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QUANTITATIVE EVALUATION OF SALIVARY GLAND FUNCTION IN DIFFERENTIATED THYROID CANCER PATIENTS BEFORE AND AFTER TREATMENT WITH RADIOACTIVE IODINE 131 THERAPY

Medical Science

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ABSTRACT

Radioactive Iodine 131 is the major modality of treatment of Differentiated thyroid cancer. In the process of concentrating the RAI salivary glands are exposed to the damaging effects of iodine 131. Salivary gland scintigraphy can quantitatively evaluate the salivary gland function to see the effect of RAI therapy on salivary glands. This study was performed to quantitatively evaluate the salivary gland functions in DTC patients before and after treatment with RAI therapy.

Material and methods: 20 patients underwent the salivary gland scintigraphy using Tc 99m pertechnetate before RAI therapy and after treatment with RAI therapy at 3 months and 1 year. 12 age and sex matched controls were also taken.

Results: Patients shows significant decrease in Ejection fraction at 3 month at compared to base line and shows improvement at 1 year but do not reach the baseline.

Conclusion: After RAI therapy salivary gland functions temporarily decrease at 3 month but improved at 1 year but do not touch the baseline.

KEYWORDS

Radioactive Iodine(RAI), Sodium Iodide symporter(NIS), differentiated thyroid cancer(DTC), Salivary Gland Scintigraphy(SGS).

INTRODUCTION

Salivary glands are compound tubuloexocrine glands. Main salivary glands are parotid, submandibular and sublingual glands. Besides them there are 800-1000 minor salivary glands which also assist in formation of saliva[1,2]. Pair of Parotid glandsare the largest of all salivary glands and are situated on each side of the face just below the external acoustic meatus. Saliva secreted by parotid glands is mainly serous in nature and constitutes about 15-20% of the total saliva. Pair of Submandibular glands are located beneath the lower jaw superior to the diagastric muscles on each side and produce 70-75% of the saliva in the oral cavity which is both serous and mucinous in nature[2]. Saliva contains 2 major types of protein secretions, Serous which contains alpha amylase enzyme which helps in digestion of starch and Mucus secretion contains mucin for lubricating food and for surface protection[2]. Various pathological processes likeobstruction, inflammation, viral or bacterial infections or trauma. Systemic diseases like Diabetes Mellitus, Parkinsonism, Cystic Fibrosis, Sarcoidosis, Sjogren's Syndrome can cause salivary gland dysfunction. Radiation therapy to head and neck, radioactive iodine therapy for thyroid carcinoma, dehydration and certain medications like anticholinergics also causes decreased salivation[3,4,5]. Differentiated thyroid carcinoma (DTC) is a curable disease when diagnosed early. The most adequate treatment is total thyroidectomy followed by ablation with radioactive Iodine 131(RAI) and has a very good prognosis with cure in more than 80% patients with excellent long-term survival, similar to that of the population that never had cancer[6].

RAI which is one of the major modalities of treatment of DTC may also cause damage to the salivary glands resulting in their dysfunction. Iodine 131 is taken up by the thyroid gland through the sodium/iodide symporter (NIS)[7].NIS is a protein that is also expressed in salivary gland, stomach and breast tissue. In the process of concentrating RAI, salivary glands are exposed to the damaging effects of radiations after administration in therapeutic doses[8-11]. The beta radiation of iodine 131 exerts cytotoxic effects on the salivary glands because these organs are highly radiosensitive[12]. All salivary glands are involved in the transport of RAI into the saliva[13]. The iodide that is secreted into saliva has concentration varying from 20 to 100 times of that found in the serum[14,15]. It is this critical ability that causes glandular damage when I 131 is used. The principal site of iodide transport into saliva is the epithelium of the parotid gland's intralobularducts[16,17]. It has been calculated that up to 24% of the administered I 131 dose for thyroid cancer therapy is lost in the saliva[18].

Dose related damage to salivary parenchyma may occur and symptoms may develop immediately after the therapeutic dose or months later and can progress in intensity with time. The frequently encountered complications include radiation sialadenitis, taste alterations, infections, dental caries, candidiasis, facial nerve palsy, xerostomia and neoplasia[8].

The diagnosis of salivary gland disease relies mainly on the clinical presentation and in certain conditions on more specialized investigations [19,20]. Various imaging modalities like plain X ray, ultrasound, sialography, CT, MRI, scintigraphy are used for the detection of salivary gland disorders[20]. In these currently available modalities, only salivary gland scintigraphy(SGS) can be used in the quantification of salivary gland function. SGS can simultaneously quantify excretion function of all salivary glands with a single intravenous injection which is advantageous over the other imaging modalities[19,20].

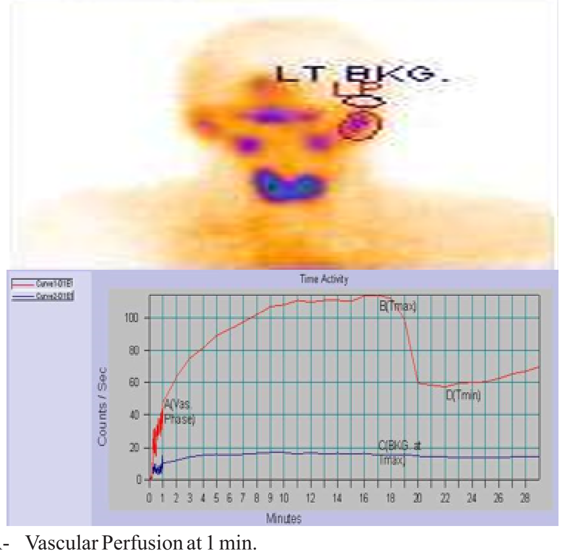
Evaluation of salivary gland function via SGS examination makes use of a single intravenously injected technetium-99m [Tc99m] pertechnetate, a radioisotope produced from molybdenum. It emits gamma radiation that can be imaged by gamma camera. Tc99m pertechnetate is trapped by the lacrimal gland, salivary glands, thyroid gland and gastric mucous membrane[21].

SGS can provide quantitative data about excretion fraction to measure glandular function[20,22]. In addition, physiologic intervention by administration of a sialogogue such as lemon juice provides information on the patency of the salivary ducts and on the overall functional integrity of the system.

MATERIAL AND METHODS:

Aim of the study wasquantitative evaluation of salivary gland function by using ejection fraction as the parameter with the help of Tc99m pertechnetate SGS in patients of DTC before and after treatment with radioactive iodine 131 at 3 month and 1 year follow up.Thiswas a prospective case control study conducted inDepartment of Nuclear Medicine SKIMS, Srinagar from October 2013 to May 2015.Ethical clearance for the study was obtained from the SKIMS ethical Committee. Patients and controlswith history of salivary gland disorders, and pregnant females and lactating women were excluded from the study. Written and informed consent taken before the study. Study consist four groups: **Group A:** 12 normal healthy individuals. **Group B:** Included 20 patients diagnosed as cases of DTC who were taken for SGS (Pretreatment). **Group C:** Same patients of DTC after surgery and RAI therapy underwent SGS using Tc99m pertechnetate at 3 months(Post treatment). **Group D:**Patients underwent SGS at 1 year after radioactive I 131 therapy(Post treatment). All patients were euthyroid at the time of scan. Age and sex of controls were matched with the study Group.Patients and controls were properly hydrated prior to the scan.Tc99m pertechnetate produced from molybdenum generator was used for SGS. Comfortable supine positionwith head and neck extension to avoid superimposition of thyroid gland over salivary glands was used facing the detector of gamma camera fitted with a low energy, parallel hole collimator. 128×128 matrix size was taken and Gamma Camera Pre Set at Tc99m (140 keV) and Energy Window 140 ± 15 %. After intravenous administration of 185MBq of Tc99m pertechnetate dynamic salivary gland scintigraphy was performed for a total of 30 minutes comprising of two phases. Phase 1(vascular phase) comprising of 60 frames of 1 second each and Phase 2 comprising of 29 frames of 60 seconds duration each. At 20 minutes of the study 3ml concentrated lemon juice was given to the patient through syringe and scintigraphy was continued for the next 10 minutes. For Data analysis Region of interest (ROI) was drawn around the right and left parotid and Submandibular glands and background was placed on respective temporal region(as shown in Fig.1) Time activity curve(TAC) was generated for parotid and submandibular glands. Following points were designed on time activity curve:A. Vascular phase (Initial 60 seconds).B. Maximum count before stimulation (Tmax.).C. Background count at the time of peak activity.D. Minimum count after stimulation (Tmin.). Ejection fraction was calculated from the TAC.

Fig 1.ROI drawn and Time activity curve drawn around the Left Parotid gland and Left Temporal as background.



A- Vascular Perfusion at 1 min.
B- Tmax(Maximum count before stimulation)
C- Background counts at the Tmax.
D- Tmin(Minimun count after stimulation)

$$EF\% = \frac{Tmax.-Tmin.}{Tmax.} X\ 100$$

Results: Ejection Fraction

Table 1: Comparison of Ejection Fraction (EF) of Group A Vs Group B

%Ejection Fraction (Mean±SD)	Group A (n=12)	Group B (n=20)	P value
RP	64.6 ± 13.1	63.4 ± 9.25	.76(NS)
LP	63.03 ± 10.4	60.1 ± 8.6	.399(NS)
RS	49.9 ± 14.6	49.35 ± 12.3	.914(NS)
LS	49.6 ± 14.3	45.9 ± 10.96	.425(NS)

P Value is non-significant (P<.05)

Table 2: Comparison of Ejection Fraction of Group B Vs Group C

%Ejection Fraction (Mean±SD)	Group B (n=20)	Group C (n=20)	P value
RP	63.4 ± 9.25	55.3 ± 9.93	.001(Sig.)
LP	60.1 ± 8.6	54.4 ± 9.2	.004(Sig.)
RS	49.3 ± 12.3	43.5 ± 9.96	.032(Sig.)
LS	45.98 ± 10.9	39.7 ± 8.4	.003(Sig.)

P Value is significant in all the glands (P<.05)

Table 3: Comparison of Ejection Fraction of Group B Vs Group D

%Ejection Fraction (Mean±SD)	Group B (n=20)	Group D (n=20)	P value
RP	63.4 ± 9.2	57.97 ± 15.87	.160(NS)
LP	60.1 ± 8.6	55.1 ± 13.4	.205(NS)
RS	49.35 ± 12.34	47.68 ± 10.89	.557(NS)
LS	45.98 ± 10.9	42.8 ± 9.7	.223(NS)

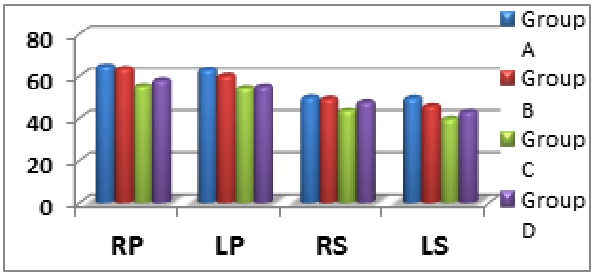


Fig.2 Comparison of EF of Group A Vs Group B Vs Group C Vs Group D at 3 month and at 1 year. Significant decrease (P<.05) in EF of all the glands at 3 months.Non-significant increase in the EF at 1 year as compared to 3 months.

DISCUSSION:

RAI therapy is an effective treatment for DTC but it may also cause damage to the salivary glands resulting in their dysfunction since NIS is also expressed in salivary glandsthrough which iodine 131 is taken up by the cells[6]. In the process of treatment of DTC with radioactive I131, salivary glands are exposed to the damaging effects of beta radiations after administration in therapeutic doses[7,8-10]. The present study was conducted for the quantitative evaluation of salivary gland functions by using SGS in patients of DTC before and after radioactive I 131 therapy at 3 months and 1 year. Ejection Fraction (EF) was used as the parameter for salivary gland function calculation. 20 patients were included in the study comprising of 14(70%) female and 6(30%) were male. Mean age of the patients was 37.5±13.4 (range: 20-60 year). 11 out of 20 patients were in the age group of 20-40 year and 9 were in the age group of 40-60 years. Mean dose of radioactive Iodine131 administered to the patients was 100 mCi (range from 72 - 116) and median dose was also 100 mCi. Lemon juice as a sialogogue was started within 1 hour of high dose therapy. Patients were advised to increase the intake of fluids post I 131administration. Patients were divided into 4 groups. Group A were healthy controls, Group B include patients not treated with I-131(pretreatment or baseline), Group C includes post RAI treated patients at 3 month, Group D includes post RAI treated patients at 1 year.

A significant decrease in the ejection fraction was observed in patients, on comparison of Group A (Controls) and Group B (Pretreatment) with Group C (post treatment with radioiodine 131 at 3 month) (P<.05) (Table 1&2; Fig.2). EF improved in the Group D (post treatment with radioiodine at 1 year) however the improvement was non-significant when compared to Group B (P>.05) (Table3; Fig.2). Similarstudy by Jonklaas et al[23]who performed SGS in 15 patients at baseline, 3 month and 1 year after RAI therapy in DTC patients and they found that there was marked decrease in uptake ratio and ejection fraction of salivary glands at 3 month which improved at 1 year. Chian-Yung Lin et al[24] studied the effect of radiotherapy on salivary gland function in 62 patients of head and neck cancers and found that after 1st month of radiotherapy there was significant (P < 0.0001) decrease in salivary flow rate but recovered from the 3rd month to the 6th month however flow rate could not return to pretreatment level. In our study we observed that after first high dose radioactive I 131 therapy in differentiated thyroid cancer patients, there is a significant decrease in the ejection fraction of all the glands at 3 month which showed improvement at 1 year. However the ejection fraction did not reach the baseline ejection fraction of the study group or that of controls.

Conclusion:

SGS can be used to calculate the effect of RAI therapy on salivary gland functions in DTC patients. We concluded that Ejection Fraction was significantly decreased at 3 months in DTC patients post RAI therapy when compared to the pretreatment levels. Although an improvement in ejection fraction was observed at 1 year as compared to the 3 month, the improvement did not reach the baseline (pretreatment levels). A long follow up of these patients maybe needed to confirm that improvement in glandular function reaches the baseline.

Conflict of interest: None

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