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Title: Taste Changes during Radiotherapy for Head and Neck Cancer

Abstract

Introduction

Taste changes (dysgeusia) during radiotherapy for head and neck cancer are associated with malnutrition, tube feeding and reduced toleration of treatment.

Method

The MD Anderson symptom inventory – head and neck (MDASI-HN) questionnaire was completed by patients in a single department receiving radical radiotherapy or chemo-radiotherapy for head and neck cancer during weeks 1 and 4 of radiotherapy. Participants who developed dysgeusia in week 4 completed supplementary questions exploring what foods they could taste and how they managed taste changes.

Results

At week 4, 97% of 61 participants reported taste changes, 77% reporting moderate or severe changes. 30% of participants reported taste changes during week 1. Patients with oropharyngeal, oral cavity and parotid gland tumours were most likely to develop dysgeusia. Females were more likely than males to report taste changes. A soft, semi-liquid diet was reportedly easier to tolerate as the more food was chewed the worse the taste became.

Conclusions

Patients having radiotherapy for all head and neck cancers should be warned of the very high risk of developing taste changes and the time scale for this. Patients with taste changes should be advised a softer diet requiring less chewing will be better tolerated. The finding that females are more at risk than males of dysgeusia needs further investigation.

Implications for Practice

Patients with all head and neck cancer diagnoses should be educated to expect taste changes from the start of radiotherapy. Patients with dysgeusia should be advised that soft, semi-liquid foods that require less chewing before swallowing are easier to tolerate.

Keywords: Taste changes; dysgeusia; head and neck cancer, radiotherapy

Introduction

Taste changes (dysgeusia), loss of taste (ageusia) and reduced sensitivity to taste (hypogeusia) are common for patients undergoing radiotherapy (RT) for head and neck cancers (HNC). Between 60 - 95% of patients report problems tasting their food.¹⁻³ The patient experience of radiation-induced dysgeusia is poorly understood by healthcare professionals and carers,^{4,5} with both often questioning why the patient cannot “just eat anyway” despite the patient reporting that everything tastes awful. Altered taste is associated with reduced appetite, weight loss, malnutrition and reliance upon tube feeding, which in turn increases hospital admissions and leads to poor treatment outcomes and reduced quality of life (QoL).⁶⁻⁸ Malnourished patients struggle to tolerate RT, leading to detrimental unplanned gaps in treatment.^{7,9} Reliance upon tube feeding risks chronic dysphagia due to atrophy of the swallowing muscles and hence difficulty in regaining lost swallow function.^{10, 11} For the purpose of this paper the term dysgeusia encompasses any form of taste distortion reported by participants.

The aim of this study was to describe the incidence of dysgeusia across tumour sites, treatment regimen and time and explore how patients manage dysgeusia. A secondary aim was to identify patients with dysgeusia to participate in interviews for the second part of the study.

Methods

Design and Ethics

A review of information provided to HNC patients by RT centres was conducted during the design phase. This single site study used an explanatory mixed methods design. The study consisted of two parts: the first, largely quantitative part, used the validated MD Anderson Symptom Inventory – Head and Neck (MDASI-HN)¹² questionnaire, to measure dysgeusia, symptom burden and symptom interference with their life. Those participants who scored themselves $\geq 5/10$ for problems tasting their food in week 4 of radiotherapy were asked to complete the following supplementary questions (SQ):

Are you able to taste any foods? YES/NO

Do you find the texture of some foods puts you off eating them? YES/NO

3. Do you find the smell of some foods puts you off eating them? YES/NO

What advice, if any have you been given to help you cope with taste changes?

What advice would you give to someone else going through the same treatment who has taste changes?

These participants were invited to take part in the second, qualitative part of the study which involved a semi-structured interview (SSI) to discuss in depth their experience. The SQ data was used to plan the questions for the SSI. The results of part one of the study are presented here and the interview data will be presented separately for clarity.

Ethical approval for the study was granted by Wales REC 3 panel, reference number: 224517 17-WA-0309.

Recruitment and Consent

All adult patients undergoing radical RT or chemo-radiotherapy (CRT) for a primary HNC site where dysgeusia was likely due to taste buds being located in the treatment field (oropharynx, oral cavity, parotid, nasopharynx, larynx, hypopharynx and ethmoid sinus) between November 2017 and May 2018 were approached to participate. A range of tumour and nodal stages were included and all patients were receiving volumetric-modulated arc radiotherapy (VMAT) and doses 60 - 70 Gray in 30 - 35 treatments over 6 - 7 weeks.

Exclusion criteria were any of: existing pre-treatment taste changes as reported by the patient, diagnoses other than primary HNC, prescribed palliative RT.

Patients were approached on day 2 of RT when they attended their routine RT review clinic appointment. Those interested in taking part were given an information leaflet and the MDASI-HN data collection tool. The researcher met patients the following day when they attended for RT, answered any questions and gained written consent from willing patients.

Data Collection

The MDASI-HN questionnaire was selected as it is a patient-reported HNC specific tool that measures problems with tasting food, using a scale of 0-10, and also quantifies symptom

burden and symptom interference. The questionnaire is validated to measure individual symptoms, including taste change or to combine the score for 22 symptoms to provide an overall symptom burden score.¹² Additionally, it measures 6 symptom interference items which generate a total symptom interference score. Together this data provides a holistic assessment of symptom burden and the associated life impact.

A score of 0 on MDASI-HN indicates that taste is normal and has not been affected by RT and a score of 10 indicates that taste is severely affected, as bad as the participant can imagine.¹² Guidelines for use of MDASI-HN¹² suggest that patients reporting scores of 5-6 are experiencing moderate symptoms and scoring 7 \geq represent severe symptoms. This study used a score of ≥ 5 to indicate that the participant was experiencing taste changes.

Procedures

Participants completed the MDASI-HN in week 1 of RT (before #3 at latest) and in week 4 when dysgeusia is expected to peak.¹ Participants either completed the questionnaire while in the department, or alternatively, they could complete it at home and return it the next day. It was emphasised that the participant completed the questions from their own perspective and that their responses were not influenced by members of staff.

Participants scoring ≥ 5 in week 4 were asked to complete SQ. These SQ were designed after consultation regarding the clinical needs of the local HNC multidisciplinary team (MDT) in addition to patient feedback during clinics. The aim of the SQ was to gather relevant information about dysgeusia from participants who declined an interview and to inform the interview schedule for part two of the study. The SQ enabled a wider range of perspectives to be collected, strengthening representativeness of the data and thus increasing the transferability of the findings.

Data analysis

MDASI-HN data were analysed using descriptive statistics, figures and tables. The SQ were analysed using a descriptive content analysis.¹³ Only participants who completed the MDASI-HN at both time points were included in the analysis, however, participants did not need to have completed all SQ.

Results

Sixty-four participants were recruited to the study with 61 completing the MDASI-HN at both time points included in the analysis. One participant failed to complete and return either questionnaire and the other two did not return the MDASI-HN in week 4. The characteristics of the study sample including the 47 who developed taste changes are summarised in Table 1.

Characteristic		Total sample (N = 61)	Taste changes sub-group (MDASI-HN ≥ 5) (n = 47)
Sex -n (%)	Male	48 (79)	35 (75)
	Female	13 (21)	12 (25)
Age - years - mean(SD)		63.2 (10.2)	61.3 (9.86)
Range – years		36 - 88	36 - 82
Treatment modality - n (%)	RT only	28 (46)	18 (38)
	CRT	33 (54)	29 (62)
Feeding tube - n (%)	Gastrostomy	18 (30)	17 (36)
	NG tube	15 (24)	12 (26)
	No tube	28 (46)	18 (38)
	during RT		

Table 1: demographic data and treatment regimens of participants

Table 1 demonstrates similar patient and treatment-related characteristics for participants who developed dysgeusia, except that the former were more likely to be tube fed and/or females. 29/33 (88%) of participants having chemotherapy reported dysgeusia compared with 64% in the RT only group.

97% of participants reported some degree of problem tasting food by week 4 of treatment with 77% reporting moderate or severe problems. Almost a third of participants had already reported mild to moderate taste changes by the end of the first week of RT compared to normal sense of taste at the start of the week (Figure 1).

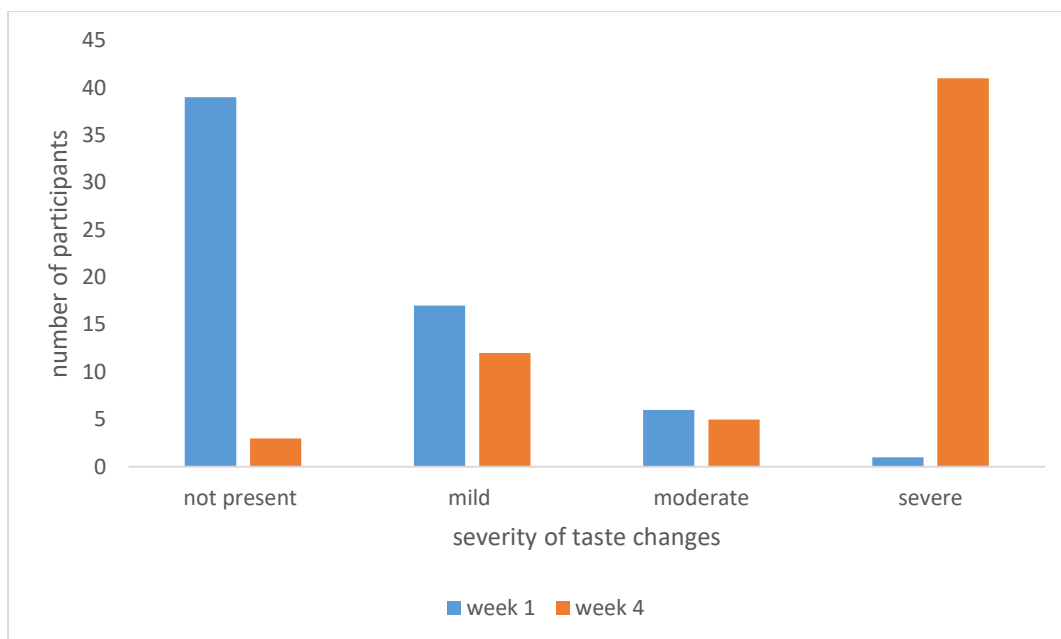


Figure 1. Number of participants reporting taste changes weeks 1 and 4 of radiotherapy

Table 2 shows the distribution of taste changes across the different HNC diagnoses of participants in the study in week 4 of RT. Study eligibility selected patients with HNC diagnoses **of all stages** considered at risk of developing taste changes and this is reflected in the data.

Diagnosis	Study sample N =61	Taste changes sub-group (MDASI-HN ≥5) n=47	Numbers having CRT in taste changes sub-group (MDASI-HN ≥5) n = 29
Oropharynx – n (%)	32 (53)	28 (88)	23 (82)
Oral cavity- n (%)	7 (11)	5 (71)	2 (40)
Larynx – n (%)	8 (13)	3 (38)	1 (33)
Parotid – n (%)	5 (8)	4 (80)	0
HNC +neck nodes – n (%)	4 (7)	2 (50)	0
Pyriform sinus – n (%)	2 (3)	2 (100)	1 (50)
Ethmoid sinus – n (%)	2 (3)	2 (100)	1 (50)
Nasopharynx – n (%)	1 (2)	1 (100)	1 (100)

Table 2: Number of participants with taste changes by diagnosis and receipt of CRT

Participants with a diagnosis of oropharyngeal cancer were most likely to report moderate or severe dysgeusia (28/32), with those with cancers of the parotid gland (4/5) and oral cavity (5/7) also frequently reporting this level of taste change.

Symptom Burden

Figure 2 shows the percentage of participants reporting individual symptoms on the MDASI-HN in weeks 1 and 4 of treatment group.

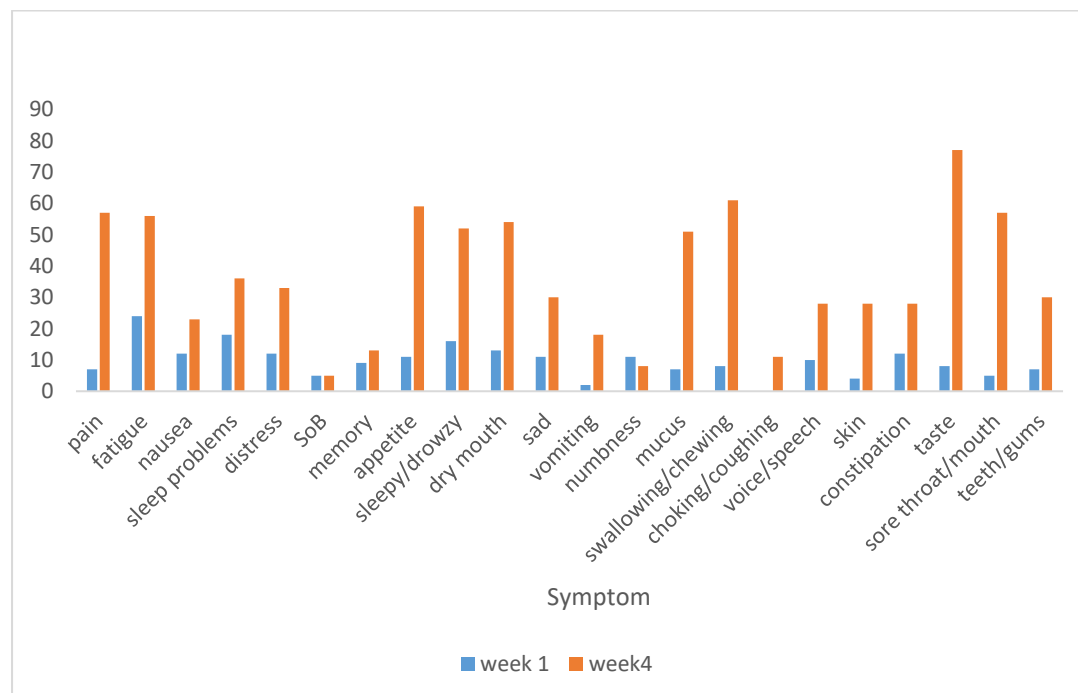


Figure 2 Percentage of participants reporting individual symptoms in weeks 1&4 of radiotherapy

Figure 2 indicates that the majority of symptoms, including taste problems, increased from week 1 to week 4. The most prevalent symptoms during week 1 were fatigue (24%) and disturbed sleep (18%). By week 4 the most commonly reported symptoms were all related to eating and nutrition: problems tasting food (77%); difficulty swallowing or chewing food (61%); lack of appetite (59%); pain (57%); sore mouth/throat (57%).

Symptom Interference with Daily Life Scores

The symptom interference (SI) scores from the MDASI-HN provide a measure of how much symptoms are interfering with daily life for patients. Respondents are asked to grade from 0-10 how much symptoms have affected their general activity, mood, work (including housework) relations with other people, walking and enjoyment of life.

Table 3 shows the mean SI scores for the whole sample, the taste changes and non-taste changes groups, demonstrating a greater level of SI in participants with dysgeusia compared with those whose taste had not been affected.

Symptom Interference	Whole Group week 4 n=61	Taste changes sub- group (MDASI-HN ≥5) week 4 n =47	Non-taste changes sub-group week 4 n=14
Mean score	22.9	26.5	11.17
Standard deviation	14.8	14.5	8.1
Range	0 - 58	0 - 58	0 - 22

Table 3 Symptom interference scores for whole sample, taste changes and non-taste changes groups
0 indicates no symptom interference; maximum score 60 indicating total symptom interference

Supplementary questions results

All 47 participants who scored ≥5 for problems tasting food in week 4 answered at least one of the 5 supplementary questions.

Responses about foods that could be tasted are summarised in Table 4. Eighteen of the 44 participants who answered question 1 were not able to taste any foods. Some reported that although they could taste some foods, they did not taste normal.

Response	Number of taste changes sub- group giving response n=44
Nothing	18
Sweet or very sweet foods e.g. trifle, custard, rice pudding	12
Everything is salty	3
Everything is bland	3
Sharp foods	4

Citrus fruits	2
Porridge/cereals	6
Pasta	4

Table 4: Responses to supplementary question 1: Are you able to taste any foods?

The most commonly tolerated foods were puddings such as custard, rice pudding and trifle and cereals such as porridge.

Sometimes only a very limited and specific list of foods could be tasted:

“Weetabix™ with sugar, butter (not margarine) on bread, fish cooked in butter, treacle sponge cake and leek and potato soup (home-made only).” Participant 24

In addition to taste, over 60% of participants found food textures unpalatable, particularly anything with bits in it that required extra chewing. Some participants commented that the more time you spent chewing food the worse the taste became making it difficult to trigger the swallow mechanism.

“I have gone over to puree diet as mouth too sore to chew food. I find the texture of pureed food not very nice at all, but I have to eat something. I hold my nose while eating so cannot taste or smell.” Participant 28

Almost all (11/13) female participants found the texture of some foods unpalatable.

Approximately one third of participants found the smell of food unpleasant particularly fried foods. Females (50%) were more likely than males (28%) to find the smell of food put them off eating it.

40% of participants reported not receiving any advice to help them manage dysgeusia during RT. Participants wanted to provide practical and moral support to future patients but often were not sure themselves what helped. The most common advice that participants suggested was to keep trying different foods and to persevere because taste changed day-to-day and what did not taste good one day may taste better in coming days. They suggested that the more you must chew food the worse the taste becomes, therefore recommending soft or semi-liquid foods.

“Persevere. Make sure the food is not too salty or too acidic. Eat slowly and chew food slowly.” Participant 44

“Be open minded to foods that you normally wouldn’t eat – try different things. Eat as much as you can when you feel like eating.” Participant 39

Participant 43 acknowledged how difficult it was to know what would help saying: *“I don’t know, I’m experimenting myself.”*

Discussion

The MDASI-HN and SQ have provided new information regarding the prevalence, timing, and self-management of dysgeusia for patients undergoing RT for HNC.

97% of participants reported some abnormal taste changes in week 4 of RT, with 77% moderate to severe at this point. This reflects the findings of previous studies.^{1, 14, 15, 16} What has not been reported previously is a higher proportion of females (12/13) than males (41/68) who experienced dysgeusia. General population data suggests that females have more taste buds on their tongue and a better sense of taste than males¹⁷ but this has not previously been related to the phenomena of RT induced taste change. It might be that the greater density of female taste buds translates into greater taste impairment when damaged by RT. SQ data revealed that females were also more likely to report finding the smell and texture of foods offensive. It has been suggested¹⁸ that females experience worse side effects than males in general and this may be what has been seen in this study. The small number of females included in this study means the observed phenomena should be treated with caution but it should be borne in mind that female patients with HNC may be more likely to experience dysgeusia that can impact upon nutritional status, treatment tolerance and QoL.^{6, 7} Statistical analysis has not been carried out due to the small numbers.

Participants undergoing CRT for oropharyngeal cancer (88%) were most likely to report dysgeusia with patients with oral cavity (71%) and parotid cancers (80%) also reporting a high incidence of dysgeusia. It is not surprising that adding chemotherapy increases the likelihood of taste changes as both treatments are known to cause dysgeusia.¹⁹ Previous studies have provided conflicting results as to whether the addition of chemotherapy to RT worsens taste changes for patients with HNC,^{19, 20} however, in this study 88% of those having CRT reported dysgeusia. It is thought that RT and chemotherapy affect the taste buds in different ways, with RT having a direct effect in damaging taste buds²¹ and chemotherapy more likely to influence appetite and enjoyment of foods.²² Further appropriately designed

studies are needed to determine whether patients receiving CRT for HNC are more likely to report taste changes than those having radical RT alone, enabling care to be targeted towards those most at risk of dysgeusia.

Taste buds are located on the tongue, soft palate, pharynx, larynx, uvula, and upper third of oesophagus, lips and cheeks³ so patients with cancers of any of these sites, including early laryngeal cancers are at risk of developing dysgeusia during RT. This should be reflected in the advice given to patients prior to RT so that they are prepared for this effect.

Almost a third of participants reported some degree of dysgeusia by the end of the first week of treatment; sooner than patients are currently warned to expect dysgeusia in clinical practice, with most patients advised to expect side effects after 2 weeks²³ or not mentioning time scale at all.²⁴ The recently published study by Asif et al²⁵ also reports that patients experience an immediate significant reduction in taste sensation after beginning RT for HNC. Asif et al²⁵ used taste strips and QoL tool to measure taste changes. The current study produced similar results using a patient self-report questionnaire, so strengthening confidence in the finding. It is acknowledged that measuring taste perception reliably and quickly is difficult in a busy clinic¹⁶ and is one of the reasons that taste changes are often not addressed, however, these results suggest that asking patients on a scale of 1-10 to report their taste perception will provide reliable information. We know that taste changes are one of the earliest symptoms to appear from HNC irradiation, often preceding oral mucositis,^{1, 26} but studies do not report a timescale for symptom development. The timing of taste changes should be added to the pre-treatment information provided to patients to address concerns if they do develop problems tasting their food very early in a course of RT. When symptoms develop sooner than expected, patients are naturally concerned that something has gone wrong.^{27, 28}

The MDT decides whether a gastrostomy tube will be placed prior to the patient with HNC starting RT. The factors considered include the patient's current nutritional status, the likelihood that treatment toxicity will impact upon their nutritional intake due to the volume and position of RT fields, whether chemotherapy is planned and patient preference. Of the 18 patients who had a gastrostomy tube, 94% reported problems tasting their food indicating that gastrostomy tubes had been placed in an appropriate patient cohort. It is unlikely that dysgeusia would be the only symptom leading to patients feeding via a

gastrostomy tube but alongside pain, dysphagia and poor appetite it is known to play a major part.⁶ Of the 15 participants who needed a naso-gastric (NG) tube placed during RT, 12 reported taste changes indicating that this were likely to have contributed to reduced oral intake leading to enteral feeding. The symptom burden scores suggest that patients who experience dysgeusia are more likely to experience other symptoms, such as fatigue and distress, which may also cumulatively impact upon their nutritional status.

Forty percent of participants with dysgeusia reported that they had not been given any advice on how to manage taste changes. One of the aims of this study is to enable better support and advice for future patients with taste changes. No studies were identified that provide this advice for patients during treatment, however, some studies have reported patient experience of dysgeusia following RT for HNC.^{23, 26, 27}

Participants gave the impression of food being tolerated rather than enjoyed. The longer food spent in the mouth the worse the taste became. Participants reported that the first mouthful of food does not taste too bad but the more the food was chewed the worse the taste became, so food that required more chewing was less tolerable than softer foods that could be swallowed without spending as much time in their mouth. They therefore chose soft, semi-liquid foods such as porridge, pasta or puddings. This finding has not been reported previously in patients undergoing RT for HNC and needs to be considered when giving advice, alongside the need for patients to continue with a textured diet for as long as they are able.^{10, 28} However, the alternative of tube feeding if the patient were not able to tolerate an oral diet would potentially have a worse functional outcome for swallowing function. So long as patients continue with swallowing exercises the semi-liquid diet should not be detrimental to their swallow in the longer term¹⁰ and has clear benefits nutritionally during treatment and recovery. This is a subject for future research.

Implications for Practice

Patients with all head and neck cancer diagnoses should be educated to expect taste changes from week 1 of radiotherapy. They should be advised that soft, semi-liquid foods that require less chewing before swallowing are easier to tolerate.

Study Limitations

This study was carried out in a single radiotherapy department with patients who were predominantly white, which is representative of the local population. Including participants from other departments with more diverse backgrounds would improve the generalisability of our findings. A larger sample size with more females would increase confidence in the transferability of results, particularly the novel findings about sex differences.

Conclusions

Almost all participants had developed some degree of dysgeusia by week 4 of treatment and one third during week 1. Patients with all HNC diagnoses should be educated to expect their sense of taste may be affected from the start of RT and to expect a deterioration through the course of treatment. Staff should be aware that females with HNC may be more likely to report dysgeusia and aversions towards food smell and texture. Participants reported that soft semi-liquid foods that required less chewing were more easily tolerated. Translating findings into patient advice will help to limit the impact of dysgeusia on nutritional status and treatment outcomes.

Conflicts of Interest: There are no conflicts of interest to be declared.

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