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Dentistry Section

Assessment of Salivary Gland Function Using Salivary Scintigraphy in Pre and Post Radioactive Iodine Therapy in Diagnosed Thyroid Carcinoma Patients

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ABSTRACT

Introduction: Thyroid carcinoma represents less than 1% of all cancers. The first line of treatment for thyroid cancer is partial/total thyroidectomy. High-dose Iodine^{131} therapy using Iodine radioisotopes is commonly used in patients with well differentiated thyroid carcinoma after total thyroidectomy. In this process, the non-thyroidal tissues, such as, salivary gland, stomach and breast tissues also take up radioactive iodine. Salivary gland scintigraphy is widely accepted as a sensitive and valid method for evaluation of salivary gland dysfunction after Radioactive Iodine^{131} Therapy (RIT).

Aim: To assess and compare the salivary flow rates, relative uptake and ejection fractions in parotid and submandibular glands just before and one month after Iodine^{131} therapy.

Materials and Methods: The study was conducted on 24 patients diagnosed with well differentiated thyroid carcinoma who underwent partial/total thyroidectomy and were due for radioactive iodine therapy. These patients were divided into two groups based on the lesion based dosimetry (Group A: 60-100Gy; Group B: 100-150Gy). Salivary gland assessment was done by salivary gland scintigraphy before and after RIT.

Statistical Analysis: The data collected was tabulated and statistically analysed using SPSS software version16 using paired t-test and individual sample t-test.

Results: A statistically significant difference in the uptake percent and ejection fraction percent in the parotid and submandibular glands before RIT and one month after RIT was observed in the study.

Conclusion: We inferred from the study that there was an overall decrease in uptake percent and ejection fraction percent one month post RIT in both parotid and submandibular glands. Also, a statistically significant difference was noted in the uptake and ejection fraction percent between Group A and Group B concluding the fact that the damage is dose related.

Keywords: Radionuclide imaging, Radioisotopes, Xerostomia

INTRODUCTION

Thyroid gland is an endocrine gland which is situated in the lower part of the front and sides of the neck. It regulates the basal metabolic rate, stimulates somatic and psychic growth, plays an important role in calcium metabolism [1,2]. It is made up of two types of secretory cells, the follicular cells which secrete tri-iodothyronin and tetra-iodothyronin and the parafollicular cells which produce thyrocalcitonin. Thyroid carcinoma is the most common endocrine malignancy, although it represents less than 1% of all cancer cases. Differentiated Thyroid Cancer (DTC), consisting of papillary and follicular thyroid cancer, constitutes approximately 90% of all thyroid malignancies. Women have a significantly higher incidence of thyroid cancer than men and account for a larger percentage of the increased incidence [3,4]. Prognosis of the disease is generally excellent. The lifetime recurrence rate is relatively high, reaching 10–30%. High-dose Iodine^{131} (I^{131}) therapy is commonly used in patients with differentiated thyroid cancer after total or sub -total thyroidectomy to ablate normal thyroid tissue or to treat remaining thyroid cancer tissue, and thus, to reduce the risks of recurrence and associated mortality.

The expression of Sodium Iodide Symporter (NIS) plays an important role in uptake of I^{131} by cancer tissues [5]. Certain non-thyroidal tissues like salivary gland, stomach and breast are also known to express NIS and hence take up I^{131}. It is reported that the concentration of I^{131} in salivary gland could be about 30 to 40 times to that in plasma [6].

The damage caused by I^{131} to salivary glands is dose limited. The initial symptoms could be subtle but may gradually progress in intensity to stomatitis xerostomia, taste alterations, infections, increase in caries, facial nerve involvement, stomatitis, candidiasis, and neoplasias [7]. Estimation of the absorbed dose of I^{131} causing this damage can be useful in adopting measures to protect the salivary glands in patients receiving I^{131}. Salivary gland scintigraphy is reported as a widely accepted, valid and sensitive method for evaluating the salivary gland function post RIT [8].

AIM

The present study was aimed to assess and compare the salivary flow rates, the uptake and ejection fractions of right and left parotid and salivary glands before and one month after the RIT in thyroid carcinoma patients.

MATERIALS AND METHODS

The study was conducted on a total sample size of 24 (n=24) from February to March 2013. The inclusion criteria was, patients with well differentiated thyroid carcinoma treated with radioactive iodine therapy. Informed consent was obtained from all the subjects and the study was started after obtaining the ethical clearance from the institutional ethical committee. Patients previously treated for any other malignancies by chemo and/or radiotherapy, other head and neck cancers, patients with xerostomia due to any other reason, other systemic disorders, patients with any deleterious habits and patients on medications like anti-cholinergic, anti histaminics and other drugs causing xerostomia were excluded from the study.

Newly diagnosed thyroid carcinoma patients treated by total/partial thyroidectomy and eligible for RIT were subjected to scintigraphy.

Group		Pre		Post		Mean difference		
		Mean	SD	Mean	SD	Mean	SD	p-value
A	UPTAKE (Parotid)	.59	.06	.53	.07	0.06	0.04	<0.001*
	EF (Parotid)	52.18	4.91	50.38	4.57	1.81	2.41	0.001*
	UPTAKE (Sub-mandibular)	.27	.04	.22	.03	0.05	0.03	<0.001*
	EF (Sub-mandibular)	38.55	4.55	40.26	6.86	-1.71	3.25	0.017*
B	UPTAKE (Parotid)	.25	.08	.05	.01	0.20	0.08	<0.001*
	EF (Parotid)	40.82	7.17	10.26	1.85	30.56	8.94	<0.001*
	UPTAKE (Sub-mandibular)	.34	.10	.14	.10	0.20	0.17	<0.001*
	EF (Sub-mandibular)	44.22	3.47	15.13	5.76	29.08	9.15	<0.001*

[Table/Fig-1]: Showing comparative mean values of uptake and ejection fraction in parotid and submandibular glands.
*The p-value was set as significant at p<0.005.

Scintigraphy was done using intravenous administration of Technetium- 99 m pertechnetate 5-10 millicurie and sequential images of parotid and submandibular glands, with 1 min each were acquired upto 30 minutes. The procedure was performed for both the right and the left parotid and submandibular glands of each subject. Fifteen minutes post injection, 3 ml of lemon juice was administered intraorally. The patient was then asked to swish and swallow the lemon juice to achieve maximum stimulation of salivary gland secretion. Generation of time activity curves for determination of half-life was performed for each of the parotid and submandibular salivary glands for qualitative and quantitative analysis. Radioactive Iodine was then administered as oral administration as per the treatment protocol for thyroid carcinoma. The subjects were divided into two groups based on the absorbed dose threshold of Iodine dose measured in Gray (lesion based dosimetry) [9]. Group A included patients with absorbed dose of iodine in the range of 60–100 Gray (Gy) and Group B included patients with absorbed dose of iodine in the range of 100 - 150 Gy. Both the groups were subjected to scintigraphy again as per the aforementioned procedure one month after the RIT. Results thus obtained were statistically analysed using paired t-test and individual sample t-test.

RESULTS

It was observed that in Group A subjects, a significantly reduced percentage uptake was observed post RIT when compared to pre RIT in both parotid and submandibular glands (p≤0.001) [Table/Fig-1]. The findings were similar in the right and left glands with a significant p-value (p≤0.001).

However, the ejection fraction in parotid and submandibular glands did not show a significant lower value post RIT when compared to pre RIT on both the right and left sides [Table/Fig-1].

In Group B, a significantly reduced percentage uptake and ejection fraction was observed post RIT when compared to pre RIT in both parotid and submandibular glands (p≤0.001) [Table/Fig-1].

The present study also compared the percentage uptake and ejection fractions of both the glands in Group A and Group B. It was observed the mean values of both relative uptake and ejection fractions were significantly lower in Group B when compared to that in group A. This suggested that the salivary gland function is dose related as the time activity curves depicted significantly lower values in Group B who were receiving higher dose than in Group A [Table/Fig-2].

Difference	Group				
	A		B		
	Mean	SD	Mean	SD	p-value
Uptake (Parotid)	.06	.04	.20	.08	<0.001*
EF (Parotid)	1.81	2.41	30.56	8.94	<0.001*
Uptake (Sub-mandibular)	.05	.03	.20	.17	<0.001*
EF (Sub-mandibular)	-1.71	3.25	29.08	9.15	<0.001*

[Table/Fig-2]: Showing the difference between pre and post RIT as compared between group A and B
*The p-value was set as significant at p<0.005.

DISCUSSION

In the present study, it was observed that there was a statistically significant difference among pre and post radiation uptake in parotid and submandibular glands wherein the uptake was significantly lower in post radiation subjects in both Group A and Group B. This was in accordance with a similar study conducted by Caglar et al., who also concluded that the parotid glands were more affected than the submandibular glands. This could be attributed to the fact that the parotid glands have more sensitive serous acini [10]. A similar finding was observed in a study conducted by Kang JY et al., who performed salivary gland scintigrahy to assess the salivary gland function in both parotid and submandibular glands in 28 Sjogren's syndrome patients and 92 thyroid cancer patients who had undergone high dose radioactive iodine therapy. They concluded that the parotid ejection was significantly lower in post RIT patients suggesting that the parotid gland is more affected than the submandibular [11].

It was also observed that the percentage change in the uptake and ejection fraction in both parotid and submandibular glands was significantly higher in Group B than in Group A, indicating that the impairment worsened with increased dose. Mandel et al., in his study has reported a similar finding suggesting that dose related damage to the salivary parenchyma results from I^{131} irradiation and worsens with increase in dose [12]. He has also reported that the symptoms worsened in intensity with time. In another study conducted by Jeong SY et al., it was found that there was a significant salivary gland dysfunction assessed by salivary gland scintigraphy five years after a single radioactive iodine ablation, especially in patients who received high dose radioactive therapy for thyroid cancer [13].

It was also observed in the present study that the salivary gland dysfunction correlated well with the administered dose. The maximum secretion and uptake ratio were found to be sufficiently sensitive to distinguish the severity of the damage which correlates well with the study conducted by Kohn WG et al., [14]. Bohuslavizki KH et al., in one study concluded that salivary gland scintigraphy can be recommended in all patients prior to and after RIT in order to quantify and to document possible parenchymal impairment induced by I^{131} [7]. A similar conclusion was drawn from the present study. Further, in his later study, Bohuslavizki KH et al., has observed that the quantitative salivary gland function improved significantly after using aminofestine in patients with well differentiated thryroid carcinoma undergoing RIT [15]. This can pave way to further elaborate studies using salivary gland scintigraphy post administration of radioprotectors.

LIMITATIONS

The present study used a small sample size which was due to inability to obtain consent from patients for salivary gland scintigraphy and because the procedure was relatively expensive. A bigger sample size can be used in further studies for better interpretation of results. Further, the study did not include evaluation of salivary gland function in follow up visits three months post RIT.

CONCLUSION

We inferred from the study that there was an overall decrease in uptake, relative uptake and ejection fractions in the scintigraphy of patients post radioactive iodine therapy. Also, this difference was significant with higher doses of radiaoactive iodine therapy. This is because damage to the salivary parenchyma is dose related. In focusing on the treatment of a disease, the other structures important for vital functions are often forgotten leading to adverse complications further causing a lot of distress to the patients. We recommend, that a proper assessment of the salivary gland damage be done and pre and post radiation prophylactic measures are mandated to improve the quality of life in patients undergoing radioiodine therapy for differentiated thyroid carcinoma.

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