

Effects of Radioiodine Treatment on Salivary Gland Function in Patients with Differentiated Thyroid Carcinoma: Experience at INMAS, Mitford

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ABSTRACT

Background: Radioiodine therapy is very effective and popular method of choice for the treatment of carcinoma thyroid. Dry mouth is a common side effect after radioiodine therapy and sequel of the salivary gland dysfunction. Many of the patients are suffering from this side effect. This study was designed to evaluate the function of the salivary gland of the patients treated with radioiodine therapy.

Materials and methods: This cross sectional study was done in the Institute of Nuclear Medicine and Allied Sciences Mitford Dhaka for about 06 months from August 2019 to March 2020. About 51 patients were enrolled for this study having single dose of radioiodine therapy. Dynamic sialo scintigraphy with citrus stimulation was done after intravenous injection of 02 mCi of Tc-99m. After 10 minutes of dynamic study lemon juice was given orally for the augmentation of the gland function. Result was interpreted as salivary gland dysfunction when a curve was uprising after lemon juice augmentation and normal functioning when fall off curve. Then data were compiled and analyzed by SPSS version 22.

Results: The mean age of the study subjects were 35.1 ± 9.8 , age ranged from 14–56 years, six were male and 45 were female participants. The mean dose was 4.3 ± 1.1 GBq, ranges from 1.8–7.4 GBq. The proportion of salivary gland dysfunction was 60.8% while 39.2% had normal salivary gland function. Right salivary gland dysfunction was found in 52.9% patients while 54.9% patient showed left salivary gland dysfunction. A little above a decile (13.7%) showed right submandibular gland dysfunction while a little less than that (7.8%) showed left submandibular gland dysfunction. Salivary gland dysfunction was related to the dose of the radioiodine therapy ($p < 0.5$). Higher dose of RAIT produced the odds of dysfunction in right parotid gland as 1.01, that of left parotid as 0.04, that of right submandibular as 0.09 and that of left submandibular 0.60.

Conclusion: Higher dose of radioiodine therapy was related with salivary gland dysfunction.

Key words: Radioiodine therapy, Salivary gland, Carcinoma thyroid.

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INTRODUCTION

Radioiodine therapy for the ablation of the residual thyroid tissue and distant metastases in thyroid carcinoma is very effective method of choice (1). Initial effects of radioiodine therapy is rare but gradually most of the patients experience dry mouth, taste alteration, difficulty in swallowing, pain in the parotid and submandibular salivary gland regions. These effects are related to the dose of the radioiodine which patients had received during their therapy (2). The radioiodine therapy cause damage to the salivary gland which has carrier mediated mechanism similar to the thyroid gland (3). Among all side effects dryness of mouth is very common problem of the patients received radioiodine therapy (4). This cross sectional study was conducted to evaluate the function of salivary gland who had given therapy for the treatment of thyroid cancer.

PATIENTS AND METHODS

This study was carried out in the Institute of Nuclear Medicine and Allied Sciences (INMAS), Mitford, Dhaka over a period of six months from August 2019 to March 2020 for dynamic sialo scintigraphy. All the study subjects in this study was treated with single dose of radioiodine therapy from the year 2012 to 2020. The study was conducted among 51 patients. Informed written consent was obtained from all the patients. Dynamic image was obtained by Siemens dual head gamma camera with parallel view, low energy all purpose collimator, acquisition matrix 64X164, orientation head out,

zoom 1.23, photopeak centered at 140 Kev. Dynamic sialoscintigraphy was done immediately after intravenous injection of 02-03 mCi of Tc-99m and anterior view was taken for about 20 minutes. 10ml of lemon juice augmentation was done after 10 minutes. Regions of interest were drawn over both parotid and submandibular salivary glands and one for background correction over the forehead. The time activity curve was generated and data were analyzed for each parotid and submandibular salivary glands. Qualitative analysis was done for time activity curves explained as normal functioning salivary gland if the curve falls after citrus juice administration and if the time activity curve did not fall after citrus juice administration-suggesting salivary gland dysfunction. Then data were compiled and analyzed e.g. bivariate analysis such as Chi-square test was done. Here the dose, duration of treatment and gender in the regression model as factors that could have been associated with the adverse outcome of salivary gland. In each analysis, level of significance was 0.05 and P value < 0.05 considered as statistically significant.

RESULTS

Total study subjects were 51, among them 45 were female and six were male. The study subjects received radioiodine therapy from the year 2012 to 2020.

The characteristics of study subjects are described in table 1.

Table 1: Characteristics of the study subjects (n = 51)

Study subjects	Characteristics
Total patients	51
Male with mean age	6 Mean ± age 39±9.9
Female with mean age	45 34.6±9.8
Mean Dose in male patients	4.3±0.9 GBq
Mean Dose in female patients	4.3±1.1 GBq

The study was conducted after the radioiodine therapy of about 1.8-2.3 years. This study showed that increase of right parotid gland, among 06 male patients 50% and 53.3% had decreased salivary function. About 50% male and 55.6% female had decreased left parotid gland salivary gland dysfunction. About 33.3% male and 11.1% patient had right submandibular salivary gland dysfunction. This study also showed that 16.7% male patients and 6.7% had female patients had left submandibular dysfunction.



Figure -1a. Salivary Gland (Parotid) dynamic sialoscintigraphy

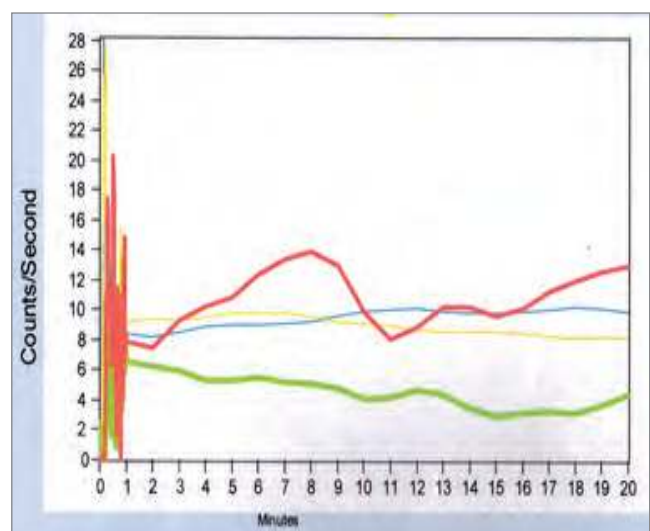


Figure-1b. Curve represent right (green curve- uprising after citrus juice stimulation-suggesting normal functioning & left (red curve)- non rising curve showing salivary gland dysfunction.



Figure-2a: Dynamic Sialoscintigraphy of both submandibular salivary glands.

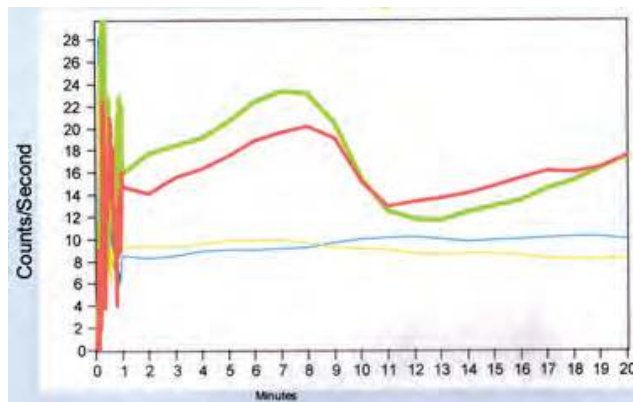


Figure-2b: Both the submandibular salivary glands show upriser curve after citrus juice stimulation after 10 minutes citrus juice—suggesting normal functioning.

Regarding effect of dose on the salivary gland this study showed 27 had right parotid gland dysfunction with radioiodine dose 4.5 ± 1.1 GBq with mean duration of 28.57 ± 26.95 months. Left parotid gland showed that, 28 had salivary gland dysfunction with mean dose 4.6 ± 1.1 GBq with duration of treatment 26.22 ± 28.92 months. The table given below showed the effect of dose on the four salivary glands.

Table 2: Dose of radioiodine therapy, functional status and duration of treatment

Salivary Gland	Functional status	Number (Percentage)	Dose GBq Mean \pm SD	P value	Duration of treatment	P value
Right parotid	Normal function	24 (47)	4.1 ± 1.1	0.17	2.3 ± 2.2	0.70
	Dysfunction	27(52)	4.5 ± 1.1		2.1 ± 2.3	
Left parotid	Normal function	23(45)	3.9 ± 1.0	0.31	2.2 ± 2.1	0.83
	Dysfunction	28 (54)	4.6 ± 1.1		2.1 ± 2.3	
Right submandibular	Normal function	44(86)	4.2 ± 1.1	0.09	2.2 ± 2.2	0.74
	Dysfunction	07(14)	5.0 ± 0.9		1.9 ± 2.6	
Left submandibular	Normal function	47(92)	4.3 ± 1.1	0.62	2.2 ± 2.2	0.73
	Dysfunction	04(08)	4.6 ± 1.0		1.8 ± 2.8	

The regression model of this study has described below in four tables:

Table 3: Regression model of right parotid salivary gland

Rt Parotid	OR	Lower	Upper	Sig.
Dose (GBq)	1.013	.994	1.033	.175
Female	1.131	.200	6.389	.890
Duration >2.7yrs	1.013	.278	3.682	.985

The above table shows the regression model on right parotid gland. It shows that for each unit increase of dose (GBq) there is 1.3% increased chance of dysfunction in right parotid gland, the females are 13.1% at increased risk of suffering from dysfunction in right parotid gland and for duration of >2.7 years, there is 1.3% increased chance of dysfunction in right parotid gland, though there is no significance in this prediction.

Table 4: Regression model for left parotid salivary gland

Lt. Par	OR	Lower	Upper	Sig.
Dose (GBq)	1.022	1.001	1.043	.039
Female	1.200	.201	7.170	.841
Duration >2.7yrs	1.394	.361	5.388	.630

The above table shows the regression model on left parotid gland. It shows that for each unit increase of dose (GBq) there is 2.2% increased chance of dysfunction in left parotid gland (p=0.04), the females are 20.0% at increased risk of suffering from dysfunction in left parotid gland and for duration of >2.7 days, there is 39.4% increased chance of dysfunction in left parotid gland; here only the dose is significantly predicting the likelihood of dysfunction leaving other non-significant.

Table 5: Regression model for right submandibular salivary gland

Rt Sub man	OR	Lower	Upper	p
Dose (GBq)	1.02	.996	1.057	.090
Female	.199	.025	1.595	.128
Duration >2.7 yrs	1.21	.179	8.257	.843

The above table shows the regression model on right submandibular gland. It shows that for each unit increase of dose (GBq) there is 2.6% increased chance of dysfunction in right submandibular gland, the females are 80% less chance of dysfunction in right submandibular gland and for duration of >2.7years , there is 21.4% increased chance of dysfunction in right submandibular gland, and none of these variables are significantly predicting the outcome.

Table 6: Regression model for left submandibular salivary gland

Left Sub man.G	OR	Upper	Lower	P value
Dose (GBq)	1.009	.975	1.045	.596
Female	.346	.029	4.075	.399
Duration >2.7 years	.999	.091	10.956	.999

The above table shows the regression model on left submandibular gland. It shows that for each unit increase of dose (GBq) there is 0.09% increased chance of dysfunction in left submandibular gland, the females have 66.4% less chance of dysfunction in left submandibular gland and for duration of >2.7 years, there is 0.1% less dysfunction in left submandibular gland, and none of these variables are significantly predicting the outcome.

DISCUSSION

Salivary gland dysfunction after radioiodine therapy is a common phenomenon and reversible situation in most of the cases. The study was conducted among the 51 patients, among them six was male and 45 was female. Patients received radioiodine therapy in this study was female predominate. This findings were consistent with the other studies Riachy et al. and kang et al. showed that carcinoma thyroid were more common among female patients in their study (4,5). Another study conducted by Toft D showed that among the study subjects 76% were female that is female predominate.

Among the study subjects mean age among the male patients were 39±9.9 and in the female patients were 34.6±9.8. The male patients received 4.3±0.9 GBq and the female patients received 4.3±1.1 GBq of radioiodine.

Kang et al. conducted a study on thyroid cancer patients with radioiodine therapy also showed similar number of patients with mean age 46.2±12.9 years with dose of I-131 5.2±1.5 GBq (5).

A study conducted by Grewal et al. also showed similar findings of 66% female with mean age 45±16yrs who had got 5.25±2.62Gbq single dose of radioiodine therapy for the treatment carcinoma thyroid (6)

All the subjects in this study were treated with single dose of radioiodine therapy and prepared with thyroid hormone (TSH) withdrawal.

Similar studies of Solans et al. and Hyer et al. showed that their patients were prepared with withdrawal of thyroid hormone for the single dose of radioiodine therapy (7,8).

This study showed that in case of right parotid gland, among 06 male patients 50% and 53.3% had decreased salivary function. About 50% male and 55.6% female had decreased left parotid gland salivary gland dysfunction. In case of right submandibular gland 33.3% male and 11.1% patient had salivary gland dysfunction. This study also showed that 16.7% male patients and 6.7% had female patients had left submandibular dysfunction.

This study showed that 54% right parotid, 52% left parotid, 14% right submandibular gland and 08% left submandibular gland. Similar findings found in a study conducted by Toft J. Daniel showed that at least one parotid was affected, 54% had bilateral parotid, 10% had submandibular gland damage (9).

Another study conducted by Cagler et al. (2002) showed that objective experience of salivary gland dysfunction was found in 69% (31 of 45) of patients. The parotid glands were affected about 81% and the submandibular glands showed had dysfunction about 13%. Both the salivary glands affected among 6% patients (< 0.000001) (10).

Regarding effect of dose on the salivary gland this study showed 27 had right parotid gland dysfunction with radioiodine dose 4.5 ± 1.1 GBq with mean duration of 28.57 ± 26.95 days. Left parotid gland showed 28 had salivary gland dysfunction with mean dose 4.6 ± 1.1 GBq with duration of treatment 26.22 ± 28.92 days.

Regarding dose another study conducted by Roh et al (2016) showed that Among 63 patients the mean age was 55.4 ± 10.4 years and the mean RAI dose was 5.3 ± 1.2 MBq (11).

A study conducted by Toft J. Daniel also depicted that dose was the main cause of the salivary gland damage and patients treated with radioiodine showed 47% salivary gland damage (9).

Another study conducted by Jonklass et al. (2015) also found that parotid glands are more affected than the submandibular glands (12).

Similar findings also observed in the study conducted by Malpani et al. that the parotid glands were more affected than the submandibular gland (13).

The regression analysis of this study showed that each unit increase of dose, 1.3% increased chance of damage of right parotid gland, 2.2% increased chance of damage of left parotid gland, 2.6% chance of damage of right submandibular gland and 0.09% increase chance of left submandibular gland.

Similar findings showed in the study conducted by the Grewal et al. that the salivary gland dysfunction more related with the administered dose, that is larger dose have more side effects and less dose have less side effects (6).

A study conducted by Tanwar et al. also found that salivary gland function decreases after radioiodine treatment and parotid glands are more affected than the submandibular salivary glands (14).

CONCLUSION

Radioiodine therapy for the treatment of carcinoma thyroid causes parotid gland dysfunction more than the submandibular gland. The damage of the salivary gland is dose dependent e.g. higher dose causes more damage.

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