The Effects of an Integrated Supportive Programme on Xerostomia and Salivary Characteristics in Patients With Head and Neck Cancer Undergoing Radiotherapy: a Randomized Controlled Trial

Nan Jiang (✉ beifang24@126.com)

Tian Jin Medical University <https://orcid.org/0000-0002-3524-5388>

Yue Zhao

Tianjin Medical University

Malin Stensson

Jönköping University: Jonkoping University

Jan Mårtensson

Jönköping University: Jonkoping University

Research Article

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Abstract

Aim: This study evaluates the effect of an integrated supportive programme on xerostomia and saliva characteristics at a one-year follow-up of patients with head and neck cancer (HNC) undergoing radiotherapy (RT).

Methods: Participants were randomly allocated to an intervention group (n=47) or a control group (n=45). The intervention group received usual care and an integrated supportive programme, which included three steps: face-to-face education; face-to-face coaching at one-month post RT; and four telephone coaching sessions at 2-, 3-, 6-, and 9-months post RT. The face-to-face education consisted of oral hygiene instruction, oral self-care strategies, facial and tongue muscle exercises, and salivary gland massage. Adherence to the intervention was evaluated using a questionnaire completed during the nine-month follow-up. The control group received usual care. The unstimulated saliva flow rate, saliva pH, buffering capacity, and xerostomia were assessed in both groups.

Results: A total of 79 participants (40 in the intervention group and 39 in the control group) completed the 12-month follow-up. There were statistically significant differences between the groups in level of xerostomia at the 3- and 12-month follow-up ($P=0.027$ and $P<0.001$, respectively) and in the mean value of unstimulated saliva flow rate at the 12-month follow-up ($P=0.035$), with better outcome in the intervention group. The adherence of the intervention was good but decreased slightly during the follow-up.

Conclusion: This integrated supportive programme with good adherence relieved xerostomia and had a positive effect on unstimulated saliva flow rate among patients with HNC during the 12-month follow-up.

Introduction

Head and neck cancer (HNC) is a common malignancy with a high level cancer burden on the healthcare systems in China [1]. Treatments for HNC include external radiotherapy (RT) often in combination with surgery and chemotherapy. The duration of RT for HNC is six to eight weeks, with a dose 1.5~2.0 Grey/day (5 day/week) [2]. Common oral side effects among patients with HNC during and following RT are xerostomia (i.e., the subjective feeling of oral dryness) and changes in saliva characteristics, including salivary gland hyposalivation, decrease in salivary production, low saliva pH, and decreased buffering capacity. Patients exposed to head and neck irradiation usually have xerostomia or hyposalivation for several months or years or for their whole life, which can cause difficulties speaking, chewing, and swallowing and increase the risk for oral disease. Consequently, these problems have a negative impact on oral health and quality of life [3,4].

Several non-pharmacological interventions have been used for the management of xerostomia and hyposalivation; however, the available treatments are generally ineffective and the effect of saliva substitutes is limited and generally received with low satisfaction [5,6]. No compelling evidence has been found that favours a specific intervention for patients with HNC. Oral hygiene instructions aimed at adults

and the elderly who have some degree of salivary gland function have shown a positive effect on improving xerostomia, saliva pH, and buffering capacity [7-10]. Short- or long-term participation in oral functional exercise programmes among elderly patients have resulted in increased oral function and fewer problems associated with xerostomia and hyposalivation [11-14]. Furthermore, soft massage of the major salivary glands can alleviate xerostomia by increasing blood circulation and parasympathetic activity in elderly patients [14,15]. However, the target population of these strategies has been the elderly who do not have cancer and therefore have not received RT.

To our knowledge, there are no consensus standards of intervention for managing radiation-induced xerostomia and change of saliva characteristics among patients with HNC. Therefore, an integrated supportive programme with multicomponent oral care was designed to determine such a programme's effects on prevalence and severity of xerostomia and saliva characteristics in patients with a diagnosis of HNC during the first year after RT.

Material And Method

Participants

Patients with a confirmed histological diagnosis of HNC were recruited consecutively from one tertiary hospital in Tianjin, China between February 2019 and September 2020. Other eligibility criteria included an age of ≥ 18 years, Karnofsky performance scale of 80 or more, primarily received definitive RT or surgery with postoperative RT (dose of ≥ 60 grey) with concurrent or induction chemotherapy or both, and ability to attend regular re-examination within the 12-month follow-up period. Patients were excluded if they had other cancers, had total edentulism, had other causes for xerostomia (i.e., Sjögren syndrome, diabetes mellitus, use of drugs that could interfere with salivary flow, removed bilateral salivary glands), or exhibited severe cognitive impairment (i.e., dementia) or psychiatric disorders that interfered with the ability to complete the questionnaire package.

A power analysis was performed to determine the sample size. As no previous literature was identified that evaluates the effectiveness of oral care intervention on xerostomia in patients with HNC, the authors conducted a pre-test study with 15 participants in each group without any significant differences in demographic and disease-related characteristics or XQ score at baseline. The pre-test used the XQ score at the three-month follow-up to calculate the sample size (mean=32.67; SD=5.55) for intervention group and control group (mean=36.41; SD=4.86). A sample size of 68 (34 in each group) was required to detect significant differences between the two groups, with a statistical power of 80% and a two-sided 5% level of statistical significance. Ten patients in each group were added to compensate for possible loss to follow-up.

The randomization was conducted by a statistician using a simple online binomial randomization programme to assign participants to either an intervention group or a control group, stratified by gender and site and stage of tumour. At baseline, 47 participants were in the intervention group and 45 participants were in the control group (Figure 1).

Study Groups

The integrated supportive programme

The integrated supportive programme was developed by the research group based on evidence from literature reviews [7-16] and the research team's experience. The programme included three steps led by the same researcher (NJ, the first author), a trained coach with experience being a coach in other intervention studies and with rich experience in oncology care for HNC. Details of the programme are shown in Table 1.

Step 1

A researcher (NJ) established trust with the participant and introduced the cause of xerostomia and saliva alteration and their negative effects on oral health and quality of life. The participants received a handbook about the programme and viewed a five-minute instruction video about the Bass technique of teeth brushing, the muscle exercises, and the salivary gland massage.

Step 2

Face-to-face coaching was conducted by the researcher (NJ) at the outpatient department after one-month post RT. At the end, the researcher collaboratively worked with participants to develop short-term realistic goals. The average time was around 15–20 minutes.

Step 3

Telephone coaching was performed by the researcher (NJ) 2-, 3-, 6-, and 9-months post RT. The researcher kept track of progress of participants' goals at subsequent telephone coaching sessions. Each telephone coaching session lasted for approximately 15–20 minutes.

The usual care

Before RT, a ward nurse provided usual care, which included face-to-face group-based health education consisting of the following instructions: (1) brush teeth using toothpaste and a soft toothbrush after meals; (2) replace the toothbrush every month; (3) if using dentures, immerse denture in antimicrobial solution for ten minutes; (4) avoid smoking, alcohol, and irritating food; and (5) gargle with medicine (i.e., lidocaine) when experiencing pain due to radiation-induced mucositis. The group-based health education was about 10–15 mins and was offered to both the intervention and the control group.

Data collection

Data regarding demographics, xerostomia, saliva characteristics, and adherence were collected using questionnaires and tests.

Measurement of xerostomia

Xerostomia was evaluated using a self-report instrument (XQ) and clinical oncologists' assessment (The National Cancer Institute Common Toxicity Criteria for Adverse Events Version 5.0 [CTCAE v5.0]) at baseline, at the end of RT, and 3- and 12-months post RT.

XQ is an eight-item instrument with four items related to oral dryness while chewing/eating and four items related to oral dryness while not chewing/eating [17]. Each item is scored on a numeric rating scale, ranging from 0 to 10. A total XQ score is calculated by multiplying the sum of the eight items by 1.25 to obtain a final summary score with a range from 0 to 100. Higher scores indicate greater discomfort/dryness [17]. The Chinese version of XQ, which has excellent validity and reliability, is used to evaluate xerostomia among HNC in China [18].

CTCAE v5.0, criteria for standardized classification of adverse effects in cancer treatment, is widely used in the HNC population [19]. The level of xerostomia consists of three grades: Grade 1 – symptomatic (e.g., dry or thick saliva) without significant dietary alteration; Grade 2 – moderate symptoms with oral intake alterations (e.g., copious water, other lubricants, diet limited to purees and/or soft, moist foods); and Grade 3 – inability to adequately aliment orally, tube feeding, or total parental nutrition indicated.

Measurement of saliva characteristics

Unstimulated whole salivary secretion, in vitro test pH, and buffer capacity of unstimulated saliva were measured. The saliva measurements were performed by a PhD student between 8AM and 11AM at the clinic. Patients were asked not to eat, drink, or brush their teeth for at least two hours before collection. No other conscious movements of the oral musculature were made during collection. Patients were invited to sit down and asked to swallow residual saliva present in the mouth. Next, unstimulated whole saliva samples were collected for 5 min and the secretion rate was expressed in ml/ min. The normal unstimulated saliva flow rate may vary between 0.3ml/min and 0.4ml/min; less than 0.1ml/min is considered to be a very low level.

The pH and buffer capacity of unstimulated saliva was performed according to the manufacturer's instructions (Shenzhen Kang Sheng Bao Bio-technology Co. LTD, China) immediately after saliva collection and judged by the colour of the test strip. The pH with a range of 5.0 to 5.8, 6.0 to 6.6, and 6.8 to 7.8 indicate highly acidic, moderately acidic, and healthy acidic, respectively. The buffering capacity from 0 to 5, 6 to 9, and 10 to 12 represent very low, low, and normal/high capacity, respectively. The unstimulated saliva flow rate, pH, and buffering capacity were assessed at baseline and 3- and 12-months post RT.

Adherence Questionnaire

The 15 questions included in the adherence questionnaire were based on the content of the programme. Participants in the intervention group completed the adherence questionnaire at the outpatient department at the one-month face-to-face coaching session. A researcher (NJ) assessed the adherence to this questionnaire through telephone interviews at 2-, 3-, 6-, 9-month coaching sessions.

Data analysis

The SPSS 22.0 (IBM Corp, Armonk, New York) was used to analyse the data. The Student's t-test and Chi-square test were used to compare baseline data between two groups. Repeated-measures analysis of variance and independent sample t-test were performed to compare differences in mean scores of xerostomia between the test and control groups. The Mann-Whitney U test was used to compare differences in saliva characteristics between the two groups. $P < 0.05$ was considered statistically significant.

Results

Participant characteristics

A total of 92 participants were enrolled, and 79 (86%) completed the 12-month follow-up. The mean age was 50 (SD 10.93) years, and 71 (77.2%) of the participants were male. The most common tumour site was nasopharynx (40.2%), and 76 (82.6%) had an advanced stage of cancer. More than half of the participants (54.3%) received chemotherapy and RT (Table 2). There were no significant differences in demographic or disease-related characteristics at baseline between the two groups.

Changes in xerostomia

A significant increase in the mean score of XQ was observed at the end of RT, and the mean scores for XQ had decreased at the 3- and 12-month follow-up in both groups. The interaction effect between time and group showed that the intervention group recovered significantly better than the control group ($P = 0.049$). The difference was statistically significant at the 3- and 12-month follow-up ($P = 0.027$ and $P < 0.001$, respectively) (Table 3).

Around 90% of patients in both groups did not report xerostomia at baseline. The number of grade 2 participants for both groups were similar (32 intervention vs. 33 control) at the end of RT. At the 12-month follow-up, the number of grade 2 participants had decreased in both groups: ten (25%) in the intervention group and 20 in the control group (51.3%). Grade 3 was only experienced at the end of RT: eight participants (20.0%) in intervention group and six participants (15.4%) in control group. There were no significant differences between the two groups in grade level of xerostomia at baseline, at the end of RT, or after three months, but the grade of xerostomia was significantly lower in the intervention group at the 12-month follow-up ($P = 0.046$) (Table 4).

Changes in saliva characteristics

The study included the analysis of 79 unstimulated saliva samples at baseline, 53 after three months, and 79 after 12 months (Table 5). No significant differences were found between the groups in salivary characteristics at baseline. There was a significant reduction in unstimulated saliva flow after three months in both groups, followed by a recovery after 12 months. The mean unstimulated saliva flow did not return to baseline after 12 months in either group. However, a statistically significant difference

between the groups was found after 12 months ($P=0.035$) (Table 5) with better recovery in the intervention group. There were no significant differences in pH values or a buffering capacity at the one-year follow-up.

Adherence to the intervention

The adherence to the intervention was generally good, especially for the first three months, slight decreasing after three months. The level of adherence to the muscle exercise regime (facial and tongue) and salivary gland massage one time or more a day were 37.5–65% and 62.5–87.5%, respectively. High adherence was seen for frequently sipping water/fluid as each participant did this at least three times a day, and 62.5–77.5% decreased their consumption of sweet foods and drinks. Lowest adherence was found in use of mouth-wetting agents (47.5–65% never used these agents) and in the use of sugar-free chewing gum and sucking tablets (only 20–30% used this strategy one day or more) (Appendix).

Discussion

This is the first multicomponent intervention study that combines face-to-face education, face-to-face coaching, and telephone coaching in an integrated supportive programme for patients with HNC. This programme significantly relieved xerostomia and improved unstimulated saliva flow rate in patients with HNC during the 12 months following RT.

In a qualitative study of patients with HNC undergoing radiotherapy in China, the majority of patients continued to suffer from xerostomia after radiotherapy, partly because of a lack of professional support, including the inability of nurses to provide oral health care [4]. In the present study, the peak in XQ score was at the end of RT in both groups and then significantly decreased during the following visits (three- and 12-months post RT), results that align with findings from previous studies [20, 21]. This decrease may have been caused by the obvious decrease in saliva flow rate and altered saliva composition [22]. Nurses should strengthen oral care for xerostomia for patients at the beginning of their RT. This study shows that strategies such as oral function exercises and salivary gland massage included in the intervention programme could relieve xerostomia and increase saliva secretion. It is also important to use oral hygiene strategies, such as the ones included in this study, to maintain good oral health in irradiated patients with HNC. Decreased saliva flow rate can affect individuals in different ways, including increasing the risk for oral disease and difficulty speaking, chewing, and swallowing [3]. Therefore, patients should be advised about anticipated oral complications and be instructed about effective oral hygiene practice, fluoride supplement, and dietary modification [23]. In addition, nurses should motivate patients to prioritize oral hygiene strategies, oral function exercises, and salivary gland massage as an integral part of oncology care before RT and continue for several years after follow-up or until a patient's oral health status is largely recovered.

In the present study, the unstimulated saliva flow rate for both groups were normal at baseline, decreased at the three-month follow-up, and then slowly increased at the 12-month follow-up. These findings are supported by results from a previous study about unstimulated whole saliva flow rate changes during

and after RT among HNC [24]. The first stage of functional deterioration in salivary secretion usually occurs during the first week of RT. For many patients, their salivary flow rate decreases continuously, becoming undetectable by the end of a 6–8 week course of treatment [24]. This finding was confirmed by our study: 26 patients could not produce any measurable saliva by the end of their treatment. Furthermore, the second stage of a dramatic loss of salivary gland function may happen within a few months (1–6 months) post RT and is accompanied by progressive and irreversible changes in the salivary gland tissue with no significant recovery in gland function [25,26]. Therefore, artificial saliva/saliva substitutes and intensive oral care are needed to provide patients help coping with the adverse effects of reduced saliva secretion.

Interestingly, a significantly higher mean value of unstimulated saliva flow rate was observed in the intervention group at the 12-month follow-up compared with the control group, a finding that suggests this programme had positive long-term effects on improving unstimulated saliva flow. This result might be questioned as RT often affects salivary glands so much that they take a long time to recover or do not recover at all. However, the differences in unstimulated saliva flow rate between the two groups might be related to different irradiation salivary glands and their functions. The level of salivary gland hyposalivation depends on differential damage of glands as the result of different irradiation volumes and doses [27]. If minor glands are damaged, xerostomia increases; if major glands are damaged, the incidence of hyposalivation increases [27].

Adherence has been identified as prerequisite for good outcomes. The adherence to this programme was generally good, but decreased slightly after the three-month follow-up. The suggestion is to extend the follow-up time to five years post RT (i.e., a brief coaching intervention every three or six months for the first five years). This may be possible to implement in China, where patients with HNC regularly visit a physician in the clinic for re-examination to check for reoccurrence of cancer within five years after cancer treatment. Physicians and outpatient nurses could be trained in the coaching intervention although this might increase the workload of a clinician. The intervention may be difficult to follow when participants are seriously ill and have a demanding treatment. Therefore, the intervention requires a motivated patient and a fairly significant effort from the healthcare staff.

Workload might be reduced by using mHealth, a new model of remote health delivery via mobile phone, which is increasingly used in China and has proved to be a useful way to increase adherence to care instructions in patients with chronic diseases [28]. It would be interesting to test adherence to this programme using mHealth. For example, mHealth could be used to provide weekly text message reminders about health care instructions post RT. Self-report in a logbook using a phone application could also be beneficial. In addition, in future research, a healthcare professional might provide personalized monthly counselling and feedback through mHealth. However, mobile phone technology is less keenly embraced in some groups of the population, such as people 65 and older and people with lower education levels [29].

Limitations

There are some limitations that need to be considered. First, the study was conducted at one tertiary hospital with a relatively small sample size. This large hospital has coverage of patients with cancer from all over the country and nearly 500 patients with HNC are admitted annually. However, to ensure that patients could complete all follow-up visits, only patients who participated in regular re-examinations were included in this study, which might have an effect on the generalizability of the findings and reflect a selection bias. Future research should explore whether these findings can be replicated in a large multicentre context with large sample sizes. Second, patients with a Karnofsky performance scale of 80 or more were included in this study. The scale ratings ranging from 80 to 100 reflect the clinical status of person who is able to carry out normal activities (e.g., work) with or without effort. Patients with a score of 80 to 100 were in a better performance status during and after RT and therefore were probably more able and willing to complete long-term intervention and follow-up. This may be attributed to good adherence and less data loss in this intervention. However, this might also make the generalizability of the findings difficult. Third, unstimulated saliva flow rate was assessed in the study, but stimulated saliva flow rate was not. One reason for this was because even if stimulated saliva is more common in research, unstimulated saliva is likely more representative of a patient's daily symptoms and best reflects basic saliva production. Fourth, the researcher (NJ) did the intervention and assessed the adherence of intervention, introducing a potential bias. This arrangement was necessary because no other researchers/clinicians with the necessary qualifications and experience to be a coach were available. In fact, there are few oncology nurses with coaching qualifications in China. Therefore, more nurses will need to be trained as a coach if similar follow-up interventions are to be tested. Lastly, there was a risk of contamination or dissemination of the first step of intervention to the control group since the participants were inpatients in one hospital. However, contamination or dissemination of the second and third step intervention was unlikely as patients were outpatients with little risk of meeting again. This study is the first randomized control trial with a multicomponent oral care intervention for patients with HNC, and despite the above limitations this study adds valuable knowledge within this highly important research area.

Conclusion

The present study shows that an integrated supportive programme with good adherence was effective at relieving xerostomia and increasing unstimulated saliva flow rate among patients with HNC during a 12-month follow-up post RT. Further study is needed to refine this intervention and evaluate the effects of the intervention on stimulated flow rate.

Declarations

Funding

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Conflicts of interest

No conflicts of interest exist.

Availability of data and material

Data can be shared based on specific requests to the corresponding author.

Code availability

Not applicable

Authors' contributions

All authors contributed to the study design and the interpretation of the results. Nan Jiang did the data analysis and written the first draft of the manuscript. All authors commented on previous versions of the manuscript. All authors approved the final the manuscript.

Ethics approval

This study was approved by Tianjin Medical University Ethics Committee (TMUHMEC 2015008), and the principles of the Declaration of Helsinki were followed.

Consent to participate

All the participants were given a written and a verbal explanation about the purpose and method of the study. After receiving this information, the participants provided written informed consent. Participants were informed of their rights to privacy and confidentiality and the option to drop-out of the study at any time

Consent for publication

All authors consent to publication of this article in Support Care Cancer

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Tables

Table 1. Contents of the integrated supportive programme

Step 1	Face-to-face education at baseline at the ward
Session 1: Oral hygiene instruction	<p>Provide information about the importance of oral hygiene</p> <p>Provide oral hygiene advice (i.e., modified bass teeth brushing method (video), the selection of toothbrush, fluoride toothpaste, and alcohol-free rinses)</p>
Session 2: Self-care instruction	<p>Smoking and drinking alcohol cessation if appropriate</p> <p>Use of mouth-wetting agents</p> <p>Use of sugar-free chewing gum, sucking tablets</p> <p>Frequently sipping water or fluid</p> <p>Intake adequate amount of water/fluid</p> <p>Have fluid food or food with fluid</p> <p>Decrease the frequency of sugar-use</p> <p>Avoid irritating agents</p> <p>Use of air humidifier if appropriate at night</p>
Session 3: Facial and tongue muscle exercise (video)	
Facial muscle	<p>Deep breathes; tightly close eyes and pull lips to both sides of the face (smile)</p> <p>Fully open eyes and mouth</p> <p>Tightly close mouth, fill the mouth with air, and move the air in mouth right and left</p>
Tongue muscle	<p>Extend tongue out far and retract</p> <p>Hold tongue out as far as possible, move it left and right, and move it up and down to lick nose and chin</p> <p>Turn tongue to lick around mouth</p> <p>Push upper and lower lips with tongue</p> <p>Alternately push the left and right cheeks with tongue</p>
Session 4: Salivary gland massage (video)	<p>Check the position of major salivary glands (parotid gland, sublingual gland, and submandibular gland) and massage the glands softly with fingers.</p>
Step 2	Face-to-face coaching at outpatient department 1-month post RT
	<p>Nurse coach/participant interactions</p> <p>Listen to participant's experience of doing programme</p> <p>Assess the adherence of doing programme</p>

	<p>If adherence was poor or the goals were not being met, explore the possible issues that influenced adherence and discuss solutions</p> <p>Health goals discussion and set a revised plan</p>
Step 3	Telephone coaching at 2-, 3-, 6- and 9-months post RT
	<p>Nurse coach/participant interactions</p> <p>Listen to participant's experience with the programme</p> <p>Evaluate the adherence of doing programme</p> <p>Conduct a motivational interview to discuss barriers, possible reasons and solutions.</p> <p>Health goals discussion and set a revised plan</p>

Table 2. Demographic and disease-related characteristics of the participants, n (%) (n=92)

Characteristics		Intervention group (n=47)	Control group (n=45)	χ^2/t	<i>P</i>
Age (years), mean $\pm$ SD		48.11 $\pm$ 10.75	51.93 $\pm$ 10.89	-1.696	0.093
Body weight (kg), mean $\pm$ SD		73.73 $\pm$ 10.35	72.44 $\pm$ 11.680	0.561	0.576
BMI, mean $\pm$ SD		25.23 $\pm$ 3.26	25.29 $\pm$ 2.40	-0.098	0.922
Sex, n (%)	Male	38(80.9)	33 (73.3)	0.738	0.390
	Female	9(19.1)	12(26.7)		
KPS (score), n (%)	80	14(29.8)	12(26.7)	1.175	0.556
	90	32(68.1)	30(66.7)		
	100	1(2.1)	3(6.6)		
Marital status, n (%)	Married/cohabitant	41(87.2)	35(77.8)	1.431	0.232
	Widowed/Divorced/Single	6(12.8)	10(22.2)		
Education level, n (%)	Primary or below	8(17.0)	7(15.6)	0.779	0.678
	Secondary	23(48.9)	26(57.8)		
	Tertiary	16(34.1)	12(26.6)		
Smoking, n (%)	Never smoker	6(12.8)	11(24.4)	2.913	0.233
	Current smoker	20(42.6)	13(28.9)		
	Ex-smoker	21(44.6)	21(46.7)		
Alcohol consumption, n (%)	None, n (%)	29(61.7)	34(75.6)	2.044	0.153
	Drinks > 1 standard glass per week	18(38.3)	11(24.4)		
Economic situation, n (%)	Very good	4(8.6)	3(6.7)	0.263	0.967
	Good	19(40.4)	20(44.4)		
	Problematic	19(42.4)	18(40.0)		
	Very problematic	5(10.6)	4(8.9)		
Living arrangement, n (%)	Living with partner	43(91.5)	39(86.7)	0.552	0.458
	Living alone	4(8.5)	6(13.3)		
Working status, n (%)	Working	17(36.2)	15(33.3)	0.169	0.982
	On sick-leave	15(31.9)	14(31.2)		

	Unemployed	9(19.1)	10(22.2)		
	Retired	6(12.8)	6(13.3)		
Physical exercise, n (%)	Inactive	32(68.1)	28(62.2)	0.348	0.555
	At least 30 minutes per day	15(31.9)	17(37.8)		
Tumour site, n (%)	Nasopharynx	20(42.6)	17(37.8)	2.037	0.729
	Larynx	7(14.8)	6(13.3)		
	Hypopharynx	6(12.8)	3(6.7)		
	Oropharynx	6(12.8)	8(17.8)		
	Oral cavity	8(17.0)	11(24.4)		
TNM stage, n (%)	I	8(17.0)	8(17.8)	1.918	0.383
	II	29(61.7)	22(48.9)		
	III	10(21.3)	15(33.3)		
Treatment modality, n (%)	RT and chemotherapy	25(53.2)	25(55.6)	0.074	0.964
	RT, chemotherapy and surgery	18(38.3)	16(35.5)		
	RT	4(8.5)	4(8.9)		

Abbreviations: KPS, Karnofsky performance status; TNM stage, tumour node metastasis staging system; RT, radiotherapy

Table 3. The effects of an integrated supportive programme on subjective xerostomia (n=79)

Group	Baseline	End of RT	3-month post RT	12-month post RT	F time*group	P
Intervention group	12.7±3.5	55.2±9.4	35.1±5.9	18.5±4.1	3.062	0.049
Control group	12.4±3.2	55.8±8.3	38.0±5.9	22.8±4.3		
t	0.420	-0.293	-2.254	-4.453		
P	0.676	0.770	0.027	<0.001		

Abbreviation: RT, radiotherapy

Table 4. The effects of an integrated supportive programme on CTCAE, n (%) (n=79)

Variable	Group	CTCAE				χ^2	<i>P</i>
		Grade 0	Grade 1	Grade 2	Grade 3		
Baseline	Intervention group	37(92.5)	3(7.5)	-	-	0.186	0.666
	Control group	35(89.7)	4(10.3)	-	-		
End of RT	Intervention group	-	-	32(80.0)	8(20.0)	0.288	0.591
	Control group	-	-	33(84.6)	6(15.4)		
3-month post RT	Intervention group	-	14(35.0)	26(65.0)	-	2.942	0.086
	Control group	-	7(17.9)	32(82.1)	-		
12-month post RT	Intervention group	7(17.5)	23(57.5)	10(25.0)	-	6.176	0.046
	Control group	6(15.4)	13(33.3)	20(51.3)	-		

Abbreviation: CTCAE, Common Terminology Criteria for Adverse Events; RT, radiotherapy; Grade 0, no xerostomia; Grade 1, symptomatic (e.g., dry or thick saliva) without significant dietary alteration; Grade 2, moderate symptoms, oral intake alterations (e.g., copious water, other lubricants, diet limited to purees and/or soft, moist foods); Grade 3, inability to adequately aliment orally, tube feeding, or total parental nutrition indicated.

Table 5. The effects of an integrated supportive programme on saliva characteristics (n=79)

Saliva characteristics	Follow-up time	Group	Mean±SD	Z	P
Unstimulated flow rate, ml/min	Baseline	Intervention group	0.48±0.12	-0.271	0.786
		Control group	0.49±0.10		
	3-month post RT	Intervention group	0.06±0.04	-0.797	0.425
		Control group	0.05±0.05		
	12-month post RT	Intervention group	0.16±0.08	-2.111	0.035
		Control group	0.12±0.07		
pH	Baseline	Intervention group	7.00±0.27	-0.916	0.360
		Control group	7.05±0.24		
	3-month post RT	Intervention group ^a	6.72±0.30	-1.058	0.290
		Control group ^b	6.60±0.32		
	12-month post RT	Intervention group	6.76±0.29	-1.332	0.183
		Control group	6.69±0.24		
Buffering capacity	Baseline	Intervention group	9.75±1.37	-0.553	0.581
		Control group	9.51±1.45		
	3-month post RT	Intervention group ^a	8.53±1.43	-1.146	0.252
		Control group ^b	8.17±1.11		
	12-month post RT	Intervention group	8.55±1.52	-1.641	0.101
		Control group	8.00±1.36		

Abbreviation: RT, radiotherapy

^a30 saliva samples for analysis in intervention group at 3-month post RT

^b23 saliva samples for analysis in control group at 3-month post RT

Figures

Figure 1

Flow chart describing how patients with HNC were screened, included and followed up in the study