI ET AL. 2016), non-mint flavor (TURNER ET AL. 2013; ELAD ET AL. 2015) and free of sodium lauryl sulfate (ANDREWS & GRIFFITHS 2001; PILOTTE ET AL. 2011; ELIYAS ET AL. 2013; ELAD ET AL. 2016). In the absence of such toothpastes, a children's toothpaste may serve as a suitable alternative (PILOTTE ET AL. 2011; PINNA ET AL. 2015; ELAD ET AL. 2016).

D Bicarbonate-based toothpastes (ANDREWS ET AL. 2001) were found to be effective in lowering the acidity of the mouth's pH (JOSHI 2010).

D Toothpastes containing casein phosphopeptide-amorphous calcium phosphate (CPP-ACP) have been suggested for the prevention of caries (KÖSTLER ET AL. 2001; CHAI ET AL. 2006; RANKIN ET AL. 2008; JAWAD ET AL. 2015; PALMIER ET AL. 2020). In case of incipient carious lesions, the use of these toothpastes has been shown to aid in remineralizing the teeth (JOSHI 2010).

Mouthwash

A It is strongly recommended to use a 0.05% fluoride mouthwash daily prior to undergoing oncological treatment and to continue using it after the treatment has been completed (CARVALHO ET AL. 2018).

A/B Two systematic reviews support the use of 0.12% alcohol-free chlorhexidine for individuals with difficulty controlling bacterial biofilm (CARVALHO ET AL. 2018; HONG ET AL. 2018). It is recommended to rinse the oral cavity with the solution once or twice daily for the reduction of plaque buildup and *S. mutans* counts (HONG ET AL. 2018).

Toothbrushing techniques

D The recommended toothbrushing techniques included the Bass and the modified Bass technique (RAY-CHAUDHURI ET AL. 2013; PETERSON ET AL. 2015).

Fluoride application

A It is essential to use fluoride daily at the start of oncological treatment in order to prevent caries in patients undergoing head and neck radiation therapy and to continue its use afterwards (CARVALHO ET AL. 2018).

A An intraoral fluoride-releasing system (IFRS) that contains sodium fluoride was found to be as effective as a custom-made fluoride carrier with stannous fluoride gel in preventing caries (CHAMBERS ET AL. 2006). IFRS is recommended as a viable alternative, especially for patients with low compliance.

B The choice of fluoride delivery system did not have a significant impact on the level of caries in post-head and neck radiation patients (HONG ET AL. 2018).

D The use of a custom-made carrier for 1% sodium fluoride gel application has been recommended by some experts (VISSINK ET AL. 2003; KIELBASSA ET AL. 2006; RANKIN ET AL. 2008; SCHWEYEN ET AL. 2011; COHEN ET AL. 2016; SHEIKH ET AL. 2020).

D It has been advised to use a brush-on technique to apply either 0.4% stannous fluoride or 1.1% sodium fluoride to the teeth (TOLJANIC & SAUNDERS 1984; KEENE & FLEMING 1987; CHAMBERS ET AL. 1995).

Management of xerostomia

A systematic review assessed topical treatments for reducing radiation-induced dry mouth (FURNESS ET AL. 2011). Two clinical treatment trials compared the efficacy of chewing gum to artificial saliva or standard care in reducing xerostomia, with both studies finding that chewing gum was more effective, though without statistically significant results (DAVIES 2000; KAAE ET AL. 2020). These studies were rated to have a high risk of bias owing to methodological limitations. Another RCT (CHAMBERS ET AL. 2006) compared the use of intraoral fluoride-releasing systems and fluoride carriers, with no differences in caries rates between the two fluoride systems. The findings are summarized in Table V and Table VI.

Guidelines for saliva substitutes and stimulants

A Artificial saliva should be used to lubricate the oral mucosa in cases of xerostomia. It should be applied before meals, before sleeping, and whenever necessary to promote lubrication of the oral cavity (CARVALHO ET AL. 2018).

A A systematic review evaluated saliva stimulants and substitutes and found that the oxygenated glycerol triester saliva substitute spray was more effective than an electrolyte spray. Additionally, chewing gum was equally effective in increasing saliva production for individuals with xerostomia compared to saliva substitutes (FURNESS ET AL. 2011). This conclusion was confirmed by a recent randomized controlled trial (KAAE ET AL. 2020).

D A case series by WARDE ET AL. (2000) found that using a combination of Biotene mouthwash, toothpaste, chewing gum, and Oralbalance gel could alleviate many symptoms of xerostomia caused by radiation therapy.

D A mixture of baking soda, salt, and water was found to effectively alleviate symptoms of xerostomia (COHEN ET AL. 2016).

Discussion

The aim of this scoping review was to assess the recommendations for maintaining oral health in patients undergoing chemotherapy, radiation therapy, or both. A total of 53 articles were evaluated and categorized into three groups based on their treatment objective: oral mucositis management, radiation caries prevention, and xerostomia management. The recommendations varied depending on the intended treatment outcome. Chlorhexidine was not advised for preventing oral mucositis in patients receiving head and neck radiation therapy, however, it was effective in preventing caries.

Most of the articles included in this scoping review were based on expert opinions with low levels of evidence, but the review also included ten systematic reviews and one meta-analysis with high levels of evidence. This demonstrates the availability of robust evidence for oral care in these patients.

The studies included in this review are found to entail risks of bias, such as ascertainment bias, comparison bias, and performance bias, leading to a lower rating of the level

of evidence and grade of recommendation according to the SIGN Guidelines. Furthermore, the use of different mucositis severity gradings, such as the WHO Oral Toxicity Scale and Eiler's Oral Assessment Guide, made it difficult to compare the studies. In some cases, recommendations could not be made owing to a dearth of data. The MASSC/ISOO study group was unable to provide guidelines for the use of saline or sodium bicarbonate mouthwashes in preventing oral mucositis, but suggested that their use might be beneficial for oral hygiene. A systematic review by (FURNESS ET AL. 2011) found that an oxygenated glycerol triester saliva substitute was more effective for treating xerostomia than an electrolyte spray, but there was not enough evidence to strongly recommend its use.

This scoping review incorporated a broad range of articles, including both high- and low-evidence-based sources, but was limited by the fact that the eligibility assessment was conducted by only one investigator. It was unable to establish a standardized oral care protocol. Instead, it provided recommendations that should be considered as potential management approaches based on the current evidence base. However, it is crucial to consider that further research in the form of

randomized controlled clinical trials, systematic reviews, and meta-analyses are needed to establish more robust evidence-based recommendations.

Conclusions

This scoping review analyzed guidelines for oral health management in patients undergoing oncological treatments, including the management of oral mucositis, radiation caries, and xerostomia. The following recommendations were based on high-quality evidence:

- Oral mucositis management: Oral care protocols and professional oral care are effective in alleviating symptoms of oral mucositis. Honey and curcumin were found to be helpful in the management of oral mucositis.
- Radiation caries management: Daily use of a fluoride toothpaste with ≥ 1100 ppm, a 0.05% fluoride mouthwash, topical fluoride application, and a fluoride-releasing system are recommended for reducing the burden of radiation caries.
- Xerostomia management: Saliva stimulants and substitutes may lubricate the oral cavity, and chewing gum was found to be as effective as saliva substitutes in increasing saliva production.

Tab.1 Overview of the evidence derived from systematic reviews and meta-analyses on the management of oral mucositis

Author and title	Evidence level	Objective	Methodology	Study quality	Type of studies	Outcome
Yu YY et al. 2020: Effects of 9 oral care solutions on the prevention of OM: a network meta-analysis of randomized controlled trials	1++	Effect of different oral care solutions on the prevention of OM in patients that had chemotherapy or radiation therapy	PubMed, Embase, Scopus, Cochrane Library, Google Scholar	Cochrane Handbook, risk ratios (RR) with 95% confidence intervals (CIs), inconsistency test, network meta-analysis	RCT (n = 28)	Chlorhexidine, benzydamine, honey and curcumin were more effective than placebo ($p < 0.05$); honey and curcumin were more effective than povidone-iodine ($p < 0.05$). Probability ranking according to the Surface Under the Cumulative Ranking curve showed the following treatments: curcumin > honey > benzydamine > chlorhexidine > allopurinol > sucralfate > granulocyte-macrophage colony-stimulating factor > povidone-iodine > aloe > placebo.
Hong CHL et al. 2019: Systematic review of basic oral care for the management of OM in cancer patients and clinical practice guidelines	1+	Update clinical practice guidelines for the use of basic oral care interventions for the prevention and treatment of OM	PubMed, Web of Science	Levels of evidence by Somerfield criteria, flaws by Hadorn criteria	RCT (n = 8), comparative studies (n = 7), non-comparative studies (n = 2)	Oral care protocol is beneficial (level of evidence III). Chlorhexidine should not be used to prevent OM in patients that are undergoing head and neck radiation therapy (level of evidence III). No guideline was possible for professional oral care, patient education, saline, sodium bicarbonate.

Tab. II Overview of the evidence derived from clinical treatment trials on the management of oral mucositis

Author and title	Study type	Evidence level	Number of patients	Patient characteristics	Intervention	Comparison	Length of follow-up	Outcome measure	Effect size
Cheng KKF et al. 2001: Evaluation of an oral care protocol intervention in the prevention of chemotherapy-induced oral mucositis in paediatric cancer patients	cohort study	2+	n = 42: intervention (n = 21), control (n = 21)	Children (6–17 years), had high-dose or combination chemotherapy for haematological malignancies or solid tumors, were capable to brush or rinse	Intervention group: toothbrush: soft bristles for 90 s mouth rinse: 60 ml of 0.9% sodium chloride for 30 s, 10 ml of 0.2% chx for 30 s technique: Bass Sulcular	Effect of oral care protocol	8 months	Severity of mucositis (Eilers' Oral Assessment Guide), oral mucositis-related pain (Faces Scale)	Intervention group: significant reduction of severity of oral mucositis (p = 0.000002) and related pain (p = 0.0001)
General note: Risk of bias: no blinding of subjects and investigators.									
Cheng KKF et al. 2004: Prevention of oral mucositis in paediatric patients treated with chemotherapy: a randomised crossover trial comparing two protocols of oral care	RCT	2-	n = 40: 1st group: chx (n = 20), 2nd group: benzydamine (n = 20)	Children (6–17 years), had high-dose or combination chemotherapy for haematological malignancies or solid tumors, were capable to brush or rinse	Mouth rinse: saline, 0.2% chx gluc or 0.15% benzydamine hydrochloride Technique: Bass	chx vs benzydamine	6 weeks	Severity of mucositis (Eilers' Oral Assessment Guide), occurrence of ulcerative lesions	chx group: significant reduction in ulcerative lesions (p < 0.05) and severity of mucositis (p < 0.05)
General notes: Compliance of >80% achieved, monitored by assessing the frequency of oral care recorded in the diary and determination amount of rinse left in the bottle. Risk of bias: this study did not include a control group; poor description of randomization; no blinding of subjects and investigators.									
Dodd MJ et al. 2000: Randomized clinical trial of the effectiveness of 3 commonly used mouthwashes to treat chemotherapy-induced mucositis	RCT	2+	n = 200: 1st group: chx (n = 51), 2nd group: magic (n = 42), 3rd group: salt and soda (n = 49)	Adults (>18 years), are receiving stomatoc chemotherapy, presence of mucositis	toothbrush: 90 s mouth rinse: 0.12% chx gluc or magic mouthwash (lidocaine, benadryl and maolox) or salt and soda mouthwash 4 t/d/20 s	chx gluc vs magic mouthwash vs salt and soda	Until cessation of signs and symptoms of OM, or 12 days	Severity of mucositis (Eiler's Oral Assessment Guide), time of cessation, pain score	Nonsignificant differences between these three mouth rinses
General note: Risk of bias: this study did not include a control group; poor description of randomization.									
Djuric M et al. 2006: Mucositis prevention by improved dental care in acute leukemia patients	RCT	1-	n = 34: intervention (n = 15), control (n = 19)	adults (>19 years), had acute leukemia, are receiving induction remission therapy, at least 10 teeth	Intervention group: prechemotherapy: scaling and polishing, restorative measurements toothbrush: round-ended soft nylon bristles or cotton buds, 2 t/d mouth rinse: 0.12% chx gluc mixed with 3% H ₂ O ₂ and nystatin, 3 t/d technique: Stillman Control group: mouth rinse: 0.12% chx gluc mixed with 3% H ₂ O ₂ and nystatin, 3 t/d	Effect of dental care program	28 days	OHI, GI, WHO Oral Toxicity Scale	Intervention group: lower mean values of GI, OHI and mucositis score, but not statistically significant on most of the examination days
General note: Risk of bias: poor description of randomization; no concealment method; no blinding of subjects and investigators; groups were not treated equally at baseline: intervention group became dental treatment before chemotherapy consisting of scaling, polishing and restorative measurements, whereas control group did not receive any.									
chx: chlorhexidine, chx gluc: chlorhexidine gluconate, F: fluoride, GI: gingiva index, OHI: oral hygiene index, OM: oral mucositis, QOL: questionnaire for quality of life, VAS: visual analogue scale, EORTC QLQ-C30: European Organisation for the Research and Treatment of Cancer Quality of Life Core 30 Questionnaire.									

Tab. II Overview of the evidence derived from clinical treatment trials on the management of oral mucositis

Author and title	Study type	Evidence level	Number of patients	Patient characteristics	Intervention	Comparison	Length of follow-up	Outcome measure	Effect size
Huang B et al. 2017: The effectiveness of a saline mouth rinse regimen and education programme on radiation-induced oral mucositis and a quality of life in oral cavity cancer patients: A randomised controlled trial	RCT	1++	n = 96: intervention (n = 51), control (n = 45)	Adults (>20 years), diagnosed with oral cavity cancer and undergoing postoperative adjuvant radiation therapy and concurrent chemotherapy	Intervention group: mouth rinse: 0.9% saline with wet dressing gauze 4 t/d/8 w Control group: mouth rinse: boiled water	Saline mouth rinse and education program vs standard care	8 weeks	WHO Oral Toxicity Scale, MSS-moo, UW-QOL	Intervention group: significant decrease of physical and social-emotional QOL (p < 0.05), WHO Oral Toxicity Scale and MSS-moo no significant difference
General notes: MSS-moo: radiation-induced oral mucositis-related symptoms. UW-QOL: physical function and social-emotional function.									
Kartin PT et al. 2014: Effect of an oral mucositis protocol on quality of life of patients with head and neck cancer treated with radiation therapy	RCT	1-	n = 50: intervention (n = 20), control (n = 30)	Adults (>18 years), nasopharyngeal, laryngeal, gingival, hypopharyngeal, tongue and salivary gland head neck cancers, absence of oral mucositis	Intervention group: toothbrush: soft-bristled, after every meal and before bed mouth rinse: sodium bicarbonate 4 t/d, water or oral care solution after meals, before bed and during night technique: Stillman other aids: dental floss, sugar-free chewing gum, ice chips, tongue cleaner	Effect of oral care and nutrition protocol	20 months	WHO Oral Toxicity Scale, VAS, SGA, EORTC QLQ-C30	Intervention group: significant decrease of VAS (p = 0.014), mucositis degree (p < 0.001) and malnutrition (p < 0.05)
General notes: Risk of bias: poor description of randomization; no concealment method; no blinding of subjects and investigators. SGA: Subjective Global Assessment.									
Niikura N et al. 2020: Oral care evaluation to prevent oral mucositis in estrogen receptor-positive metastatic breast cancer patients treated with everolimus (Oral Care-BC): A randomized controlled phase III trial	RCT	1+	n = 175: intervention (n = 82), control (n = 87)	Women aged 20 years or older, postmenopausal, metastatic hormone receptor-positive, HER1-negative breast cancer, adequate renal function, newly prescribed everolimus 10 mg and exemestane 25 mg	Intervention group: periodontal treatment: scaling, crown polishing brushing: tongue cleaning mouth rinse: 0.2% Neostein Green other aids: dexaltin ointment control group: mouth rinse: saline	Professional oral care before everolimus treatment	8 weeks	Incidence of oral mucositis	Significant decrease of incidence of grade 1 and 2 oral mucositis in the intervention group (p = 0.34, p = 0.15, respectively)
General note: Risk of bias: no referring to blinding of the subjects or investigators.									
chx: chlorhexidine, chx gluc: chlorhexidine gluconate, F: fluoride, Gi: gingiva index, OHI: oral hygiene index, OM: oral mucositis, QOL: questionnaire for quality of life, VAS: visual analogue scale, EORTC QLQ-C30: European Organisation for the Research and Treatment of Cancer Quality of Life Core 30 Questionnaire.									

Tab. III Overview of the evidence derived from systematic reviews and meta-analyses on the management of radiation caries

Author and title	Evidence level	Objective	Methodology	Study quality	Type of studies	Outcome
Carvalho CG et al. 2018: Guide for health professionals addressing oral care for individuals in oncological treatment based on scientific evidence	1++	Guide for oral care of oncological patients	PubMed, Cochrane, EBSCOHost	SIGN, PICO, AMSTAR, MERGE	n = 54: RCT, systematic review of RCT	Oral assessment and professional and home care before, during and after oncological treatment Treatment of xerostomia with saliva substitute and hydration
General notes: AMSTAR: Assessing the Methodological Quality of Systematic Reviews. MERGE: Method for Evaluating Research and Guideline Evidence.						
Cohen EEW et al. 2016: American Cancer Society Head and Neck Cancer Survivorship Care Guideline	2+	Guideline that provides recommendations on best practices in the management of adults after head and neck cancer treatment	PubMed	Level of evidence, expert panel was convened to develop guideline based on this systematic review	RCT, cohort studies, case-control	Most evidence is not sufficient to provide a strong recommendation. Brushing with remineralizing dentifrice, use of dental floss and fluoride use (1.1% sodium fluoride as dentifrice or incustomized delivery trays)
Hong CHL et al. 2018: A systematic review of dental disease management in cancer patients	1+	Update efficiency of dental strategies in preventing dental-related complications in cancer patients	PubMed, Embase	Electronic collection form customized for reviewing dental disease data, level of evidence by Somerfield criteria, flaws by Hadorn criteria	n = 59: RCT, cohort studies, case series, cross-sectional studies	Use of fluoride products to prevent dental caries. Type of fluoride delivery system does not significantly influence caries activity (level of evidence II, grade of recommendation B). Use of chx mouth rinse 0.12 - 0.2% once or twice daily (level of evidence II, grade of recommendation B)

Tab. IV Overview of the evidence derived from clinical treatment trials on the management of radiation caries

Author and title	Study type	Evidence level	Number of patients	Patient characteristics	Intervention	Comparison	Length of follow-up	Outcome measure	Effect size
Papas A et al. 2008: Caries remineralising toothpaste in radiation patients	RCT	1++	n = 57: Enamelon (n = 28), conventional (n = 29)	Adults (>18 years), had radiation to the head and neck; reduction of unstimulated salivary flow to below 0.2 ml/min, at least 10 teeth	Enamelon toothpaste 1100 ppm with additional calcium phosphate (intervention group), conventional fluoride toothpaste 1100 ppm (control group); mouthrinse: 0.05% sodium fluoride 1t/d Other aids: topical fluoride varnish, dental floss, pilocarpine	Enamelon toothpaste with 1100 ppm and additional calcium phosphate vs conventional toothpaste 1100 ppm	12 months	root caries, coronal caries, salivary flow rate, PI, GI, level of <i>S. mutans</i> and lactobacillus	toothpaste: significant lower root caries (p = 0.03), no significant difference for coronal caries

Tab. V Overview of the evidence derived from a systematic review on the management of xerostomia

Author and title	Evidence level	Objective	Methodology	Study quality	Type of studies	Outcome
Furness S et al. 2011: Interventions for the management of dry mouth: topical therapies	1++	Topical treatments that are effective in reducing xerostomia	Cochrane, Medline, Embase, Cimahl, Amed, Cancerlit	Data extraction form, RR with 95% CIs, risk of bias using two-part tool by Cochrane reviews, sensitivity analysis	RCT (n = 36)	No strong evidence that any topical therapy is effective for relieving the symptom of dry mouth. Oxygenated glycerol triester saliva substitute spray is more effective than an aqueous electrolyte spray. Chewing gum increases saliva production, but there is no evidence that gum is better or worse than saliva substitution.

Tab. VI Overview of the evidence derived from clinical treatment trials on the management of xerostomia

Author and title	Study type	Evidence level	Number of patients	Patient characteristics	Intervention	Comparison	Length of follow-up	Outcome measure	Effect size
Chambers MS 2005: Clinical evaluation of the intraoral fluoride releasing system in radiation-induced xerostomic subjects. Part 2: Phase I study	RCT	1++	n = 22: intervention group (n = 10), control group (n = 12)	Adults (>18 years), undergone radiation therapy min 40 Gy at least 3 months prior to study, unstimulated salivary flow less than 0.3 g/min	Toothbrush: Colgate-Palmolive Toothpaste: 1100 ppm fluoride 2t/d Intervention group: intraoral fluoride-releasing system Control group: custom-made fluoride carriers with 0.4% stannous fluoride gel, 1t/d/10 min	Intraoral fluoride-releasing system vs fluoride carriers	48 weeks	Caries, hematologic and renal parameters	No significant differences in caries rate, hematologic or renal complications
Davies AN 2000: A comparison of artificial saliva and chewing gum in the management of xerostomia in patients with advanced cancer	RCT	2-	n = 43, crossover design	Xerostomia, malignant disease, estimated prognosis of 2 weeks	Artificial saliva: mucin-based Saliva Orthana in spray form 4t/d Chewing gum: sugar-free Freedent 4 t/d/10 min, 2 pieces at a time	Chewing gum vs artificial saliva	12 days	VAS, questionnaire	No statistically significant difference in VAS Questionnaire: relief of xerostomia, but side effect
General note: Risk of bias: this study did not include a control group, poor description of randomization, no blinding of subjects and investigators, no concealment method, high drop-out rate of 36%.									
Kaaze JK et al. 2020: A randomized phase III trial for alleviating radiation-induced xerostomia with chewing gum	RCT	1+	n = 109: 1st group: chewing gum (n = 68), 2nd group: standard care (n = 41)	Adults (>18 years), physician-assessed xerostomia, >6 months after radiation therapy, disease-free and able to chew gum	1st group: chewing gum tasteless and sugar-free, 5 t/d/5 min 2nd group: saliva substitutes or stimulants	Chewing gum vs standard care	1 month	EORTC QLQ-H&N35, GRX questionnaire, salivary flow and viscosity	Both groups: reduction of dry mouth scores, salivary flow increase and viscosity decrease, but no significant differences between these two groups
General notes: Risk of bias: no blinding of subjects and investigators, no concealment method. EORTC QLQ-H&N35: scoring of dry mouth. GRX questionnaire: Groningen Radiotherapy-Induced Xerostomia.									
Warde P et al. 2000: A phase II study of Biotene in the treatment of postirradiation xerostomia in patients with head and neck cancer	Case series	3	n = 28	Post-irradiation xerostomia, more than 75% of both parotid glands included in the primary radiation field	Toothbrush: soft Toothpaste: Biotene (fluoridated and lactoperoxidase) Mouthrinse: Biotene 3 t/d Other aids: Biotene chewing gum, Oralbalance gel	Effect of Biotene dentifrice, mouthwash, chewing gum and Oralbalance gel	2 months	VAS, xerostomia questionnaire	Significant improvement of VAS, subjective improvement of oral dryness, ability to eat, oral discomfort
VAS: Visual Analogue Scale									

Zusammenfassung

Einleitung

Ziel dieses Scoping Review war, eine klinische Leitlinie für das Management der Mundgesundheit von Patienten nach Chemo- und/oder Radiotherapie zu erstellen.

Materialien und Methoden

Es wurde eine elektronische Recherche in PubMed, Embase, Cochrane und Google Scholar durchgeführt. Systematische Übersichtsarbeiten, Meta-Analysen, klinische Interventionsstudien, Fallserien und Expertenmeinungen wurden ausgewertet. Das SIGN-Guideline-System wurde verwendet, um den Evidenzgrad und die Empfehlungsklasse der eingeschlossenen Studien zu bewerten.

Ergebnisse

53 Studien erfüllten die Einschlusskriterien. Die Ergebnisse zeigten das Vorhandensein von Empfehlungen für Patienten nach Radio- und/oder Chemotherapie in drei Bereichen: das Handling von oraler Mukositis, Prävention und Kontrolle von Strahlentherapie und das Management von Xerostomie. Die Mehrheit der eingeschlossenen Studien hatten jedoch ein niedriges Evidenzniveau.

Diskussion

Dieses Review umfasst Leitlinien für medizinisches Fachpersonal, das Patienten betreut, die eine Chemo- und/oder Strahlentherapie erhalten haben. Eine einzige Standardempfehlung konnte aufgrund mangelnder hochevidenzbasierter Daten nicht erstellt werden.

References

- ANDREWS N, GRIFFITHS C: Dental complications of head and neck radiotherapy: Part 2. *Aust Dent J* 46: 174–182 (2001)
- BECKER-SCHIEBE M, LORDICK F, HOFFMANN W: Treatment of radiation-induced mucocutaneous toxicity. *Memo Mag Eur Med Oncol* 5: 39–42 (2012)
- CARVALHO C G, MEDEIROS-FILHO J B, FERREIRA M C: Guide for health professionals addressing oral care for individuals in oncological treatment based on scientific evidence. *Support Care Cancer* 26: 2651–2661 (2018)
- CHAI W L, NGEOW W C, RAMLI R, RAHMAN R A: Managing complications of radiation therapy in head and neck cancer patients: Part II. Management of radiation-induced caries. *Singapore Dent J* 28: 4–6 (2006)
- CHAMBERS M S, TOH B B, MARTIN J W, FLEMING T J, LEMON J C: Oral and dental management of the cancer patient: prevention and treatment of complications. *Support Care Cancer Off J Multinatl Assoc Support Care Cancer* 3: 168–175 (1995)
- CHAMBERS M S, MELLBERG J R, KEENE H J, BOUWEMA O J, GARDEN A S, SIPOS T, FLEMING T J: Clinical evaluation of the intraoral fluoride releasing system in radiation-induced xerostomic subjects. Part 1: fluorides. *Oral Oncol* 42: 934–945 (2006)
- CHENG K K F, MOLASSIOTIS A, CHANG A M, WAI W C, CHEUNG S S: Evaluation of an oral care protocol intervention in the prevention of chemotherapy-induced oral mucositis in paediatric cancer patients. *Eur J Cancer* 37: 2056–2063 (2001)
- CHENG K K F, CHANG A M, YUEN M P: Prevention of oral mucositis in paediatric patients treated with chemotherapy: a randomised crossover trial comparing two protocols of oral care. *Eur J Cancer Oxf Engl* 40: 1208–1216 (2004)
- COHEN E E W, LAMONTE S J, ERB N L, BECKMAN K L, SADEGHI N, HUTCHESON K A, STUBBLEFIELD M D, ABBOTT D M, FISHER P S, STEIN K D, LYMAN G H, PRATT-CHAPMAN M L: American cancer society head and neck cancer survivorship care guideline. *CA Cancer J Clin* 66: 203–239 (2016)
- DAVIES P: The relevance of systematic reviews to educational policy and practice. *Oxf Rev Educ* 26: 365–378 (2000)
- DE SANCTIS V, BOSSI P, SANGUINETI G, TRIPPA F, FERRARI D, BACIGALUPO A, RIPAMONTI C I, BUGLIONE M, PERGOLIZZI S, LANGENDIJK J A, MURPHY B, RABER-DURCHLACHER J, RUSSI E G, LALLA R V: Mucositis in head and neck cancer patients treated with radiotherapy and systemic therapies: Literature review and consensus statements. *Crit Rev Oncol Hematol* 100: 147–166 (2016)
- DJURIC M, HILLIER-KOLAROV V, BELIC A, JANKOVIC L: Mucositis prevention by improved dental care in acute leukemia patients. *Support Care Cancer* 14: 137–146 (2006)
- DODD M J, DIBBLE S L, MIASKOWSKI C, MACPHAIL L, GREENSPAN D, PAUL S M, SHIBA G, LARSON P: Randomized clinical trial of the effectiveness of 3 commonly used mouthwashes to treat chemotherapy-induced mucositis. *Oral Surg Oral Med Oral Pathol Oral Radiol Endod* 90: 39–47 (2000)
- EILERS J, MILLION R: Clinical Update: Prevention and management of oral mucositis in patients with cancer. *Semin Oncol Nurs* 27: 1–16 (2011)
- EILERS J, HARRIS D, HENRY K, JOHNSON L A: Evidence-based interventions for cancer treatment-related mucositis: Putting evidence into practice. *Clin J Oncol Nurs* 18: 80–96 (2014)
- ELAD S, RABER-DURLACHER J E, BRENNAN M T, SAUNDERS D P, MANK A P, ZADIK Y, QUINN B, EPSTEIN J B, BLIJLEVENS N M A, WALTIMO T, PASSWEG J R, CORREA M E P, DAHLÖF G, GARMING-LEGERT K U E, LOGAN R M, POTTING C M J, SHAPIRA M Y, SOGA Y, STRINGER J, STOKMAN M A, VOKURKA S, WALLHULT E, YAROM N, JENSEN S B: Basic oral care for hematology-oncology patients and hematopoietic stem cell transplantation recipients: A position paper from the joint task force of the Multinational Association of Supportive Care in Cancer / International Society of Oral Oncology (MASCC/ISOO) and the European Society for Blood and Marrow Transplantation (EBMT). *Support Care Cancer* 23: 223–236 (2015)
- ELAD S, HOROWITZ R, ZADIK Y, HOWARD S S, PILITSIS J G (EDS.): Supportive and palliative care in dentistry and oral medicine. The art and science of palliative medicine, Hong Kong (2016)
- ELIYAS S, PORTER R, BRIGGS P, PATEL R R: Effects of radiotherapy to the jaws. 2: Potential solutions. *Eur J Prosthodont Restor Dent* 21: 170–181 (2013)
- EPSTEIN J B, SCHUBERT M M: Oral mucositis in myelosuppressive cancer therapy. *Oral Surg Oral Med Oral Pathol Oral Radiol Endod* 88: 273–276 (1999)
- FURNESS S, WORTHINGTON H V, BRYAN G, BIRCHENROUGH S, MCMILLAN R: Interventions for the management of dry mouth: topical therapies. *Cochrane Database Syst Rev* 7: CD008934 (2011)
- HARRIS D J, EILERS J, HARRIMAN A, CASHAVELLY B J, MAXWELL C: Putting evidence into practice: Evidence-based interventions for the management of oral mucositis. *Clin J Oncol Nurs* 12: 141–152 (2008)
- HONG C H L, HU S, HAVERMAN T, STOKMAN M, NAPAÑAS J J, BRABER J B, GERBER E, GEUKE M, VARDAS E, WALTIMO T, JENSEN S B, SAUNDERS D P: A systematic review of dental disease management in cancer patients. *Support Care Cancer* 26: 155–174 (2018)
- HONG C H L, GUEIROS L A, FULTON J S, CHENG K K F, KANDWAL A, GALITI D, FALL-DICKSON J M, JOHANSEN J, AMERINGER S, KATAOKA T, WEIKEL D, EILERS J, RANNA V, VADDI A, LALLA R V, BOSSI P, ELAD S: Systematic review of basic oral care for the management of oral mucositis in cancer patients and clinical practice guidelines. *Support Care Cancer* 27: 3949–3967 (2019)
- HUANG B S, WU S C, LIN C Y, FAN K H, CHANG J T C, CHEN S C: The effectiveness of a saline mouth rinse regimen and education programme on radiation-induced oral mucositis and quality of life in oral cavity cancer patients: A randomised controlled trial. *Eur J Cancer Care* 27: e12819 (2018)
- JAWAD H, HODSON N A, NIXON P J: A review of dental treatment of head and neck cancer patients, before, during and after radiotherapy: part 2. *Br Dent J* 218: 69–74 (2015)
- JOSHI V K: Dental treatment planning and management for the mouth cancer patient. *Oral Oncol* 46: 475–479 (2010)
- KAAE J K, STENFELDT L, HYRUP B, BRINK C, ERIKSEN J G: A randomized phase III trial for alleviating radiation-induced xerostomia with chewing gum. *Radiother Oncol J Eur Soc Ther Radiol Oncol* 142: 72–78 (2020)

Résumé

Introduction

L'objectif de cette revue de littérature exploratoire était d'établir une ligne directrice clinique pour la gestion de la santé bucco-dentaire des patients après une chimiothérapie et/ou une radiothérapie.

Matériaux et méthodes

Une recherche a été effectuée dans PubMed, Embase, Cochrane et Google Scholar. Des revues systématiques, des méta-analyses, des études d'intervention clinique, des séries de cas et des avis d'experts ont été analysés. Le système lignes directrices de SIGN a été utilisé pour évaluer le niveau de preuve et la classe de recommandation des études incluses.

Résultats

53 études ont rempli les critères de sélection. Les résultats ont indiqué l'existence de recommandations pour les patients suivant une radiothérapie et/ou une chimiothérapie: le traitement de la mucite buccale, la prévention et le contrôle des caries radiatives et le traitement de la xérostomie. La majorité des études incluses étaient basées sur un niveau de preuve faible.

Discussion

Cette revue de littérature exploratoire contient des lignes directrices pour les professionnels de la santé qui s'occupent de patients ayant reçu une chimiothérapie et/ou une radiothérapie. Il n'a pas été possible d'établir une recommandation standard en raison du manque de données à haut niveau de preuve.

- KARTIN P T, TASCI S, SOYUER S, ELMALI F: Effect of an oral mucositis protocol on quality of life of patients with head and neck cancer treated with radiation therapy. *Clin J Oncol Nurs* 18: 118–125 (2014)
- KIELBASSA A M, HINKELBEIN W, HELLWIG E, MEYER-LÜCKEL H: Radiation-related damage to dentition. *Lancet Oncol* 7: 326–335 (2006)
- KUMAR N, BROOKE A, BURKE M, JOHN R, O'DONNELL A, SOLDANI F: The oral management of oncology patients requiring radiotherapy, chemotherapy and/or bone marrow transplantation. *Fac Dent J* 4: 200–203 (2013)
- LARSON P J, MIASKOWSKI C, MACPHAIL L, DODD M J, GREENSPAN D, DIBBLE S L, STEVEN P, PHARM I R: The PRO-SELF Mouth Aware program: an effective approach for reducing chemotherapy-induced mucositis. *Cancer Nurs* 21: 263–268 (1998)
- MCGUIRE D B, FULTON J S, PARK J, BROWN C G, CORREA M E P, EILERS J, ELAD S, GIBSON F, OBERLE-EDWARDS L K, BOWEN J, LALLA R V: Systematic review of basic oral care for the management of oral mucositis in cancer patients. *Support Care Cancer* 21: 3165–3177 (2013)
- MILLER M, KEARNEY N: Oral care for patients with cancer: a review of the literature. *Cancer Nurs* 24: 241–254 (2001)
- MOSLEMI D, NOKHANDANI A M, OTAGHSARAEI M T, MOGHADAMNIA Y, KAZEMI S, MOGHADAMNIA A A: Management of chemo/radiation-induced oral mucositis in patients with head and neck cancer: A review of the current literature. *Radiother Oncol* 120: 13–20 (2016)
- NIKURA N, NAKATUKASA K, AMEMIYA T, WATANABE K, HATA H, KIKAWA Y, TANIKE N, YAMANAKA T, MITSUNAGA S, NAKAGAMI K, ADACHI N, KONDO N, SHIBUA Y, HAYASHI N, NAITO M, KASHIWABARA K, YAMASHITA T, UMEDA M, MUKAI H, OTA Y: Oral care evaluation to prevent oral mucositis in estrogen receptor-positive metastatic breast cancer patients treated with everolimus (oral care-BC): A randomized controlled phase III trial. *The Oncologist* 25: 223–230 (2020)
- PALMIER N R, MIGLIORATI C A, PRADO-RIBEIRO A C, DE OLIVEIRA M C Q, VECHIATO FILHO A J, DE GOES M F, BRANDAO T B, LOPES M A, SANTOS-SILVA A R: Radiation-related caries: current diagnostic, prognostic, and management paradigms. *Oral Surg Oral Med Oral Pathol Oral Radiol* 130: 52–62 (2020)
- PAPAS A, RUSSELL D, SINGH M, KENT R, TRIOL C, WINSTON A: Caries clinical trial of a remineralising toothpaste in radiation patients. *Gerodontology* 25: 76–88 (2008)
- PETERSON D E, BOERS-DOETS C B, BENSADOUN R J, HERRSTEDT J: Management of oral and gastrointestinal mucosal injury: ESMO clinical practice guidelines for diagnosis, treatment, and follow-up. *Ann Oncol* 1: 139–151 (2015)
- PILOTTE A P, HOHOS M B, POLSON K M O, HUFTALEN T M, TREISTER N: Managing stomatitis in patients treated with mammalian target of rapamycin inhibitors. *Clin J Oncol Nurs* 15: 83–89 (2011)
- PINNA R, CAMPUS G, CUMBO E, MURA I, MILIA E: Xerostomia induced by radiotherapy: an overview of the physiopathology, clinical evidence and management of the oral damage. *Ther Clin Risk Manag* 11: 171–188 (2015)
- RANKIN K V, JONES D L, REDDING S W: Oral health in cancer therapy. 3rd edn, *Dental Oncology Education Program*, Texas (2008)
- RAY-CHAUDHURI A, SHAH K, PORTER R J: The oral management of patients who have received radiotherapy to the head and neck region. *Br Dent J* 214: 387–393 (2013)
- KEENE H J, FLEMING T J: Prevalence of caries-associated microflora after radiotherapy in patients with cancer of the head and neck. *Oral Surg Oral Med Oral Pathol* 64: 421–426 (1987)
- KÖSTLER W J, HEJNA M, WENZEL C, ZIELINSKI C C: Oral mucositis complicating chemotherapy and/or radiotherapy: Options for prevention and treatment. *CA Cancer J Clin* 51: 290–315 (2001)
- RUBENSTEIN E B, PETERSON D E, SCHUBERT M, KEEFE D, MCGUIRE D, EPSTEIN J, ELTING L S, FOX P C, COOKSLEY C, SONIS S T: Clinical practice guidelines for the prevention and treatment of cancer therapy-induced oral and gastrointestinal mucositis. *Cancer* 100: 2026–2046 (2004)
- SHEIKH A, KHAN F R, TABASSUM S: Topical fluorides for head and neck cancer patients subjected to surgical resection and radiation therapy in resource restraint settings. *J Coll Physicians Surg Pak* 30: 205–209 (2020)
- SIERACKI R L, VOELZ L M, JOHANNIK T M, KOPACZEWSKI D M, HUBERT K: Development and implementation of an oral care protocol for patients with cancer. *Clin J Oncol Nurs* 13: 718–722 (2009)
- SCHWEYER R, HEY J, FRÄNZEL W, VORDERMARK D, HILDEBRANDT G, KUHN T: Radiogene Karies: Ätiologie und Möglichkeiten der Prävention. *Strahlenther Onkol* 188: 21–28 (2011)
- TOLJANIC J A, SAUNDERS V W: Radiation therapy and management of the irradiated patient. *J Prosthet Dent* 52: 852–858 (1984)
- TURNER L, MUPPARAPU M, AKINTOYE S O: Review of the complications associated with treatment of oropharyngeal cancer: A guide to the dental practitioner. *Quintessence Int* 44: 267–279 (2013)
- VISSINK A, BURLAGE F R, SPIJKERVET F K L, JANSMA J, COPPES R P: Prevention and treatment of the consequences of head and neck radiotherapy. *Crit Rev Oral Biol Med* 14: 213–225 (2003)
- WARDE P, KROLL B, O'SULLIVAN B, ASLANIDIS J, TEW-GEOURGE E, WALDRON J, MAXYMIW W, LIU F F, PAYNE D, CUMMINGS B: A phase II study of Biotene in the treatment of postradiation xerostomia in patients with head and neck cancer. *Support Care Cancer* 8: 203–208 (2000)
- YU Y-Y, DENG J-L, JIN X-R, ZHANG Z-Z, ZHANG X-H, ZHOU X: Effects of 9 oral care solutions on the prevention of oral mucositis: a network meta-analysis of randomized controlled trials. *Medicine (Baltimore)* 99: e19661 (2020)