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Does the radioactive iodine dose affect smell, taste sensation and nose function?

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Main Article

Dr B Tutar takes responsibility for the integrity of the content of the paper

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Abstract

Objective. To detect whether the adverse effects of post-operative radioactive iodine therapy following differentiated thyroid cancer on smell, taste and nasal functions were associated with radioactive iodine dose.

Methods. Fifty-one patients who had undergone total thyroidectomy because of differentiated thyroid cancer were divided into two groups depending on the post-operative radioactive iodine therapy dose: low dose group (50 mCi; 21 patients) and high dose group (100–150 mCi; 30 patients). The Sniffin' Sticks smell test, the Taste Strips test and the 22-item Sino-Nasal Outcome Test were performed on all patients one week before therapy, and at two months and one year following therapy.

Results. Statistically significant differences were detected in the Sniffin' Sticks test results, total odour scores, total taste scores and Sino-Nasal Outcome Test results between the assessment time points. There was no statistically significant difference between the low and high dose groups in terms of odour, taste or Sino-Nasal Outcome Test scores either before or after therapy.

Conclusion. Radioactive iodine therapy has some short- and long-term adverse effects on nasal functions and taste and odour sensations, which affect quality of life. These effects are not dose-dependent.

Introduction

Thyroid cancer has become a notable healthcare problem because of gradually increasing incidence globally. The global thyroid cancer incidence is 6.7 per 100 000.[1] Standardisation of early diagnosis and treatment has resulted in a promising decrease in mortality.[2,3] Radioactive iodine therapy following total or near-total thyroidectomy constitutes the basic therapy for most patients with differentiated thyroid cancer. The dose is adjusted according to the risk status of the patient.[4,5]

Radioactive iodine therapy has some adverse effects with low morbidity. Such effects are usually dose-dependent, and associated with the accumulation of iodine in salivary and lachrymal glands.[6] Patients frequently suffer from taste disorder, chronically dry eyes and dry mouth.[7,8] These patients develop sialadenitis, which negatively affects quality of life. The risk of secondary haematological and salivary gland malignancy slightly increases in patients with higher radioactive iodine doses; however, these cases should be evaluated individually.[9] The adverse effects of radioactive iodine are both acute and long-term; chronic effects remain a problem in patients for whom long-term survival is expected.

Although it has been shown that radioactive iodine accumulation in the nose is normal and higher than in the mouth and parotid gland,[10] nasal complications have been neglected and only a limited number of studies have been published.[11–13] Those studies concluded that radioactive iodine caused loss of smell in patients, but the effect of dose was not investigated. This study aimed to determine whether the short- and long-term adverse effects on smell, taste and nose function are dependent on radioactive iodine dose.

Materials and methods

We prospectively studied 51 patients (41 female and 10 male) who had undergone total thyroidectomy because of differentiated thyroid cancer and who had received further radioactive iodine therapy. The average (± standard deviation) age of the participants was 40 ± 12 years (range, 19–56 years). None of the patients presented with cervical metastasis. Olfactory and taste tests were carried out, and the 22-item Sino-Nasal Outcome Test (SNOT-22) questionnaire was completed. Thyroxine (T4),

thyroid-stimulating hormone (TSH) and thyroglobulin levels were measured one week before therapy and at two months and one year following therapy.

Radioactive iodine therapy

According to our standard protocol, all patients followed a low iodine diet for two weeks before radioactive iodine therapy, and the patients did not take levothyroxine for four weeks or triiodothyronine for two weeks, to obtain a TSH level of 30 μIU/ml or more prior to the administration of radioactive iodine.

The patients were divided into two groups according to the radioactive iodine dose: the low dose group ($n = 21$) were treated with low radioactive iodine therapy (50 mCi), and the high dose group ($n = 30$) were treated with intermediate–high radioactive iodine therapy (100–150 mCi). Sialagogues such as sour candies or lemon juice were given to all the patients in order to stimulate salivary secretion and reduce the possible harmful effect of radiation on salivary gland cells.

Inclusion criteria

The inclusion criteria were adult patients who had undergone total thyroidectomy because of differentiated thyroid carcinoma, for whom post-operative radioactive iodine therapy was planned.

Exclusion criteria

Patients were excluded from the study if: they were smokers; they had any salivary gland pathology (i.e. sialadenitis or sialolithiasis); they had a malignant tumour in the oral cavity or nasal cavity; they had previously undergone sinus surgery or septoplasty, neck radiotherapy, tympanoplasty or tympanomastoidectomy; or they had a history of autoimmune disease, nasal septal deviation, or allergic rhinitis.

Olfactory and taste function measurement

The 'Sniffin' Sticks' test (Burghart Messtechnik, Wedel, Germany) is a nasal chemosensor performance test utilising felt pens that dispense odour. The Sniffin' Sticks test was performed on all patients in a bright, clean and odourless room by a single physician. The test kit consists of three subtests: odour threshold, odour identification and odour discrimination. The pen cap was removed for approximately 3 seconds for odour delivery, and the tip of the pen was then placed about 2 cm from both nostrils.[14]

Odour threshold

Threshold measurements were performed using *n*-butanol via a single-step system based on a three-alternative forced choice technique. Sixteen different dilutions were used, starting with 4 per cent *n*-butanol and decreasing geometrically. Three pens, two odourless and one odorous, were randomly smelt by the patients. The patient was asked to detect the odorous pen. Three pens were smelt subsequently at intervals of 20 seconds. The ladder step was reversed when the odour was recognised in two different tests. The threshold was identified as the average of the last four reversed steps of the seven ladder steps. The scores range between 1 and 16.

Odour discrimination

A system based on a three-alternative forced choice technique was used for the odour discrimination test. Three pens, two with the same odour and one with a different odour, were smelt by the patients randomly, and the patient was asked to identify the correct odour. An interval of 20 to 30 seconds was allowed between triple pens, and approximately 3 seconds were allowed before each pen. Sixteen triple pens were smelt, and a score between 0 and 16 was determined. The patients' eyes were closed during determination of the threshold value and discrimination scores, to prevent identification of the pens and corresponding odour.

Odour identification

Odour identification was evaluated for 16 common odours. The patient was asked to select one of four options for each odour. The scores range between 0 and 16.

The results of the three subtests (threshold, discrimination and identification) were presented as a combined total score. A total score of 16.5 or lower indicates anosmia, 16–30.5 reflects hyposmia and higher than 30.5 represents normosmia.[15]

Taste Strips test

The Taste Strips test (Burghart Messtechnik) consists of tastant-impregnated filter papers (four concentrations for each of four basic taste modalities). The following concentrations were used: sweet = 0.4, 0.2, 0.1 and 0.05 g/ml sucrose; sour = 0.3, 0.165, 0.09 and 0.05 g/ml citric acid; salty = 0.25, 0.1, 0.04 and 0.016 g/ml sodium chloride; and bitter = 0.006, 0.0024, 0.0009 and 0.0004 g/ml quinine hydrochloride.

The mouth was rinsed out with water before the implementation of each strip. The tastes were presented randomly in increasing concentration (four concentration levels per taste). The patients had to identify the taste from five identifier lists: sweet, sour, salty, bitter and no taste. The number of accurate tastes was combined into a total taste score in order to obtain an impression of general taste function. A taste score of lower than 12 points was identified as hypogeusia.[16]

Sino-Nasal Outcome Test

The SNOT-22 is the most common test used to evaluate the effects of sinonasal diseases on quality of life. The test comprises 6 sections and 22 questions (0 for no problem; 5 for the worst symptom). Increasing scores correspond to a worse quality of life.[17,18]

Statistical analysis

Statistical analysis was performed using SPSS® software version 23. Descriptive analyses were presented using means and standard deviations, or median, minimum and maximum values. The proportions were presented using tables of frequencies and percentages. The chi-square test or Fisher's exact test (when chi-square test assumptions did not hold because of low expected cell counts), was used, where appropriate, to compare these proportions in the different groups. One-way analysis of variance was utilised to compare the parameters among the groups. Levene's test was employed to assess the homogeneity of the variances. When an overall significance was observed, pairwise post-hoc tests were performed using Tukey's test. Friedman tests were conducted to test whether there was a significant change in the variables as a result of violations of parametric test assumptions

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Table 1. Demographic features of patients according to RAI therapy dose

Characteristic	RAI therapy dose			
	50 mCi	100 mCi	150 mCi	Total
Gender (*n* (%))				
– Female	17 (81.0)	18 (85.7)	6 (66.7)	41
– Male	4 (19.0)	3 (14.3)	3 (33.3)	10
Age (mean ± SD; years)	39 ± 9	41 ± 11	39 ± 6	40 ± 12

RAI = radioactive iodine; SD = standard deviation

(non-normal distribution), and the Wilcoxon test was performed to test the significance of pairwise differences using the Bonferroni correction to adjust for multiple comparisons. A *p*-value lower than 0.05 was considered to show a statistically significant result.

Results

Seventeen females and four males underwent 50 mCi radioactive iodine therapy following thyroidectomy; the average age of the participants was 39 ± 9 years (range, 19–53 years). Eighteen females and three males received 100 mCi radioactive iodine therapy following thyroidectomy; the average age of the participants was 41 ± 11 years (range, 19–56 years). Six females and three males had 150 mCi radioactive iodine therapy following thyroidectomy; the average age of the participants was 39 ± 6 years (range, 19–53 years) (Table 1).

The low dose group included patients who had received 50 mCi radioactive iodine therapy, whereas the high dose group comprised patients who had received 100 or 150 mCi radioactive iodine therapy. There was no statistically significant difference between the low and high dose groups in terms of gender or age.

The TSH, thyroglobulin and T4 levels of the patients were analysed before and after therapy (Table 2).

Olfactory function

In the low dose group, hyposmia was detected in three patients (14.3 per cent) before therapy, in 11 patients (52.4 per cent) at two months and in 8 patients (38.1 per cent) at one year following therapy (Table 3).

In the low dose group, statistically significant differences were detected between the baseline scores and two-month scores for the Sniffin' Sticks threshold and discrimination subtests ($p < 0.05$). In the same group, statistically significant differences were detected between the scores at two months and one year following therapy for the Sniffin' Sticks identification and total odour subtests ($p < 0.05$) (Table 4 and Figure 1).

In the high dose group, hyposmia was detected in 6 patients (20 per cent) before therapy, in 19 patients (63.3 per cent) at two months and in 17 patients (56.7 per cent) at one year following therapy (Table 3). Anosmia was detected in two patients (6.7 per cent) at two months following therapy.

In the high dose group, statistically significant differences were detected between baseline scores and those at two months following therapy for the Sniffin' Sticks threshold and identification subtests ($p < 0.05$) (Table 4). In the same group, statistically significant differences were detected between baseline scores and those at two months and one year following therapy for the Sniffin' Sticks discrimination and total odour subtests ($p < 0.05$) (Figure 2).

There was no significant difference in odour disorder ratios between patients enrolled in the low and high dose groups before therapy. However, the number of patients who had developed hyposmia at two months was higher in the high dose group (Table 3).

No statistically significant difference was detected when total odour scores before therapy were compared with score differences at two months and one year following therapy (Table 5).

Taste function and total taste scores

In the low dose group, hypogeusia was detected in six patients (28.6 per cent) before radioactive iodine therapy, in 13 patients (61.9 per cent) at two months and in 16 patients (76.2 per cent) at one year following therapy (Table 3).

In the high dose group, hypogeusia was detected in 16 patients (53.3 per cent) before radioactive iodine therapy, in 24 patients (80 per cent) at two months and in 25 patients (83.3 per cent) at one year following therapy (Table 2).

In the low and high dose groups, no statistically significant differences were detected when total taste scores before therapy and at two months and one year after therapy were compared ($p > 0.05$) (Table 6).

Sino-Nasal Outcome Test results

In the low and high dose groups, no statistically significant differences were detected when SNOT-22 results before therapy and at two months and one year after therapy were compared ($p > 0.05$) (Table 2).

Discussion

Radioactive iodine therapy is used to ablate the thyroid tissue remnant that remains post-operatively in differentiated thyroid cancer. However, radioactive iodine may accumulate in tissues other than the thyroid and may cause some adverse effects, including sialadenitis, dry mouth, alopecia and conjunctivitis. Nasal dysfunction and problems in odour and taste may also present as adverse effects of radioactive iodine therapy.[6,10,19] When it became evident that problems in smelling and tasting affect quality of life, the number of studies in this field increased.

Norby *et al.*[10] reported radioactive iodine accumulation in the nasal area following a 5 mCi diagnostic dose. In the same study, intranasal radioactive iodine accumulation was shown in a patient who had received a therapeutic dose of 150 mCi and developed bleeding. Van Nostrand *et al.*[19] found nasal symptoms (nose pain, nose wounds, nose dryness, blood clots inside the nose and nose bleeding) in 2 of 10 patients with metastatic, well-differentiated thyroid cancer who had received a total of 51–450 mCi radioactive iodine. These complaints appeared one to two weeks following therapy and disappeared within three months.

Jonklaas[11] retrospectively reviewed 411 patients who had received radioactive iodine therapy for lachrymal and nasal side effects. The mean dose was 109 mCi. Following therapy, 42 patients (10.5 per cent) developed adverse nasal effects, whereas 40 patients (9.7 per cent) developed lachrymal adverse effects. The mean onset period was 11 days for nasal symptoms and 10 months for lachrymal symptoms. Radioactive iodine dose and body mass index were significantly positively

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Table 2. Data for TSH, thyroxine, thyroglobulin and SNOT-22, for both dosage groups, before and after RAI therapy

	Low dose group (50 mCi RAI)		High dose group (100–150 mCi RAI)		
Parameter	Mean ± SD	Median (range)	Mean ± SD	Median (range)	*P*-value
TSH level (mU/l)	≤0.001*		≤0.001*		
– Before RAI	37.26 ± 17.48	47 (1–49)	42.59 ± 11.58	47 (7–49)	0.969
– 2 months after RAI	2.28 ± 4.68	0 (0–20)	2.74 ± 4.47	1 (0–17)	0.382
– 1 year after RAI	1.44 ± 3.77	0 (0–17)	1.10 ± 1.59	1 (0–6)	0.200
Thyroxine level (ng/l)	≤0.001*		≤0.001*		
– Before RAI	3.97 ± 3.36	3 (0–11)	2.71 ± 1.86	2 (0–9)	0.251
– 2 months after RAI	10.23 ± 2.61	10 (6–18)	11.26 ± 3.18	10 (8–18)	0.254
– 1 year after RAI	10.11 ± 2.45	10 (6–18)	10.99 ± 2.87	10 (8–18)	0.319
Thyroglobulin level (pmol/l)	≤0.001*		≤0.001*		
– Before RAI	18.04 ± 31.12	12 (0–141)	13.16 ± 14.06	14 (0–72)	0.929
– 2 months after RAI	1.72 ± 4.38	0 (0–20)	1.16 ± 3.61	0 (0–20)	0.815
– 1 year after RAI	1.38 ± 4.34	0 (0–20)	1.06 ± 3.59	0 (0–20)	0.549
SNOT-22 scores	≤0.001*		≤0.001*		
– Before RAI	8.19 ± 5.66	8 (0–23)	10.03 ± 6.02	10 (0–23)	0.213
– 2 months after RAI	24.14 ± 8.15	25 (4–38)	26.33 ± 10.10	25 (12–52)	0.766
– 1 year after RAI	16.10 ± 10.90	14 (0–35)	19.13 ± 10.12	18 (4–44)	0.319

*Indicates statistical significance. TSH = thyroid-stimulating hormone; SNOT-22 = 22-item Sino-Nasal Outcome Test; RAI = radioactive iodine; SD = standard deviation

Table 3. Anosmia, hyposmia, normosmia, hypogeusia and normal taste rates, for both dosage groups, before and after RAI therapy

Assessment time	Parameter	Low dose group (50 mCi RAI) (*n* (%))	High dose group (100–150 mCi RAI) (*n* (%))	*P*-value
Before RAI	Anosmia	0 (0)	0 (0)	0.720
	Hyposmia	3 (14.3)	6 (20.0)	
	Normosmia	18 (85.7)	24 (80.0)	
	Hypogeusia	6 (28.6)	16 (53.3)	0.079
	Normal taste	15 (71.4)	14 (46.7)	
2 months after RAI	Anosmia	0 (0)	2 (6.7)	0.362
	Hyposmia	11 (52.4)	19 (63.3)	
	Normosmia	10 (47.6)	9 (30.0)	
	Hypogeusia	13 (61.9)	24 (80.0)	0.154
	Normal taste	8 (38.1)	6 (20.0)	
1 year after RAI	Anosmia	0 (0)	0 (0)	0.192
	Hyposmia	8 (38.1)	17 (56.7)	
	Normosmia	13 (61.9)	13 (43.3)	
	Hypogeusia	16 (76.2)	25 (83.3)	0.722
	Normal taste	5 (23.8)	5 (16.7)	

RAI = radioactive iodine

and negatively associated with nasal and lachrymal adverse effects, respectively ($p = 0.04$ and $p = 0.01$, respectively).

Alexander *et al.*[6] reviewed the intermediate-term (first three months) and long-term (three months to one year) adverse effects associated with high dose (100–200 mCi) radioactive iodine therapy in 203 patients. They asked the patients 10 standardised questions. The authors reported intermediate- or long-term adverse effects in 76.8 per cent of patients (156 out of 203) following radioactive iodine therapy. Long-term adverse effects were reported in 61.1 per cent (124 out of 203 patients). Sialadenitis, smell and taste loss, and alopecia developed in 33 per cent, 27.1 per cent and 28.1 per cent of the patients, respectively. Smell and taste loss appeared several weeks following therapy and recovered within three months.

The present study reviewed smell and taste loss during the short and long term in patients who had received low (50 mCi) or high (100–150 mCi) radioactive iodine therapy doses. At two months, smell loss was detected in 62.7 per cent of patients (32 out of 51) and taste loss in 72 per cent (37 out of 51). At one year, smell loss was detected in 49.0 per cent

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Table 4. Olfactory scores, for both dosage groups, before and after RAI therapy

	Low dose group (50 mCi RAI)		High dose group (100–150 mCi RAI)		
Olfactory parameter	Mean ± SD	Median (range)	Mean ± SD	Median (range)	*P*-value
Threshold score	0.010*		≤0.001*		
– Before RAI	11.43 ± 4.26	12 (3–16)	11.33 ± 4.10	12 (3–16)	0.929
– 2 months after RAI	9.24 ± 3.90	8 (3–16)	8.03 ± 3.59	8 (2–16)	0.201
– 1 year after RAI	9.81 ± 3.49	9 (3–16)	9.67 ± 3.24	9 (4–16)	0.764
Discrimination score	0.034*		≤0.001*		
– Before RAI	12.57 ± 1.69	13 (8–15)	12.27 ± 2.23	13 (8–15)	0.875
– 2 months after RAI	11.24 ± 2.43	11 (5–16)	10.03 ± 3.01	11 (5–16)	0.070
– 1 year after RAI	11.48 ± 2.11	12 (7–15)	10.37 ± 2.82	10 (7–16)	0.075
Identification score	≤0.001*		≤0.001*		
– Before RAI	12.48 ± 2.11	13 (8–15)	11.30 ± 2.47	11 (8–16)	0.089
– 2 months after RAI	10.10 ± 2.96	10 (5–14)	9.43 ± 2.76	9 (6–14)	0.441
– 1 year after RAI	10.24 ± 2.88	10 (5–14)	10.50 ± 2.74	10 (5–14)	0.735
Total score	≤0.001*		≤0.001*		
– Before RAI	36.52 ± 5.56	37 (25–45)	34.80 ± 6.40	37 (21–45)	0.300
– 2 months after RAI	30.48 ± 6.48	32 (18–42)	26.77 ± 6.41	25 (15–37)	0.099
– 1 year after RAI	31.48 ± 5.35	33 (20–41)	30.53 ± 5.12	32 (24–38)	0.637

*Indicates statistical significance. RAI = radioactive iodine; SD = standard deviation

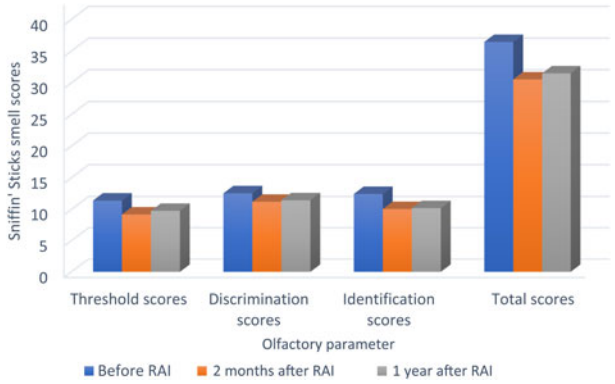

Fig. 1. Olfactory scores of the low dose (50 mCi) radioactive iodine (RAI) ablation group.

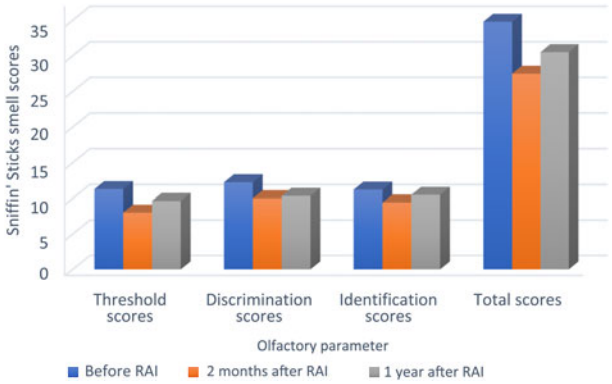

Fig. 2. Olfactory scores of the high dose (100–150 mCi) radioactive iodine (RAI) ablation group.

Table 5. Relationship between RAI dose and olfactory scores, for both dosage groups

	Low dose group (50 mCi RAI)		High dose group (100–150 mCi RAI)		
Difference	Mean ± SD	Median (range)	Mean ± SD	Median (range)	*P*-value
Before RAI & 2 months after RAI	6.05 ± 4.79	6.00 (0–23)	8.03 ± 4.46	6.50 (2.00–16.00)	0.110
Before RAI & 1 year after RAI	5.05 ± 4.24	5.00 (−1–15)	4.27 ± 6.79	5.00 (−10.00–15.00)	0.616

RAI = radioactive iodine; SD = standard deviation

of patients (25 out of 51) and taste loss in 80.3 per cent (42 out of 51). The taste loss ratio had increased at one year. Loss of smell persisted, although it had decreased over time. Increased fibrosis and loss of salivary acinus might have resulted in the increased ratio for taste loss, because saliva plays a role in tasting. There were no statistically significant differences in adverse smell and taste effects between lower dose and higher dose radioactive iodine therapy.

Server *et al.*[12] reviewed the effect of radioactive iodine therapy on nasal mucosa and nasal functions. The study included 41 patients (31 females and 10 males) who had received radioactive iodine therapy following papillary thyroid cancer. The saccharine test, nasal Schirmer test and acoustic rhinometry were used to evaluate nasal functions objectively. The investigators detected nasal dryness and congestion immediately after radioactive iodine therapy.

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Table 6. Taste scores, for both dosage groups, before and after RAI therapy

	Low dose group (50 mCi RAI)		High dose group (100–150 mCi RAI)		
Taste parameter	Mean ± SD	Median (range)	Mean ± SD	Median (range)	*P*-value
Sweet taste score	≤0.001*		≤0.001*		
– Before RAI	2.86 ± 0.85	3 (2–4)	2.93 ± 1.08	3 (0–4)	0.606
– 2 months after RAI	2.14 ± 0.91	2 (0–4)	2.50 ± 0.78	3 (1–4)	0.148
– 1 year after RAI	2.24 ± 0.83	2 (1–4)	2.50 ± 0.73	3 (1–4)	0.256
Salty taste score	0.024*		0.012*		
– Before RAI	2.86 ± 1.31	3 (0–4)	2.57 ± 1.22	3 (0–4)	0.285
– 2 months after RAI	2.14 ± 1.15	2 (0–4)	1.97 ± 0.93	2 (0–4)	0.660
– 1 year after RAI	2.52 ± 0.81	3 (1–4)	2.17 ± 0.79	2 (0–4)	0.123
Bitter taste score	0.150		0.002*		
– Before RAI	2.57 ± 1.43	3 (0–4)	2.33 ± 1.18	2 (0–4)	0.539
– 2 months after RAI	2.00 ± 1.05	2 (0–4)	1.90 ± 0.84	2 (0–4)	0.717
– 1 year after RAI	2.05 ± 1.02	2 (0–4)	1.90 ± 0.84	2 (0–4)	0.551
Sour taste score	0.001*		≤0.001*		
– Before RAI	2.81 ± 0.93	3 (1–4)	2.67 ± 0.84	3 (1–4)	0.613
– 2 months after RAI	2.00 ± 0.95	2 (1–4)	1.83 ± 0.70	2 (1–3)	0.609
– 1 year after RAI	2.00 ± 0.95	2 (1–4)	1.83 ± 0.70	2 (1–3)	0.609
Total taste score	≤0.001*		≤0.001*		
– Before RAI	11.10 ± 3.67	12 (5–16)	10.50 ± 2.98	10 (4–16)	0.494
– 2 months after RAI	8.29 ± 2.85	9 (4–14)	8.20 ± 2.25	8 (4–14)	0.692
– 1 year after RAI	8.81 ± 2.58	9 (5–14)	8.40 ± 1.98	9 (5–13)	0.543

*Indicates statistical significance. RAI = radioactive iodine; SD = standard deviation

We evaluated the effect of radioactive iodine therapy on nasal function using the SNOT-22. The SNOT-22 scores of the patients who had received radioactive iodine therapy increased at two months and one year following therapy; nasal congestion, asphyxiation and intranasal crusting, which had negative effects on quality of life, appeared. These complaints decreased but persisted between two months and one year post-therapy.

Bilici *et al.*[13] enrolled 63 patients diagnosed with papillary thyroid carcinoma. They administered the Connecticut Chemosensory Clinical Research Center odour test one week before patients received 100 mCi or 150 mCi radioactive iodine therapy, and at three weeks and one year following therapy. The odour threshold test, odour identification test and total odour scores were calculated after therapy. Before therapy, 90.5 per cent of the patients were normosmic, compared with only 54 per cent at three weeks and 56 per cent at one year. Statistically significant decreases were detected when compared with the scores before the therapy.

The Sniffin' Sticks test was implemented in the present study, including the threshold, discrimination and identification subtests, to evaluate smell sensations. We calculated the total odour score. Before therapy, 82.3 per cent of the patients were normosmic; however, only 37.3 per cent of the patients who had received either 50 mCi or 100–150 mCi radioactive iodine therapy were normosmic in the early period (at two months), and 51 per cent of the patients were normosmic at one year following therapy. Of the high dose (100–150 mCi) radioactive iodine patients, 30 per cent were normosmic at two months and 43.3 per cent were normosmic at one year following radioactive iodine therapy. In the present study, the ratio of patients with decreased smell function was higher post-therapy at 2nd month (increased scores of SNOT-22). Worse SNOT-22 questionnaire scores were seen post-therapy at 1st year, reflecting the detrimental effects on nasal functions and quality of life at two months; however, the patients continued to complain about nasal function despite the decreased scores at one year. The adverse effects of radioactive iodine on smell, taste and nasal function were dose-independent.

- Thyroid cancer has become a notable healthcare problem because of gradually increasing incidence globally
- Radioactive iodine therapy following total or near-total thyroidectomy constitutes the basic therapy for most patients with differentiated thyroid cancer
- Radioactive iodine therapy has some dose-independent short- and long-term adverse effects
- The adverse effects on nasal function, smell and taste sensation affect quality of life

Positive aspects of the present study include the evaluation of the effects on nasal function, smell and taste in patients who received low or high radioactive iodine therapy doses. Patients were followed up for one year in order to avoid biases associated with hypothyroidism.[20,21] The patients' thyroid parameters were assessed at the time of the tests. All patients were euthyroid at two months and at one year. It was concluded that subclinical hypothyroidism can also cause taste and smell disorders, and that this can be remedied within an average of three months.[20]

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The shortcomings of the present study include the limited number of patients and the restricted period for evaluation of function.

Conclusion

Radioactive iodine therapy has some dose-independent short- and long-term adverse effects. The adverse effects on nasal function and smell and taste sensations negatively affect quality of life. It is important to develop individual patient assessments and approaches to improve quality of life.

Competing interests

None declared

References

1 Ferlay J, Colombet M, Soerjomataram I, Mathers C, Parkin DM, Pineros M *et al.* Estimating the global cancer incidence and mortality in 2018: Globocan sources and methods. *Int J Cancer* 2019;**144**:1941–53

2 La Vecchia C, Malvezzi M, Bosetti C, Garavello W, Bertuccio P, Levi F *et al.* Thyroid cancer mortality and incidence: a global overview. *Int J Cancer* 2015;**136**:2187–95

3 Choi YM, Kim TY, Jang EK, Kwon H, Jeon MJ, Kim WG *et al.* Standardized thyroid cancer mortality in Korea between 1985 and 2010. *Endocrinol Metab (Seoul)* 2014;**29**:530–5

4 Jeong JH, Kong EJ, Jeong SY, Lee SW, Cho IH, Ah Chun K *et al.* Clinical outcomes of low-dose and high-dose postoperative radioiodine therapy in patients with intermediate-risk differentiated thyroid cancer. *Nucl Med Commun* 2017;**38**:228–33

5 Haugen BR, Alexander EK, Bible KC, Doherty GM, Mandel SJ, Nikiforov YE *et al.* 2015 American Thyroid Association Management Guidelines for Adult Patients with Thyroid Nodules and Differentiated Thyroid Cancer: The American Thyroid Association Guidelines Task Force on Thyroid Nodules and Differentiated Thyroid Cancer. *Thyroid* 2016;**26**:1–133

6 Alexander C, Bader JB, Schaefer A, Finke C, Kirsch CM. Intermediate and long-term side effects of high dose radioiodine therapy for thyroid carcinoma. *J Nucl Med* 1998;**39**:1551–4

7 Almeida JP, Sanabria AE, Lima EN, Kowalski LP. Late side effects of radioactive iodine on salivary gland function in patients with thyroid cancer. *Head Neck* 2011;**33**:686–90

8 Klein Hesselink EN, Brouwers AH, de Jong JR, van der Horst-Schrivers AN, Coppes RP, Lefrandt JD *et al.* Effects of radioiodine treatment on salivary gland function in patients with differentiated thyroid carcinoma: a prospective study. *J Nucl Med* 2016;**57**:1685–91

9 Dingle IF, Mishoe AE, Nguyen SA, Overton LJ, Gillespie MB. Salivary morbidity and quality of life following radioactive iodine for well-differentiated thyroid cancer. *Otolaryngol Head Neck Surg* 2013;**148**:746–52

10 Norby EH, Neutze J, Van Nostrand D, Burman KD, Warren RW. Nasal radioiodine activity: a prospective study of frequency, intensity, and pattern. *J Nucl Med* 1990;**31**:52–4

11 Jonklaas J. Nasal symptoms after radioiodine therapy: a rarely described side effect with similar frequency to lacrimal dysfunction. *Thyroid* 2014;**24**:1806–14

12 Server EA, Kirgezen T, Celebi OO, Yildiz M, Yigit O, Cermik TF. How does radioactive iodine affect the nose? *Laryngoscope* 2017;**127**:2698–702

13 Bilici S, Edizer DT, Yiğit Ö, Yıldız M, Cermik TF. The effects of radioactive iodine therapy on olfactory function. *Am J Rhinol Allergy* 2016;**30**:206–10

14 Tekeli H, Altundağ A, Salihoğlu M, Cayönü M, Kendirli MT. The applicability of the "Sniffin' Sticks" olfactory test in a Turkish population. *Med Sci Monit* 2013;**30**:1221–6

15 Hummel T, Kobal G, Gudziol H, Mackay-Sim A. Normative data for the "Sniffin' Sticks" including tests of odor identification, odor discrimination, and olfactory thresholds: an upgrade based on a group of more than 3,000 subjects. *Eur Arch Otorhinolaryngol* 2007;**264**:237–43

16 Landis BN, Welge-Luessen A, Brämerson A, Bende A, Mueller CA, Nordin S *et al.* "Taste Strips"-a rapid, lateralized, gustatory bedside identification test based on impregnated filter papers. *J Neurol* 2009;**256**:242–8

17 Morley AD, Sharp HR. A review of sinonasal outcome scoring systems - which is best? *Clin Otolaryngol* 2006;**31**:103–9

18 Cakir Cetin A, Kumus O, Keskinoglu P, Sutay S, Ecevit MC. Turkish validation of the Sino-Nasal Outcome Test-22. *Clin Otolaryngol* 2019;**44**:557–64

19 Van Nostrand D, Neutze J, Atkins F. Side effects of "rational dose" iodine-131 therapy for metastatic well-differentiated thyroid carcinoma. *J Nucl Med* 1986;**27**:1519–27

20 Baskoy K, Ay SA, Altundag A, Kurt O, Salihoglu M, Deniz F *et al.*. Is there any effect on smell and taste functions with levothyroxine treatment in subclinical hypothyroidism? *PLoS One* 2016;**11**:e014997

21 Świdziński T, Linkowska-Świdzińska K, Czerniejewska-Wolska H, Wiskirska-Woźnica B, Owecki M, Głowacka MD *et al.* Hypothyroidism affects olfactory evoked potentials. *Biomed Res Int* 2016;**2016**:9583495

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