Radioiodine Induced Salivary and Lacrimal Gland Dysfunction in Differentiated Thyroid Carcinoma Patients: An Observational Study

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ABSTRACT

Background: This study was carried out to assess the radioiodine (I131) induced salivary and lacrimal gland damage in differentiated thyroid carcinoma (DTC) patients.

Material and Methods: A total 124 patients with differentiated thyroid carcinoma (DTC) were included in this observational study. These patients underwent radioiodine (I131) ablation following total thyroidectomy at INMAS, Mitford and completed a minimum follow-up period of 60 months. Symptoms indicative of salivary and lacrimal gland damage (xerostomia, dysphagia, salivary gland pain, swelling, dysgeusia, dry eye, excess lacrimation) were evaluated during follow up using standard questionnaires. Morphological changes of major salivary glands were assessed using high resolution ultrasound.

Result: A total of 46 (37.10%) patients experienced salivary gland symptoms where xerostomia (34, 27.4%) was the most common. Lacrimal gland symptoms found in 12 (9.60%) patients. Ultrasound features of chronic sialadenitis were observed in 10 (7.80%) patients.

Conclusion: Salivary gland damage is a common manifestation of thyroid cancer patient after radioiodine ablation.

Keywords: Salivary gland, differentiated thyroid carcinoma, sialadenitis, xerostomia, dysgeusia

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INTRODUCTION

Differentiated thyroid carcinoma (DTC) accounts for 90–95% of all thyroid tumors, with papillary (PTC) and follicular (FTC) being the most common subtypes. For over 70 years, radioactive iodine (RAI) therapy has reached a great rate of success along with surgery in DTC treatment. RAI specifically targets vesicular thyroid cells but is also taken up by salivary glands, lacrimal glands and nasal mucosa through the sodium-iodide symporter resulting dysfunction of these glands. While the side effects are generally benign, they can significantly impact the patient's quality of life. This study aimed to evaluate both the immediate and long-term effects of ^{113}1 therapy on salivary and lacrimal gland function in DTC patients (1,2)

PATIENTS AND METHODS

Total 124 DTC patients were enrolled in this retrospective observational study who underwent at least one course of radioiodine ablation (^{113}1) after total thyroidectomy at INMAS, Mitford and completed minimum 60 months (5 years) of follow up. Initial dose of RAI varied depending on the stage and morphological type of tumor and ranging from 50mci to 150 mci. In most cases, a single therapeutic dose achieved the desired ablative effect. To reduce treatment related salivary gland damage, patients were advised to increase their fluid intake and use sialagogues like citric fruit, vitamin c tablet, prickles and chewing gum starting 24 hours after RAI ingestion. Symptoms of salivary and lacrimal gland damage (xerostomia, dysphagia, salivary gland pain, swelling, dysgeusia, dry eye, excess lacrimation) were assessed during follow up with self-structured standard questionnaires. Morphological changes (volume and echotexture) of major salivary glands (parotid and salivary glands) were assessed using high resolution ultrasound (HRUS).

Statistical analysis was performed using SPSS statistical software version 20.0. Clinical parameters were presented in terms of mean and SD for quantitative variables and frequency (%) for qualitative variables. To identify the relationship between studied quantitative parameters, correlation analysis was used and spearman's rank correlation coefficients were calculated P value <0.05 was considered as statistically significant.

RESULT

A total of 124 (13 men and 111 women) patients of DTC (PTC 110, 88.7% and FTC 14, 11.3%) aged 15 to 63 years (mean age 34.5±10.8 years) underwent total thyroidectomy with lymph node dissection. Depending upon the stage and morphological variety of tumor, 3 (2.4%) patients received 50mci, 26 (21.0%) patients received 75mci, 79 (63,70%) received 100mci and 16 (12.0%) patients received 150mci RAI. 21 (16.90%) patients needed second dose and 4 (3.20%) patients needed third doses of RAI. Mean follow up period was 88.2±39.9 months with range between 60-240 months.

Table-1: Different dose of Radioiodine according to gender

RAI Dose (mci)	Female	Male	Total Number of patients
50	3 (2.42%)	0 (0.0%)	3 (2.42%)
75	21 (16.94%)	5 (4.03%)	26 (20.97%)
100	73 (58.87%)	6 (4.84%)	79 (63.71%)
150	14 (11.29%)	2 (1.61%)	16 (12.90%)

Among 124 patients, 78 (62.90%) did not report any salivary gland problems in the early (within 6months) and late (after 6 months) post ablative periods but 46 (37.10%) patients reported at least one symptom of salivary gland damage. Xerostomia or dry mouth was the most commonly experienced side effect (34, 27.40%). Eight (6.4%) patients experienced dry mouth in the early post radiation period, which recurred only when they failed to maintain proper hydration. 26 (20.97%) patients experienced dry mouth after 6 months of therapy with intermittent recurrence in 24 (19.30%) patients when fail to maintain adequate hydration. 2 (1.60%) patients experienced permanent dry mouth which affected their quality of life.

Table-2: Salivary and lacrimal adverse effects on different dose of RAI

Dose (mci)	Any Symp		Dry Mouth		Dysphagia		Pain		Swelling		Dysgeusia		Dry eye		Excess tear	
	No	Yes	No	Yes	No	Yes	No	Yes	No	Yes	No	Yes	No	Yes	No	Yes
50	3	0	3	0	3	0	3	0	3	0	3	0	3	0	3	0
	100.0	0.0	100.0	0.0	100.0	0.0	100.0	0.0	100.0	0.0	100.0	0.0	100.0	0.0	100.0	0.0
75	12	14	16	8	24	2	16	10	17	9	24	2	25	1	26	0
	46.2	53.8	61.5	30.8	92.3	7.7	61.5	38.5	65.4	34.6	92.3	7.7	96.2	3.8	100.0	0.0
100	52	27	56	23	72	7	70	9	75	4	76	3	70	9	78	1
	65.8	34.2	70.9	29.1	91.1	8.9	88.6	11.4	94.9	5.1	96.2	3.8	88.6	11.4	98.7	1.3
150	11	5	13	3	16	0	14	2	15	1	15	1	15	1	16	0
	68.8	31.3	81.3	18.8	100.0	0.0	87.5	12.5	93.8	6.3	93.8	6.3	93.8	6.3	100.0	0.0

Discomfort or pain in salivary region was experienced by 21 (16.93%) patients. 5 (4.02%) patients experienced this discomfort during first few weeks after therapy, after which it resolved spontaneously. 16 (12.90%) patients experienced chronic discomfort occasionally in late post ablative period. Bilateral or unilateral major salivary gland (mainly parotid) swelling was found in 14 (11.29%) patients. 2 (1.60%) patients experienced swelling in early post ablative periods which it was resolved afterward. 12 (9.68%) patients experienced salivary swelling in late post ablative period which completely resolved for 1 (0.81%) patient. 11 (88.70%) experienced recurrent periodic swelling which resolved within few hours. 9 (7.26%) patients complained about dysphagia in late post ablative period which was resolved completely for 2 (1.61%) patients and recurrent periodically in 7 (5.65%) patients. 22 (17.74%) patient needed parotid massage and 1 (0.81%) needed diet modification (avoidance of sour diet) to get rid of salivary swelling and pain.

Transient taste alteration or dysgeusia was reported by 6 (4.84%) patients which developed during first week after ablation and completely resolved within two months. All cases experienced altered sensation to salty taste.

HRUS of parotid and submandibular glands revealed normal volume and echotexture of parotid glands in 114 (91.80%) patients. All patients had normal salivary gland morphology sonographically. Eight (6.50%) patients had bilateral and 2 (1.60%) patients had unilateral of chronic parotid sialadenitis (reduced volume and or inhomogeneous texture).

Among 124 patients, 12 (9.60%) patients complained about lacrimal gland side effects in late post ablative periods which resolved completely within few months. 11 (8.87%) patients experienced transient dry eyes and only 1 (0.81%) patient experience of excess tearing. All patients of dry eyes used artificial tear.

Table 3: Relationships between individual clinical symptoms in the studied patients

	Age	Sex	Dose	No. of dose	Any symptom	Dry mouth	Dysphagia	Pain	Swelling	Dysgeusia	Dry eye	Excess tear
Age	1											
Sex	-.126	1										
Dose	.141	-.134	1									
No. of dose	.015	-.095	.098	1								
Any symptom	.027	.154	.112	.065	1							
Dry mouth	.021	.151	-.013	.179*	.688**	1						
Dysphagia	.177*	-.107	-.072	.025	.364**	.385**	1					
Pain	-.058	.155	.185*	.084	.588**	.204*	-.043	1				
Swelling	-.007	.122	.227*	.128	.465**	.123	-.100	.790**	1			
Dysgeusia	-.011	.077	.076	-.023	.294**	-.054	-.063	.099	.157	1		
Dry eye	-.003	.014	-.082	.048	.171	.126	.022	.086	.068	.062	1	
Excess tear	-.142	.031	-.057	-.045	.117	.147	-.025	.200*	-.032	-.020	-.028	1

* Correlation is significant at the 0.05 level (2-tailed).
** Correlation is significant at the 0.01 level (2-tailed).

Statistical analysis of obtained data revealed specific relationships between individual clinical symptoms in the studied patients (Table-3). Strong correlation was observed between salivary region pain and swelling (P-value <0.01). There was also strong correlation between dry mouth and dysphagia (P-value <0.01). However, no significant relation found between salivary and lacrimal adverse effect with age, sex, total dose of RAI and the number of RAI courses.

DISCUSSION

Radioactive iodine (RAI) therapy is a well-established approach for ablating residual thyroid tissue after total thyroidectomy in the management of differentiated thyroid carcinoma (DTC). Salivary and lacrimal gland damage induced by ^{131}I has been recognized since the widespread adoption of RAI therapy for DTC patients. RAI enters these glands through periductal capillaries, is excreted via the glandular ducts and is transported into the oral cavity in case of salivary gland and nasal cavity in case of lacrimal gland through the ductal system. The concentration of RAI in salivary glands is reported to be approximately 30–40 times higher than in the bloodstream. This elevated concentration leads to aseptic inflammation and obstruction of the salivary and lacrimal ducts resulting reduced salivation, changes in saliva composition and diminished or excess lacrimation.

Consequently, patients may experience symptoms such as dry mouth, salivary gland pain, swelling, dysphagia, altered taste sensation, dry eyes and excessive tearing which may interfere with quality of life (1-3).

Acute radiation-induced sialadenitis primarily occurs due to saliva retention in the early post-ablation period with an incidence ranging from 2% to 67%. These symptoms are generally transient and often resolve spontaneously or with minimal intervention. According to Viktoriia et al., salivary pain is the most common immediate adverse effect following ablation, followed by swelling and dry mouth (1, 4). In our study, radiation-induced sialadenitis was observed in 6.45% of cases during the early post-ablation period, with most cases resolving without intervention. Dry mouth was the most frequently reported symptom during this time, followed by dysgeusia and pain. Notably, all cases of dysgeusia and pain in our study resolved within a few weeks.

In contrast, more severe and chronic salivary gland disorders typically emerge during the late post-ablation period that can decrease the quality of life. Commonly reported symptoms include xerostomia and chronic pain, often linked to salivary gland thickening and interstitial fibrosis. Literature reports indicate that the frequency of xerostomia in the late post-radiation period varies significantly, ranging from 2% to 43% (1, 3). In our study, 22.6% of patients experienced chronic sialadenitis with periodic symptom recurrence. Xerostomia was the most common late adverse effect which became permanent in 2 patients.

Parotid glands are more affected by RAI than the submandibular glands, with an impact ratio of approximately 1.5:1 (1, 5). In our study, 6.5% of patients showed sonological evidence of bilateral parotitis, while 1.6% revealed unilateral parotitis. No sonological evidence of chronic submandibular gland involvement was observed.

Despite being reasonably safe, I131 therapy may induce some ophthalmic adverse effect like dry eye, excess tearing and conjunctivitis mainly due to RAI induced inflammation of lacrimal gland and nasolacrimal duct obstruction. Risk of ophthalmic complications is associated with various factors, including the administration of high 131I doses, age of more than 45 years and time to event within the first 12 months (6). Our study found only two complains (dry eye and excess tear) related to lacrimal gland dysfunction among the study population. Both are transient and resolved completely within two months of development. Patents used artificial tear for symptomatic relief of dry eye according to physicians' advice.

Our study identified a significant association between pain and swelling, consistent with the findings of Viktoriia et al. These symptoms are indicative of either acute or chronic sialadenitis and/or saliva retention. While Hesselink et al., Viktoriia et al., Baudin et al. and Upadhyaya et al. reported a significant relationship between salivary gland damage and factors such as RAI dose and the number of treatment courses, our study did not find any convincing association in this regard (1, 7-10). Additionally, no significant differences were observed based on age, sex, or duration of follow-up.

Adverse effects of RAI therapy are believed to presumed from the salivary glands' ability to concentrate RAI. To minimize salivary gland damage during therapy, the use of sialagogues and adequate water intake are widely recommended. Sialagogues stimulate salivation, thereby reducing RAI concentration in the glands, while sufficient water intake helps to maintain hydration. Although certain drugs may mitigate salivary gland damage, their use is not endorsed by various guidelines (7, 11, 12). At our center, all patients were advised to intake sialagogues, vitamin-C and adequate water to prevent salivary gland damage. However, we were unable to gather sufficient data to evaluate the quantitative intake of water and sialagogues.

Our study had several limitations. First, the sample size was relatively small, which may limit the generalizability of our findings. Second, the study design was retrospective, which could introduce biases. Future studies with larger sample sizes and prospective designs are needed to validate our findings and provide more robust insights.

CONCLUSION

Salivary and lacrimal gland symptoms are not uncommon following radioiodine therapy and usually develops after months or years of administration. Preventive measures can reduce the damage and improve the quality of life.

CONFLICT OF INTEREST

None

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