THE EFFECT OF ELECTROSTIMULATION ON SALIVARY PRODUCTION IN PATIENTS UNDERGOING RADIOTHERAPY FOR HEAD AND NECK CANCER

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In Partial Fulfilment for the Degree of

MASTER OF DENTAL SURGERY

BRANCH IX

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THE TAMILNADU Dr. M.G.R. MEDICAL UNIVERSITY

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DECLARATION BY THE CANDIDATE

I hereby declare that this dissertation titled **"THE EFFECT OF ELECTROSTIMULATION ON SALIVARY PRODUCTION IN PATIENTS UNDERGOING RADIOTHERAPY FOR HEAD AND NECK CANCER"** is a bonafide and genuine research work carried out by me under the guidance of **Dr. P.VENKATALAKSHMI APARNA, M.D.S.**, Reader, Department of Oral Medicine & Radiology, Ragas Dental College and Hospital, Chennai.

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This is to certify that this dissertation titled **"THE EFFECT OF ELECTROSTIMULATION ON SALIVARY PRODUCTION IN PATIENTS UNDERGOING RADIOTHERAPY FOR HEAD AND NECK CANCER"** is a bonafide record of work done by **Dr. N. NARMATHA** under my guidance during her postgraduate study period 2017–2020.

This dissertation is submitted to **THE TAMILNADU Dr. M.G.R.MEDICAL UNIVERSITY,** in partial fulfilment for the degree of **MASTER OF DENTAL SURGERY, BRANCH IX – Oral Medicine & Radiology.**

It has not been submitted (partial or full) for the award of any other degree or diploma.

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LIST OF ABBREVIATION

S.NO	ABBREVIATION	EXPANSION
1	SF	Salivary flow
2	TENS	Transcutaneous electric nerve stimulation
3	IMRT	Intensity modulated radiation therapy
4	3DCRT	3 dimensional conventional radiotherapy
5	Hz	Hertz ,unit of frequency
6	RT	Radiotherapy

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Introduction

INTRODUCTION

The oral cavity is a moist environment; a film of fluid called saliva constantly coats its inner surfaces and occupies the space between the lining oral mucosa and the teeth. Saliva is a complex fluid, whose important role is to maintain the well-being of oral cavity.[1] There are three major salivary glands namely parotid, submandibular and sublingual, along with 300 to 500 minor salivary glands, which produce about 1 to 1.5 litres of whole saliva daily.[2]

The saliva circulating in the mouth at any given time is termed whole saliva and comprises of secretions from the major and minor salivary glands, gingival crevicular fluid, oral bacteria, desquamated epithelial cells and food debris.[3] At rest, a small, continuous salivary flow (SF), denominated basal unstimulated secretion, is present. Stimulated saliva is produced under mechanical, gustatory, olfactory or pharmacological stimulus, contributing to around 80 to 90% of daily salivary production.

The salivary flow (SF) index is a parameter allowing stimulated and unstimulated salivary flow to be classified as normal, low, or very low (hyposalivation). In adults, normal total stimulated SF ranges from 1 to 3 ml/min, low-ranges from 0.7 to 1.0 ml/min, while hyposalivation is characterized by a SF of less than 0.7 ml/min. The normal unstimulated SF ranges from 0.25 to 0.35 ml/min, low-ranges from 0.1 to 0.25 ml/min, while

hypo salivation is characterized by a SF of less than 0.1 ml/min. However, the values denominated exhibit large biological variations.[4]

Saliva has many important functions. It maintains neutral pH, is an essential for maintaining enamel mineralization, lubricates the mouth and upper pharynx, modulates oral flora, aids in digestion of food, facilitates speech and swallowing and plays a role in oral immunology.[5]

Without saliva there will be dryness of mouth; altered taste; a deviant sense of smell; lack lustre singing; difficulty in speaking and swallowing; increased dental caries; wedge-shaped erosion; bad breath; heart burn and esophagitis; burning tongue; cracked lips; yeast infections. [6] Salivary gland hypofunction or hypo salivation is the condition of having reduced saliva production which leads to the subjective complaint of oral dryness termed xerostomia.[7] This is associated with various local and systemic conditions which include diseases of salivary glands (Sjogren's syndrome, Sarcoidosis, Diabetes Mellitus, and others), iatrogenic causes (medications, radiation to head and neck region, chemotherapy, chronic graft *vs* host diseases) and other rare causes, such as salivary gland agenesis, amyloidosis etc.[8]

Palliative management of xerostomia includes topical agents, such as ice chips and saliva substitutes, increasing water intake, chewing sugar free gum, sucking sour lemon drops, paraffin and citric acid containing lozenges and rinses. Systemic agents, like pilocarpine and cevimeline stimulate salivary flow but often have unfavourable side effects, such as profuse sweating,

rhinitis, dyspepsia, etc. Acupuncture also has shown improvement in xerostomic and healthy patients.[9]

Transcutaneous electrical nerve stimulation is well-known physical therapy. First described in dentistry by Shane and Kessler in 1967, it has been widely used for relief of acute and chronic pain.[9] Electrostimulation to produce saliva was studied in the past and showed moderate promise but never became part of mainstream therapy.11 Transcutaneous electrical nerve stimulation may be a viable treatment option in the management of salivary gland hypofunction. Research in this area has been sparse, and hence this study was undertaken to evaluate the effect of TENS on salivary production in patients undergoing radiotherapy treatment.

Aim and Objectives

AIM AND OBJECTIVES

AIM

To determine the effectiveness of transcutaneous electrical nerve stimulation (TENS) in stimulating salivary flow from submandibular gland and sublingual gland in head and neck cancer patients undergoing radiotherapy.

OBJECTIVES

To compare the salivary volume between unstimulated saliva and saliva stimulated with TENS in head and neck cancer patients undergoing radiotherapy and to substantiate the role of TENS as highly effective in stimulating the salivary production in head and neck cancer patients undergoing radiotherapy.

Materials and Methods

MATERIALS AND METHODS:-

Study design :

A prospective study is carried out to evaluate the effect of electrostimulation on salivary production in patients undergoing radiotherapy for head and neck cancer , conducted in the Department of Oral Medicine and Radiology, Ragas Dental College and Hospital, Chennai, Tamilnadu.

Study sampling: Random sampling.

Study setting:

Includes patients reporting to Dr. Rai Memorial Cancer Institute, Outpatient Department, and Teynampet seeking service and who are from a wide variety of socioeconomic background.

Transcutaneous Electrical Nerve Stimulation (TENS) is used in stimulating salivary flow from submandibular gland and sublingual gland in head and neck cancer patients undergoing radiotherapy. The parotid gland saliva is blocked by cotton rolls and collection of the remaining unstimulated and stimulate saliva was done by using micropipette at various intervals. Unstimulated saliva was collected for every minute for 5 minutes in a graduated test tube, before radiotherapy, immediately after radiotherapy, at 3rd week, at 1st month. The TENS unit was activated and stimulated saliva was collected for every minute for 5 minutes in a separate graduated test tube, before radiotherapy, immediately after radiotherapy , at 3rd week, at 1st month and the volume was compared with the unstimulated salivary flow rate.

Obtaining approval from authorities:

Permission from the ethical committee of the Ragas Dental Hospital and Dr.Rai Memorial Cancer Institute was obtained before starting the study for interrogating and examining patients.

Selection criteria:

Subject of the present study consists of fifteen patients reporting to Ragas Dental College and Hospital, and Dr. Rai Memorial Cancer Institute, Outpatient Department, diagnosed with head and neck cancer undergoing radiotherapy.

Study groups :- **Age group** : Male Adults < 55 years.

INCLUSION CRITERIA:-

- Patients willing to participate
- Patients who were undergoing head and neck radiotherapy, either IMRT/3DCRT.

EXCLUSION CRITERIA:-

- Patients with pacemakers, defibrillator, hearing aid and cochlear implants
- Pregnant females
- Patients with skin lesions or abrasions on the face
- Patients who were already on medications that are known to cause xerostomia
- Patients who underwent any head and neck surgery involving salivary glands.
- Patients who were suspected of exposure more than 60- 66 GY.

Research tool:

Transcutaneous Electric Nerve Stimulation (TENS unit)

The unit with two output channels was set at a frequency of 2–150 Hz and a pulse width of 50–250 μs. Before using the unit, the operator should confirm the stimulation parameter settings and then use a protective front cover to keep the TENS unit safe. In addition, prior to each intervention, the operator should ensure that the battery is fully charged to maintain the consistency and stability during TENS.

Procedure for examination:

A Prospective cross sectional study was carried out among fifteen adult male patients visiting to Dr. Rai Memorial Cancer Institute, Outpatient Department, diagnosed with head and neck cancer undergoing radiotherapy.

Armamentarium:

1. For examining the patients

a) Physiological dental chair with provision for artificial illumination
b) Mouth mask
c) Sterile glove
d) Mouth mirror
e) Explorer
f) Kidney tray
g) Cotton
h) Tweezers

2. For electrostimulation procedure:
    a) Cotton roll
    b) Micro pore
    c) Transcutaneous electric nerve stimulation
    d) Micropipette
    e) Autoclavable graduated container

Methodology:

A prospective study is carried out with Transcutaneous Electrical Nerve Stimulation (TENS) for stimulating salivary flow from submandibular and sublingual gland in head and neck cancer patients undergoing radiotherapy. The evaluation included oral inspection with visualization of the aspect of the mucosa and the possible presence of dryness, cracking and/or hyperemia as well as the presence of saliva in the oral cavity. Clinical data on the disease and treatments were collected by means of the information provided by patients and by the computerized system of the hospital. Information was also collected on respiratory aspects, smoking and drinking habits and medicaments in use. The patients were asked about the possible interference of reduction of saliva on stomatognathic functions and the use of alternative techniques to reduce the discomfort produced by hypo salivation, e.g., water intake. Subjects were asked to refrain from eating, drinking and smoking and oral hygiene procedures for at least 1 h prior to appointment. The parotid gland saliva is blocked by cotton roll and collecting the remaining saliva by using micropipette. Unstimulated saliva was collected for every minute for 5 min in a graduated test tube, before radiotherapy, immediately after radiotherapy, at 3rd week, 1 month.

The placement of pads was approximated bilaterally over the submandibular salivary glands.The TENS unit was activated and Intensity was adjusted manually and continuously until reaching the maximum current tolerated by patients .Stimulated saliva was collected for every minute for 5 min in a separate graduated test tub, before radiotherapy, immediately after radiotherapy, at 3rd week, 1 month and the volume was compared with the unstimulated salivary flow rate. Unstimulated and stimulated saliva was collected in a autoclavable graduated tube and salivary output was noted for comparison and entered in excel sheet for statistical analysis.

STATISTICS FOLLOWED

Quantitative data were described through the mean and standard deviation for parametric distributions .The comparisons between the evaluations were performed using T test for parametric data Evaluation of the response of the salivary glands to TENS was based on the difference between the values found in the unstimulated and stimulated salivary flow output . The data were analysed using the statistical software SPSS v.23. The cut-off point used for determination of statistical significance was 5% (p-value $\leq$ 0.05).

Review of literature

REVIEW OF LITERATURE:

Literature has been reviewed under the following headings:

- Review on saliva
- Review on head and neck cancer
- Review on radiotherapy
- Review on effect of radiotherapy in salivary glands
- Review on tens and effect of tens in saliva stimulation

Review on saliva:

Saliva is a complex fluid, whose important role is to maintain the well-being of oral cavity.[10] There are three major salivary glands namely parotid, submandibular and sublingual, along with 300 to 500 minor salivary glands, which produce about 1 to 1.5 litres of whole saliva daily. The saliva circulating in the mouth at any given time is termed whole saliva and comprises of secretions from the major and minor salivary glands, gingival crevicular fluid, oral bacteria, desquamated epithelial cells and food debris.[11] At rest, a small, continuous salivary flow (SF), denominated basal unstimulated secretion, is present. Stimulated saliva is produced under mechanical, gustatory, olfactory or pharmacological stimulus, contributing to around 80 to 90% of daily salivary production.

It has been known that the nerves to the salivary glands control the secretion of saliva. Salivary secretion is normally controlled by reflex stimulation with effector nerve impulses traveling along the sympathetic as well as parasympathetic nerves to the glands.[12,13] Parasympathetic stimulation produces copious saliva of low protein concentration, whereas sympathetic stimulation produces little saliva but with high protein concentration, which may give a sensation of dryness.[14]

Review on head and neck cancer:

Cancer is the result of cell growth that is out of control. 1 In fact, the primary risk factors for head and neck cancer (with the exception of nasopharyngeal cancer) have been identified as tobacco (including smokeless tobacco) and heavy alcohol use. Other high-risk factors include human papillomavirus infection, poor oral hygiene and consumption of certain processed foods, radiation exposure, and mechanical irritation.1. In 2015, head and neck cancers globally affected more than 5.5 million people (2.4 million mouth, 1.7 million throat, and 1.4 million larynx cancer),[15] and it has caused over 379,000 deaths (146,000 mouth, 127,400 throat, 105,900 larynx cancer).[16] Together, they are the seventh most-frequent cancer and the ninth most-frequent cause of death from cancer.[17] In the United States, about 1% of people are affected at some point in their life, and males are affected twice as often as females.[18,19] The usual age at diagnosis is between 55 and 65 years

old.[20] The average 5-year survival following diagnosis in the developed world is 42-64%.[21,22]

Radiation therapy is the most common form of treatment. There are different forms of radiation therapy, including 3D conformal radiation therapy, intensity-modulated radiation therapy, particle beam therapy and brachytherapy, which are commonly used in the treatments of cancers of the head and neck. Most people with head and neck cancer who are treated in the United States and Europe are treated with intensity-modulated radiation therapy using high energy photons. At higher doses, head and neck radiation is associated with thyroid dysfunction and pituitary axis dysfunction.

Review on Radiation Therapy: [23]

RT uses high-energy x-rays to kill cancer cells. Death of cancer cells leads to shrinkage of the tumour. RT may be used as the primary treatment for small tumours, after surgery to destroy residual small pockets of cancer cells, or before surgery to shrink tumours in the hope of more successful surgical removal with fewer residual deficits.

Radiation may be administered in two ways: external-beam radiation and internal radiation. *External-beam radiation* involves aiming a high-energy radiation beam at the tumour and surrounding tissues. External-beam radiation may be applied on a conventional, once-daily schedule or on an altered fractionation schedule. The latter form of RT may increase acute toxicity, but late effects are similar between these two techniques.[24]

A newer form of external-beam radiation is known as *intensity-modulated radiation therapy (IMRT).* This procedure allows more effective doses of radiation to be delivered to the tumour while hitting less healthy tissue around the tumour. This method is intended to result in fewer side effects. Other recent advances in RT include *radio sensitization* (using drugs to make cancer cells more sensitive to radiation) and *hyper fractionation* (giving radiation in small doses several times per day). In general, treatment strategies leading to a lower dose of RT or RT to more confined anatomic regions results in less-severe and more transient dysphagia.[23,24] Side effects from RT are common both during treatment (acute toxicity) and after treatment (late effects or late toxicity). Some of these effects are transient and others are persistent. In addition, certain side effects may be latent—that is, they may not appear for a substantial period (in some cases years) after the completion of RT. Many side effects of RT to the head and neck region contribute directly to dysphagia and resulting decline in nutritional status. If these occur during treatment, patients may experience interruptions in therapy.

Dry mouth, or xerostomia, is perhaps the most clinically significant and long-lasting difficulty faced by patients who undergo RT in the treatment of head and neck cancer.

Review on effect of radiotherapy in salivary glands

Salivary glands are usually irradiated during radiotherapy for head and neck cancers, which can lead to radiation-induced damage. Radiation-induced xerostomia (oral dryness) is the most common post-radiotherapy complication for head and neck cancer patients and can reduce the patient's quality of life. Major salivary glands are situated in the lateral facial and submandibular regions where they are commonly included in or close to the target volume in radiotherapy of head and neck cancers. Parotid glands are commonly irradiated with high-radiation doses in two-dimensional (2D) radiotherapy (conventional radiotherapy) for some head and neck cancers like nasopharyngeal carcinoma (NPC) because they are usually in close proximity to, or within, the radiation field. High-radiation dose can damage salivary glands and lead to xerostomia (oral dryness owing to reduced salivary secretion from the impaired salivary glands). Saliva is produced by acinar cells, drained to the excretory duct though ductal cells and finally secreted into the oral cavity. [22] The submandibular gland is the second largest salivary gland located under the floor of the oral cavity. It is composed of both serous and

mucous acinar cells, which produce thicker and more viscous saliva. Its main salivary duct is Wharton's duct, which drains saliva near the lingual frenula. The submandibular gland mainly secretes saliva in non-stimulated conditions, producing up to 90% of total salivary output during the resting state, but contributes only 20–40% of total saliva in stimulated conditions.

Sublingual gland

The sublingual gland is the smallest among the three pairs of major salivary glands, which are located in the floor of the oral cavity and medial to mandible. Similar to the submandibular gland, the sublingual gland is composed of both serous and mucous acinar cells, which produce 2–5% of the total saliva upon stimulation. The intra glandular ducts of sublingual glands may either drain into the Wharton's duct or empty into the floor of the oral cavity directly.

Submandibular glands in the unilateral neck irradiation group demonstrated retention of about 50% of the pre-radiotherapy salivary flow in the first 3 months after radiotherapy, but the flow rate increased continually to the pre-radiotherapy level after 1 year .[23]

Review on effect of tens in saliva stimulation

Neural electrostimulation of salivary gland function, through application of electric current through the oral mucosa, on afferent nerve pathway receptors, has been reported to increase the production of saliva and to reduce the symptoms of xerostomia .[15, 16]

Transcutaneous electrical nerve stimulation (TENS) has been evaluated in stimulating salivary flow and it was found to be effective even in patients with xerostomia secondary to radiation therapy for head and neck cancer.

The only side effect of the TENS therapy was mild twitching of the facial musculature, which was also described by Hargitai *et al.*[2] It was minimal and transient and ceased immediately after the TENS unit was switched off. The modifications suggested to avoid the side effects include manufacturing small electrodes to make the electrostimulation of the parotids more effective. The mechanism by which the TENS unit worked on the parotid gland may be that it directly stimulates the auriculotemporal nerve that supplies secretomotor drive to the parotid gland. In order to electrically stimulate sympathetic salivation, higher frequencies and longer pulse duration is required. On the other hand, electric stimulation of parasympathetic nerves of the salivary glands produces copious amounts of watery saliva of the parotid gland at lower frequencies, and it is this voluminous serous saliva that would be clinically most useful in the management of xerostomia.[2]

The main advantage offered by TENS over other nonpharmacological measures, such as chewing gum or citric lozenges is that it is an extra oral device, with minimal side effects. It can be used while eating food and it does not affect the normal mastication process. Thus, the salivary production while eating would be beneficial, which is not the case with the intraoral devices.[15]

A wide range of the unstimulated and stimulated salivary flow was observed .This variation of salivary flow rate was similar to the observation made by **Becks and Wainwright,[17,18] Anderson *et al.*,[18] Heintze *et al.*,[7,18] and Yeh *et al.*[7]** there was a 21% increase in the salivary flow, which was statistically significant. The maximum increase with the TENS application was 50%. Eighty five out of the 100 responded positively to TENS therapy.

Damingo, 2004 [19] six of the 18 post radiation head and neck cancer patients demonstrated significant increase in the saliva flow during the application of TENS.

Hargitai *et al.*, 2005 [2] conducted the study by in which 15 (out of 22) healthy subjects demonstrated significant increase in the parotid salivary flow and the maximum increase was 8.75 fold greater than the baseline.

Saraf *et al.*2006 [10] showed that 85 of hundred healthy subjects demonstrated increased salivary flow when stimulated via the TENS unit.

Hargitai *et al. 2007* [12] had observed that TENS was unable to stimulate the parotid saliva in 11 subjects as there was no increase in whole saliva flow and it was interpreted that TENS may act more efficiently as an accelerator of salivary flow rather than an initiator. Therefore, it is likely to be more effective in cases of decreased salivary gland function rather than absolute absence of function.

As mentioned in different studies done by **Ghezzi *et al.*,**[20] **Ikbe *et al.*,**[21] **Percival *et al.*,**[22] **and Tylenda *et al.***[23] functional changes in the salivary glands have been reported to be associated with aging; however, there is no evidence to show that xerostomia is likely to result from aging process.

Narhi *et al. 2007* [24] reported that over a 5-year period, an elderly individual. Stimulated salivary flow had significantly decreased. In the present study, it was found that in all the age groups, there was a statistically significant increase in TENS stimulated saliva, as compared to unstimulated saliva, except in the 66.75 age group, where the difference was not significant. The reason behind this could be the less number of subjects present in the group. The unstimulated and stimulated salivary flow rates in different age groups was not statistically significant.

Thorselius *et al* 2008 [21] stated that the reason for the lower salivary rate in women was that they had smaller salivary glands and it may be

associated with postmenopausal changes. The stimulated salivary flow rate was higher for males than for females. The gender difference in salivary flow rate was similar to that observed in previous studies.[2, 21,25]

Ghezzi *et al 2009* [20] had shown that there was no significant age and gender differences in the salivary flow rates.

Strietzel, et al 2012 [21] demonstrated significant decrease in dryness in the mouth following TENS therapy. Its effectiveness depends on functional capability of glands; it will not be effective if there is absolute absence of salivary secretion

Pattipati, et al. in 2013 [24] showed an increase in salivary flow rate on giving TENS and Salivary flow was persistent even after one hour of the treatment.

Vijayan, et al. 2014 [25,26] observations are also in congruence with the other studies as it was found to be effective supportive therapy in the management of xerostomia in post irradiation patients of Oral cancer.

Aggarwal H, et al.2015 [21] Conducted study and shown approximately 13% increase in the mean salivary flow rate.

Anusha Rangare Lakshman, G. Subhas Babu, Suresh Rao conducted a study on 40 subjects. The apparatus used was a strong low rate conventional mode of TENS model-NS Electro pulse that generates current through AC at a continuous frequency of 500 Hz and sweep of 0.5-2 Hz. The control group (no xerostomia) showed increased salivary flow rate after stimulation by TENS therapy compared to the unstimulated salivary flow and patients who were undergoing radiotherapy with weekly TENS therapy (0th week, 3rd week, 6th week and after a month) there was no significant improvement in salivary flow. [24]

Vilas SK, et al. **2016** [23] stated four patients out of 100 reported decreased salivary flow with the application of TENS.

Mittal Kumud, Keluskar Vaishali, Kapoor Shekhar 2015 evaluated effect of Transcutaneous Electrical Nerve Stimulation (Tens) at pulse rate of 50 Hz on salivary flow in patients with xerostomia and revealed that there was statistically significant difference between the unstimulated and stimulated salivary flow by TENS therapy.

Neha bhasin, et al. 2015 reported no increase in whole saliva flow in four subjects and also Vilas SK et al, reported that 11 subjects out of 100 demonstrated absence of increase in saliva flow in response to TENS stimulation.[29]

Manu Dhillon, et al.2016 evaluated the relationship of TENS therapy and gender, age and found that there was difference in the stimulatory salivary output between the age groups of 20-40 years and more than 60 years but there was no difference between the genders.[31]

Aparna et al 2017, stated that males produced significantly more saliva when compared to females after stimulation with TENS which was consistent previous study.[32]

Results

RESULTS

A Prospective cross sectional study was carried out among fifteen adult male patients visiting to Dr. Rai Memorial Cancer Institute, Outpatient Department, diagnosed with head and neck cancer undergoing radiotherapy.

Table 1: Shows Group statistics for unstimulated saliva before radiotherapy having mean value of 3.7200 and standard deviation of 0.45857 and Group statistics for stimulated saliva before radiotherapy having mean value of 4.0467and standard deviation of 0.33989.

Table 2: Shows Independent Samples test before radiotherapy with significant P value of 0.035 and mean difference of - 0.32667.

Comparison of unstimulated and stimulated saliva before radiotherapy was found to be statistically significant with P value of 0.035.

Table 3: Shows Group statistics for unstimulated saliva after radiotherapy having mean value of 3.5467 and standard deviation of .46270 and Group statistics for stimulated saliva after radiotherapy having mean value of 3.9227 and standard deviation of 0 .41368.

Table 4: Shows Independent Samples test after radiotherapy with significant P value of 0 .026 and mean difference of - 0.37600.

Comparison of unstimulated and stimulated saliva after radiotherapy was found to be statistically significant with P value of 0.026.

Table 5: Shows Group statistics for unstimulated saliva at third week of radiotherapy having mean value of 3.2800 and standard deviation of 0.38210 and Group statistics for stimulated saliva after radiotherapy having mean value of 3.6733 and standard deviation of 0 .28900

Table 6: Shows Independent Samples test at third week of radiotherapy with significant P value of 0.035 and mean difference of -0.32667.

Comparison of unstimulated and stimulated saliva at third week of radiotherapy was found to be statistically significant with P value of 0.035.

Table 7: Shows Group statistics for unstimulated saliva at 1st month of radiotherapy having mean value of 3.5467 and standard deviation of 0.37007 and Group statistics for stimulated saliva after radiotherapy having mean value of 3.8600 and standard deviation of 0.29713.

Table 8: Shows Independent Samples test at 1st month of radiotherapy with significant P value of 0.016 and mean difference of -0.31333.

Comparison of unstimulated and stimulated saliva at first month of radiotherapy was found to be statistically significant with P value of 0.016.

Table 9: Shows T –TEST –paired samples statistics for unstimulated saliva

- Before radiotherapy with mean value of 3.7200 and standard deviation of 0.4585.
- After radiotherapy with mean value of 3.5467and standard deviation of 0.46270.
- At third week with mean value of 3.2800 and standard deviation of 0.38210.
- At first month with mean value of 3.5467 and standard deviation of 0.37007.

Table 10: Shows T –TEST –paired samples statistics for stimulated saliva

- Before radiotherapy with mean value of 4.0467 and standard deviation of 0.33989
- After radiotherapy with mean value of 3.9227and standard deviation of 0.41368
- At third week with mean value of 3.6733 and standard deviation of 0.28900
- At first month with mean value of 3.8600 and standard deviation of 0.28900

Tables and Graphs

Table 1: Shows group stastics for unstimulated and stimulated saliva before radiotherapy

Group Statistics					
	Type of Saliva	**N**	**Mean**	**Std. Deviation**	**Std. Error Mean**
Radiotherapy – Before	Unstimulated Saliva	15	3.7200	.45857	.11840
	Stimulated Saliva	15	4.0467	.33989	.08776

Table 2: Independent Samples Test before radiotherapy

Independent Samples Test								
		Levene's Test for Equality of Variances		**t-test for Equality of Means**				
		F	**Sig.**	**t**	**df**	**Sig. (2-tailed) (P value)**	**Mean Difference**	**Std. Error Difference**
Radiotherapy - Before	**Equal variances assumed**	1.746	.197	-2.217	28	.035	-.32667	.14738
	Equal variances not assumed			-2.217	25.816	.036	-.32667	.14738

P Value – 0.035

Table 3: Shows group stastics for unstimulated and stimulated saliva after radiotherapy

Group Statistics					
	Type of Saliva	**N**	**Mean**	**Std. Deviation**	**Std. Error Mean**
Radiotherapy – After	Unstimulated Saliva	15	3.5467	.46270	.11947
	Stimulated Saliva	15	3.9227	.41368	.10861

Table 4: Independent Samples Test after radiotherapy

Independent Samples Test								
		Levene's Test for Equality of Variances		**t-test for Equality of Means**				
		F	**Sig.**	**t**	**df**	**Sig. (2-tailed) (P value)**	**Mean Difference**	**Std. Error Difference**
Radiotherapy – After	Equal variances assumed	.305	.585	-2.346	28	.026	-.37600	.16026
	Equal variances not assumed			-2.346	27.656	.026	-.37600	.16026

P Value – 0.026

Table 5: Shows group stastics for unstimulated and stimulated saliva at third week of radiotherapy

Group Statistics					
	Type of Saliva	**N**	**Mean**	**Std. Deviation**	**Std. Error Mean**
Radiotherapy – Third week	Unstimulated Saliva	15	3.2800	.38210	.09866
	Stimulated Saliva	15	3.6733	.28900	.07462

Table 6: Independent Samples Test at third week of radiotherapy

Independent Samples Test								
		Levene's Test for Equality of Variances		**t-test for Equality of Means**				
		F	**Sig.**	**t**	**df**	**Sig. (2-tailed) (P value)**	**Mean Difference**	**Std. Error Difference**
Radiotherapy – Third week	Equal variances assumed	1.602	.197	-2.217	28	.035	-.32667	.14738
	Equal variances not assumed			-2.217	25.816	.036	-.32667	.14738

P Value – 0.035

Table 7: Shows group stastics for unstimulated and stimulated saliva at 1st month of radiotherapy

Group Statistics					
	Type of Saliva	**N**	**Mean**	**Std. Deviation**	**Std. Error Mean**
Radiotherapy – First month	Unstimulated Saliva	15	3.5467	.37007	.09555
	Stimulated Saliva	15	3.8600	.29713	.07672

Table 8: Independent Samples Test at 1st month of radiotherapy

Independent Samples Test								
		Levene's Test for Equality of Variances		**t-test for Equality of Means**				
		F	**Sig.**	**T**	**df**	**Sig. (2-tailed) (P value)**	**Mean Difference**	**Std. Error Difference**
Radiotherapy – First month	Equal variances assumed	1.247	.274	-2.557	28	.016	-.31333	.12254
	Equal variances not assumed			-2.557	26.751	.017	-.31333	.12254

P Value – 0.016

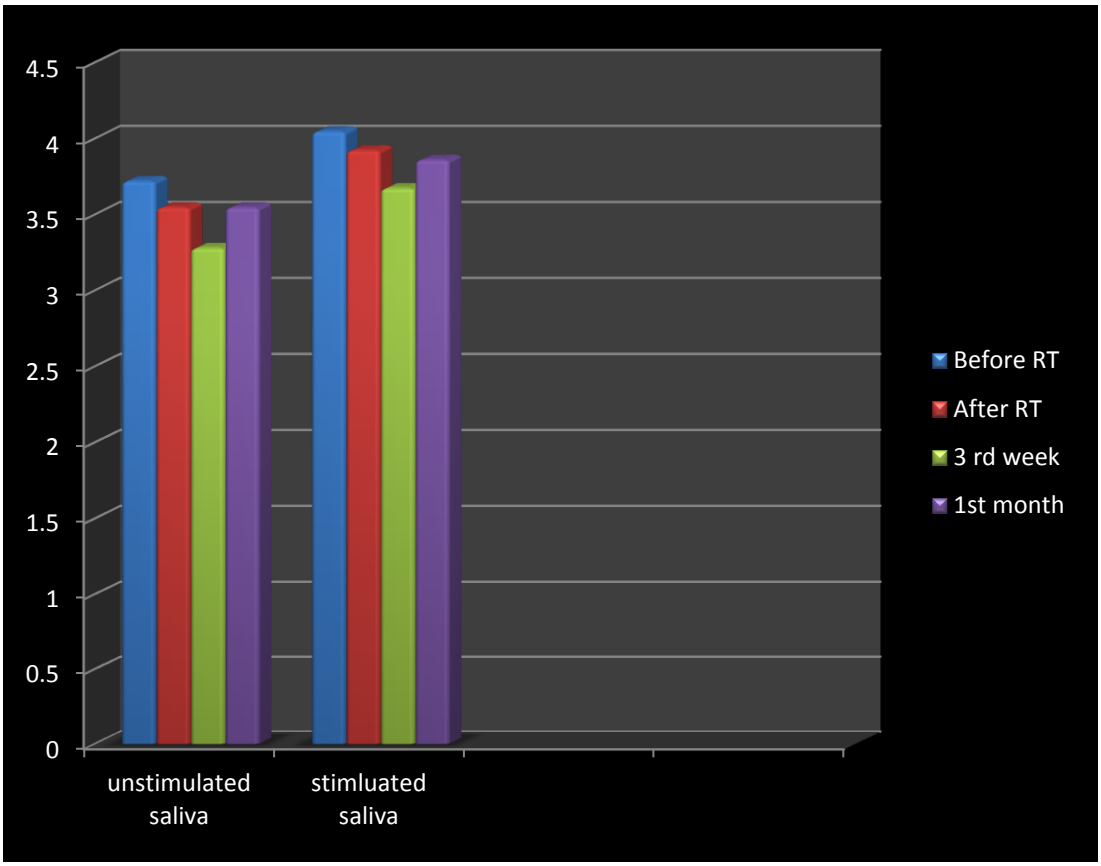
Table 9: T –TEST –paired samples stastics for unstimulated saliva

Paired samples stastics		Mean	Std. Deviation
Pair 1	Radiotherapy - Before	3.7200	.45857
	Radiotherapy - After	3.5467	.46270
Pair 2	Radiotherapy - Before	3.7200	.45857
	Radiotherapy - Third Week	3.2800	.38210
Pair 3	Radiotherapy - Before	3.7200	.45857
	Radiotherapy - First Month	3.5467	.37007
Pair 4	Radiotherapy - After	3.5467	.46270
	Radiotherapy - Third Week	3.2800	.38210
Pair 5	Radiotherapy - After	3.5467	.46270
	Radiotherapy - First Month	3.5467	.37007
Pair 6	Radiotherapy - Third Week	3.2800	.38210
	Radiotherapy - First Month	3.5467	.37007

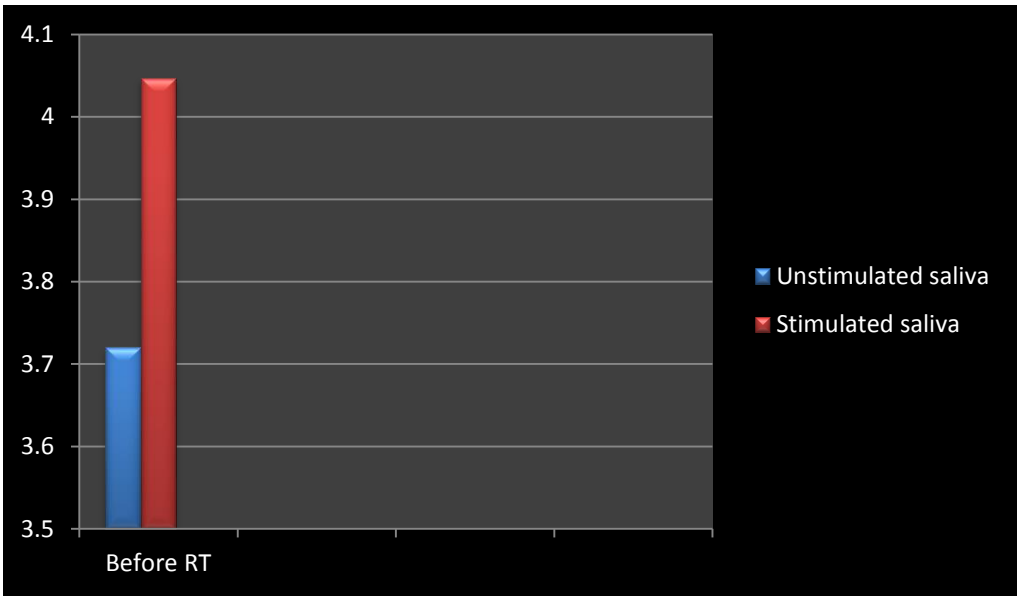
Table 10: T –TEST –paired samples stastics for stimulated saliva

Paired samples stastics		Mean	Std. Deviation
Pair 1	Radiotherapy - Before	4.0467	.33989
	Radiotherapy - After	3.9227	.41368
Pair 2	Radiotherapy - Before	4.0467	.33989
	Radiotherapy - Third Week	3.6733	.28900
Pair 3	Radiotherapy - Before	4.0467	.33989
	Radiotherapy - First Month	3.8600	.29713
Pair 4	Radiotherapy - After	3.9227	.41368
	Radiotherapy - Third Week	3.6733	.28900
Pair 5	Radiotherapy - After	3.9227	.41368
	Radiotherapy - First Month	3.8600	.29713
Pair 6	Radiotherapy - Third Week	3.6733	.28900
	Radiotherapy - First Month	3.8600	.29713

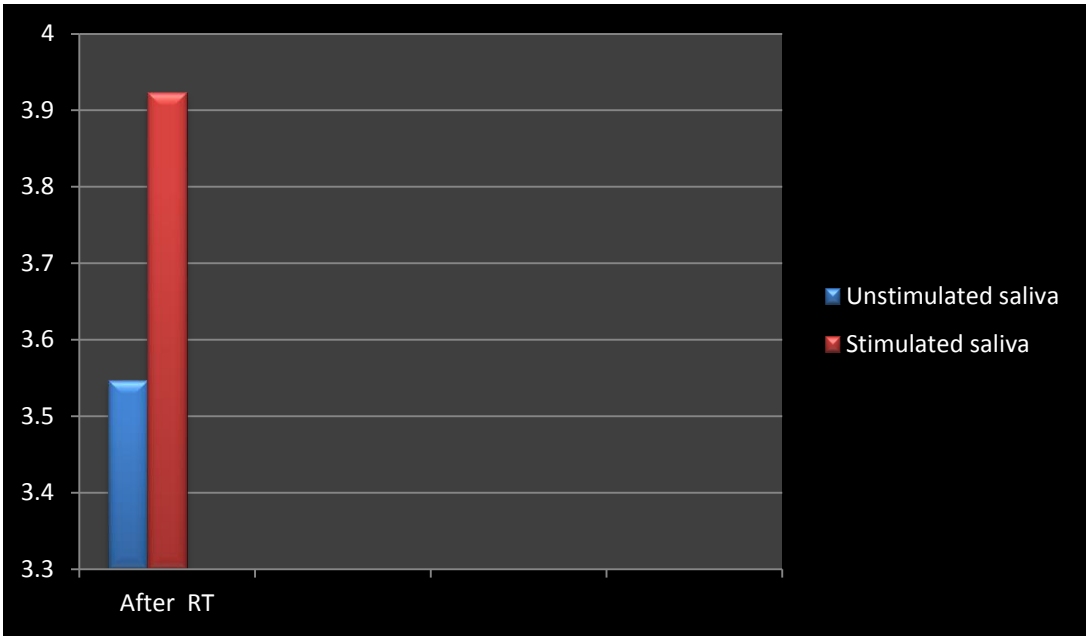
Graph 1: Paired sample stastics showing Mean difference between unstimulated and stimulated saliva



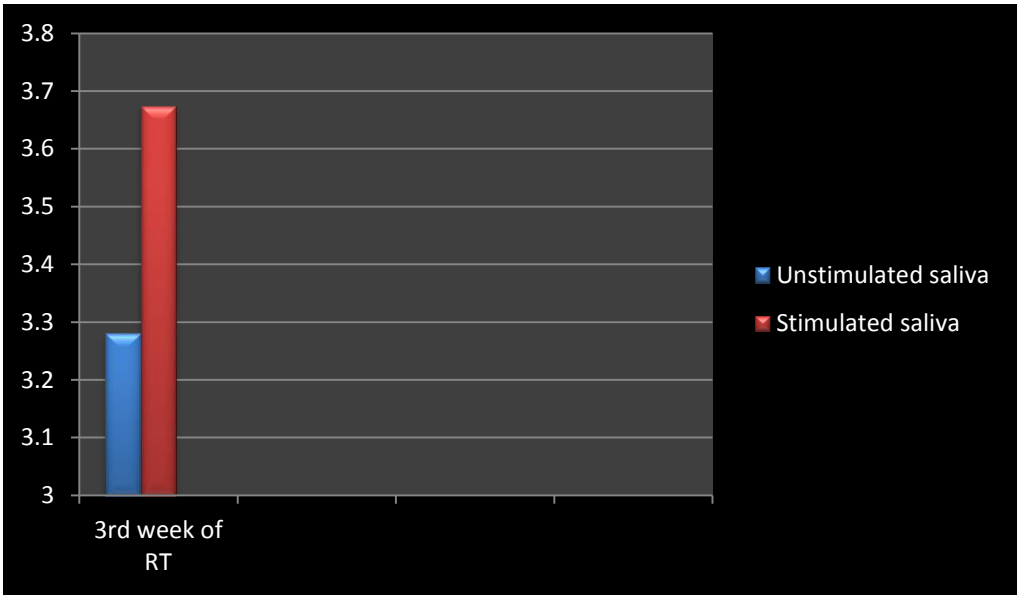
Graph 2: Mean difference between unstimulated and stimulated saliva before radiotherapy



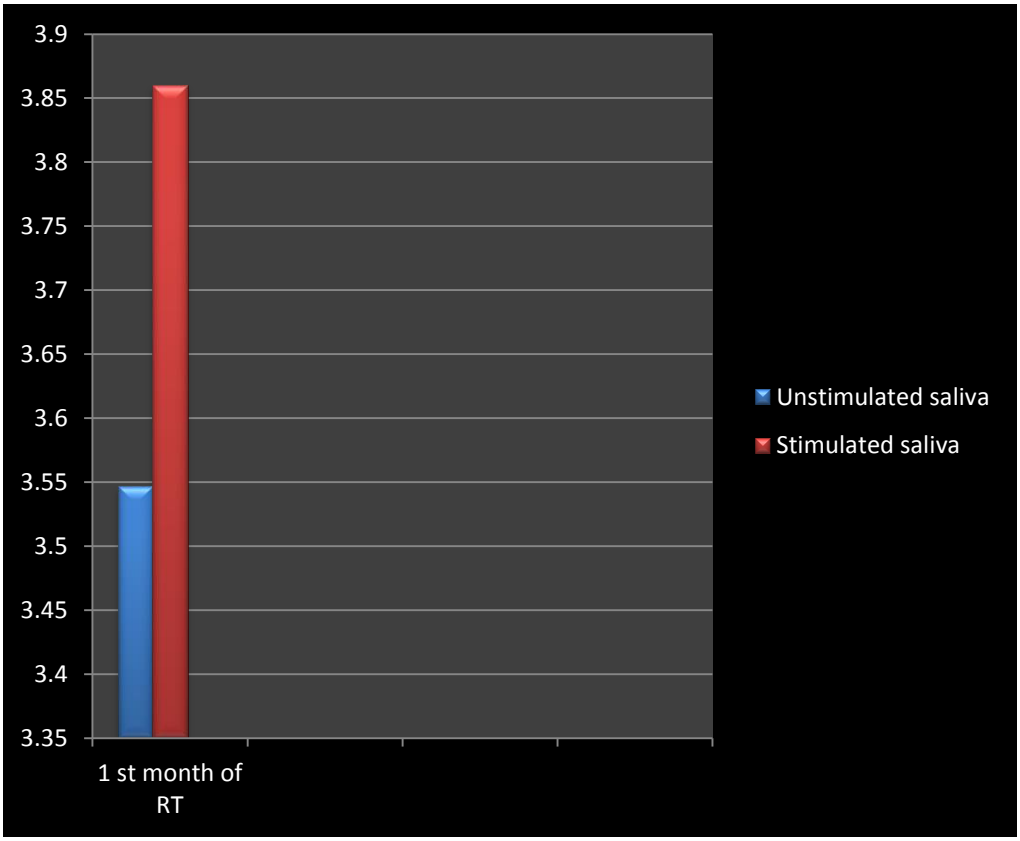
Graph 3: Mean difference between unstimulated and stimulated saliva after radiotherapy



Graph 4: Mean difference between unstimulated and stimulated saliva at 3rd week of radiotherapy



Graph 5: Mean difference between unstimulated and stimulated saliva at 1st month of radiotherapy



Figures

FIGURE 1: DIAGNOSTIC INSTRUMENTS

FIGURE 2: ARMAMENTARIUM FOR STUDY

FIGURE 3: COLLECTION OF UNSTIMULATED SALIVA USING MICROPIPETTE

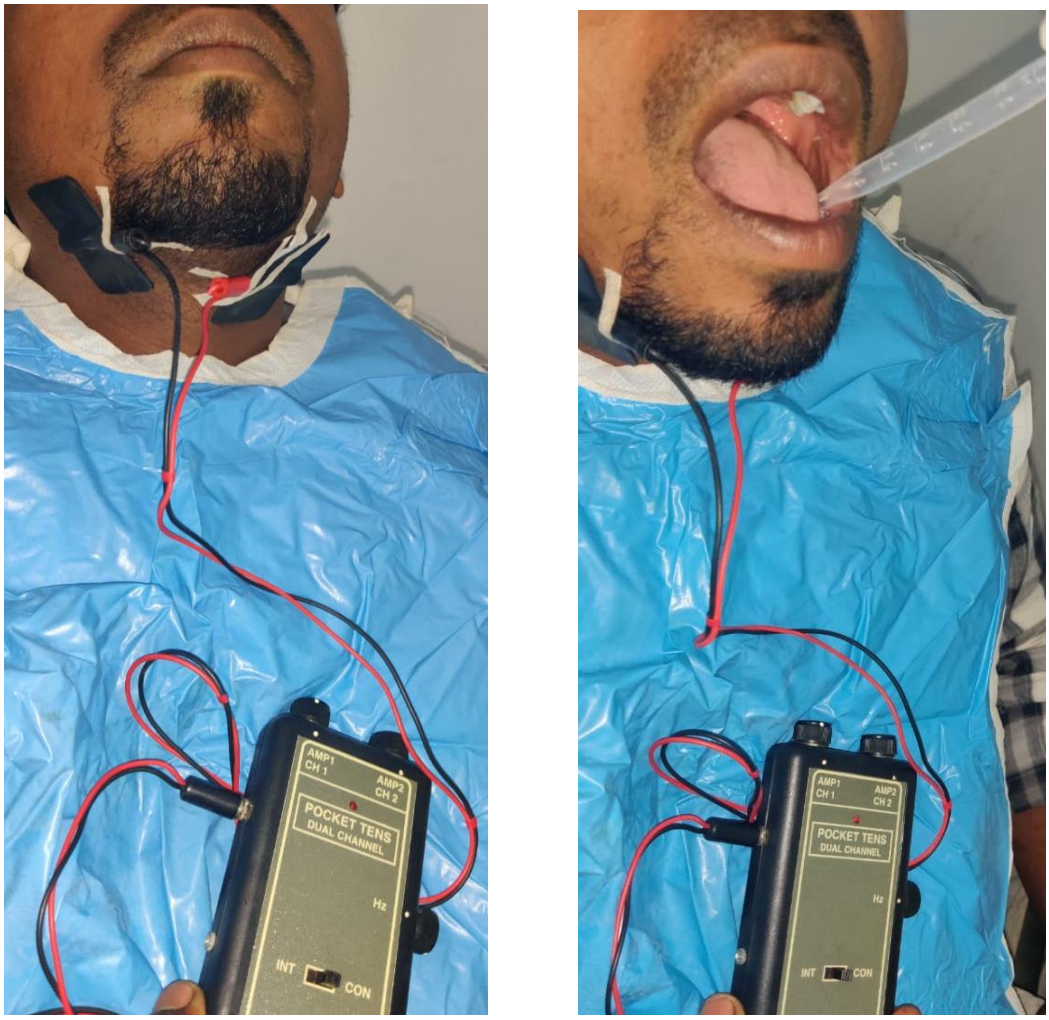
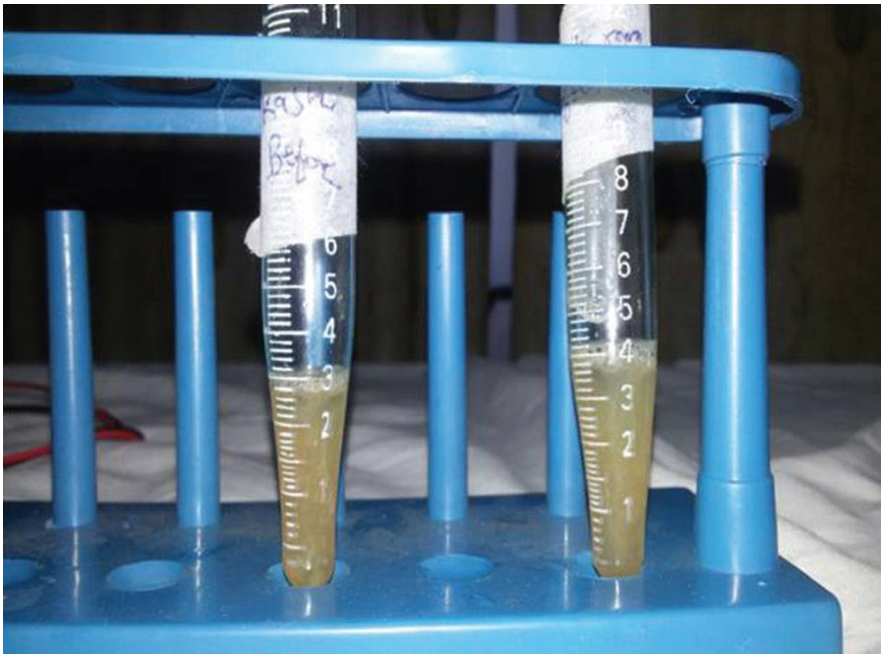


FIGURE 4: COLLECTION OF STIMULATED SALIVA USING MICROPIPETTE WITH ACTIVATING TENS UNIT

FIGURE 5: COMPARISION OF UNSTIMULATED AND STIMULATED SALIVA



Discussion

DISCUSSION:

The results of the present study showed that TENS significantly increased the salivary flow of the patients with head and neck cancer and RT-induced hypo salivation.

An important point of these findings was a moderate positive correlation between intensity of the applied electrical stimulation and response of the salivary flow. In parallel, the dose of ionizing radiation used in RT also influenced the response of the salivary glands to electrostimulation, but negatively. Apparently, the higher the intensity of the electric current, the greater is the production of saliva in response to TENS, while the higher the dose of ionizing radiation, the lower the salivary flow after application of TENS. This indicates that the greater the dose used in RT, the greater the gland damage, which justifies part of the low functionality of these glands even when stimulated artificially.

This study includes patients reporting to Dr. Rai Memorial Cancer Institute, Outpatient Department, and Teynampet seeking service and who are from a wide variety of socioeconomic background.

The patients included in this study were randomly selected who were undergoing IMRT/3DCRT, but the treatment is planned with a basis on an X-ray image, which offers little accuracy for visualization of soft tissues, thereby increasing the exposure of healthy tissues to ionizing radiation. Although IMRT/3DCRT focuses on the region of the tumour, healthy cells of adjacent structures are affected unnecessarily; for example, the salivary glands. When patients undergo three-dimensional intensity-modulated radiotherapy (IMRT),

there may be adverse effects such as deglutition and salivation disorders but to a lesser degree. [35, 36]

The physical-chemical changes of saliva, as well as the reduction or even a complete absence of salivary flow, affects the functions of speech and deglutition by reducing the lubrication of the oral cavity and impairing the proper preparation of the alimentary bolus .[20,21]

The patients in this study reported these changes in the initial assessment. These changes were not evaluated separately; only the participants' self-perception about their stomatognathic functions was considered. The most affected salivary glands are the major ones, which are often involved in the radiation field.[22]

There are different theories that propose divergent mechanisms on how radiation affects the salivary glands by decreasing their secretion. Some suggest that this effect is related to damage to the plasma membrane of acinar cells. In a late phase, the effect would be due to the reduction in the amount of the functional acinar cells.[23]

The main factors that influence the severity of this disorder are the dose of RT, the amount of salivary tissue exposed and individual characteristics.[25] In addition to the reduction of volume, the saliva becomes thicker [26] a characteristic present in the complaints of the patients in this study.

However, regardless of the pathophysiological mechanism that leads to reduced salivary flow, the results of this study showed that TENS, within the parameters described previously, was able to improve the functioning of the salivary glands after a single session, although, in some cases, the normal value could not be re-established (1.0 mL/min).

All the patients shown significant increase in SF after transcutaneous electrical nerve stimulation. All the patients who participated in the study had residual saliva before stimulation; this may be the fact why most of patients showed increase in SF. One of the previous studies showed that TENS by itself is less likely to be effective in cases where there is no baseline saliva and in cases where there is residual salivary function TENS appears to be potential. TENS may act more efficiently as an accelerator of SF rather than an initiator.

Still, the technique is a potential alternative, since even a small increase in salivary flow can provide individuals with greater comfort and possibly oral positive influence on deglutition, speech and mastication. The present findings show that the median of the stimulated salivary flow increased by 100% in patients with RT-induced hypo salivation.

The results of our study are in accordance with the results of study conducted by **Lakshman et al, Vijayan et al, Longman et al, Saraf *et al* , Pattipati, et al.**

In the study conducted by **Lakshman et al** [32] TENS (500Hz) was used in bilateral parotid glands. The authors found an increase in salivary flow with a variation of 3.7% to 140% in the intervention groups. Likewise in our present study the stimulated salivary was increased with significant p value of 0.32667.

Vijayan et al [13] applied TENS (500HZ) in bilateral parotid glands and found an average increase of 0.06 mL/min, which represents an increase by 130%. Their findings are similar to the ones in the present study. Together, these findings reinforce the effect of TENS on the excretion function of the salivary glands, which manifest themselves both acutely and late.

Longman et al [27] found an increase in salivary flow by 71% (pre-test = 0.07 ± 0.03 mL/min; post-test = 0.12 ± 0.03 mL/min) after a single application of electrical stimulation. The mechanism of action of TENS in the glands is not yet clear, but it is believed that the electric current acts upon the direct stimulation of the secretomotor-auriculotemporal nerve. These nerve bundles are located bilaterally and are afferent paths that carry sensory information (action potentials) to the salivatory nuclei (centre of salivation) in the medulla oblongata, which, in turn, send efferent responses of the reflex responsible for salivation (30)

Pattipati, et al. in 2013[28] showed an increase in salivary flow rate on giving TENS and Salivary flow was persistent even after one hour of the treatment.

The results of the study are in contrary to the to study reported by **Hargitai *et al*, Strietzel, et al, Anusha Rangare Lakshman, G. Subhas Babu, Suresh Rao.**

In 11 subjects, there was no increase in whole saliva flow. In a previous study, **Hargitai *et al*** [2] had observed that TENS was unable to stimulate the parotid saliva.

Strietzel, et al [20] demonstrated significant decrease in dryness in the mouth following TENS therapy. Its effectiveness depends on functional capability of glands, it will not be effective if there is absolute absence of salivary secretion .

Anusha Rangare Lakshman, G. Subhas Babu, Suresh Rao conducted a study on 40 subjects. The control group (no xerostomia) showed increased salivary flow rate after stimulation by TENS therapy compared to the unstimulated salivary flow and patients who were undergoing radiotherapy with weekly TENS therapy (0th week, 3rd week, 6th week and after a month) there was no significant improvement in salivary flow.

Summary and Concluion

SUMMARY AND CONCLUSION

The present study titled "**THE EFFECT OF ELECTROSTIMULATION ON SALIVARY PRODUCTION IN PATIENTS UNDERGOING RADIOTHERAPY FOR HEAD AND NECK CANCER**" was conducted in the Department of Oral Medicine and Radiology, Ragas Dental College and Hospital, Uthandi, Chennai and Dr. Rai Memorial Cancer Centre, Chennai to evaluate the effectiveness of electrostimulation on salivary production in patients undergoing radiotherapy for head and neck cancer.

A total of 15 patients undergoing radiotherapy for head and neck cancer were selected for the study.

The study documents the following data:

All the patients participated in this study shown significant value at 5 level with P value ranging from 0.011 – 0.050. There was a significant increase in the stimulated salivary output by electrostimulation with TENS unit.

There are very few studies published to show TENS having a potential for increasing the salivary flow and all the studies have also shown that TENS therapy is effective in parotid saliva stimulation. In our study, the effect of TENS on salivary flow rate on submandibular and sublingual glands was evaluated and it was found to be effective in stimulating saliva.

Thus, despite their results, they do not have enough theoretical bases to justify the choice of this method for treatment of hypo salivation after RT. This evidence must be proven in controlled studies with a larger sample size, in view of the high variability found in the salivary flow records of these patients.

However, the application of this preliminary study is relevant because there is a shortage of research on the use of this technique of stimulation of submandibular and sublingual salivary glands in patients after treatment for head and neck cancer. It should also be noted that other types of electric stimulation can positively stimulate salivary flow, but the findings in this study open up a prospect for new studies on the treatment of hypo salivation, because the TENS technique is an easy to apply, safe if applied by skilled professionals, non-invasive and widely used.

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Annexures

Annexure -I

CASE SHEET

RAGAS DENTAL COLLEGE & HOSPITAL

2/102, EAST COAST ROAD, Uthandi, Chennai – 600119

DEPARTMENT OF ORAL MEDICINE & RADIOLOGY

THE EFFECT OF ELECTROSTIMULATION ON SALIVARY PRODUCTION IN PATIENTS UNDERGOING RADIOTHERAPY FOR HEAD AND NECK CANCER

Date:

S.No :

OP.No :

Study group :

Name : *Annexures*

Age/Sex :

Address :

Phone number :

Occupation :

Monthly income :

Past medical /surgical/dental /history :

Personal history :

ETIOLOGY	PRESENT	ABSENT
Smoking		
Tobacco chewing		
Sharp tooth		
Others		

Provisional Diagnosis :

Investigation & Reports :

Final Diagnosis :

Annexure II

RAGAS DENTAL COLLEGE AND HOSPITAL

DEPARTMENT OF ORAL MEDICINE AND RADIOLOGY

CONSENT LETTER

I ……., undersigned hereby give my consent for the performance of Diagnostic study for **"The effect of electrostimulation on salivary production in patients undergoing radiotherapy for head and neck cancer."** by **Dr.N.NARMATHA** under the able guidance of **Dr.S.Kailasam** Professor and head , Department of Oral Medicine and Radiology, Ragas Dental College and Hospital, Chennai-600119. I have been informed and explained the procedure and the purpose of the study. I also understand and accept this as a part of the study protocol there by voluntarily, unconditionally and freely give my consent without any fear or pressure in a mentally sound and conscious state to participate in the study.

Witness/Representative: Signature:

Date:

Annexure II

RAGASDENTALCOLLEGE AND HOSPITAL

DEPARTMENT OF ORAL MEDICINE AND RADIOLOGY

ஒப்புதல் கடிதம்

நான் _____ என்னுடைய முழு ஒப்புதலை டாக்டர்.ந.நர்மதா மற்றும், டாக்டர்.எஸ். கைலாசம், பேராசிரியர் மற்றும் தலைவர், வாய்வழி மருத்துவம் மற்றும் கதிரியக்கவியல் துறை, ராகஸ் பல் கல்லூரி மற்றும் மருத்துவமனை, சென்னை -600119.

“தலை மற்றும் கழுத்து புற்றுநோய்க்கான கதிரியக்க சிகிச்சைக்கு உட்படுத்தப்பட்ட நோயாளிகளில் உமிழ்நீர் உற்பத்தியில் எலக்ட்ரோஸ்டிமுலேஷனின் விளைவு" என்பதற்கான நோயறிதல் ஆய்வின் செயல்திறனுக்காக , எனக்கு, செயல்முறை மற்றும் ஆய்வின் நோக்கம் குறித்து விளக்கப்பட்டுள்ளது. ஆய்வில் பங்கேற்பதற்கான மனரீதியான மற்றும் நனவான நிலையில் எந்த பயமும் அழுத்தமும் இன்றி தானாக முன்வந்து, நிபந்தனையின்றி மற்றும் சுதந்திரமாக எனது சம்மதத்தை அளிப்பதன் மூலம் இதை அங்குள்ள ஆய்வு நெறிமுறையின் ஒரு பகுதியாக நான் புரிந்துகொண்டு ஏற்றுக்கொள்கிறேன் .

Annexure III

RAGAS DENTAL COLLEGE & HOSPITAL

(Unit of Ragas Educational Society)
Recognized by the Dental Council of India, New Delhi
Affiliated to The Tamilnadu Dr. M.G.R. Medical University, Chennai - 600 032

2/102, East Coast Road, Uthandi, Chennai - 600 119. INDIA
Tele : (044) 2453 0002 - 06. Principal (Dir) 2453 0001 Fax : (044) 24530009

TO WHOM SO EVER IT MAY CONCERN

Date: 20.12.2019

Place: Chennai

From

The Institutional Review Board

Ragas Dental College and Hospital

Uthandi, Chennai – 119

The Project titled **"THE EFFECT OF ELECTROSTIMULATION ON SALIVARY PRODUCTION IN PATIENTS UNDERGOING RADIOTHERAPY FOR HEAD AND NECK CANCER"**, submitted by **Dr.N.Narmatha** has been approved by the Institutional Review Board of Ragas Dental College and Hospital.

Dr.N.S .Azhagarasan,MDS

Member secretary,

The Institutional Review Board

Ragas Dental College and Hospital

Uthandi, Chennai – 119

Annexure IV

S.NO	BEFORE RADIOTHERAPY	AFTER RADIOTHERAPY	3 RD WEEK	IST MONTH	TYPE OF SALIVA ml / 5 mins
1	3.5	3.5	3	3.2	UNSTIMULATED SALIVA
2	4	3.8	3.5	3.8	UNSTIMULATED SALIVA
3	4	4.2	3.5	3.8	UNSTIMULATED SALIVA
4	3	3	2.5	3	UNSTIMULATED SALIVA
5	3.5	3.5	3	3.2	UNSTIMULATED SALIVA
6	4.2	4	3.5	4	UNSTIMULATED SALIVA
7	4	3.8	3.5	3.5	UNSTIMULATED SALIVA
8	3.8	2.5	3	3.5	UNSTIMULATED SALIVA
9	4	4	3.5	4	UNSTIMULATED SALIVA
10	3.5	3.2	3	3.2	UNSTIMULATED SALIVA
11	3	3	3.2	3	UNSTIMULATED SALIVA
12	3.8	3.6	4	4	UNSTIMULATED SALIVA
13	4.5	4	3.8	4	UNSTIMULATED SALIVA
14	3	3.5	3	3.5	UNSTIMULATED SALIVA
15	4	3.6	3.2	3.5	UNSTIMULATED SALIVA
1	4.2	4	3.5	3.8	STIMULATED SALIVA
2	4.5	4.2	3.8	4	STIMULATED SALIVA
3	4.2	4.5	4	4	STIMULATED SALIVA
4	3.5	3.8	3	3.2	STIMULATED SALIVA
5	4	3.8	3.5	3.8	STIMULATED SALIVA
6	4.5	4.2	3.8	4.2	STIMULATED SALIVA

Annexure IV

7	4.2	4	3.8	3.6	STIMULATED SALIVA
8	4	2.8	3.5	3.8	STIMULATED SALIVA
9	4.4	4.2	3.8	4.2	STIMULATED SALIVA
10	3.8	3.5	3.5	3.6	STIMULATED SALIVA
11	3.5	3.6	3.6	3.5	STIMULATED SALIVA
12	4	4	4.2	4.2	STIMULATED SALIVA
13	4.2	4.4	4	4.2	STIMULATED SALIVA
14	3.5	3.84.2	3.5	4	STIMULATED SALIVA
15	4.2	4	3.6	3.8	STIMULATED SALIVA

Annexure V

URKUND

Urkund Analysis Result

Analysed Document:	2 introduction-merged.pdf (D62788941)
Submitted:	1/21/2020 10:41:00 PM
Submitted By:	narmadabds11@gmail.com
Significance:	9 %

Sources included in the report:

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