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Therapeutic Diet for Xerostomia in Head and Neck Cancer Patients: A Narrative Review

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ABSTRACT

Xerostomia significantly disrupts nutritional status, increases oral complications, and reduces quality of life in head and neck cancer (HNC) patients. This systematic review aimed to determine the best dietary interventions for the management of xerostomia in HNC patients by examining available therapies and their effects. A search of PubMed, Web of Science, and Scopus was conducted for randomised controlled trials, interventional, and observational studies published between December 2000 and December 2021. English articles involving adult HNC patients undergoing or having completed anti-cancer therapy were included. Non-HNC xerostomia causes and abstracts were excluded. Risk of bias was assessed using the Cochrane and Joanna Briggs Institute (JBI) tools. Fifteen studies were included out of 533 articles. Acidic candy, ginger extract, chewing gum, vitamin C/E supplements, and thyme honey were identified as helpful in reducing xerostomia. Dietary counselling and awareness of diet modifications improved symptoms, nutrition, and quality of life. Acidic candy was particularly effective in stimulating salivary flow but may cause dental enamel erosion, and timing precautions were necessary for thyroid patients' post-radioactive ablation. Hydration techniques were commonly adopted by patients for symptom alleviation. Dietary modifications show promise in managing xerostomia in HNC patients, although further large-scale, randomised trials are needed to confirm these findings and explore new interventions.

Keywords: *Hyposalivation; nutrition; quality of life; radiation induced toxicity; xerostomia*

INTRODUCTION

Head and neck cancer (HNC) comprises a diverse group of malignancies that affect the oral cavity, pharynx, and larynx. Globally, it ranks as the sixth most common cancer, with over 930,000 new cases and 467,000 deaths reported annually (Sung *et al.*, 2021). In Malaysia, nasopharyngeal carcinoma (NPC) is prevalent and has ethnic predisposition for Chinese (49%), followed by the natives of Sabah and Sarawak (28%) and Malay (22%) (Pua *et al.*, 2008). HNC is a clinically serious condition, often requiring

multimodal treatment including surgery, radiotherapy, and chemotherapy, which are associated with high rates of functional and psychosocial morbidity.

Patients with HNC are often impacted by xerostomia, a condition characterised by a subjective feeling of dryness of the mouth and significant reduction in salivary flow, leading to challenges in mastication, swallowing, and speech (Marimuthu *et al.*, 2021), as well as increasing the risk of dental caries, oral infections, and mucosal lesions. For dentists, oral and maxillofacial surgeons, and head and neck surgeons, managing xerostomia is critical, as it profoundly affects both oral health and patients' quality of life (Leong *et al.*, 2020).

The aetiology of xerostomia is multifactorial, often stemming from radiotherapy, chemotherapy, or surgical extirpation of salivary glands. Studies have shown a sizable proportion of HNC patients suffering from late toxicities such as xerostomia, dysphagia, mandibular osteoradionecrosis, trismus, and hearing loss, especially with radiation therapy (Brook, 2013/2021; Azman *et al.*, 2015; Cohen *et al.*, 2016; Leong *et al.*, 2020). As cancer treatment increases life expectancy and prolongs life, the number of HNC survivors living with xerostomia is likely to increase. One study showed that NPC survivors have a good quality of life score of 76% despite 96.8% having xerostomia (Leong *et al.*, 2020), with symptoms affecting eating, speech, and social interaction.

Current treatment options for xerostomia largely depend on pharmacological agents. A systematic review highlighted the effectiveness of cholinergic drugs, Pilocarpine (Salagen®) and Cevimeline (Evoxac®), for xerostomia management and saliva substitutes (U.S. Food and Drug Administration, 2000; 2003; Pinna *et al.*, 2015). These medications, however, require frequent regular dosing to maintain their effectiveness, are associated with adverse reactions, and are contraindicated in certain patient populations, with pilocarpine being contraindicated in asthmatics, hypertensives, ischemic heart disease, and beta-blocker users. Apart from that, two reviews suggested dietary modifications and improved oral hygiene as potential strategies for improvement of xerostomia symptoms, but both lacked adequate evidence (Pinna *et al.*, 2015; Cohen *et al.*, 2016).

Given the increasing incidence of HNC and the consequent rise in xerostomia cases, there is a pressing need for evidence-based dietary strategies as supportive care. Diet-based interventions are generally low risk, accessible, and may complement medical therapy by stimulating saliva production, improving oral comfort, and enhancing overall well-being. This narrative review aims to describe the complementary dietary approach for managing xerostomia in HNC survivors. The findings could provide additional understanding and benefit healthcare professionals and patients.

MATERIAL AND METHODS

Protocol

The review was prepared following the Preferred Reporting Items for Systematic Reviews and Meta-Analyses Protocol (PRISMA) guidelines to ensure transparency and methodological rigour (Fig. 1). The protocol was not registered in a public database, but it guided the systematic approach to study selection and data extraction. Data was extracted across 13 predefined topics, including study design, population characteristics, cancer and treatment types, xerostomia definitions and assessments, dietary interventions outcome measures, and follow-up duration. In total, 18 specific data items were consistently collected from each study to ensure comprehensive comparison and synthesis.

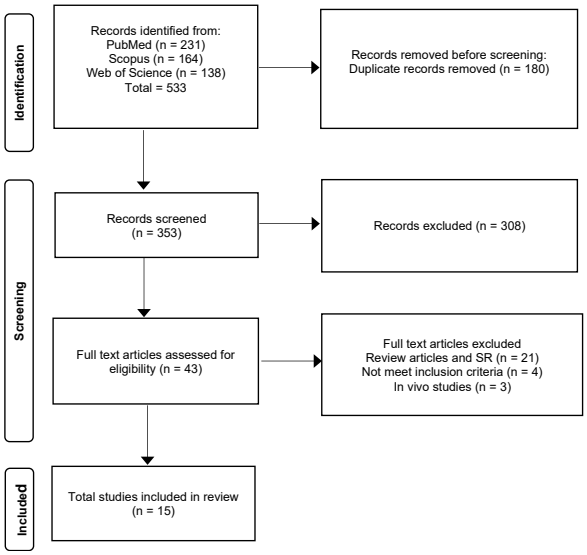

Fig. 1 PRISMA flow chart of the search strategy and study selection.

Data Sources and Search Strategy

A systematic literature search for articles published between 1st December 2001 till 30th November 2021 was conducted using three electronic databases. PubMed, Web of Science and Scopus databases were searched using a combination of the MeSH keywords (Table 1): [Xerostomia] OR [Hyposalivation] OR [Dry Mouth] AND [Diet] OR [Nutrition] OR [Food] OR [Supplement] OR [Meal] OR [Menu] OR [Abstinence] OR [Edible] AND [Head and Neck Cancer] OR [Nasopharyn].

Table 1 Description of MESH keywords used for literature search

Parameters	MESH keywords used in PubMed, Scopus and Web of Science
POPULATION	Head and Neck Cancer OR Nasopharyn*
INTERVENTION	Diet* OR Nutrition* OR Food* OR Supplement* OR Meal* OR Menu* OR Abstinence* OR Edible*
OUTCOME	Xerostomia* OR Hyposalivation* OR Dry* mouth

Eligibility Criteria

This study included randomised controlled trial, interventional studies and observational study reports in the English language published between 1st December 2001 till 30th November 2021. The study population included adult patients with HNC who were scheduled to receive or who had received anti-cancer therapy and diagnosed with xerostomia. All non-HNC causes of xerostomia were excluded. The intervention was focused on the type of diet therapy used. Articles were excluded from the systematic review if it was abstracts not subsequently published in peer-reviewed journals; editorials, commentaries, letters, news articles, case reports, and narrative reviews; or published in a non-English language.

Study Selection

All articles were screened prior to their inclusion in this systematic review. For each manuscript, titles and abstracts were assessed by the two authors (SS and MA) to ensure inclusion and exclusion criteria were adhered to and full-text articles were obtained when they appeared to meet the eligibility criteria. We assessed the eligibility of the studies independently in a standardised manner and documented the reasons for exclusion. Any disagreement between the review authors was resolved by discussion. In the final phase, the selected papers were read, and the data carefully extracted.

Search Results

From the initial search, a total of 533 articles were identified. After removal of duplicates, title and abstracts screened, 43 full-text articles were obtained and assessed for eligibility. Following the exclusion of articles that did not meet the inclusion criteria, a total of 15 studies were selected (Fig.1).

Data Collection and Extraction

The reviewers independently extracted data from the selected manuscripts, which were presented in Table 2. Recorded variables were the authors and year, study design, population (N), type of HNC, type of treatment for HNC, dietary intervention received, duration of intervention, study outcome measures, duration of follow-up, and recommendations.

Table 2 Characteristic of studies reporting on the association between xerostomia and diet therapy

No	Authors (Year)	Study design	Population (N)	Type of head and neck cancer	Type of treatments	Study endpoint/ Xerostomia screening	Type of dietary intervention	Duration of intervention	Duration of follow-up	Recommendations
1	Shooriabi *et al*. (2016)	RCT (Randomised, double blinded, placebo-controlled trial study)	40	Head and neck cancer	Facio-cervical radiation therapy (bilateral)	1. Questionnaire. 2. Unstimulated saliva flow rate.	Ginger (*Zingiber officinale*) vs Placebo	2 weeks	–	Outcome measures improved after 2 weeks of ginger compared to control group.
2	Jensdottir *et al*. (2006)	Quasi experimental	10	Oropharyngeal carcinoma	Facio-cervical radiation therapy (unilateral)	1. Salivary flow rate (unstimulated and stimulated) saliva pH. 2. Saliva $PC0_2$. 3. Saliva degree of saturation with respect to hydroxyapatite (HAp).	Acidic hard-boiled candy (Soemods-bolcher, Copenhagen, Denmark) with tartaric acid and rhubarb flavour	–5 to 0 min (pre-unstimulated saliva) 0 to 4 min (stimulated saliva) 4 to14 min (post-unstimulated saliva)	–	Acidic candy improves salivary flow rate.
3	Guerdoux-Ninot *et al*. (2016)	Observational study (Prospective)	255	Breast (27.1%), GI tract (22.0%) Head and neck (12.9%)	Nonspecific treatment including chemotherapy, radiotherapy, surgery and others	1. Questionnaire.	Patient reported preference: 1. Salty foods (57.6%) rather than sweet ones (39.6%) ($p < 0.001$). 2. Hot (58.7%) rather than cold food (29.8%) ($p < 0.001$). 3. Cut into pieces: 27.8% Creamy (20.8%), liquid (14.1%), minced (13.7%), blended food (9.8%).	–	–	Personalised nutritional counseling should include the role of the family, patient's meal traditions, and food habits.
4	Jensdottir *et al*. (2010)	Quasi experimental	19	Oropharyngeal cancer	Facio-cervical radiation therapy (unilateral)	1. Saliva flow rates. 2. Saliva pH. 3. Saliva degree of saturation with respect to HAp. 4. Total saliva calcium concentration.	Acidic candies without calcium (control) and with calcium lactate	10 mins	Single intervention	Modification of acidic candies with calcium stimulates salivary flow and may potentially help reduce erosive side effects.
5	Crowder *et al*. (2020)	Observational study (Qualitative study)	31	Stage I to IV primary cancer of the oral cavity, oropharynx, hypopharynx, nasopharynx or larynx	6 months to 10 years post concurrent chemoradiation	1. Interview (50 mins) Based on patient-reported symptoms.	Xerostomia (n = 30), taste alterations (n = 29), dysphagia (n = 22), bothered chewing (n = 20).	–	–	Highlights the high prevalence of xerostomia among study subjects.

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Table 2 *(Continued)*

No	Authors (Year)	Study design	Population (N)	Type of head and neck cancer	Type of treatments	Study endpoint/ Xerostomia screening	Type of dietary intervention	Duration of intervention	Duration of follow-up	Recommendations
6	Ravasco *et al*. (2005)	RCT (Prospective Randomised Controlled Trial)	75	Cancer of the base of the tongue, nasopharynx, oropharynx, and larynx	All patients were referred for preoperative RT, having been previously treated with chemotherapy (5-fluorouracil + cisplatin + folinic acid–based regimen). RT treatment of 70 Gy administered in 35 fractions and absence of renal disease and/or diabetes mellitus	1. Nutritional assessment by Ottery's Patient Generated Subjective Global. Assessment (PG-SGA) a validated nutritional assessment tool for patients with cancer. 2. QOL assessed at the three time points using the EORTC Quality of Life Questionnaire version 3.0 (EORTC QLQ-C30).	Dietary counselling in Group 1 Oral nutrition commercial supplements in Group 2 (Supplements of the same commercial brand, two cans/day (Each 200 mL can provides 20 g of protein and 200 kcal)	Start of RT, End of RT and 3 months post RT	3 months	Adding oral nutritional supplements to an individualised dietary counseling did not seem to be as effective as counseling only. Early intervention and sensible partnerships with patients are key to success.
7	Ganzer *et al*. (2015)	Observational study (mixed-method approach)	10	Cancer of the base of the tongue, nasopharynx, oropharynx, and larynx	Primary or adjuvant concurrent chemoradiation therapy	The Vanderbilt Head and Neck Symptom Survey version 2.0 scores (VHNSS 2.0)	Drinking water/ fluid with meals Limiting foods Adapting how food is prepared	–	–	Patients adopt a food modification or food avoidance. Nutrition professional can help patients optimise dietary intake and the eating experience.
8	Logemann *et al*. (2003)	Quasi experimental	30	Advanced-stage cancer of the oropharynx	Chemoradiation therapy	1. Questionnaire. 2. Stimulated whole saliva production. 3. Videofluorographic study.	–	Pre-treatment and at 3, 6 and 12 months after completion of their treatment	–	Reduced saliva weight does not correlate with slowed or inefficient swallow. Instead, reduced saliva weight seems to change patients' perceptions of their swallowing ability and, on that basis, their diet choices.
9	Barnhart *et al*. (2018)	Observational study (Prospective cohort)	96	Cancer of the base of the tongue, nasopharynx, oropharynx, and larynx	Chemoradiation therapy	1. Questionnaire functional oral intake scale 2. Interviews (exploratory questions)	Prophylactic swallowing and active jaw exercises during treatment and in the acute recovery phase.	End of treatment and 3, 6, 12, 24, and 36 months post-treatment	36 months	Mealtime strategies and support help patients cope with permanent toxicities such as xerostomia and dysgeusia.

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Table 2 *(Continued)*

No	Authors (Year)	Study design	Population (N)	Type of head and neck cancer	Type of treatments	Study endpoint/ Xerostomia screening	Type of dietary intervention	Duration of intervention	Duration of follow-up	Recommendations
10	Kaae *et al*. (2020)	RCT (Prospective non-blinded randomised trial)	109	Cancer oropharynx and oral cavity survivors without loco-regional disease	Mean radiation dose: Arm A: 27.29 Gy to parotid and 53.72 Gy to submandibular glands Arm B: 23.84 Gy to parotid and 52.31 Gy to submandibular glands	1. Questionnaire EORTC QLQ-H&N35 and GRIX questionnaire. 2. Unstimulated whole saliva (UWS) and stimulated whole saliva (SWS) sialometry.	Stimulant was a customised sugar-free chewing gum developed by Fertin Pharma. The gum was non-flavoured, had a soft texture and each piece of gum weighted 1 g.	1 month	–	Categorised scores found reduction of dry mouth to be significantly higher in Arm A than Arm B, but no difference was seen for salivary flow rate and viscosity.
11	Charalambous *et al*. (2017)	RCT (Parallel randomised controlled trial)	72	Cancer of the base of the tongue, nasopharynx, oropharynx, and larynx	Radiotherapy or/ and chemotherapy or/and surgery	1. Xerostomia grading scale adapted by the National Cancer Institute (NCI) (version 3.0) (Primary endpoint). 2. Xerostomia questionnaire (secondary endpoints).	Oral rinses: 1. 20 ml of thyme honey diluted in 100 ml of purified water in trial group. 2. Normal saline rinses in control group. During radiation therapy, then 3 times a day for four weeks post radiation	During RT at 4 weeks Post RT 1 and 6 months	6 months	Thyme honey oral rinses is safe and efficacious for treatment induced xerostomia.
12	Nakada *et al*. (2005)	Quasi experimental	105 in group A and 125 in group B	Differentiated thyroid cancer	Radioiodine ^{131}I ablative therapy	1. Interviews with patients. 2. Visual analog scale. 3. Salivary gland scintigraphy using 99mTc-pertechnetate.	Group A: 1 or 2 lemon candies every 2–3 hours immediately after 131I ablative therapy Group B: 1 or 2 lemon candies every 2–3 hours for 24 hours after 131I ablative therapy	5 days	4-6 months post-intervention	An early start of sucking lemon candy may induce a significant increase in salivary gland damage. Lemon candy should not be given until 24 hours after radioiodine therapy.

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Table 2 *(Continued)*

No	Authors (Year)	Study design	Population (N)	Type of head and neck cancer	Type of treatments	Study endpoint/ Xerostomia screening	Type of dietary intervention	Duration of intervention	Duration of follow-up	Recommendations
13	Chung *et al.* (2016)	RCT (Prospective, randomised, double blinded, placebo-controlled trial)	45	Cancer of the base of the tongue, nasopharynx, oropharynx, and larynx	Intensity-modulated RT	1. Patient-reported xerostomia questionnaire (XQ). 2. Observer-rated xerostomia score (XS). 3. Salivary scintigraphy.	Vitamin C/E complex supplementation (trial group) 200 IU of Vitamin E + 1,000 mg of Vitamin C daily placebo supplementation (control group)	Supplement started 1 week before RT and continued up to 1 month post RT completion average duration (3months)	1. Before RT. 2. At 1 month post RT completion. 3. 6 months post RT completion	Short-term supplementation with an antioxidant vitamin E/C complex exerts a protective effect against RT-induced xerostomia.
14	Pauloski *et al.* (2013)	RCT (Randomised controlled trial)	51 treated head and neck cancer patients 64 healthy adult control subjects	Head and neck cancer (Nasopharynx, oral cavity, oropharynx, larynx, hypopharynx)	Primary radiotherapy +/- chemotherapy or primary surgery	1. Modified barium swallow procedure with videofluoroscopy. 2. Weight of stimulated saliva. 3. Stimulated whole-mouth saliva production	1. Sour bolus. 2. Sweet bolus. 3. Salty bolus.	3 assessment points: 1. 7 to 10 days after treatment completion. 2. 1 month after treatment completion. 3. 3 months after treatment completion. Healthy control subjects received a single assessment.	3 months	Sour flavour influenced the swallow of patients treated for HNC, as well as that of control subject. Sour flavour may improve the speed of pharyngeal transit in patients post-treatment for HNCs.
15	Leistra *et al.* (2015)	Quasi experimental	95: individualised dietary counseling 95: usual nutritional care	Head and neck cancer (oral cavity, oropharynx, hypopharynx larynx, nasal cavity, nasopharynx)	Primary radiotherapy +/- chemotherapy or primary surgery	1. Weight change (weight and BMI). 2. Major complications. 3. Length of hospital stay	1. Individualised dietary counselling. 2. Usual counselling.	Start and end of primary treatment	First outpatient to post-treatment visit	The study could not demonstrate an effect of early individualised dietary counselling compared to usual care.

RESULTS

Study Characteristics

The summary of characteristics of the selected studies is shown in Table 3. They were six randomised controlled trials, four observational studies, and five quasi-experimental studies. In relation to the type of malignancy among the HNC survivors, there were 10 general head and neck malignancies, 4 oropharyngeal carcinoma, and 1 thyroid carcinoma. Five publications had HNC patients who received single-modality treatment with radiotherapy. Ten out of 15 involved HNC patients who received combination treatment modalities of chemotherapy, radiotherapy, or surgery. One study had 230 patients with well-differentiated thyroid carcinoma who were treated with radioactive iodine (RAI). Various screening tools were used to demonstrate xerostomia, which included six studies that used subjective tools like questionnaires, three studies that used objective tools such as salivary flow rate, and six studies that utilised a combination of both. The dietary interventions reported were categorised into three distinct groups, which included seven studies on specific food or supplement, six studies on diet modification, and two studies on diet counselling as the type of intervention.

Risk of Bias, Heterogeneity, and Publication Bias

A total of six randomised controlled trial studies were evaluated using the Cochrane Risk of Bias Tool for randomised trials (RoB 2) Short Version (Cribsheet) (Table 3) (Sterne *et al.*, 2019). We identified three studies as low risk, two of intermediate risk, and one as high risk. The Joanna Briggs Institute (JBI) checklist for observational studies (Table 4) showed all four studies were high-quality studies with low risk of bias (Joanna Briggs Institute, 2017). JBI checklist for quasi-experimental studies (Table 5) showed three high-quality studies and two moderate-quality studies (Joanna Briggs Institute, 2020). All 15 studies were included in this narrative systematic review. The study design, type of malignancy, treatment received, type of dietary intervention, as well as the xerostomia assessment tool, were the source of heterogeneity. No evidence of publication bias was seen.

Table 3 Characteristic of studies reporting on the association between xerostomia and diet therapy

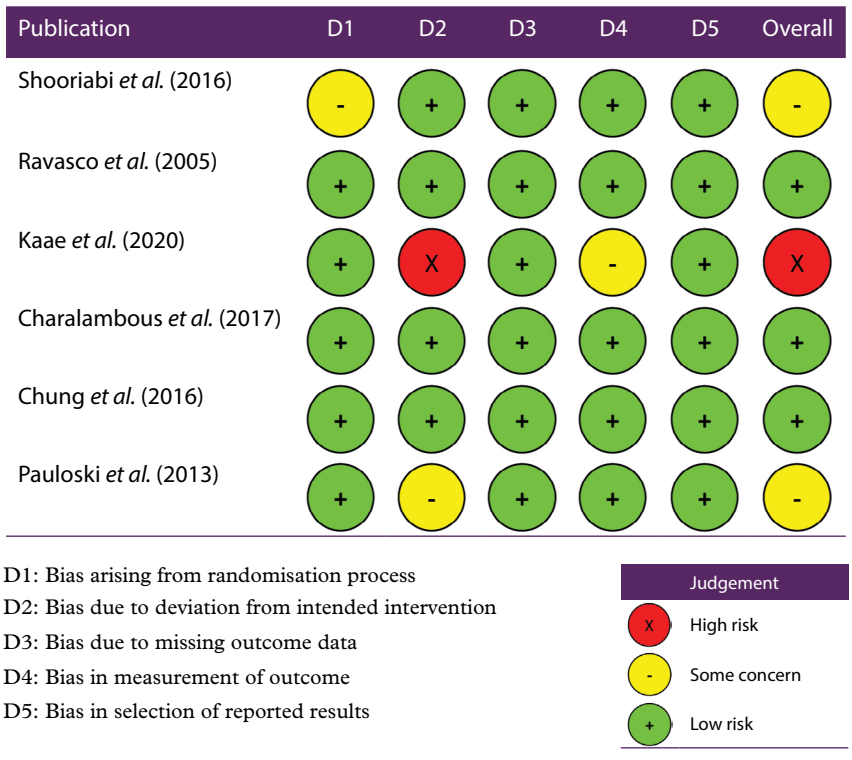

Table 4 JBI critical appraisal checklist for observational studies

Author(s) and publication year	Q1 Were the criteria for inclusion in the sample clearly defined?	Q2 Were the study subjects and the setting described in detail?	Q3 Was the exposure measured in a valid and reliable way?	Q4 Were objective standard criteria used for measurement of the condition?	Q5 Were confounding factors identified?	Q6 Were strategies to deal with confounding factors stated?	Q7 Were the outcomes measured in a valid and reliable way?	Q8 Was appropriate statistical analysis used?	Q9 Was appropriate statistical analysis used?
Guerdoux-Ninot *et al.* (2016)	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Crowder *et al.* (2020)	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Ganzer *et al.* (2015)	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Barnhart *et al.* (2018)	Yes	Yes	No	Yes	Yes	Yes	Yes	Yes	Yes

Table 5 JBI critical appraisal checklist for quasi-experimental studies

Author(s) and publication year	Q1 Is it clear in the study what is cause and what is the "effect' (There is no confusion about which variable comes first)?	Q2 Were the participants included in any comparisons similar?	Q3 Were the participants included in any comparisons receiving similar treatment/ care, other than the exposure or intervention of interest?	Q4 Was there a control group?	Q5 Were there multiple measurements of the outcome both pre and post the intervention/ exposure?	Q6 Was follow-up complete and if not, were differences between groups in terms of their follow-up adequately described and analysed?	Q7 Were the outcomes of participants included in any comparisons measured in the same way?	Q8 Were outcomes measured in a reliable way?	Q9 Was appropriate statistical analysis used?
Jensdottir *et al.* (2006)	Yes	Yes	No	No	Yes	Yes	Yes	Yes	Yes
Jensdottir *et al.* (2010)	Yes	Yes	No	Yes	Yes	Yes	Yes	Yes	Yes
Logemann *et al.* (2003)	Yes	No	Yes	No	Yes	Yes	Yes	Yes	Yes
Nakada *et al.* (2005)	Yes	Yes	No	Yes	Yes	Yes	Yes	Yes	Yes
Leistra *et al.* (2015)	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes

Description of Studies

Dietary therapies for xerostomia in HNC patients

Dietary therapies described for xerostomia in HNC patients were classified into three distinct categories: 1) specific food or supplements; 2) dietary modifications; and 3) dietary counseling. Three distinct categories of diet intervention were identified from the 15 included studies. Most studies used specific foods or supplements, which functioned as either saliva stimulants or saliva substitutes. The food items included acidic candy, ginger, chewing gum, thyme honey and vitamin C/E supplements. Acidic candy was the most used item, with a total of three studies documenting its use for patients with xerostomia. Another six studies captured various dietary modification techniques that were employed to reduce the impact of xerostomia. All the six studies with dietary modifications reported on food preparation via augmentation to taste, temperature, texture, or consistency. Dietary counselling was also described in two studies as an intervention for xerostomia in HNC patients.

The effect of diet therapy on xerostomia

Specific food/supplement

Acidic candies were the most frequently used as salivary stimulants, as evidenced in three studies. The study by Jensdottir *et al.* (2006) recruited patients with unilaterally radiated oropharyngeal carcinoma who were instructed to suck acidic candies and had the salivary flow rates measured at pre-stimulatory, stimulatory, and post-stimulatory intervals. The study reported significant oral dryness improvement after sucking acidic candy based on findings of a tenfold increase in salivary flow rate as compared to the pre-stimulatory phase, which persisted up to 10 mins post stimulation, signified continued stimulation

even after removal of acidic candy. In another study by Jensdottir *et al.* (2010), modified calcium-enhanced acidic candy was compared to conventional acidic candies. While both types showed similar positive effects in stimulating saliva, the modified candy also demonstrated additional protective dental benefits, including reduced hydroxyapatite (HAp) dissolution in the saliva. The third study, which used acidic candy, was Nakada *et al.* (2005), which demonstrated the two different effects of lemon candy based on the timing it was given to patients with post-surgical undifferentiated thyroid carcinoma following RAI treatment. The study demonstrated statistically significant damaging effects on the salivary gland if lemon candy was administered within 24 hours post-RAI versus the protective effect the lemon candy had as a sialagogue when administered after the first 24 hours, with reduced incidences of xerostomia, as proven in salivary scintigraphy studies.

For HNC patients with established xerostomia, having had completed treatment between 3 months to 6 months, the findings of two individual studies that used ginger extract and chewing gum respectively, were compared. Shooriabi *et al.* (2016), who used ginger extract, showed statistically significant improvement in symptoms of xerostomia as well as an increase in unstimulated saliva secretion after 2 weeks of intake of ginger extract. In comparison, chewing gum that was used for 1 month in a randomised phase III trial study by Kaae *et al.* (2020) showed no significant objective improvement in salivary flow rates and saliva viscosity in both patients and the control arm. There was, however, an overall reduction in dry mouth scores based on xerostomia assessed by European Organization for Research and Treatment of Cancer Quality of Life Questionnaire – Head and Neck Module (35 items) for both groups, but patients using chewing gum had a significantly greater self-reported reduction in xerostomia. Based on these two studies, the ginger extract produced both objective and subjective improvement in xerostomia as compared to chewing gum that only produced subjective improvement, however the duration of intervention in both studies was short, ranging from 2 weeks to 1 month.

A longer intervention period was reported in two separate studies that used thyme honey and vitamin C/E, respectively, in HNC patients undergoing treatment. Both studies were performed on patients at the start of anti-cancer treatment, and completed at least 1 month post-treatment, with an average of 3 months duration of intervention. The use of thyme honey oral rinses showed the positive effect of this intervention when used during and up to 4 weeks post-treatment with radiotherapy (Charalambous *et al.*, 2017). There were significantly lower grades of xerostomia during radiation therapy, up to 6 months post-radiotherapy, as well as overall improved quality of life scores in patients with the oral thyme honey intervention. A study that utilised Vitamin C/E complex supplement during radiotherapy reported greater improvements in xerostomia questionnaire scores when compared between 1 month and 6 months post-radiotherapy (Chung *et al.*, 2016). There was no significant difference objectively, with similar findings for ejection fraction as well as maximal accumulation on salivary scintigraphy observed between the two groups at 1 month and 6 months post-radiotherapy. However, a significant increase in pre- and post-stimulatory saliva was noted 1 month post-radiotherapy in the intervention group, with no similar increase observed at 6 months post-treatment.

Diet modification

Six studies reported on diet modification techniques. In a French study, 48.6% of patients experienced dry mouth affecting eating and drinking, with preferences for salty foods (57.6%), hot food (58.7%), and various textures such as cut pieces (27.8%), creamy (20.8%), liquid (14.1%), minced (13.7%), and blended (9.8%) (Guerdoux-Ninot *et al.*, 2016). Patients preferred soft,

moist foods, spices or seasonings, and sauces or gravies, employing techniques like increased mealtime, cutting food smaller, consuming less food, more fluid intake, and avoiding citrus fruits, raw vegetables, dry food, and meat (Crowder *et al.*, 2020). Patients also adopted food modification or avoidance and downplayed challenges, using techniques such as alternating water intake, limiting certain foods, and adjusting meal preparation styles to cope with xerostomia (Ganzer *et al.*, 2015). Advanced oropharyngeal cancer patients treated with chemoradiation showed diet choices based on food consistency evolved from thin liquids, thick to soft masticated, and crunchy food over time despite persistence of xerostomia, although crunchy food was avoided in 43% of patients up to 1 year post treatment (Logemann *et al.*, 2003). Xerostomia did not significantly hinder oral intake at 3 months post-treatment, and the strategy of alternating food and fluids frequently used as an adaptation with 48.6% continuing this practice at 36 months post-treatment (Barnhart *et al.*, 2018). Sour flavour enhanced food bolus did not improve xerostomia but significantly shorted the swallowing process in HNC patients (Pauloski *et al.*, 2013). Overall, hydration techniques were the most used as seen across three studies with 48% using this strategy up to 3 years post-treatment. Other techniques included food avoidance, increased mealtime duration, as well as swallowing maneuvers (Ganzer *et al.*, 2015; Barnhart *et al.*, 2018; Crowder *et al.*, 2020).

Diet counselling

A total of two studies explored the use of dietary counselling on xerostomia and its complications. Ravasco *et al.* (2005) demonstrated an overall positive effect of dietary counselling using regular foods, with reduced xerostomia incidence and severity as well as radiotherapy-induced toxicity at 3 months post-intervention. This was in comparison to two other groups that did not receive diet counseling, however, had regular diet with oral nutritional supplement and another group maintaining intake ad lib, respectively. There was no statistically significant difference in the severity of xerostomia between early individualised dietary counseling (counseling at the first outpatient visit/diagnosis) and the usual care of dietary counseling at the point of primary anti-tumor treatment (Leistra *et al.*, 2015). Both studies concluded that dietary counselling together with modification of regular diets was most beneficial in xerostomia symptom burden reduction.

The effect of diet therapy on xerostomia related complications

Several studies captured secondary outcomes in relation to the effect of diet therapy on both local and systemic xerostomia-related complications. Acidic candy was most frequently used in HNC survivors to stimulate salivary production, but the timing and formulations are important. In one study, an associated increased risk of dental enamel erosion was observed, as evidenced by higher salivary saturation with HAp and increased dissolution of HAp in acidic candy-stimulated saliva among cancer patients compared to the healthy control group. To mitigate this effect, the study used modified acidic candies with calcium to reduce the effects of dental enamel erosion in irradiated patients, which proved successful (Jensdottir *et al.*, 2010). The use of acidic candy after 24 hours to 5 days post-RAI was protective towards the salivary glands and was attributed to reduced rates of hypogeusia and sialadenitis (Nakada *et al.*, 2005). Another study showed sour flavour enhanced food bolus reduced dysphagia as there was significantly shortened pharyngeal transit time across all evaluations (first post-treatment, followed by 1-month and 3-month post-treatment) in HNC patients (Pauloski *et al.*, 2013). There were reported improved nutritional intake, reduced weight loss, as well as lower postoperative complications among HNC patients who received dietary counselling interventions (Ravasco *et al.*, 2005; Leistra *et al.*, 2015).

Improved quality of life function scores were demonstrated using oral thyme honey, hydration techniques, and the use of dietary counselling (Ravasco *et al.*, 2005; Ganzer *et al.*, 2015; Charalambous *et al.*, 2017).

DISCUSSION

Xerostomia in HNC causes significant morbidity functionally, emotionally, and socially as impairment in eating and swallowing leads to poor nutrition, oral and dental complications, as well as poor quality of life. The ability to eat and the enjoyment of food are important for cancer survivors' quality of life. A key ingredient in the enjoyment of food involves being able to appreciate texture, colours, and flavours. Understanding that certain foods can stimulate residual salivary reserves makes chewing easier, and the eating experience more pleasant in HNC survivors (Pedersen *et al.*, 2002; Pinna *et al.*, 2015)

This review highlights short-term improvements in salivation occurring with saliva stimulants such as acidic candies, chewing gum, and ginger. This aligns with findings by Jensen *et al.* (2010), which explained that sugar-free lozenges, acidic candies, or chewing gum may potentially provide transitory relief from xerostomia by stimulating residual salivary gland tissue. However, the salivary composition in cancer survivors is altered compared to normal subjects (Jensen *et al.*, 2010; Pinna *et al.*, 2015). Although acidic candies relieve xerostomia, patients must be aware of potential dental erosions due to low pH in saliva, which persists after removal of the candy stimulus. Low pH values in saliva are caused by low buffer capacity, low saliva flow rates, slower acid clearance, and higher concentration of acid from candy stimulus in HNC patients (Napeñas *et al.*, 2009) better alternative is calcium-enhanced acidic candies, which mitigate demineralisation of the tooth by higher release of calcium into saliva (Jensdottir *et al.*, 2013; Amaechi *et al.*, 2015).

An intriguing discovery involves the use of lemon or acidic candies in patients following RAI therapy. The parotid gland has an active iodine transporter that absorbs high levels of RAI, causing salivary gland damage (Charalambous *et al.*, 2017). Sialagogues were used to flush out the effect of accumulated RAI in the salivary glands, but too early intervention resulted in increased damage to the glands. Administration of these candies 24 hours after RAI administration, up to 5 days post RAI was more effective and safer (Nakada *et al.*, 2005).

Ginger, a common culinary ingredient, was shown in this study to improve patients overall satisfaction and alleviate xerostomia symptoms. Ginger increases salivation due to its direct parasympathomimetic effect on post-synaptic M3 receptors and possible repressive effect on presynaptic muscarinic autoreceptors. Ginger also improves oral health due to its antifungal properties, reducing oral candidiasis, dental caries, and mouth ulcers (Ghayur *et al.*, 2007; Rashmi & Tiwari, 2016).

Vitamin C, vitamin E and beta-carotene are known antioxidants that minimise free radical cellular damage. Fresh fruits and vegetables are excellent sources of vitamin C, although care in preparation is vital as it is vulnerable to oxygen and heat. Vitamin E is found in vegetable oils, margarine, salad dressings, vegetables, fish and poultry (Johnson *et al.*, 2003). Ascorbic acid (vitamin C) has saliva stimulatory function and short-term use of vitamin E and C complex during radiotherapy has protective roles against xerostomia via preservation of submandibular gland function (Visvanathan & Nix, 2010; Park *et al.*, 2012).

Chewing gums function as a saliva stimulant by activation of chemoreceptors (gustatory receptors) and mechanoreceptors (Karami-Nogourani *et al.*, 2011). However, a study by Davies (2000) found no significant difference between chewing gum and artificial mucin for xerostomia in advanced cancer patients.

Honey contains various organic acids, such as ascorbic acid, citric acid, and malic acid. Its function includes saliva stimulation, reduction of oral infections and weight maintenance in patients undergoing radiotherapy and chemotherapy (Bardy *et al.*, 2008; Davies *et al.*, 2010).

One of the most significant findings from this systematic review was that diet modification techniques plays a pivotal role in long term management of xerostomia. Food adaptation using sauces and gravy, along with augmentation of food texture allowed the incorporation of a wider range of healthy foods into the diet of HNC patients. Hydration techniques by intake of water or ice chips were commonly used to alleviate the oral dryness encountered. Patients reported preferences for soft, less spicy, with smaller bites to enhance their eating experience. These findings align with local recommendations from the Medical Nutrition Therapy Guidelines for Cancer in Adults Working Group Committee in Malaysia (Lian *et al.*, 2012). Despite persistent xerostomia, patients' coping skills, and their perception of disease burden improved once they adopted diet modifications. The diet modification techniques highlighted in this review were similar to findings in studies on xerostomia in geriatric and Sjogren syndrome patients (de Figueiredo *et al.*, 2023; Müller *et al.*, 2023).

This study reinforces the importance of dietary counselling in reducing xerostomia and xerostomia-related complications. While early intervention at the first outpatient visit may not benefit all HNC patients, high-risk individuals with pre-existing nutritional deficiencies, low BMI or malnutrition may require early referral to dietitians and possible enteral feeding. Local Malaysian guidelines recommend that dieticians should provide medical nutritional therapy consisting of pre-treatment evaluation and weekly visits during radiation treatment for head and neck cancer to improve outcomes. The need for follow-up varies, with some patients requiring two to three weekly visits during treatment. Post-treatment, patients should receive a minimum of fortnightly dietitian visits for at least 6 weeks (Lian *et al.*, 2012).

Individualised dietary counselling allows dieticians to cater to each patient's needs and preferences. The use of regular, familiar foods was sustainable and provided longer-lasting relief. Patients also benefit from professional advice on swallowing techniques, food hygiene and food preparation skills (Talwar *et al.*, 2016). This review demonstrates that the use of oral nutritional supplement (ONS) without diet counseling does not enhance patient care as efficiently as ONS combined with counselling. When ONS were used together with nutritional counselling for HNC patients undergoing treatment, it resulted in better weight maintenance, increased protein-calorie intake, improved quality of life and better tolerance of anti-cancer treatment (Cereda *et al.*, 2018).

Strength and Limitation

This systematic study utilised comprehensive literature search and detailed data synthesis for all head and neck cancer patients with xerostomia. There was exclusive focus on dietary interventions to incorporate the various dimensions of a therapeutic diet for head and neck cancer patients with xerostomia. The study highlighted the presence of research gaps with the need for more standardised outcome measures in future studies. It also reinforced the multidisciplinary roles of dietitians, clinicians and oral health personnel when dealing with xerostomia patients. Identification of specific foods and food modification techniques allows the formation of practical clinical guidelines to be employed by patients for better nutrition and quality of life.

Several limitations were identified in this systematic review of a therapeutic diet for xerostomia. The primary issue was a small number of high-quality studies, with only

15 studies recruited compared to extensive research on pharmacological interventions and salivary substitutes. Another significant limitation was the heterogeneity in interventions and outcome measures, with various subjective and objective assessments used. Furthermore, the studies encompassed diverse HNC, ages and treatments used in this cancer. The exclusion of HNC with enteral feeding resulted in a loss of a significant patient cohort. Valuable studies involving in vivo research, Sjogren's syndrome and geriatric xerostomia were excluded due to strict inclusion criteria. Additionally, the complexity of natural products made reproducibility difficult, and incorrect preparation may lead to loss of beneficial properties and distorted results. Other limitations included short follow-up periods, reliance on self-reported outcomes, and lack of consensus on outcome measures. These limitations highlight the need for larger, more rigorous studies to validate these findings.

Clinical Applicability and Generalisability

This study highlighted evidence-based dietary interventions for xerostomia that treating physicians and dietitians can guide patients, especially incorporating beneficial foods and dietary habits that improve overall quality of life and reduce xerostomia-related complications. Structured dietary counselling can be constructed to focus on foods with saliva-stimulating properties and food modification techniques. It also advocates oral health education and correction of bad dental practices. There is potential for the establishment of individualised xerostomia menus for affected oncological and hospitalised patients, like diabetic diets and low salt diet plans. Specific foods that stimulate salivary production can inspire culinary dishes tailored for xerostomia patients, supported by recipe books and mobile food applications to simplify meal preparation for patients or caregivers.

Future Recommendations

Future recommendations include randomised controlled study comparing saliva-stimulating and standard diet for HNC patients post treatment. A standardised, universal approach to patient-reported outcomes using the Xerostomia Inventory, as it is a comprehensive tool for assessment of frequency and impact of dry mouth on various aspects of life. Objective monitoring of xerostomia should preferably involve salivary flow rate measurement which involves collection and measurement of stimulated or unstimulated saliva over a specific period of time. Longitudinal studies with standardised methods should document patient food preferences and dietary modifications, especially for oropharyngeal and NPC patients with irreversible xerostomia secondary to high-dose radiation, as well as severe Sjogren syndrome. These studies will help identify an optimal diet for patients with hyposalivation and ease the adaptation to living with xerostomia. Incorporating local diet and food sources will also benefit local populations by including familiar and locally available food.

CONCLUSION

This review found three modes of dietary approach consisting of specific food/ supplements, dietary modification, and dietary counselling, which have been prescribed to HNC patients with xerostomia. The effects of these approaches on xerostomia vary, with favourable outcomes identified when ginger extract, thyme honey, calcium-modified candies, chewing gum, and individualised dietary counselling were utilised. Based on the detailed literature survey conducted above, future studies on dietary interventions for xerostomia in HNC patients must use standardised outcome measures such as stimulated whole saliva, questionnaires, to enable meta-analyses that can verify the efficacy of specific interventions.

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