ROLE OF RG4 (AN AYURVEDIC FORMULATION) IN THE MANAGEMENT OF SIDE-EFFECTS OF RADIOTHERAPY OF ORAL CAVITY CANCERS

A thesis submitted to

TILAK MAHARASHTRA VIDYAPEETH, PUNE

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Subject	**:**	**Kayachikitsa**
Under Faculty of	**:**	**Ayurved**
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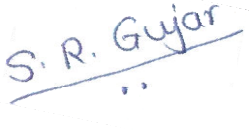
Under the Guidance of Name of the Guide	**:**	**Dr. Vineeta V. Deshmukh**
Name of the Department	**:**	**Ayurved**
Month & Year	**:**	**September 2015**

DECLARATION

I hereby declare that the thesis entitled "Role of RG4 (an Ayurvedic formulation) in the management of side-effects of Radiotherapy of oral cavity cancers" completed and written by me has not previously formed the basis for the award of any degree or other similar title or any other university or examining body.

Place - Pune

Date – 01/09/2015



Vd. Mrs. Shweta Rakesh Gujar

CERTIFICATE

This is to certify that the thesis entitled,

"Role of RG4 (an Ayurvedic formulation) in the management of side-effects of Radiotherapy of oral cavity cancers" which is being submitted herewith for the award of the Degree of Vidyavachaspati (Ph. D.) in Ayurveda of Tilak Maharashtra Vidyapeeth, Pune is the result of original research work completed by **Vd . Mrs. Shweta Rakesh Gujar** under my supervision and guidance. To the best of my knowledge and belief the work incorporated in this thesis has not formed the basis for the award of any degree or similar title of this or any other University or examining body.

Place - Pune

Date – 01/09/2015

Deshmukh

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Vd. Mrs. Shweta R. Gujar
Research Scholar.

INDEX

LIST OF ABBRIVATIONS

Texts

च. सं.	Ch.Sa.	Charak Samhita (चरक संहिता)
सु. सं.	Su.Sa	Susrut Samhita (सुश्रूत संहिता)
अ. ह्र.	Ah.Sa.	Asthang Sangraha (अष्टांग ह्रदय)
का.सं.	Ka.S.	Kashyap Samhita (काश्यप संहिता)
भा.प्र.	Bh.P.	Bhavprakash (भावप्रकाश)
यो.र.	Y.R.	Yogratnakar (योगरत्नाकर)
र.यो.सा.	R.Y.S.	Rasyogsagar (रसयोगसागर)

Topics

सू. स्था.	Su.	Sutrasthan (सुत्र स्थान)
नि. स्था.	Ni.	Nidansthan (निदान स्थान)
उ. स्था.	U.	Uttarsthan (उत्तर स्थान)
चि. स्था.	Chi.	Chikitsasthan (चिकित्सा स्थान)

TABLE DETAILS

GRAPH DETAILS

No.	Title of Graphs
1	Age wise distribution of oral cancer patients under Radiotherapy.
2	Sex wise distribution of oral cancer patients under Radiotherapy
3	Socio – economical distribution of oral cancer patients under radiotherapy
4A	History of addiction of oral cancer patients under radiotherapy
4B	Distribution of forms of tobacco consumption in oral cancer patients under radiotherapy
5	Histopathological Grade wise presentation of oral cancer patients under radiotherapy
6	Surgical status of oral cancer patients under radiotherapy
7	Status of adjuvant chemotherapy of oral cancer patients under radiotherapy
8A	Gradation of stomatitis in oral cancer patients treated with radiotherapy
8B	Graphical representation of statistical analysis of gradation of stomatitis in oral cancer patients treated with radiotherapy
9A	Gradation of xerostomia in oral cancer patients treated with radiotherapy
9B	Graphical representation of statistical analysis of gradation of xerostomia in oral cancer patients treated with radiotherapy
10A	Gradation of loss of taste in oral cancer patients treated with radiotherapy
10B	Graphical representation of statistical analysis of gradation of loss of taste in oral cancer patients treated with radiotherapy
11A	Gradation of excessive salivation in oral cancer patients treated with radiotherapy
11B	Graphical representation of statistical analysis of gradation of excessive salivation in oral cancer patients treated with radiotherapy
12A	Gradation of trismus in oral cancer patients treated with radiotherapy
12B	Graphical representation of statistical analysis of gradation of trismus in oral cancer patients treated with radiotherapy
13A	Gradation of dysphagia in oral cancer patients treated with radiotherapy
13B	Graphical representation of statistical analysis of gradation of dysphagia in oral cancer patients treated with radiotherapy
14A	Gradation of nausea in oral cancer patients treated with radiotherapy

No.	Title of Graphs
14B	Graphical representation of statistical analysis of gradation of nausea in oral cancer patients treated with radiotherapy
15A	Gradation of percentage of weight loss in oral cancer patients treated with radiotherapy
15B	Graphical representation of statistical analysis of gradation of percentage of weight loss in oral cancer patients treated with radiotherapy
16A	Change of Karnofsky score in oral cancer patients under radiotherapy
16B	Mean values depicting Karnofsky score in oral cancer patients under radiotherapy
16C	Graphical representation of statistical analysis Karnofsky score in oral cancer patients under radiotherapy
17A	Change in Functional score of quality of life in oral cancer patients under radiotherapy
17B	Mean values depicting Functional score of QOL in oral cancer patients under radiotherapy
17C	Graphical representation statistical analysis Functional score of QOL in oral cancer patients under radiotherapy
18A	Change in symptom score of quality of life in oral cancer patients under radiotherapy
18B	Mean values depicting symptom score of QOL in oral cancer patients under radiotherapy
18C	Graphical representation statistical analysis symptom score of QoL in oral cancer patients under radiotherapy
19A	Change in global score of quality of life in oral cancer patients under radiotherapy
19B	Mean values depicting global score of QoL in oral cancer patients under radiotherapy
19C	Graphical representation statistical analysis global score of QoL in oral cancer patients under radiotherapy
20A	Change in H & N symptom score of quality of life in oral cancer patients under radiotherapy

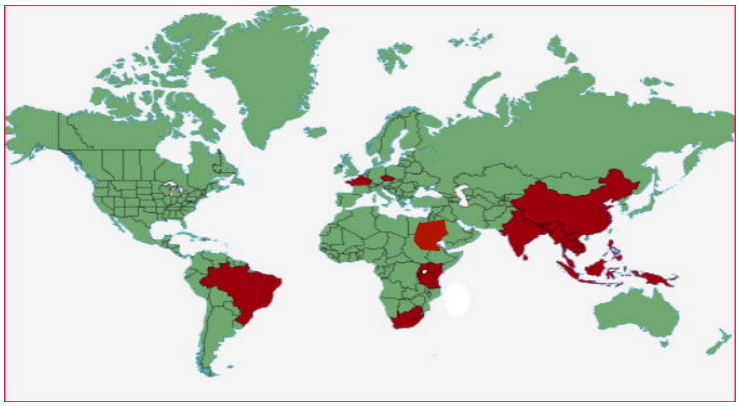
No.	Title of Graphs
20B	Mean values depicting H & N symptom score of QoL in oral cancer patients under radiotherapy
20C	Graphical representation statistical analysis H & N symptom score of QoL in oral cancer patients under Radiotherapy

STATISTICAL TABLE DETAILS

No	Title Statistical Tables
1	Gradation of stomatitis in oral cancer patients treated with radiotherapy
2	Gradation of xerostomia in oral cancer patients treated with radiotherapy
3	Gradation of loss of taste in oral cancer patients treated with radiotherapy
4	Gradation of excessive salivation in oral cancer patients treated with radiotherapy
5	Gradation of trismus in oral cancer patients treated with radiotherapy
6	Gradation of dysphasia in oral cancer patients treated with radiotherapy
7	Gradation of nausea in oral cancer patients treated with radiotherapy
8	Gradation of percentage of weight loss in oral cancer patients treated with radiotherapy
9	Mean values depicting Karnofsky scaore in oral cancer patients under radiotherapy
10	Mean values depicting Functional score of QoL in oral cancer patients under radiotherapy
11	Mean values depicting Symptom score of QoL in oral cancer patients under radiotherapy
12	Mean values depicting Global score of QoL in oral cancer patients under radiotherapy
13	Mean values depicting H &N Symptom score of QoL in oral cancer patients under radiotherapy

INTRODUCTION

Prevalence of Cancer is increasing rapidly to such an extent that in each family we find at least one near one, a family friend or a colleague diagnosed with it. This is due to changing lifestyle and advance in technology in developed as well as in developing countries. Oral cancer is rapidly becoming global health priority. In India it ranks among top three cancers[1]. The prevalence of oral cancer is high among men[2].



Oral cancer is a significant disease affecting public health as it is diagnosed in late stages; as a result, the treatment outcome is poor with respect to considerably costly and unaffordable treatments.

Oral cancer mainly affects those from lower socioeconomical groups due to greater consumption of tobacco as a result of illiteracy. 90 % of oral caners are due to tobacco use and alcohol consumption. Several studies now confirm that evidence of smokeless tobacco is a major factor causing oral cancer[3].

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1. Challenges of the Oral Cancer Burden in India, Ken Russell Coelho,(2012) Journal of Cancer Epidemiology, Volume 2012 , Article ID 701932, pp17.
   http://www.hindawi.com/journals/jce/2012/701932/
2. Strengthening the prevention of oral cancer: the WHO perspective, Blackwell Munksgaard ,(2005),Community Dentistry Oral Epidemiology, 33:pp397–399
   http://www.who.int/oral_health/publications/CDOE05_vol33_397_9/en
3. Smoking tobacco, oral snuff, and alcohol in the etiology of squamous cell carcinoma of the head and neck, (1998) FreddiLewin., Staffan E. Norell Hemming Johansson ,Per Gustavsson , Johan Wennerberg , Anders Biörklund and Lars Erik Rutqvist , Cancer, Volume 82, Issue 7, pp 1367–1375
   http://www.ncbi.nlm.nih.gov/pubmed/9529030

Oral cancer is dangerous as many times it remains unnoticeable by the patient in early stages and frequently progressed without pain or any symptom. The patients, who survive a first encounter with the disease, have up to a 20 times higher risk of developing secondaries. Patient is under risk for 5-10 yrs after first encounter of the disease.

90 % of oral cancers are squamous cell carcinomas. In modern medicines available treatment modalities includes identification of population which is at high risk, eduation of the patients, timely management of lesions with the help of conventional treatment options.

Radiotherapy is a common treatment option as per Indian Council of Medical Research Guidelines for Management of Buccal Mucosa Cancer irrespective of stage of cancer (whether it is in stage I-IV)[4].

Efficacy of Radiotherapy in oral cavity cancer

Role of radiotherapy is evident in oral cavity cancer patients. Small mucosal tumours can be successfully treated only with radiotherapy instead of surgery with similar results and by avoiding surgical hazards and lifelong deformities. Extensive nodal metastatic disease in oral cavity cancers are managed by combined modalities like surgery, radiotherapy and chemotherapy. Thus radiotherapy is integral part of treatment in oral cavity cancers.[5]

4. Indian Council of Medical Research consensus document for the management of buccal mucosa cancer ,(2014),GouraKishorRath, Purvish M Parikh, Shelley Hukku, BalakrishnanRajan, Sandeep Kumar, Hemant Malhotra, SeenuVuthaluru, DayaNand Sharma, Amish Vora, Deepak Kumar Shukla, Tanvir Kaur, Ajeet Kumar Gandhi , Indian Jpournal of Medical and Paediatric Oncology , Volume : 35 , Issue : 2 , pp 136-139 http://www.ncbi.nlm.nih.gov/pmc/articles/PMC4152629/
5. Cancer Principal and Practice of oncology, Vincent T. Devita, Jr. , Samuel Hellman , Steven A. Rosenberg, 7th edition,Chapter26.2,pp681

Radiotherpy hazards –

Radiotherapy, which is often given as adjuvant therapy following surgery, affects tumour cells as well as healthy cells depending upon field of radiotherapy. Radiotherapy when given in oral cancers induces stomatitis, xerostomia, trismus, loss of taste etc in patients. It directly impacts upon oral health, and swallowing ability[6]**.**The inability to eat has significant consequences. This has impact on quality of life and performance status. The patients with poor quality of life and performance generally have poor prognosis.

Selection of topic:

Main goal of cancer treatment are to cure the disease, prolong the life of patients and to give best possible quality of life to cancer patients.

Ayurvedic drugs used for centuries in India are known for less toxicity and accepted for chronic diseases[7]. They are also known to improve the generalised weakness and also boost up immunity which is particularly hampered in oral cancer patients. These medicines can help to maintain quality of life in cancer patients. Recently combinations of Ayurvedic drugs are also recommended for cancer as an adjunct therapy as Ayurvedic drugs are commonly used to improve quality of life and to improve immune response. As mentioned above radiotherapy is one of the main stream treatments for oral cancer. Side effects occurring due to radiotherapy often leads to pitta vruddhi, raktadushti and dehoshma vrudhhi (Jwara). In oral cavity cancers, it additionally hampers Jatharagni, produces vrana in oral cavity. Thus in many pateintsit causes discontinuation of therapy jeopardising its effects and also in compromising quality of life of cancer patient.

6. Oral complications of cancer radiotherapy (1977), Denizen, Daly TE, Drane JB, Brown LR , Postgraduate Medicine , 61(2), pp85-92 http://europepmc.org/abstract/med/12108892
7. Tripathi B (2003) CharakSamhita, vol. 2, ChaukhambaSurabharatiPrakashan, Varanasi, Rasayana 1/1/4, pp3

Various Ayurvedic drugs such as Mauktikyukta Praval Panchmrut, Mauktikyukta Kamdudha, Yashtimadhu (*Glycyrrhiza glabra*), Ananta (*Hemidesmus indicus*) have properties as chardighna (antiemetic), pittashamak (antacids), raktashodhak (Improving quality of blood), jwarahara (anti pyretic) and vranropak (Antiulcer). It is with this consideration in mind, I have selected various preperations of above mentioned medicines to minimize side-effects of radiotherapy in oral cavity cancer patients. In our centre, we are using combination of these medicines in oral cavity cancer patients undergoing radiotherapy and found to be effective in minimizing these side effects and improving QoL. It is with this consideration in mind I have selected the topic.

AIMS AND OBJECTIVES

Aim -

To study role of RG4 (an Ayurvedic formulation) in the management of side-effects of radiotherapy in oral cavity cancer patients.

Objectives –

1) To evaluate status of quality of life hampered due to side effects of radiotherapy in oral cancer patients.
2) To assess wellbeing and ability to conduct activities of daily life hampered due to side effects in oral cancer patients undergoing radiotherapy.

LITERATURE REVIEW

A) LITERATURE REVIEW OF CANCER FROM ALLOPATHIC PERSPECTIVE

A-I) CANCER

Cancer can start anywhere in the body. The body is made up of trillions of cells. Normally human cells grow and divide to form new cells as the body needs them. When cells grow old or become damaged, they die, and new cells take their place. When cancer develops, however, this orderly process breaks down. As cells become more and more abnormal, old or damaged cells survive when they should die, and new cells form when they are not needed. These extra cells can divide without stopping and may form growths called tumours [8].

It is a complex genetic disease derived from the accumulation of various genetic changes. These genetic alterations include activation of protooncogenes and inactivation of tumour suppressor genes. It is a group of diseases, which arise by initial mutation hit in a single cell in any of the multiple cell regulatory systems. It can remain dormant for any length of period. Additional mutation hits drives the initiated cell into proliferation of cells and additional mutations selecting cells with growth advantage, invasive and metastatic properties. Cancer occurs in functionally differentiating cells. Cancer is characterised by invasion of normal tissue and metastasis at distant organs. Metastatic cells have different biochemical and immunological properties conducive of spread of the disease [9].

Many cancers form solid tumours, which are masses of tissue. Cancers of the blood, such as leukemias, generally do not form solid tumours which are called non solid tumours. Cancerous tumours are malignant, which means they can spread into, or invade, nearby tissues. In addition, as these tumours grow, some cancer cells can break off and travel to distant places in the body through the blood or the lymph system and form new tumours far from the original tumour.

8. http://www.cancer.gov/cancertopics/what-is-cancer
9. Cancer Principal and Practice of oncology, Vincent T. Devita, Jr. , Samuel Hellman , Steven A. Rosenberg, 7th edition, chapter26,pp653

Unlike malignant tumours, benign tumours do not spread into, or invade, nearby tissues. Benign tumours can sometimes be quite large, however, when removed; they usually don't grow again, whereas malignant tumours sometimes can reaccure. Unlike most benign tumours elsewhere in the body, benign brain tumours can be life threatening.

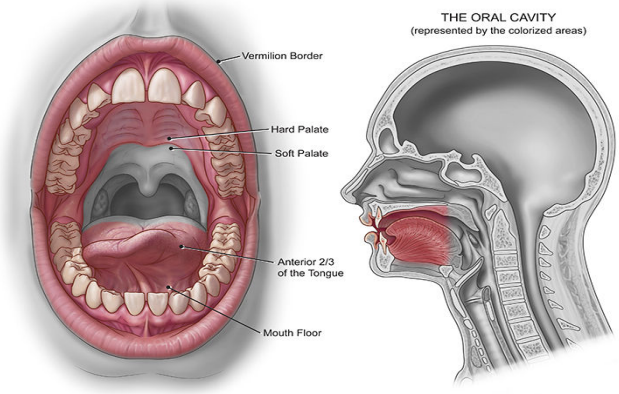
A-II) ORAL CANCER

a. ANATOMY AND PHYSIOLOGY OF ORGANS OF ORAL CAVITY

The oral cavity begins at the border between the skin and the lips (vermillion border). The roof of the mouth is formed by the hard palate. The oral cavity leads into the oropharynx, which includes the soft palate, the back of the tongue and the tonsils. The inner surface of the cheeks forms the sides of the oral cavity. The lowest part of the oral cavity is the floor of the mouth, which is covered by the tongue [10].

The oral cavity can be divided into specific areas, including:

- lips
- labial mucosa (inner lining of the lips)
- commissure of lips (where the upper and lower lips meet at the corner of the mouth)
- vestibule (a space bounded by the teeth and gums on the inside and the mucosal surface of the lips and cheeks on the outside)
- oral tongue (the front two-thirds of the tongue)
- floor of the mouth
- buccal mucosa (the inner lining of cheeks)
- gingiva (gums)
- retromolar trigone (the area just behind the back molars in the lower jaw)
- hard palate (the bony part at the front of the roof of the mouth)
- teeth
- lower jaw (mandible)
- upper jaw (maxilla)



10. Basic Human Anatomy – A regional Study of Human Structure, Ronan O'Rahilly, Fabiola Müller, Stanley Carpenter, Rand Swenson, Chapter 51: The mouth tongue and teeth. https://www.dartmouth.edu/~humananatomy/

b. HISTOLOGY OF ORAL CAVITY CANCER

The vast majoritry of head and neck malignant neoplasms arise from the surface of epithelium and are therefore **squamous cell carcinoma** or one of its variants, including lympho-epithelioma, spindle cell carcinoma, verrucous carcinoma and undifferentiated carcinoma. Lymphomas and wide variety of other malignant and benign neoplasms make up the remaining cases [11]

Lymphopho-epithelioma is a carcinoma with a lymphoid stroma. It occurs at anatomical sites with lymphoid aggregates in the submucosa, namely, the nasopharynx, tonsil, and base of the tongue. It may also occur in the major salivary glands.

In the **spindle cell** variant, found in 2% to 5% of upper aerodigestive tract malignancies, there is a component of spindle cells that resembles sarcoma intermixed with squamous cell carcinoma. For the most part, these lesions can not be distinguished grossly from the usual squamous cell carcinoma.

Verrucous carcinoma is a low grade squamous cell carcinoma found most often in the oral cavity, particularly in the gingio and buccal mucosa. It usually has an indolent growth patteren and is often associated with the chronic use of snuff or chewing tobacco. A verrucous tumour resembles a wart. These carcinomas rarely develop lymph node metastasis.

Small cell neuroendocrine carcinoma occurs rarely throughout the head and neck region and usally managed by radiotherapy and chemotherapy.

11. Cancer Principal and Practice of oncology, Vincent T. Devita, Jr. , Samuel Hellman , Steven A. Rosenberg, 7th edition, chapter26.2,pp 662

c. ORAL CAVITY CANCER -RISK FACTORS

A risk factor is a cause associated with increased risk of disease or infection. Oral cancer has multiple etiological factors but tobacco use and alcohol consumption are widely considered to be its major risk factors[12].

1) ADDICTION

i. Smokeless Tobacco (Snuff and Chewing Tobacco)

Tobacco that is not burned is known as smokeless tobacco. It has many names like chewing tobacco, spit, spitting tobacco, chew, dip or snuff. People in many countries like Northern Europe, North America, India and other Asian countries, part of Africa are commonly using smokeless tobacco. While chewing tobacco i.e placing loose leaves between cheek and lower lip and then spitting or swallowing saliva. In this process nicotine in the tobacco is absorbed through the mouth lining.

There are two main types of smokeless tobacco:

a. **Snuff** - Snuff is finely cut or powdered tobacco sold in different scents and flavors. It is packaged moist or dry, available loose or in small pouches similar to tea bags. The user places a pinch or pouch of moist snuff between the cheek and gums or behind the upper or lower lip. Another name for moist snuff is snus pronounced "snoose". Some people inhale dry snuff into the nose.

Chewing Tobacco- Chewing tobacco is a type of smokeless tobacco product consumed by placing a portion of the tobacco between the cheek and gum or upper lip teeth and chewing. Nearly all modern chewing tobaccos are produced via a process of leaf curing, cutting, fermentation and processing or sweetening. **Gutka** or **Gutkha** is a preparation of sweeten tobacco along with crushed betal nut, slaked lime etc. It is a mild stimulant manufactured in India and exported to a few other countries in small, individual-sized packets that cost between 2 and 10 rupees per packet. Gutka is consumed by placing a pinch of it between the gum and cheek and gently sucking and chewing.There is no safe form of tobacco.

12. Squamous cell carcinoma of the oral cavity, maxillary antrum and lip in a Zimbabwean population: A descriptive epidemiological study,(2006) Midion Mapfumo Chidzonga, Leonard Mahomva , oral oncology , Volume 42 , Issue 2 , pp 184 – 189. http://www.oraloncology.com/article/S1368-8375(05)00224-1/abstract

ii. Alcohol -

Alcohol is already the second largest risk factors for the development of oral cancer. Addiction of alcohol consumption alongwith tobacco increases the risk of developing oral cavity cancers. The dehydrating effect of alcohol affected mouth tissues; additionally, nutritional deficiencies associated with heavy drinking can lower the body's natural ability to use antioxidants to prevent the formation of cancers. Eliminating the use of tobacco and reducing intake of alcohol immediately reduces risk of developing oral cancer [13].

iii. Cigarettes

Evidence from various epidemiological studies has shown the association between cigarette smoking and oral cancer [14].

The mortality risk for oral cancer in cigarette smokers is substantially greater than who are non smokers. Furthermore, the risk for death from oral cancer is related to number of cigarettes consumed in smokers. The more cigarettes consumed daily and the more years one has smoked, the greater the risk. In numerous studies examining the relative risk for oral cancer among former smokers have found that the risk for oral cancer was lower among former smokers after the first few years of non smoking than for those who continued to smoke. These studies have found that after 3 to 5 years of smoking abstinence, oral cancer risk decreased by about 50%[15].

13. Risk factors for oral cancer in Brazil: A case-control study,(1998) Eduardo L. Franco, Luiz P. Kowalski, Benedito V. Oliveira, M. Paula Curado, Raimunda N. Pereira , M. Estela Silva, Antonio S. Fava, Humberto Torloni, International Journal of Cancer , Volume 43, Issue 6, pp 992–1000.
http://onlinelibrary.wiley.com/doi/10.1002/ijc.2910430607/abstract

14. Effect of Cigarette Smoking and Alcohol Consumption in the Aetiology of Cancer of the Oral Cavity, Pharynx and Larynx ,(1991)Soo Yong Choi and Hiroaki Kahyo , International Journal of Epidemiology . Volume 20, Issue 4 ,pp 878-885
http://www.ncbi.nlm.nih.gov/pubmed/1800426

15. US Department of Health and Human Services. The health consequences of smoking: cancer. Rockville, MD: US Department of Health and Human Services, Public Health Service, Office of Smoking and Health, 1982. DHHS publication no. (PHS) 82-50179. http://www.surgeongeneral.gov/library/reports/50-years-of-progress/full-report.pdf

iv. Cigars and Pipes

Cigarette smoking being a direct form of tobacco increases risk of oral cavity cancer. At the same time regular use of cigars and pipes which have indirect contact of tobacco, also showed increased incidence of oral cancer. Both prospective and retrospective studies have consistently documented that pipe and cigar smokers experience mortality rates for oral cancer either similar or higher than those risks observed among cigarette smokers[16, 17].

2) MOUTHWASH

There is some concern that mouthwashes might cause oral cancer because they have high alcohol content and are used frequently. The link between oral cancer and mouthwash is less clear. The association was only significant when looking at very frequent use (three times a day) [18].

3) DIET

Linking of deficient diet and oral cavity cancer is not as evident to that of tobacco and alcohol consumption. In some studies low beta-carotene intake has been associated with an increased risk of lung, laryngeal, gastric, ovarian, breast, cervical, and oral cancers.

Several studies have shown that a low intake of fruits and vegetables, which are the primary sources of beta-carotene, is also related to a generalized increased cancer risk and mortality [19].

16. IARC Working Group. Tobacco smoking. In: IARC Working Group, ed. Monographs on the evaluation of the carcinogenic risk of chemicals to humans. vol. 38. Lyon, France: International Agency for Research on Cancer, 1986. http://monographs.iarc.fr/ENG/Monographs/vol1-42/mono38.pdf
17. World Health Organization. Smoking and its effects on health. Report of a WHO expert committee. Geneva: World Health Organization, 1975. Technical Report Series 568. http://whqlibdoc.who.int/trs/WHO_TRS_568.pdf
18. Oral cancer and mouthwash use: evaluation of the epidemiologic evidence,(1995), Elmore JG, Horwitz RI Otolaryngol Head Neck Surg; 113, pp253-261.http://www.ncbi.nlm.nih.gov/pubmed/7675486
19. Beta-carotene and vitamin E in oral cancer prevention, (1993)Garewal HS, J Cell Biochem Suppl. ; 17F:262-9. http://onlinelibrary.wiley.com/doi/10.1002/jcb.240531039/abstract

4) ACTINIC RADIATION

Sunlight, through actinic radiation, helps to produce cancer along the vermilion border of the lip. These "sunlight" induced cancers are much more common in fair-skinned individuals exposed to the outdoor life than in individuals with darker pigmentation. It appears that darker pigment protects against actinic radiation damage [20].

5) DENTAL FACTORS

Poor oral hygiene, improperly fitting dental prostheses, defective dental restorations, or misaligned or sharp teeth promotes oral cancer [21].

6) VIRUSES AND THEIR INTERACTIONS WITH ONCOGENES –

The human papilloma virus (HPV) is a double-stranded DNA virus. It infects the epithelial cells of skin and mucosa. The moist epithelial surfaces (squamous cells) include all areas covered by skin and/or mucosa such as the mouth interior, throat, tongue, tonsils, vagina, cervix, vulva, penis and anus. Transmission of the virus occurs when these areas come into contact with a virus, allowing it to transfer between epithelial cells. While it is established now that sexual contacts, both conventional and oral, are means of transferring the HPV virus through direct skin to skin contact[22]. HPV plays a tole in some head and neck cancers.

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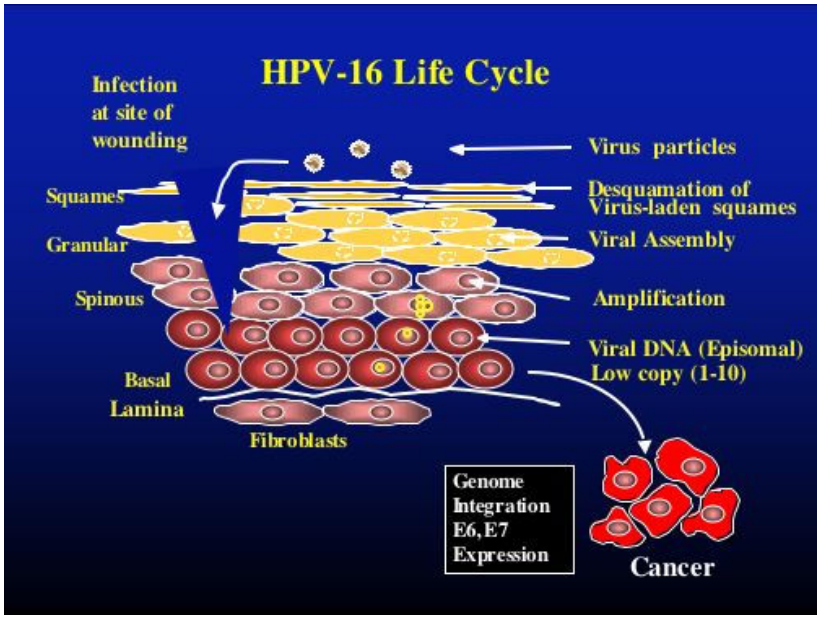
20. Solar cheilosis: An ominous precursor, (2009), Yuri T.Jadotte, Robert A. Schwartz, Journal of the American Academy of Dermatology, Vol. 66, Issue 2, pp173–184
http://www.jaad.org/article/S0190-9622%2811%2901196-0/abstract

21. Poor dental status increases acetaldehyde production from ethanol in saliva: a possible link to increased oral cancer risk among heavy drinkers, (2001) , N Homann, J Tillonen, H Rintamäki, M Salaspuro, C Lindqvist , J.H Meurman, oral oncology , Volume 37, Issue 2, pp 153–158
http://www.ncbi.nlm.nih.gov/pubmed/11167142

22. Human Papillomavirus and Oral Cancer: The International Agency for Research on Cancer Multicenter Study,(2003),Rolando Herrero, Xavier Castellsagué, Michael Pawlita, Jolanta Lissowska, Frank Kee,Prabda Balaram, Thangarajan Rajkumar, Hema Sridhar, Barbara Rose, Javier Pintos,Leticia Fernández,Ali Idris, María José Sánchez, Adoración Nieto, Renato Talamini,Alessandra Tavani, F. Xavier Bosch, Ulrich Reidel, Peter J. F. Snijders, Chris J. L. M. Meijer,Raphael Viscidi, Nubia Muñoz, Silvia Franceschi and For the IARC Multicenter Oral Cancer .JNCI J Natl Cancer Inst ,Volume 95, Issue 23, pp 1772-1783. http://jnci.oxfordjournals.org/content/95/23/1772.full

HPV positive oropharyngeal tumours compose a distinct clinical and pathological disease entity casually associated with HPV [23].



23. Cancer Principal and Practice of oncology, Vincent T. Devita, Jr. , Samuel Hellman , Steven A. Rosenberg, 7th edition,chapter26.1, pp 658

d. ORAL CAVITY CANCER –SCREENING FOR EARLY DETECTION

Screening of cancer means looking for a cancer before a patient has any symptoms. Appropiate cancer screening should lead to early detection of asymptomatic or unrecognized disease by the application of acceptable, inexpensive tests or examinations on large number of persons. The main objective of cancer screening is to detect cancer at an early stage when it is treatable and curable [24].

There is no standard or routine screening test for oral cancer.

Screening for oral cancer may be done during a routine check-up by a dentist or medical doctor. The exam will include looking for lesions, including areas of leukoplakia (an abnormal white patch of cells) and erythroplakia (an abnormal red patch of cells). Leukoplakia and erythroplakia lesions on the mucous membranes may become cancerous.

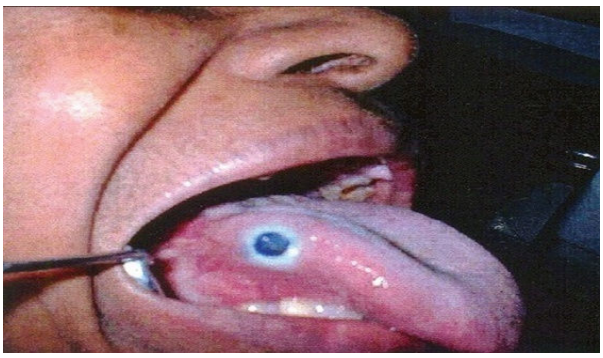
If lesions are seen in the mouth, the following procedures may be used to find abnormal tissue that might develop into oral cancer:

i. **Exfoliative cytology:** A procedure to collect cells from the lip or oral cavity. A piece of cotton, a brush, or a small wooden stick is used to gently scrape cells from the lips, tongue, mouth, or throat. The cells are viewed under a microscope to find out if they are abnormal.

24. Cancer Principal and Practice of oncology, Vincent T. Devita, Jr. , Samuel Hellman , Steven A. Rosenberg, 7th edition,chapter22,pp -567

ii. **Fluorescence staining:** A procedure in which lesions in the mouth are viewed using a special light. After the patient uses a fluorescent mouth rinse, normal tissue looks different from abnormal tissue when seen under the light.

iii. **Toluidine blue stain**: A procedure in which lesions in the mouth are coated with a blue dye. Areas that stain darker are more likely to be cancer or become cancer.



iv. **Brush biopsy:** The removal of cells using a brush that is designed to collect cells from all layers of a lesion. The cells are viewed under a microscope to find out if they are abnormal.

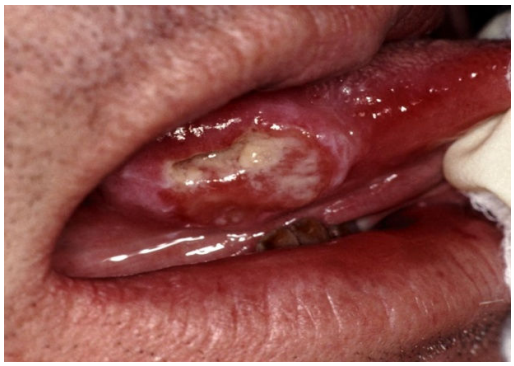
More than half of oral cancers have already spread to lymph nodes or other areas by the time they are found. No studies have shown that screening would decrease the risk of dying from this disease [25, 26].

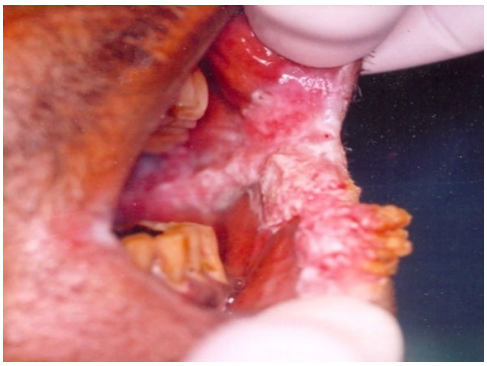
25. http://www.cancer.gov/cancertopics/pdq/screening/oral/Patient/page3
26. Harrison's Principal of Internal Medicine, Fauci, Braunwald, Kasper, Hauser, Longo,Jameson, Loscalzo, 17 th edition, Part 6, Chapter 78 , pp489-490

e. ORAL CAVITY CANCER - SIGNS AND SYMPTOMS

Manifestations of oral cavity cancer vary according to the stage and primary site of tumour. Carcinoma of oral cavity commonly present with following Signs and symptoms[27.]

1. A patch in the mouth which is rough and does not heal within two weeks
2. Small lump inside the inner lining of oral cavity
3. Erosions around lips and gums
4. Numbness, loss of feeling and sensation inside the oral cavity
5. Loosening of teeth and bad breathe
6. Decreased tongue mobility
7. Loss of taste
8. Altertions in speech
9. Loss of appetite
10. Severe weight loss
11. Difficulty in swallowing
12. Trismus
13. Lymphadenopathy in neck region





27. Harrison's Principal of Internal Medicine, Fauci, Braunwald, Kasper, Hauser, Longo,Jameson, Loscalzo, 17 th edition, Part 6, Chapter 86 , pp548-549

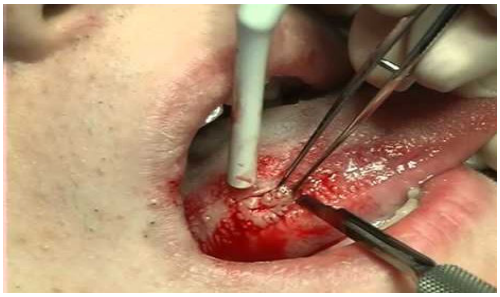
f. ORAL CAVITY CANCER – DIAGNOSIS

Diagnostic work up in oral cancer can be done as follows [28.]

1. **History and physical examination** – The initial evaluation includes a thorough head and neck examination by one or more physicians. The location and extent of the primary tumour and any clinically positive cervical lymph node documentation can be done through this.

2. **CT scan / MRI –** Almost all patients undergo contrast enhanced CT or MRI or both for further defining the extent of local regional disease. The scan should be obtained before biopsy so that changes of biopsy are not confused with tumour.

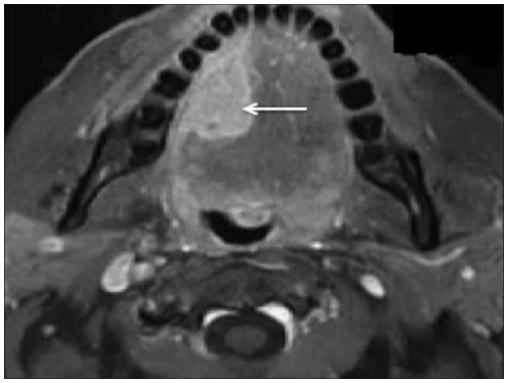
3. **Biopsy -** If any abnormalities are found during the examination, a small tissue sample, or biopsy, is usually taken. This procedure is completed under local anaesthesia.



4. **Fine-needle-aspiration biopsy (FNA):** Patients presenting with a metastatic node from an unknown primary site undergo FNA of the node.

28. Cancer Principal and Practice of oncology, Vincent T. Devita, Jr. , Samuel Hellman , Steven A. Rosenberg, 7th edition, Chapter 26.2,pp 665.

5. **Ortho Pan Tomogram (OPG)-** OPG or plain radiograph of mandible will be done if the lesion extends to lower GB sulcus or lower alveolus.



6. A **chest radiograph** is obtained to determine the presence of distant metastases.

7. Positron emission tomography **(PET)** may be useful to dertermine peripheral metastasis.

8. Complete blood counts, renal function tests including creatinine clearance & liver function tests may be needed.

g. STAGES OF ORAL CAVITY CANCER

The staging for the primary lesions (T) is given in the site specific section oral cavity. The American Joint Committee on Cancer (AJCC) (2002) neck staging (N) is common to all head and neck sites, except the nasopahrynx [29].

TNM STAGING SYSTEM

Method of staging oral carcinomas is referred as the TNM method. In this method T describes the tumour, N describes the lymph nodes, and M describes distant metastasis[30].

T – (Tumour) TX - Primary tumour cannot be assessed.

- **T0** - No evidence of primary tumour.
- **T1** - Tumour 2 cm or less in greatest dimension.
- **T2** - Tumour more than 2 cm but not more than 4 cm in greatest dimension.
- **T3** - Tumour more than 4 cm in greatest dimension.
- **T4** - Tumour invades adjacent structures e.g., through cortical bone, into deep [extrinsic] muscle of tongue etc.

N- (Lymph nodes) NX- Regional lymph nodes cannot be assessed.

- **N0** - No regional lymph node metastasis.
- **N1** - Metastasis in a single ipsilateral lymph node, 3 cm or less in greatest dimension.
- **N2** - Metastasis in a single ipsilateral lymph node, more than 3 cm but not more than 6 cm in greatest dimension and in multiple ipsilateral lymph nodes, none more than 6 cm in greatest dimension; in bilateral or contralateral lymph nodes, none more than 6 cm in greatest dimension.

29. American Joint Committee on Cancer. Lip and Oral Cavity. In: AJCC Cancer Staging Manual, 7th ed. New York, Springer: 2010; 29–35.
30. Cancer Principal and Practice of oncology, Vincent T. Devita, Jr. , Samuel Hellman , Steven A. Rosenberg, 7th edition, Chapter 26.2,pp 665.

N2a - Metastasis in single ipsilateral lymph node more than 3 cm but not more than 6 cm in greatest dimension.

N2b - Metastasis in multiple ipsilateral lymph nodes, none more than 6 cm in greatest dimension.

N2c - Metastasis in bilateral or contralateral lymph nodes, none more than 6 cm in greatest dimension.

N3 - Metastasis in a lymph node more than 6 cm in greatest dimension.

M (Metastasis) MX- Presence of distant metastasis cannot be assessed

M0 - No distant metastasis.

M1 - Distant metastasis.

The format for combining T and N stages into an overall stage is as follows –

Stage 0	**Tis**	**N0**	**M0**
Stage I	**T1**	**N0**	**M0**
Stage II	**T2**	**N0**	**M0**
Stage III	**T3**	**N0**	**M0 /**
	T1-T3	**N1**	**M0**

Satge IV can further devide into -

Stage IV A	**T4a**	**N0-N1**	**M0 /**
	T1-T4a	**N2**	**M0**
Stage IV B	**Any T**	**N3**	**M0 /**
	T4b	**Any N**	**M0**
Stage IV C	**Any T**	**Any N**	**M1**

h. ORAL CAVITY CANCER MANAGEMENT

Surgery and radiation therapy are the only curative treatments for carcinoma arising in the head and neck. Chemotherapy is useful in the adjunct setting; used alone, it is not curative[31].

Advantage of surgery with radiation therapy may include following –

1. A limited amount of tissue is exposed to treatment.
2. Treatment time is shorter.
3. The risk of immediate and late side effects can be avoided.

Advantage of irradiation may include the following –

1. The risk of a major postoperative complication is avoided.
2. No tissues are removed so that the probability of a functional or cosmetic defect may be reduced.
3. Elective irradiation of the lymph nodes can be included with little added morbidity, whereas the surgeon must observe the neck or proceed with an elective neck dissection (sometimes bilateral depending on the primary site).
4. The surgical salvage of irradiation failure is probably more likely than the salvage of a surgical failure.

31. Cancer Principal and Practice of oncology, Vincent T. Devita, Jr. , Samuel Hellman , Steven A. Rosenberg, 7th edition, Chapter 26.2,pp 665-728.

Treatment options for oral cavity cancer by stage–

(Practice Guidelines for Buccal mucosa cancer (SCC) in India according to Indian Council of Medical Research Guidelines)[32].

The type of treatment depends on the stage of cancer and tumour site.

Stage (TNM)	**Initial treatment planning**
T1 N0 M0	Surgery or Radiotherapy (RT) (EBRT+ISI Boost)
T2 N0 M0	Surgery (Primary + SOHND or RT(EBRT +ISI boost)
T3/ T4a N1/N2 M0	Surgery followed by CT-RT (or RT) or Radical CT + RT.
T3/ T4 N1/N2 M0 Borderline Resectable	Induction chemotherapy followed by surgery or CT + RT
T4B or N3(Fixed Node)	Chemotherapy /RT
Occult primary (SCC on biopsy)	Surgery or CT +RT
Recurrent disease < 6 months old	CT + RT if patient had undergone surgery earlier and surgery if CT + RT earlier
Recurrent disease > 6 months after initial treatment	Surgery if resectable / CT + RT if unresectable and RT Naive
Recurrent disease advanced	Palliative chemotherapy or best supportive care.

32. Indian Council of Medical Research Guidelines for Management of Buccal Mucosa CancerIndian Council of Medical Research, New Delhi – 110029, 2010

i ORAL CANCER TREATMENT -RADIOTHERAPY

Radiation therapy uses high-energy x-rays or particles to destroy cancer cells or slow their rate of growth. Radiation therapy can be prescribed before surgery, after surgery, or sometimes as the only treatment. Although radiation damages both cancer cells and normal cells, healthy cells are able to repair themselves and return to proper functioning. The total dose of radiation therapy prescribed by the radiation oncologist is broken down into small amounts (fractions) which are given on a daily basis, usually five days in a row with a two day break each week. It has been found that patients better tolerate the smaller daily doses while still receiving the maximum benefit of the treatments.

Radiation therapy can be used in following situations for oral cancers:

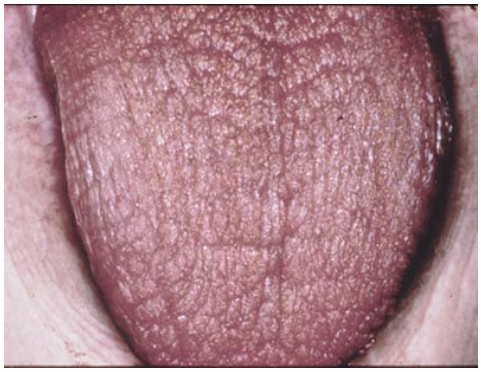
- It can be used as the main treatment for small cancers.
- Patients with larger cancers may need both surgery and radiation therapy or a combination of radiation therapy and chemotherapy or a targeted drug.
- After surgery, radiation therapy can be used, either alone or with chemotherapy, as an additional (adjuvant) treatment to try to kill any small deposits of cancer that may not have been removed during surgery. This is known as **adjuvant radiation therapy**.
- Radiation may be used (along with chemotherapy) to try to shrink some larger cancers before surgery. This is called **neo adjuvant therapy**. In some cases this makes it possible to use less radical surgery and remove less tissue.
- Radiation therapy can also be used to relieve symptoms of more advanced cancer, such as pain, bleeding, trouble swallowing, and problems caused by bone metastases.

j. ORAL CANCER TREATMENT – RADIOTHERAPY – SIDE EFFECTS

Xerostomia

Xerostomia, commonly called dry mouth, occurs when the salivary glands do not make enough saliva, or spit, to keep the mouth moist. Because saliva is needed for chewing, swallowing, tasting, and talking, these activities may be more difficult with a dry mouth[33].

Xerostomia is experienced by the patient receiving radiation therapy to the head and neck region. The parotid and the submandibular glands are the main contributors to salivary flow, contributing approximately 90% of salivary volume. The secretory unit of the salivary gland is constructed of acinar cells, myoepithelial cells; intercalated ducts, striated ducts and excretory ducts. The acini are responsible for secreting serous and mucous constituents of saliva. Severity of xerostomia dependant on radiation dosage and location, and volume of exposed salivary glands. Xerostomia can affect oral confort, fit of prostheses, speech and swallowing. Many of the enzymes found in patients with xerostomia contribute to the growth of caries- producing organisms, and the decrease in quantity and quality of saliva can be harmful to the dentures [34].



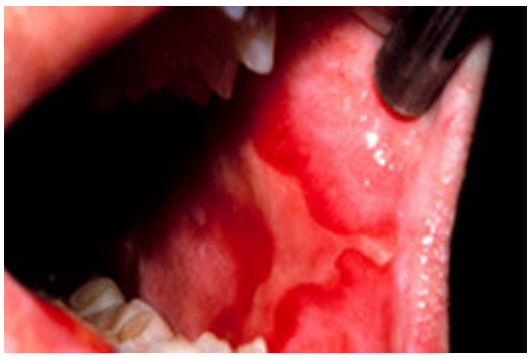
33. Xerostomia and hypofunction of the salivary glands in cancer therapy ,(2003), Siri Jensen , Anne Pedersen, Jesper Reibel, Birgitte Nauntofte , Supportive Care in Cancer , , Volume 11, Issue 4, pp 207-225 http://link.springer.com/article/10.1007%2Fs00520-002-0407-7
34. Cancer Principal and Practice of oncology, Vincent T. Devita, Jr. , Samuel Hellman , Steven A. Rosenberg, 7th edition, Chapter 26.2,pp2526-2527.

Excessive Salivation

The stringy saliva is the initial phase of dry mouth. The damaged saliva glands are still working but are not able to produce the lighter type of saliva, thus only the thicker type remains.

Stomatitis / Oral Mucositis

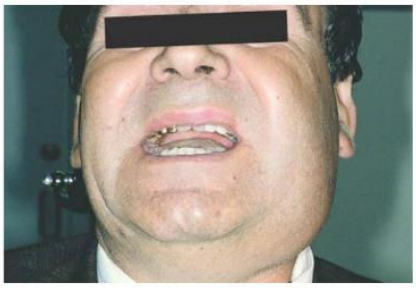
Oral mucositis is probably the most common, debilitating complication of radiotherapy. Radiation induced mucositis is initiated by direct injury to basal epithelial cells and cells in the underlying tissue. It can lead to several problems, including pain, nutritional problems as a result of inability to eat, and increased risk of infection due to open sores in the mucosa. It has a significant effect on the patient's quality of life and can be dose-limiting (i.e., requiring a reduction in subsequent radiotherapy doses) [35].



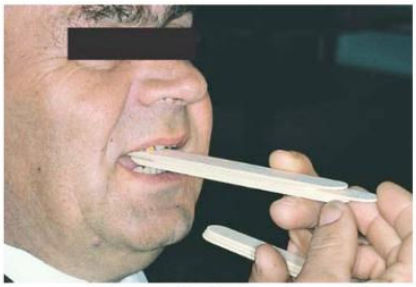
35. Radiation Induced Oral Mucositis,(2009)Satheesh Kumar PS, Anita Balan, Arun Sankar, and Tinky Bose, Indian J Palliat Care.; 15(2), pp 95–102. http://www.ncbi.nlm.nih.gov/pmc/articles/PMC2902123/

Trismus

The term 'trismus' has been used to describe any restriction to mouth opening, including restrictions caused by trauma, surgery or radiation. This limitation in the ability to open the mouth can have serious health implications [36].



Reduced aperture of the mouth due to trismus



Attempt to open mouth with physiotherapy, in a case of trismus

Problems caused by trismus are as follows -

- Eating issues - Limited mouth opening frequently results in reduced nutrition. The inability to open the mouth to receive more than a very small amount of food makes eating quite difficult. Patients with this condition may experience significant weight loss, and may have significant nutritional deficits.
- Limited mouth opening may also result in compromised airway clearance.

36. Predicting the severity and prognosis of trismus after intensity-modulated radiation therapy for oral cancer patients by magnetic resonance imaging ,(2014),Hsieh LC, Chen JW, Wang LY, Tsang YM, Shueng PW, Liao LJ, Lo WC, Lin YC, Tseng CF, Kuo YS, Jhuang JY, Tien HJ, Juan HF, Hsieh CH , PLoS One. ; 9(3):e92561
http://www.ncbi.nlm.nih.gov/pubmed/24658376

- Oral hygiene issues - Limited mouth opening can result in compromised oral hygiene. In cancer patients who have received radiation oral hygiene is of particular importance.
- Swallowing and speech issues - Many persons with limited mouth opening also present with difficulty in swallowing and speech. Speech is compromised when the mouth is unable to open sufficiently to create normal sounds. Swallowing is compromised when, due to muscle damage, surgery or radiation, the larynx is unable to be properly elevated, or when the timing of the elevation does not coincide with the passage of the bolus.
- Joint Immobilization - Although the most apparent signs of trismus involve the ability to open the mouth, it is important to realize that there are likely to be problems within the joint, as well. When a joint is immobilized, degenerative changes occur within the joint. These changes may mimic arthritic changes, and may be accompanied by inflammation and pain.

Weight Loss

Patients when treated with radiotherapy in head and neck cancer can lose weight because of dry mouth, poor appetite, taste changes, due to treatment and difficulty in swallowing due to soreness or swelling in throat. These effects may be temporary and will gradually go back to normal after a few months when the treatment ends.

k. ORAL CANCER - REHABILITATION

Rehabilitation is an essential phase of cancer care and should be considered from the time of diagnosis in a complete and comprehensive treatment plan. Post treatment functional limitations may result from any treatment for head and neck cancer. Combined modality treatments multiples the risk for functional deficit after treatment. Surgical resections often create large defects accompanied by dysfunction and disfigurement, and radiation therapy produces significant morbidity and unique tissue-management problems. Speech, swallowing, control of saliva, and mastication can all be adversely affected. This dispersion of potential deficits extends beyond the scope of any single professional. Thus patients benefit most from multidisciplinary rehabilitation efforts. If these cosmetic and functional impairments are not corrected or minimized, the patient may be unable to resume a normal working and social life [37]

The primary objective of rehabilitation is the restoration of appearance and function. How successfully this is accomplished, depends upon both the judgment and skill of the therapist, and the post-treatment anatomic, physiologic, and psychological makeup of the patient.

Rehabilitation of the head and neck cancer patient requires a team approach, which includes many specialists. In addition to the surgeon, the dental oncologist and the prosthetic doctor, there are many other individuals involved as part of the restorative team. As there may be conditions which alter eating habits, dietitians advise patients on proper nutrition. Occupational and physical therapists help retrain altered muscular systems, and the speech pathologist can help patients to adapt speech mechanisms to prosthetic appliances, and altered physiology. Dental hygienists provide prophylaxis and oral-health-care instruction.

37. Cancer Principal and Practice of oncology, Vincent T. Devita, Jr. , Samuel Hellman , Steven A. Rosenberg, 7th edition, Chapter 26.2,pp732- 743

B) AYURVEDIC LITERATURE REVIEW

B-I) ANUKTA VYADHI FROM AYURVEDIC PERSPECTIVE

Cancer is not directly mentioned in Ayurvedic text as one disease. Many diseases which are described in Ayurvedic text show similes with cancer. Etiology (Nidan) pathogenesis (samprapti), treatment (chikitsa) of cancer can be described by considering the basic principles of Ayurved**.**

विकारनामाकुशलो न जिह्रीयात् कदाचन।
न हि सर्वविकाराणां नामतोस्ति ध्रुवा स्थितिः।।४४।।
स एव कुपितो दोषः समुत्थानविशेषतः।
स्थानान्तरगतश्चैव जनयत्यामयान् बहून्।।४५।।
तस्माद्विकारप्रकृतीरधिष्ठानान्तराणि च।
समुत्थानविशेषांश्च बुद्ध्वा कर्म समाचरेत् ।।४६।।
यो ह्येतत्त्रितयं ज्ञात्वा कर्माण्यारभते भिषक् ।
ज्ञानपूर्वं यथान्यायं स कर्मसु न मुह्यति।।४७।।

च. सू. - १८/४४-४७

Acharya Charaka has clearly mentioned that a physician should not bother too much to understand name of the disease. On the contrary he has to understand thoroughly Vikaraprakruti - state of vitiated, dosha, dhatu, mala causing disease, Adhisthanantarani - site of vitiated dosha and samutthanavishesha - cause of vitiation of dosha [38].

38. Charak Samhita, Vol.1, Tripathi B (2003) ChaukambhaSubharatiPrakashan, Varanasi, Sutrasthan -18/44-47, pp378

त एव अपरिसंख्येया भिद्यमाना भवन्ति हि ।

रूजावर्णसमुत्थानस्थानसंस्थाननामभिः ।।

व्यवस्थाकरणं तेषां यथास्थूलेषु संग्रहः ।

तथा प्रकृतिसामान्यं विकारेषु उपदिश्यते ।।

च. सू. १८ । ४२ - ४३

सर्व एव निजा विकारा नान्यत्र वातपित्तकफेभ्यो निर्वर्तन्ते;

यथा हि - शकुनि सर्व दिवसमपि परिपतन् स्वां छायां नातिवर्तते,

तथा स्वधातुवैषम्यनिमित्तः सर्वे विकारा वातपित्तकफान्नतिवर्तन्ते;

वातपित्तश्लेष्मणां पुनः स्थानसंस्थानप्रकृतिविशेषनभिसमीक्ष्य

तदात्मकानपि च सर्वविकारांस्तानेवोपदिशन्ति बुध्दिमन्त ।

च. सू. १९ /५

A vitiated dosha can exhibit various diseases according to different causes of vitiation & different sites. One, who treats the disease by the knowledge of these 3 things, achieves success in the **t**reatment[39, 40]**.**

39. Charak Samhita, Vol.2, Tripathi B (2003) ChaukambhaSubharatiPrakashan, Varanasi, Sutrasthan -18/42-43, pp 377.

40. Charak Samhita, Vol.2, Tripathi B (2003) ChaukambhaSubharatiPrakashan, Varanasi, Sutrasthan -19, pp385.

B-II) DIAGNOSIS OF CANCER FROM AYURVEDIC PERSPECTIVE

Cancer is not mentioned in Ayurvedic Samhitas as a single disease. Varius diseases mentioned in Ayurvedic texts like Dushta Vrana, Dushta Granthi, Dushta Arbuda, Dushta Vranashotha, Dushta Nadivrana, Dushta Visarpa show simili with cancer. Malignant tumours are divided as solid tumours and non-solid tumours in modern literature. Non solid tumours which mainly include Leukemia, Hodgkin's diseases and Non-Hodgkin's disease resemble

1. Rasa-Rakta Dhatugata Jwara- (Fever pertaining to Rasadhatu & Raktadhatu)
2. Raktapitta - (Bleeding Disorders)
3. Pandu - (Anemia)
4. Raktaja Krumi - (Worms's causing skin disorders)

Solid malignant tumoursare similar to diseases like

1. Dushta Shotha - (Malignant Oedema)
2. Dushta Vrana - (Malignant Wounds / Ulcers)
3. Dushta Granthi - (Malignant Nodes)
4. Dushta Arbuda - (Malignant Tumours)
5. Dushta Visarpa - (Malignant Spreading Cellulitis)
6. Dushta Nadivrana - (Malignant Fistula / Sinus)
7. Dushta Mansapradoshaja Vikara - (Malignant Diseases caused due to vitiation of Mansa dhatu)

ग्रंथादिभ्यो विलक्षणः पृथुर्ग्रथितः समो विषमो वा त्वङ्मांसस्थायी
दोषसंघातः शरीरैकदेशोत्थितः शोफ इत्युच्यते ।

सु.सू. १७-३

All these diseases are various forms of Vranashotha as explained by Acharya Sushruta[41].

41. Sushrut Samhita with commentary Ayurveda Tatvasandipika by Kaviraj Ambikadatta Shastri, Chaukhamba Sanskitti Sansthan, Varanasi (2005), sutrsthan, 17/3,pp70

रोगाश्चोत्सेधसामान्यदधिमांसार्बुदादयः ।

विशिष्टा नामरुपाभ्यां निर्देश्याः शोथसङ्ग्रहे ।।

च. सू. १८/३३

It is clearly mentioned by Charakacharya in trishothiya Adhyaya that Shotha developed at various sites, forms various diseases like adhimansa, arbud, shleepad etc[42].

42. Charak Samhita, Vol.2, Tripathi B (2003) ChaukambhaSubharatiPrakashan, Varanasi, Sutrasthan -18/33, pp 375

B-III) STAGES OF CANCER FROM AYURVEDIC PERSPECTIVE

Basically Granthi, Arbuda, Vidradhi, Visarpa, Nadivrana and Mansapradoshaja Vikara are various forms of Shotha (oedema), because Utsedha (growth / swelling) is the common and predominant symptom in them.

- **Ayurvedic treatment differs in various avastha (stages) of the disease.**
- **Stages of cancer are described in following manner in Ayurvedic Samhitas –**

a) According to progression of Shotha[43]

1. Aama Avastha
2. Pachyamana Avastha
3. Pakwa Avastha (i.e. Acutely Tender Stage) of Shotha (Oedema)

आमं विपच्यमानं च सम्यक् पाकघ्न यो भिषक् ।
जानीयात् स भवेद्वैद्यः शेषास्तस्करवृत्तयः ।।

सु. सू. १७/११

The Aama (unripped stage), Pachyamana (semi -ripped stage) and Pakwa avastha (stage of inflammation), which are described in Shotha (Swelling), are also observed in above-mentioned diseases.

b) According to gati and swarupa of Dushta Dhatu causing disease

1. Dhatugata Awastha[44]
2. Dhatupaka Awastha[45]

मांसदोषेण जानीयात् अर्बुदं मांससंभवम् ।
शीर्यन्ते यस्य मांसानि यत्र सर्वाः च वेदना ।।
विद्यात् तं मांसपाकं तु सर्वदोषकृतं भिषक् ।

सु. नि. १४ । १५

43. Sushrut Samhita with commentary Ayurveda Tatvasandipika by Kaviraj Ambikadatta Shastri, Chaukhamba Sanskitti Sansthan, Varanasi (2005), Sutrasthan 17/11pp 72.
44. Acharya Narendranath Shastri (2002), Madhav Nidan of Acharya Madhav with Madhukoshcommentary,edn. 3rd , Motilal Banarsidas, Chapter 2/66- 73,Pg. 151 – 159
45. Sushrut Samhita with commentary Ayurveda Tatvasandipika by Kaviraj Ambikadatta Shastri, Chaukhamba Sanskitti Sansthan, Varanasi (2005), Nidansthan 14/15pp 290

c) According to Sadhya - Asadhya avastha of the disease. (curable & non-curable stage)

1. Sadhya Vyadhi
2. Asadhya Vyadhi

सुखसाध्यं मतं साध्यं कृच्छ्रसाध्यमथापिच च ।
व्दिविधं चाप्यसाध्यं स्याद् याप्यं यच्चानुपक्रमम् ।।
साध्यानां त्रिविधश्चाल्पमध्यमोत्कृष्टतां प्रति ।
विकल्पो न त्वसाध्यानां नियतानां विकल्पना ।।

च. सू. १०/७

In Sushrut samhita along with Charak sutrasthan, adhyaya tenth, mahachatushapad criteria of sadhya – asadhya vyadhis are mentioned. As in many patients, cancer is diagnosed in late stage i.e. in Dhatupaka avastha (Stage of loss of tissues) and Dhatugata avastha; these are the signs of Asadhyatwa (Non-curable stage). At this stage also, physician should try his best to control further growth, to give relief to the patients suffering in miserable conditions[46].

46. Charak Samhita, Vol.2, Tripathi B (2003) ChaukambhaSubharatiPrakashan, Varanasi, Sutrasthan -10/07 , pp-218

B-IV) MUKHAGATA ROGA

Shalakya Tantra is one of the eight branches of Ayurveda which particularly deals with the diseases occurring in head, neck, eyes, ear and oral cavity. Mukhagata Roga is described in ancient Ayurvedic texts like Sushrut Samhita, Charak Samhita, Astanga Sangraha, Yoga Ratnakar, Madhav Nidan, etc.

Mukha– Mukha (Oral cavity) consists of 7 different parts –

ओष्ठौ च दंतमूलानि दन्ता जिव्हा च तालु च ।
गलो गलादि सकलं सप्तांगं मुखमुच्यते ।।

यो.र.भा. २ पा.४८२

तत्रायतनानि-ओष्ठौ, दन्तमूलानि, दंताः जिव्हा, तालु कंठः, सर्वाणि चेति ।

सु.नि. १६-३

1. Oshtha (Lips)
2. Dantmoola (Gums)
3. Danta (Teeth)
4. Jivha (Tongue)
5. Talu (Palate)
6. Gala (Throat)
7. Mukhadi (All of the above mentioned parts as a whole)[47,48]

47. Yogratnakar with Vidyodini Hindi Commentary of Shri Laxmipati Shastri Chaukhamba Prakashan (2012) ,pp 482.
48. Sushrut Samhita with commentary Ayurveda Tatvasandipika by Kaviraj Ambikadatta Shastri, Chaukhamba Sanskitti Sansthan, Varanasi (2005), Nidansthan 16-3 pp294.

Aetiological factors (Nidan) of Mukhagata Roga –

Following etiological factors are taken into consideration while describing Mughgat Roga in ancient literature -

मत्स्यमहिषवाराहपिशितामलकमूलक्रम ।
माषसूपदधिक्षीरसुक्तेक्षुरसफाणितम् ।
अवाक् शय्या च भजतो व्दिषतो दंतधावनम् ।
धूतच्छर्दनगंडूषानुचितं च सिराव्यधम् ।

वा.उ.२१-१, २

Dietary factors like fish, buffalo meat, pork which are heavy to digest; ash gourd, raddish, soup of black gram, curds, milk and milk products, vinegar, sugarcane juice and jaggery syrup consumed in excessive proportion can cause diseases of Oral cavity. Also, consumption of excessive hot and spicy food items can lead to diseases of oral cavity[49].

Sleeping in prone position (Avakchhaya), improper brushing habits, not following procedures like Dhoompana (inhalaling medicated fumes), Vaman (emesis), Gandush (gargling with medicated decoctions) and Raktamokshan (blood letting) whenever required can also lead to diseases of oral cavity.

Pathogenesis (Samprapti) –

Pathogenesis of oral diseases is described as follows -

क्रुध्दाः श्लेष्मोल्बणा दोषाः कुर्वंत्यंतर्मुखे गदान् ।

वा.उ.२१-३

Improper dietary habit and improper behavioral habit leads to vitiation of tridosha to develop oral cavity diseases[50].

49. Ashtanghridya, Vagbhat with Sarvasunder commentary of Arundatta and Ayurved Rasayan commentary of Hemadry, Chaukhamba Surbharati Prakashan, Varanasi (2010) , Uttarsthan 21-1,2 , pp 845
50. Ashtanghridya, Vagbhat with Sarvasunder commentary of Arundatta and Ayurved Rasayan commentary of Hemadry, Chaukhamba Surbharati Prakashan, Varanasi (2010) , Uttarsthan 21-3, pp 845

Types of Mukha Roga –

मुखरोगाः पंचषष्टिर्भवन्ति सप्तस्वायतनेषु ।

तत्राष्टावोष्ठयोः, पंचदश दंतमूलेषु, अष्टौ दंतेषु, पंच जिव्हायां,

नव तालुनि सप्तदश कंठे, त्रयः सर्वेष्वायतनेषु ।

सु.नि. १६-३

There are various differences of opinion regarding the Samkya Samprapti or number of types of Mukha Roga[51].

Table 1 – showing types of Mukhgat rog described in the ancient texts

Site	Sushrut Samhita	Astanga Hridaya	Charak Samhita	Yoga Ratnakar	Madhav Nidan
Oshtha	08	11	-	08	08
Dantmoola	15	13	-	16	15
Dant	08	10	-	08	08
Jivha	05	06	-	05	05
Talu	09	08	-	09	09
Kanta	17	18	-	18	17
Sarvamukha	03	08	-	03	03
Ganda	-	01	-	-	-
Total	**65**	**75**	**64**	**67**	**65**

51. Sushrut Samhita with commentary Ayurveda Tatvasandipika by Kaviraj Ambikadatta Shastri, Chaukhamba Sanskitti Sansthan, Varanasi (2005), Nidansthan 16-3 pp294.

Symptoms of mukhagata rog (Samanya Lakshanas)-

The general symptoms of Mukha roga have been mentioned in the Vedana Adhaya of Kashyap Samhita in context with pediatric group. These are as follows –

लालास्त्रवणमत्यर्थं स्तनव्देषारतिव्यथाः ।

पीतमुद्गिरति क्षीरं नासाश्वासी मुखामये ।।

का.सं.सू. २५-८

These symptoms can be co-related to other age group also. These symptoms can be in the form of [52] -

1. Excessive salivation
2. Anorexia
3. Regurgitation
4. Tachypnoea
5. Loss of appetite
6. Generalised weakness.

52. Kashyap Samhita by Vruddha Jivak, Revised by Vatsya with Sanskrit introduction by Pandit Hemraj Sharma with vidyodini hindi commentary, Chaukhamba Sanskrit Samsthan,(2010), Sutrasthan , 25-8, pp 33.

Mukhagata Roga which are correlated with Oral cavity Cancer

Amongst the various diseases of oral cavities described by our Ayurvedic scholars, few of these which are relevant for the present study can be correlated with malignant manifestations. These are as follows –

Kaphaj Jivha Kantaka - This disease is mentioned under Jivha gata roga and can be correlated with chronic glossitis or Leucoplakia which is pre malignant condition of tongue cancer.

कफेन गुर्वी बहला चिता च मांसोग्दमैः शाल्मलिकंटकाभैः ।

सु.नि. १६-३७

Signs and Symptoms -In this condition, vitiated Kapha dosha causes jihva as heavy, thick, wide and is scattered with thorny buds resembling Shalmali Kantak and is associated with pain, discomfort, itching sensation and sticky salivation[53].

Treatment – The treatment described in this condition is in the form of scrapping, gargling with white seasame oil mixed with rock salt, bloodletting, local application of powder of long pepper and honey and few dietary recommendations like vegetables in the form of snake gourd, Nimba, bringal; kshara and lentil soups[54].

कंटकेषु कफोत्थेषु लिखितेष्वसृजः क्षये ।
पिप्पल्यादिर्मधुयुतः कार्यस्तु प्रतिसारणे ।।
गृह्णीयात कवलाश्चापि गौरसर्षपसैंधवैः ।
पटोलनिंबवार्ताकुक्षारयूषौश्च भोजयेत ।।

सु.चि. २२-४६, ४७

53. Sushrut Samhita with commentary Ayurveda Tatvasandipika by Kaviraj Ambikadatta Shastri, Chaukhamba Sanskitti Sansthan, Varanasi (2005), Nidansthan – 16-37 , pp 298
54. Sushrut Samhita with commentary Ayurveda Tatvasandipika by Kaviraj Ambikadatta Shastri, Chaukhamba Sanskitti Sansthan, Varanasi (2005), Chikitsasthan 22-46,47 pp 100

- Lekhana (Scrapping) or Gharshana with the leaves of Gojihva or Shephalika to remove the impure blood.
- Rakta Mokshan (Blood letting)
- Pratisaran – Local application over tongue lesions with Trikatu, Sarshapa + Saindhav + Madhu.
- Kavala and Gandusha– Gargling with Shweta Sarshapa + Saindhav.
- Yusha sevan – Yusha prepared with Patola, Nimba twak, Varthaka and Yavakshara.

Galarbuda - This disease is mentioned under Gala gata Roga and can be correlated with tumour in throat region in the vicinity of tongue.

जिव्हावसाने कंठादावपाकं श्वयथुं मलाः ।
जनयंति स्थिरं रक्तं नीरुजं तद्गलार्बुदम् ।।

वा.उ. २१-५२, ५३

Signs and Symptoms -In this condition, vitiated Vatadi doshas produces a hard, immobile, painless, non-suppurative, reddish tumour in the throat in the vicinity of tongue[55].

According to Acharya Vagbhatt, this is asadhya (incurable) type of disease.

Treatment – The treatment described in this condition is in the form of excision, gargling, nasal drops, local application and few dietary recommendations.

- Chedana (Excision) to be done if the growth is small
- Pratisaran – Local application over the lesion with Sarja kshara + Shunthi + Madhu.
- Gandusha– Gargling with Guduchi + Nimba Kashaya + Honey + Tila Tailam.
- Nasya and Abhyanga.
- Yavanna sevan.

55. Ashtanghridya, Vagbhat with Sarvasunder commentary of Arundatta and Ayurved Rasayan commentary of Hemadry, Chaukhamba Surbharati Prakashan, Varanasi (2010) , Uttarsthan, 21-52-53, pp 849

Kapharbuda = This disease is mentioned under Mukhadi Roga and can be correlated with Cancer of Buccal Mucosa.

अंतःकपोलमाश्रित्य श्यावपांडुः कफोर्बुदम् ।
कुर्यात्तत्पाटितं छिन्नं मृदितं च विवर्धते ।।

वा.उ. २१-६२, ६३

Signs and Symptoms -In this condition, vitiated Kapha dosha produces a blackish-white color tumour in the oral cavity specifically in the internal surface of Kapola i.e. cheeks. By compression, incision and excision the disease recurs and aggravates.[56]

According to Acharya Vaghbhatt, this is asadhya (incurable) type of disease.

Treatment – The treatment described in this condition is in form of excision, gargling, nasal drops, local application and few dietary recommendations.

नवेऽर्बुदे त्वसंवृध्दे छेदिते प्रतिसारणम् ।
स्वर्जिकानागरक्षौद्रैः क्वाथो गंडूष इष्यते ।।
गुडूचीनिंबकल्कोत्थो मधुतैलसमन्वितः ।
यवान्नभुक् तीक्ष्णतैलनस्याभ्यंगांस्तथाचरेत् ।।

वा.उ. २२-७७ ते ७९

- Chedana (excision) to be done if the growth is small
- Pratisaran – Local application over the lesion with Sarja kshara + Shunthi + Madhu.

56. Ashtanghridya, Vagbhat with Sarvasunder commentary of Arundatta and Ayurved Rasayan commentary of Hemadry, Chaukhamba Surbharati Prakashan, Varanasi (2010) , Uttarsthan, 21-62,63, pp 850

- Gandusha– Gargling with Guduchi + Nimba Kashaya + Honey + Tila Tailam.
- Teekshna Nasya, Dhoomapana and Abhyanga.
- Yavanna sevan.
- Kaphahara Picchu at the site of vrana (lesion or ulcer)[57].

Sarvasara Mukha Roga - They occur by spreading completely in the Mukha so named as Sarvasara mukha roga[58]. They are also called as Mukha Roga. In this the main sign is inflammation or ulceration in the oral cavity. This sign is mainly seen in all types of oral cavity cancers and also can be pre-malignant and malignant stage.

Dushta Arbuda as Mansapradoshaja Vyadhi and it's management

शृणु मांसप्रकोपजान् ।
अधिमांसार्बृदं कीलं गलाशालूकशुण्डिका ।।
पूतिमांसालजीगण्ड गण्डमालोपजिव्हिकाः ।
विद्यान्मांसाश्रयात् ।।

च. सू. २८/१३-१४

मांसजानान्तु संशुध्दिः शस्त्रज्ञाराग्निकर्म्म च ।

च. सू. २८/२६

Dushta arbud is mentioned as one of mansapradoshja vyadhi in Charak Samhita. The line of treatment in this condition is shastrakrma, agnikarma and ksharakarma[59, 60].

57. Ashtanghridya, Vagbhat with Sarvasunder commentary of Arundatta and Ayurved Rasayan commentary of Hemadry, Chaukhamba Surbharati Prakashan, Varanasi (2010) , Uttarsthan, 22-77-79, pp 855-856
58. Ashtanghridya, Vagbhat with Sarvasunder commentary of Arundatta and Ayurved Rasayan commentary of Hemadry, Chaukhamba Surbharati Prakashan, Varanasi (2010) , Uttarsthan, 21-58,59, pp 850
59. Charak Samhita, Vol.1, Tripathi B (2003) Chaukambha Subharati Prakashan, Varanasi, Sutrasthan 28 , pp 548
60. Charak Samhita, Vol.1, Tripathi B (2003) Chaukambha Subharati Prakashan, Varanasi ,Sutrasthan 28 ,pp 550

Agni karma, Kshara Karma and Shastra Karma in treatment of Cancer

विपाट्य चोद्धृत्य भिषक् सकोशं
शस्त्रेण दग्ध्वा व्रणवच्चिकित्सेत् ।
अदग्ध ईषत् परिशेषितश्च प्रयाति भूयोऽपि शनैर्विवृध्दिम् ।।
तस्मादशेषः कुशलैः समन्ताच्छेद्यो भवेव्दीक्ष्य शरीरदेशान् ।

च.चि. १२-८२, ८३

क्षाराग्निशस्त्राण्यसकृव्दिदध्यात् प्राणानहिंसन् भिषगप्रमत्तः ।

सु.चि. १६ – ३८

Kshara Karma, Agani Karma & Shastra Karma are the choice of treatment in Arbuda & Granthi. These treatment need to be carried out without injuring / causing harm to the vital organ involved.

According to Ayurveda generally complete excision of granthi / arbuda (tumour) is recommended. After excising the tumour growth, Agnikarma (type of cauterization) is to be carried out. This is helpful in complete removal of tumour. Growth which is not removed completely, recurrence may take place.

Therefore it is advisable to remove the tumour in accordance to the organ involved.

As per the modern terminology, surgery can be correlated to Shastrakarma, Chemotherapy to Kshara Karma & Radiation therapy to Agni Karma [61, 62].

61. Charak Samhita, Vol.2, Tripathi B (2003) ChaukambhaSubharatiPrakashan, Varanasi, Chikittsasthan 12/82-83
62. Sushrut Samhita with commentary Ayurveda Tatvasandipika by Kaviraj Ambikadatta Shastri, Chaukhamba Sanskitti Sansthan, Varanasi (2005), Chikitsasthan 16-38, pp 78

B-V) PATHOGENESIS OF SIDE-EFFECTS OF RADIOTHERAPY IN ORAL CAVITY CANCERS AS PER AYURVEDIC PERSPECTIVE

I) Talushosha (Xerostomia)

शोषोऽत्यर्थ दीर्यते चापि तालुः श्वासो वातात्तालुशोषः सपित्तात् ।

सु.नि. १६-४५

Talushosh arises due to vitiation of Vata and Pitta. In this condition, there is dryness in the talu region, sometimes it might bifurcate (as seen in cleft palate) and is associatiated with shwas (Dyspnoea) [63].

स्नेहस्वेदौ तालुशोषे विधिश्चानिलनाशनः ।

सु.चि. २२/५८

Treatment – The treatment described in this condition is in the form of gargling, nasal drops, local application and few dietary recommendations[64].

- Vata pitta har chikitsa.
- Intake of ghee after meals.
- Amla dravya or sneha dravya gandush.
- Kshirisarpi nasya (Ghee + Milk).

II) Mukhapaka – (Stomatitis)

There are 5 types of Mukha Paka –

i) Vataj Mukha Paka – This condition can be correlated with Stomatitis.

Signs and Symptoms -In this, vitiated Vata dosha causes a single or multiple ulcers in the oral mucosa with acute inflammatory changes. The disease is progressive in nature, very painful, mucosa becomes dry and rough. The associated symptoms are inflammed lips, tongue and palate, difficulty in opening the mouth and sensitivity to cold items, etc.

63. Sushrut Samhita with commentary Ayurveda Tatvasandipika by Kaviraj Ambikadatta Shastri, Chaukhamba Sanskitti Sansthan, Varanasi (2005), Nidansthan, 16/45,pp299
64. Sushrut Samhita with commentary Ayurveda Tatvasandipika by Kaviraj Ambikadatta Shastri, Chaukhamba Sanskitti Sansthan, Varanasi (2005), Chikitsasthan, 22/58,pp101

करोति वदनस्यांतर्वणान्सर्व्रसरो ऽ निलः ।

संचारिणो ऽ रुणान् रुक्षानोष्ठौ ताम्रौ चलत्वचौ ।।

जिव्हा शीतासहा गुर्वी स्फुटिता कंटकाचिता ।

विवृणोति च कृच्छ्रेण मुखपाको मुखस्य च ।।

वा.उ. २१-५८, ५९

Treatment –

- Nidan Parivarjan (avoiding causative factors)
- Snehan, swedana (oleation and Fomentation)
- Shodhana Karma (vaman, Virechan, Nasya, Rakta mokshan)
- Kavalgraha / Gandush with Triphala Kashaya, Rasnadi Kashaya, Dashmoola Kashaya, Vatahara Taila or Ghrita.
- Snehika Dhoomapana (medicated smoking) with Shalaphadi drugs, sarjarasa, khadiradi vati, etc.
- Snehana Nasya with Vatahara Taila or Ghrita.
- Lekhana and Pratisaran[65].

ii) Pittaj Mukha Paka – This condition can be correlated with Acute Stomatitis.

Signs and Symptoms -In this, vitiated pitta dosha causes inflammation and ulceration of oral mucosa. Smaller reddish yellow papules develop throughout the mouth and causes severe burning, altered taste, difficulty in mastication and deglutition.

तिक्तवक्त्रता । क्षारोक्षितक्षतसमा व्रणाः ।

Treatment –

- Nidan Parivarjan (avoiding causative factors)
- Snehan, swedana (oleation and fomentation)
- Shodhana Karma (Vaman, Virechan, Nasya, Rakta mokshan)

65. Ashtanghridya, Vagbhat with Sarvasunder commentary of Arundatta and Ayurved Rasayan commentary of Hemadry, Chaukhamba Surbharati Prakashan, Varanasi (2010) , Uttarsthan, 21-58,59, pp850

- Kavalgraha / Gandush with Panch valkal Kashaya, Pancha Tikta Kashaya, Yashtimadhu Kashaya, milk, sugarcane juice and ghee.
- Shaman Dhoomapana (Medicated Smoking)
- Nasya with Sheeta virya, Pittahara Taila or Ghrita or Kashaya.
- Lekhana and Pratisaran[66].

iii) Kaphaj Mukha Paka – This condition can be correlated with Sub acute or chronic Stomatitis.

Signs and Symptoms -In this, vitiated Kapha dosha causes inflammation and ulceration of oral mucosa. The mouth becomes sweet and sticky with itching sensation and negligible pain. Small cysts or tumours develop and become more severe by compression and excision.

कफजे मधुरास्यत्वं कंडूमत्पिच्छिला व्रणा : ।

वा.उ. २१-६२

Treatment –

- Nidan Parivarjan (avoiding causative factors)
- Snehan, swedana (oleation and fomentation)
- Shodhana Karma (Vaman, Virechan, Nasya, Rakta mokshan)
- Kavalgraha / Gandush with Khadiradi Taila, Haridradi Taila, Trikatu Kashaya.
- Virechanika Dhoomapana (Medicated Smoking)
- Lekhana / Bhedhan / Chedan and Pratisaran[67].

iv) Sannipataja Mukha Paka – All the symptoms of Tridosha and Rakta dosha are present in this disease.

Treatment – Tridosha hara Chikitsa should be given. Pratisaran with Haridra + Kasis + Rasanjan + Mocha rasa + Madhu

66. Ashtanghridya, Vagbhat with Sarvasunder commentary of Arundatta and Ayurved Rasayan commentary of Hemadry, Chaukhamba Surbharati Prakashan, Varanasi (2010) , Uttarsthan, 21-61, pp850
67. Ashtanghridya, Vagbhat with Sarvasunder commentary of Arundatta and Ayurved Rasayan commentary of Hemadry, Chaukhamba Surbharati Prakashan, Varanasi (2010) , Uttarsthan, 21-62, pp 850

v) Raktaj Mukha Paka – All the signs and symptoms and treatment are like Pittaja Mukha Paka.[68]

रक्तेन पित्तोदित एक एव कैश्चित् प्रदिष्टो मुखपाकसंज्ञः ।।

सु.नि. १६-६४ ते ६६

III) Talupak (Stomatitis)

पित्तं कुर्यात् पाकमत्यर्थघोरं तालुन्येनं तालुपाकं वदन्ति ।

सु.नि. १६-४५

Vitiated Pitta causes severe dreadful ulceration in talu region. Sometime the ulcer may be painful and pus discharging [69].

Treatment -

तालुपाके तु कर्तव्यं विधानं पित्तनाशनम् ।
सु.चि. २२-५८

Treatment – The treatment described in this condition is in the form of gargling, nasal drops, local application and few dietary recommendations[70].

- Pitta- visarp har chikitsa.
- Kaval with shita, Kashaya and Madhur dravyas like Kakolyadi Gana.

68. Sushrut Samhita with commentary Ayurveda Tatvasandipika by Kaviraj Ambikadatta Shastri, Chaukhamba Sanskitti Sansthan, Varanasi (2005), Nidansthan 16-64-66 , pp302
69. Sushrut Samhita with commentary Ayurveda Tatvasandipika by Kaviraj Ambikadatta Shastri, Chaukhamba Sanskitti Sansthan, Varanasi (2005), Nidansthan, 16/45,pp299
70. Sushrut Samhita with commentary Ayurveda Tatvasandipika by Kaviraj Ambikadatta Shastri, Chaukhamba Sanskitti Sansthan, Varanasi (2005), Chikitsasthan, 22/58,pp101

IV) Hanugraha (Trismus)

जिव्हातिलेखनात् शुष्कभक्षणादभिघाततः ।

कुपितो हनुमूलस्थः स्त्रंसयित्वाऽनिलोहनू ।।

करोति विवृतास्यत्वमथवा संवृत्तास्यताम् ।

हनुस्त्रंसः स तेन स्यात्कृच्छ्राच्चर्वणभाषणम् ।।

वा.नि. १५-२९, ३०

In this condition there is difficulty in opening of mouth and disability in movement of jaw[71].

हनुस्त्रंसे हनू स्निग्धस्विनौ स्वस्थानमानयेत् ।

उन्नामयेच्च कुशलश्चिबुकं विघृते मुखे ।

नामयेत्संवृते शोषमेकायामवदाचरेत् ।।

वा.चि. २१-४०, ४१

Snigdha Chikitsa is mentioned for Hanugraha in chikitsasthan[72].

71. Ashtanghridya, Vagbhat with Sarvasunder commentary of Arundatta and Ayurved Rasayan commentary of Hemadry, Chaukhamba Surbharati Prakashan, Varanasi (2010) , Nidansthan15/29, pp533

72. Ashtanghridya, Vagbhat with Sarvasunder commentary of Arundatta and Ayurved Rasayan commentary of Hemadry, Chaukhamba Surbharati Prakashan, Varanasi (2010) , chikitsasthan, 21/40-41, pp 725

V) Aruchi and Hrullas (Loss of taste and Nausea)

अश्रध्दा चारुचिश्चास्यवैरस्यमरसज्ञता ।

ह्रल्लासो गौरवं तन्द्रा सङ्गमर्दो ज्वरस्तमः ।।

च. सू. २८/९

Aruchi and Hrullas are caused due to Rasavaha srotodushti. In this condition there is loss of taste sensation and nausea[73].

Treatment -

रजसजानां विकाराणां सर्वम् लङ्घनमौषधम् ।

च. सू. २८/२५

Treatment – The treatment described in this condition is Langhan[74].

73. Charak Samhita, Vol.1, Tripathi B (2003) Chaukambha Subharati Prakashan, Varanasi ,Charak Sutrasthan 28/9 pp 548

74. Charak Samhita, Vol.1, Tripathi B (2003) Chaukambha Subharati Prakashan, Varanasi ,Charak Sutrastrhan28/25, pp 550

C) DRUG REVIEW

Combination of Ayurvedic drugs which are selected for this study on the basis of following review -

त्वग्निवर्णोष्यतेऽत्यर्थ न च स्फोटसमुद्भवः ।
वा.सू. ३०-४७

As mentioned in Vagbhatt the signs of ati daghdha can be correlated with side effects caused due to radiotherapy. These can be charring of the skin associated with blackish discoloration along with Jwara, Daha, Trushna and Murchha[75].

मधूच्छिष्टं समधुकं रोध्रं सर्जरसं तथा ।
मंजिष्ठा चंदन मूर्वा पिष्ट्वा सर्पिर्विपाचयेत ।।
सर्वेषां अग्निदग्धानां एतद्रोपणमुत्तमम् ।
स्नेहदग्धे क्रियां रुक्षां विशेषेणावचारयेत् ।।
सु.सू. १२-२७ ते २९

Treatment –

Ropan chikitsa is the best line of treatment in such conditions. For This Madhur, Kashay, Tikta rasatmak, Shit Veeryatmaka, Snigdha Gunatmak dravyas are used which pacifies Pitta and Rakta and ultimately cause Pitta shaman, Daha shaman and Raktta prasadan. Selection of drugs in our study has been done keeping in mind this chikitsa sutra [76].

75. Ashtanghridya, Vagbhat with Sarvasunder commentary of Arundatta and Ayurved Rasayan commentary of Hemadry, Chaukhamba Surbharati Prakashan, Varanasi (2010) , Sutrasthan30/47, pp 359
76. Sushrut Samhita with commentary Ayurveda Tatvasandipika by Kaviraj Ambikadatta Shastri, Chaukhamba Sanskitti Sansthan, Varanasi (2005), Sutrasthan, 12/27-29,pp42

I) Mouktikayukta Kamdudha[77]

मौक्तिकस्य प्रवालस्य मुक्ताशुक्ति भवस्य च ।
वराटिकायाः शंखस्य भस्मानि गैरिकं तथा ।।
गुडुचिकाभ्दवं सत्वं समभागानि कारयेत् ।
अजानिकासिताभ्याञ्च गृहीयाद्राक्तिकाव्दयम् ।।
जीर्णज्वरभ्रमोन्मादपित्तरोगेषु शस्यते ।
अम्लपित्ते सोमरोगे योज्यः कामदुधारसः ।
र.यो.सा. २६०

Table 2– Details of contents of Mouktikayukta Kamdudha

Sr. No	Dravya Name	English Name	Rasa (Taste)	Veerya (Potency)	Vipaka (Post-digestive test)	Doshghnata (Action on doshas)	Karya (Action)
1	Praval	Coral	Madhur(Sweet), Amla (sour), Kashay (Astringent)	Sheeta (Cold)	Madhur (Sweet)	Pittashamak, Kaphaghna	Rasayan , Jwaraghna, Raktapittahar, Vishbadhahar
2	Mouktika	Pearl	Madhur (Sweet), Kashay (Astringent)	Sheeta (Cold)	Madhur (Sweet)	Tridoshshamak	Daha shamak , Balya
3	Shankha	Conch shell	Tikta (Bitter)	Ushana (Hot)	Madhur (Sweet)	Kaph pitta shamak	Chhradighna
4	Shauktika	Peral Shell	Katu (Pungent)	Sheeta (Cold)	Madhur (Sweet)	Vat Pittaghna	Arochakahar, Chhardighna
5	Kapardika	Cowrie shell	Katu (Pungent)	Sheetoshna	Madhur (Sweet)	Vat Kaphaghna	
6	Guduchi	Tinospora cordifolia	Tikta, Kashay	Ushna	Madhura	Tridoshshamak	Deepan, Pachak, Pittasarak, Balya, Raktashodhak, Jwaraghna, Dahaprashaman
7	Gairik	Red Lumber Stone	Madhur Kashay	Sheet	Madhur	Pittashamak	Pittashamak , Vishhara

77. Sharma HP Rasa Yoga Sagar Part -1, KrishnadasAyurved Series, pp 260

II) Mouktik yukta praval Panchamrut[78]

प्रवालमुक्ता फलशंखशुक्ति कपर्दिकानाञ्च समांशभागम् ।
प्रवालमात्रं व्दिगुणं प्रयोज्यं सर्वैः समांशं रविदुग्धामेव ।।
एकीकृतं तव्खलु भाण्डमध्ये क्षिप्त्वा मुखे बन्धनमंत्र योज्यम् ।
गुल्मोदरप्लीहविबध्दकासश्वासाऽग्निमान्द्यान्कफमारुतोत्थान् ।।
अजीर्णमुद्गारह्रदमायघ्नं बालग्रहार्तो परमं प्रशस्तम् ।
मेहामयं मूत्ररोगं मूत्रकृच्छ्र तथाऽश्मरीम् ।
योगोत्तमः सर्वगदाऽपहारी ।।

र.यो.सा. ९३

Table 3 – Details of contents of Mouktikayukta Praval Panchamrut

Sr. No	Dravya Name	EnglishName	Rasa (Taste)	Veerya (Potency)	Vipaka (Post-digestive test)	Doshghnata (Action on doshas)	Karya (Action)
1	Praval	Coral	Madhur (Sweet), Amla (sour), Kashay (Astringent)	Sheeta (Cold)	Madhur (Sweet),	Pittashak, Kaphaghna	Rasayan , Jwaraghna Raktapittahar, Vishbadhahar
2	Mouktika	Pearl	Madhur (Sweet), Kashay (Astringent)	Sheeta (Cold)	Madhur (Sweet),	Tridoshshamak	Daha shamak , Balya
3	Shankha	Conch shell	Tikta (Bitter)	Ushana (Hot)	Madhur (Sweet),	Kaph pitta shamak	Chhradighna
4	Shauktika	Pearl Shell	Katu (Pungent)	Sheeta (Cold)	Madhur (Sweet),	Vat Pittaghna	Arochakhar, Chhardighna
5	Kapardika	Cowrie shell	Katu (Pungent)	Ushna (Hot)	Madhur (Sweet),	Vatshamak Kaphaghna	Dahshamak, Deepan , Raktavikarhar , Pittahar
6	Arka kshira	Calotrophis giganticum	Tikta (Bitter) Lavan (salty)	Ushna (Hot)	Katu	Kaphashamak	Virechaka, Gulmahara

78. Sharma HP Rasa Yoga Sagar Part -2, KrishnadasAyurved Series, pp 93.

III) Ananta Vati[79]

सारिवायुगलं**स्वादु स्निग्ध** शुक्रकरं गुरु

अग्निमान्द्यारुचिश्वासकाससाम**विषनाशनम्** ।।

दोषत्रयास्रप्रदर**ज्वरा**तीसारनाशनम् । २३८ ।

भा.प्र. ४२६

Table 4- showing details of Ananta Vati

Dravya Name	Botanical Name	Rasa (Taste)	Veerya (Potency)	Vipaka (Post-digestive test)	Guna (Properties)	Doshghnata (Action on doshas)	Karya (Action)
Ananta	Hemidesmus indicus	Tikta (Bitter) Madhura (Sweet)	Sheet (cold)	Madhura (Sweet)	Guru	Tridosha shamak	Pittashamak, Raktaprasadak, Vishaghna, Daha shamak

79. Bhavprakash Nighantu by Bhavmishra with Vidyodini Hindi Commentary by Shree Bramha Shankar Mishra and Shree Ruplalji Vaishya, Chaukhamba Sanskrit Samsthan, (2002), 10th Eddition, Nighantu Bhag,pp 65

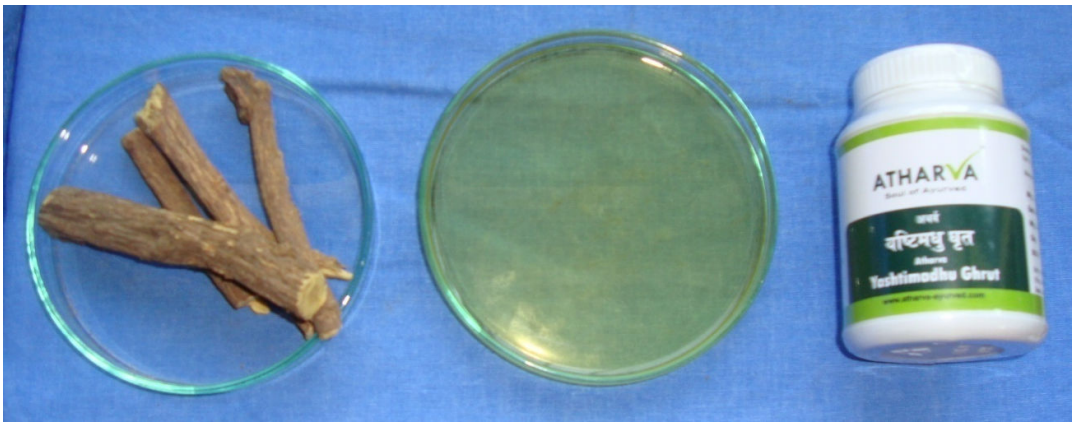
IV) Yashtimadhu Ghrut [80]

यष्टीमधु तथा यष्टीमधुकं क्लीतकं तथा ।
अन्यत्क्लीतनकं तत्तु भवेत्तोये मधूलिका ।।
यष्टी हिमा गुरु स्वादी चक्षुष्या बलवर्णकृत् ।
सुस्निग्धा शुक्रला केश्यःस्वर्या पित्तानिलास्त्रजित् ।।
व्रणशोथविषच्छर्दितृष्णाग्लानिक्षयापहा ।

भा.प्र. ६५

Table 5 – Shwoing details of Yashtimadhu Ghrut

Sr. No	Dravya Name	Botanical Name	Rasa (Taste)	Veerya (Potency)	Vipaka (Post-digestive test)	Guna (Properties)	Doshghnata (Action on doshas)	Karya (Action)
1	Yashti madhu	Glycyrrhiza glabra	Madhura (Sweet)	Sheeta (Cold)	Madhura (sweet)	Guru Snigdha	Vata Pitta Shamak	Dahashamaka, Kanthya, Varnya, Sandhaneeya, Rasayana
2	Ghrut		Madhura (Sweet)	Sheeta (Cold)	Madhura (sweet)	Guru, snigdha	Vata Pitta, Visha doshghna	Balvardhan, Agni – daghdha vrana ropak



80. Bhavprakash Nighantu by Bhavmishra with Vidyodini Hindi Commentary by Shree Bramha Shankar Mishra and Shree Ruplalji Vaishya, Chaukhamba Sanskrit Samsthan, (2002), 10th Eddition, Nighantu Bhag,pp 426

PREVIOUS WORK DONE

1. Protective effect of Yashtimadhu (Glycyrrhiza glabra) against side effects of radiation/chemotherapy in head and neck malignancies – Dr. Debabrata Das - 2011 – Jamnager, Gujrath.

2. Efficacy of Rasayana Avaleha as adjuvant to radiotherapy and chemotherapy in reducing adverse effects. Dr. Vyas P – 2010 - Smt.Maniben M.A.H. Government Ayurvedic Hospital, Asarava, Ahmedabad, India.

3. Triphala, an Ayurvedic Rasayana Drug, protects mice against radiation-induced lethality by free-radical scavenging – Dr. Ganesh Chandra Jagetia – 2004 - Kasturba Medical College, Manipal, Karnataka India.

4. Radiation protection of DNA and membrane in vitro by extract of Hemidesmus indicus, Shetty TK[1], Satav JG, Nair CK, 2005, Phytother Res. ;19(5):387-90.

MATERIAL AND METHODS

- Material –

Table 6 - showing groups of oral cavity cancer patients

Group	No. of patients	Description
Group A -Study	30	Opted for radiotherapy with conventional medication and a combination of Ayurvedic drugs (RG4) from the beginning of RT and continued for 3 month after completion of RT at ICTRC
Group B- Control	30	Opted for radiotherapy with conventional medication at ICTRC

- Type of oral cavity cancers selected for study -
  CA Tongue
  CA Buccal Mucosa

- Medicine -

Table 7 - showing details of Ayurvedic medicine (RG4) -

Sr. No.	Name of medicine	Matra	Kala	Anupana
1	Mouktikayukta Kamdudha	250 mg	Vyanodan (Morning – Evening)	Milk
2	Mouktikykta Praval Panchamrut	250 mg	Vyanodan	Milk
3	Ananta Vati	1 gm	Vyanodan	Water
4	Yashtimadhu Ghrut	5 gm	Apan (Before lunch and dinner)	Luke warm water
	Yashtimadhu Ghruta for local application internally in oral cavity.			

Inclusion criteria

- Oral cavity cancer patients of all stages planned for radiotherapy with or without concurrent chemotherapy (Inj. Cisplatin)
- Patients of age group 20-75 years
- Patient scheduled to receive radiation with external beam radiotherapy
- Total dose in between 6000 – 6600 Cgy
- Total Fractions – 25-35 # as required. In 5 - 6 wks
- Among blood parameters HB = > 9 gr. %

Exclusion criteria –

- Patient taking palliative radiotherapy.
- Oral cavity cancer patients other than Ca Tongue and Ca Buccal Mucosa.

Plan of work done -

- Patients diagnosed with oral cancer with confirmed biopsy / FNAC were selected for the study.
- References of Mukhagat Vyadhi, Agnikarma , Ksharkarma etc. were taken from Bruhat trayee and Laghu trayee
- References of oral cancer especially cancer of buccal mucosa and tongue alongwith radiotherapy were taken.
- Standardized Ayurvedic medicines (RG4) were used for the study. These medicines were tested in laboratory (FDA approved, GMP and USDA & EC certified).
- The study was open labelled controlled clinical trial.
- Patients were divided in 2 groups as mentioned above.
- Specially designed informed written consent was taken.
- Detail case was taken on specially designed CRF.
- Standard criteria for assessment were Karnofsky scoring for performance status and QLQ were noted at four time points - Before radiotherpay (a), immediate after radiotherapy (b), 1 month after radiotherapy (c), 3 Months after completing radiotherapy (d).
- Side effects were noted as per Common Toxicity Criteria (CTC) derived by Cancer Therapy Evaluation Program (CTEP). Symptoms were noted at three time

points -Immediate after radiotherapy (b), 1 month after radiotherapy (c), 3 Months after completing radiotherapy (d)

- Follow ups were taken at every 8^{th} day during RT and every 15^{th} day after RT upto 3 months.
- Investigations were done on day 1, at the end of RT & then monthly up to 3 months and in between if necessary.
- Statistical analysis was done using Man Whitney Z test for symptoms, umpaired t Test for persantage of weight loss and chi square terst for comparison of Karnofsky score, and QoL scores Chi square test was applied.

Assessment criteria –

- Symptoms like xerostomia, loss of taste, stomatitis, extensive salivation, trismus, nausea, dysphagia, weight loss were assessed as per Common Toxicity Criteria (CTC) derived by Cancer Therapy Evaluation Program (CTEP). It was used as assessment scale [81].
- According to Ayurvedic criteria for assessment, side effects were correlated on the basis of dosha, dhatu, agni and srotas.
- Measurement of opening of mouth in cm. by mouth gag for measurement of trismus.
- Photographic evaluation during follow ups
- Karnofsky scoring for performance status [82]
- QLQ (Quality of Life questionnaire) [83]
- Pathological Parameters like complete blood count (CBC), liver function test (LFT), renal function test (RFT) were noted whenever required.

81. Common Terminology Criteria for Adverse Events (CTCAE)Version 4.0,May 2009 (updated June 2010) U.S. Department Of Health and Human Services NIH, NCI
http://www.eortc.be/ services/doc/ctc/CTCAE_4.03_2010-06-14_QuickReference_5x7.pdf

82. The use of the Karnofsky Performance Scale in determining outcomes and risk in geriatric outpatients (1991), Crooks, V, Waller S, et al ,J Gerontol46, pp 139-144

83. The European organization for research and treatment of cancer QLQ-C30: a quality-of-life instrument for use in international clinical trials in oncology (1993),Aaronson NK, Ahmedzai S, Bergman B, Bullinger M, Cull A, Duez NJ, Filiberti A, Flechtner H, Fleishman SB, de Haes JC, et al. J Natl Cancer Inst 85, pp 365–376.
http://www.ncbi.nlm.nih.gov/pubmed/8433390

Side effects of Radiotherapy were graded according to Common Terminology Criteria for Adverse Events v3.0 (CTCAE) [81]

Table 8 - showing gradation of side effects of radiotherapy

Sr. No	Symptom	Grade 1	Grade 2	Grade 3	Grade 4	Grade 5
1	Stomatitis	No Symptom Noted	Patient has erythema of the mucosa	Patient has ulceration in patches with pseudomembranes	Patients has ulceration which bleeds with minor trauma	Patient has tissue necrosis, significant spontaneous bleeding.
2	Xerostomia	No Symptom Noted	Xerostomia is only symptomatic. No need of dietary ulteration. Unstimulated saliva flow present	Xerostomia is symptomatic and signicant oral intake alteration with unstimulated saliva	Xerostomia leading to inability to take orally. Tube feeding required. Saliva is unstimulated.	-
3	Loss of Taste	No Symptom Noted	Taste is altered but no change in diet required.	Taste is altered and change in diet required.	-	-
4	Extensive Salivation	No Symptom Noted	Patient has slightly thickened saliva. And slightly ultered taste.	Patient has thick and sticky saliva, markedly altered taste. Alteration of diet is indicated.	Patient has severe secreations. Symptoms interfering with ADL	Disabling
5	Trismus (Difficulty in opening of Mouth)	No Symptom Noted	Patient has decreased motion of jaw. Patient can not open for more than 4 cm.	Patient's motion of jaw decreased and required small bites, soft foods or purees. Patient can not open for more than 3 cm.	Severe restriction of jaw. Inability to hydrate orally. Patient can not open for more than 2 cm.	Patient can not open for more than 1 cm.

81. Common Terminology Criteria for Adverse Events (CTCAE)Version 4.0,May 2009 (updated June 2010) U.S. Department Of Health and Human Services NIH, NCI
http://www.eortc.be/ services/doc/ctc/CTCAE_4.03_2010-06-14_QuickReference_5x7.pdf

Sr. No	Symptom	Grade 1	Grade 2	Grade 3	Grade 4	Grade 5
6	Weight Loss	Weight loss is less than 5 % weight loss from baseline.	Weight loss is 5 to <10% from baseline which do not required intervention	Weight loss is 10 – <20% from baseline. Required nutritional support.	Weight loss is ≥20% from baseline and needs tube feeding or TPN.	-
7	Dysphasia	No symptom noted	Dysphagia is symptomatic but able to eat regular diet.	Dysphagia is symptomatic but altered dietary habits. IV fluids indicated in <24 hrs.	Dysphagia is symptomatic and severely altered eating / swallowing required IV fluids /tube feedings / TPN indicated in ≥24 hrs.	Life threatening consequences like obstruction, perforation.
8	Nausea	No Symptom Noted	Patient has nausea with loss of appetite without alteration in eating habits.	Oral intake of patient decreased without significant weight loss, but IV fluids indicated < 24 hrs.	Oral caloric or fluid intake is less , tube feeding required , TPN indicated ≥24 hrs	Due to Nausea life-threatening consequences happen.

Karnofsky scoring for performance status

Karnofsky score was used for assessment of general well-being and activities of daily life of patients to compare effectiveness of therapies. Ascending order of Karnofsky score shows improvement in well-being of patients. The assessment of these scores was as per the formulae described by Crooks et al[82].

Table 9 showing particulars regarding status of Karnofsky score

Patient do not need special care and able to carry normal day to day activity.	100	Patient is normal without complaints and evidence of disease.
	90	Patient is able to carry normal activity with minor signs and symptoms of the disease.
	80	Patient can do normal acivity with minimum effort with some signs and symptoms of the disease.
Patient can not work, only live at home and can take care for personal needs. Rarely assistance needed.	70	Patient has to take selfcare and can not perform normal activity.
	60	Patient has to take selfcare and occasionally need assistance, but can able to care for most of his personal needs.
	50	Patient requires considerable assistance with medical care.
Patient can not take care for self. Require hospital care. Disease is progressing rapidly.	40	Patient is disabled and needs hospital admission, special care and assistance.
	30	Patient is severly disabled; hospital admission is needed although not on the verge of death.
	20	Patient is very ill, hospitalized and active treatment intervention is necessary.
	10	Patient is declining state, fatal process progressing rapidly.
	0	Death.

82. The use of the Karnofsky Performance Scale in determining outcomes and risk in geriatric outpatients (1991), Crooks, V, Waller S, et al ,J Gerontol46, pp 139-144

EORTC Quality of Life Questionnaire

1. QLQ C – 30 – General Questionnaire for all types of cancer
   QLQ-C30 questionnaire is designed by European Organization for Research and Treatment of Cancer (EORTC), which consists of functional, symptom and global scores, recordedin patient's own perspective. High functional score represents high level of functioning. High symptom score represents a high level of symptomatology while overall QoL is assessed in terms of global score, the high score representing healthy status [83].
2. H&N – 35 – Specially designed Head and Neck Cancer Questionnaire for head and neck cancers by them.

83. The European organization for research and treatment of cancer QLQ-C30: a quality-of-life instrument for use in international clinical trials in oncology (1993),Aaronson NK, Ahmedzai S, Bergman B, Bullinger M, Cull A, Duez NJ, Filiberti A, Flechtner H, Fleishman SB, de Haes JC, et al. J Natl Cancer Inst 85, pp 365–376.
http://www.ncbi.nlm.nih.gov/pubmed/8433390

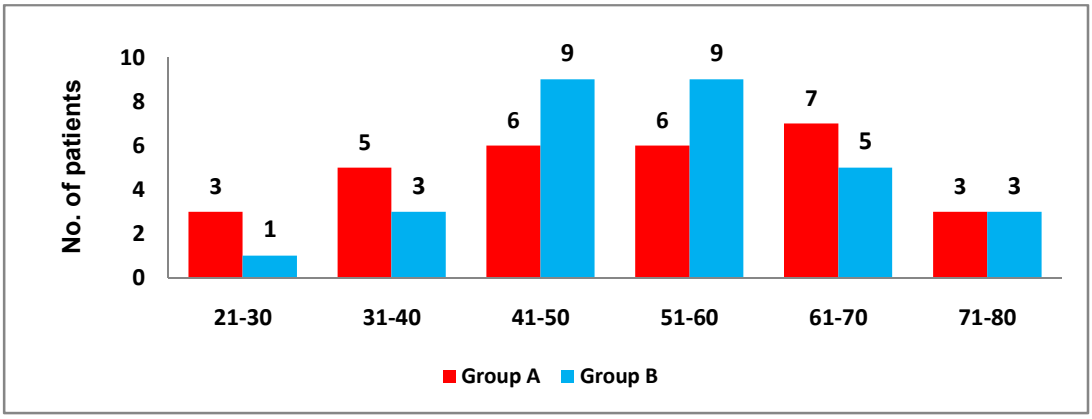
OBSERVATIONS AND RESULTS

I) Observations of demographic data

Table 10 – showing age wise distribution of oral cancer patients treated with Radiotherapy.

Sr. No	Age	Group A	Group B
1	21-30	3	1
2	31-40	5	3
3	41-50	6	9
4	51-60	6	9
5	61-70	7	5
6	71-80	3	3
	Total	**30**	**30**

Graph 1 – Graphical representation of age wise distribution of oral cancer patients treated with Radiotherapy.

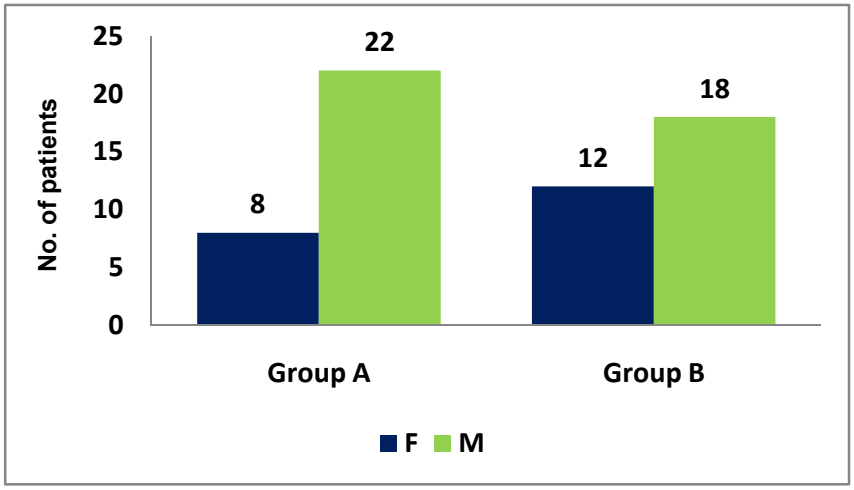


Proportion of cancer patients of oral cavity cancer who underwent radiotherapy is higher in age 41 yrs to 70 yrs.

Table 11 – showing sex wise distribution of oral cancer patients treated with Radiotherapy

Sr. No	Sex	Group A	Group B
1	Female	8	12
2	Male	22	18
	Total	30	30

Graph 2 – Graphical representation of sex wise distribution of oral cancer patients treated with radiotherapy

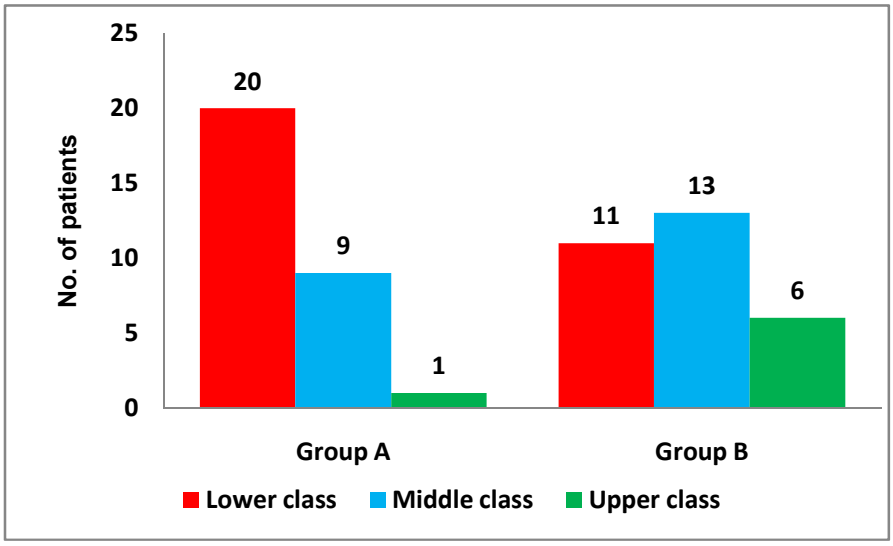


In both the groups number of male patients were more than that of female patients who underwent radiotherapy.

Table 12 – showing distribution of Socio – economical statuses of oral cancer patients treated with radiotherapy

Sr. No	Socio economical status	Group A	Group B
1	Lower class	20	11
2	Middle class	9	13
3	Upper Class	1	6
	Total	30	30

Graph 3 – Graphical representation of distribution of socio – economical status of oral cancer patients treated with radiotherapy

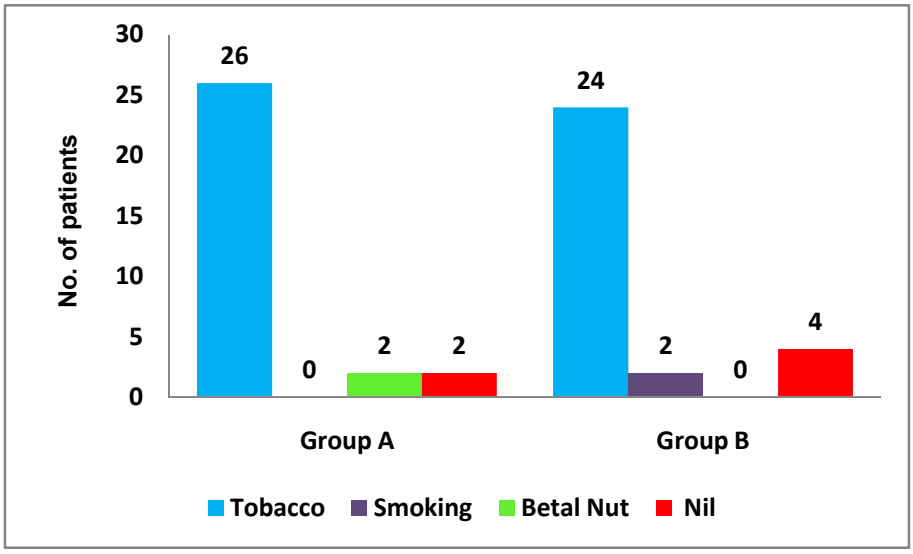


Socioeconomically lower class and middle class patients were more in both groups than upper class.

Table 13 A– showing history of addiction of oral cancer patients treated with radiotherapy

Addiction	Group A	Group B
Tobacco	26	24
Smoking	0	2
Betal Nut	2	0
No addiction	2	4
Total	30	30

Graph 4A – Graphical representation of history of addiction of oral cancer patients treated with radiotherapy

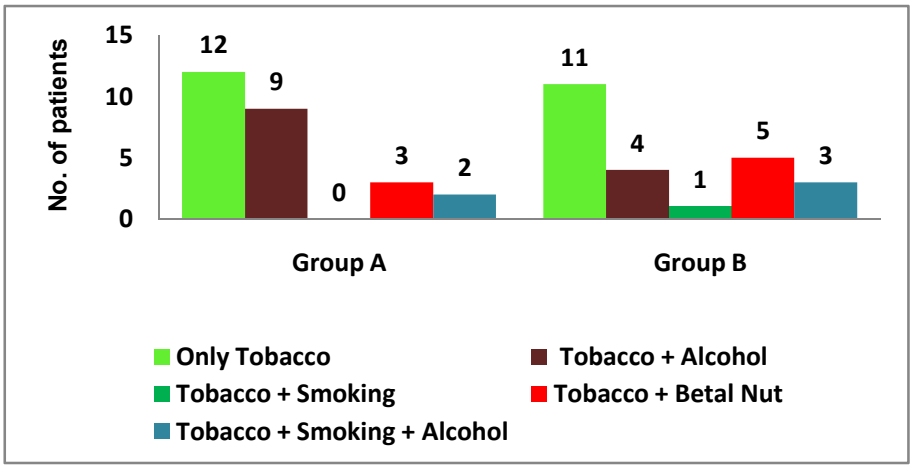


Tobacco addiction was found to be evident causative factor in both the groups. 26/30 patients in group A and 24/30 patients in group B had habit of consuming tobacco. Only 2 patients in group A and 4 patients in group B had no history of any addiction.

Table 13 B – showing combinations of addictions along with tobacco consumption in oral cancer patients treated with radiotherapy

	Group A	Group B
Only Tobacco	12	11
Tobacco + Alcohol	9	4
Tobacco + Smoking	0	1
Tobacco + Betal Nut	3	5
Tobacco + Smoking + Alcohol	2	3
Total	26	24

Graph 4B – showing combinations of addictions along with tobacco consumption in oral cancer patients treated with radiotherapy

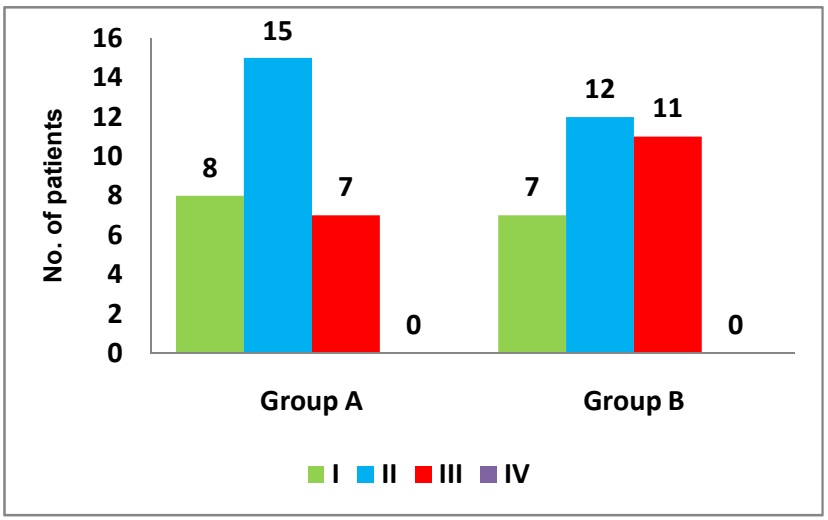


Out of 26 patients from Group A who were addicted to tobacco, 9 patients were drinking alcohol along with tobacco, 3 patients were consuming betal nut, 2 patients had habit of smoking along with tobacco and alcohol, while 12 patients were taking only tobacco. From group B, out of 24 patients who were consuming tobacco, 11 patients were consuming only tobacco, 4 patients were drinking alcohol with tobacco while 3 patients had a habit of smoking along with tobacco and alcohol.

Table 14 – showing distribution of Histopathological Grading of oral cancer patients treated with radiotherapy

Sr. No	Grade	Group A	Group B
1	I	8	7
2	II	15	12
3	III	7	11
4	IV	0	0
	Total	30	30

Graph 5 – Graphical distribution of Histopathological Grading of oral cancer patients treated with radiotherapy

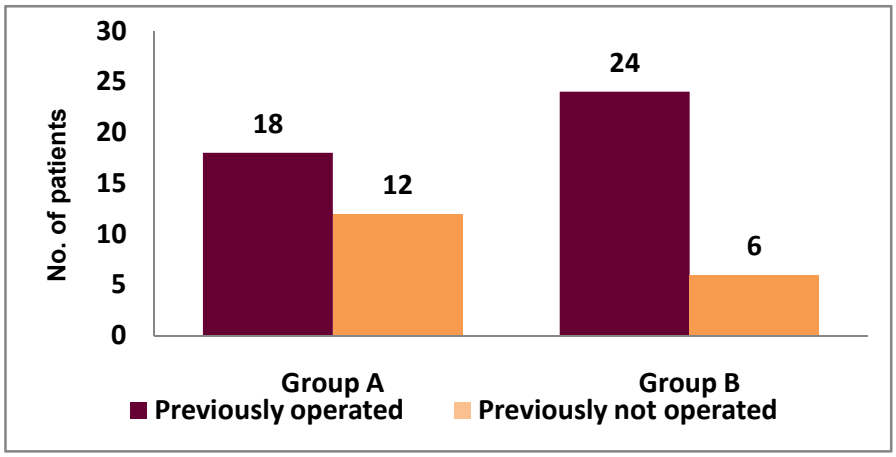


In Group A, 8 patients were histopathologically in grade I, 15 patients were in grade II, and 7 patients in grade III while no patient was in grade IV. In Group B, 7 patients were in grade I, 12 patients in grade II, 11 patients were in grade III and no patients were in grade IV.

Table 15 – showing operative history for oral cancer before radiotherapy

Sr. No	Status	Group A	Group B
1	Previously operated patients	18	24
2	Previously not operated patients	12	6
	Total	30	30

Graph 6 – Graphical representation of operative history for oral cancer before radiotherapy

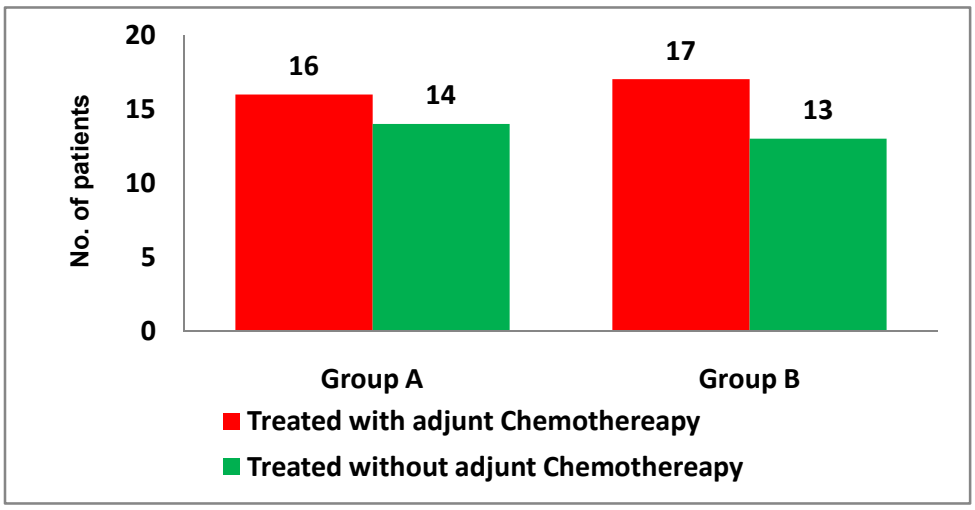


18 patients in group A and 24 patients in group B underwent surgery for oral cavity cancer before taking radiotherapy.

Table 16 – showing status of adjuvant chemotherapy (Inj. Cisplatin – 500 mg) of oral cavity cancer patients treated with radiotherapy

Sr. No	Status	Group A	Group B
1	Treated with adjunct chemotherapy (Inj. Cisplatin – 500 mg)	16	17
2	Treated without adjunct chemotherapy	14	13
	Total	30	30

Graph 7 – Graphical representation of status of adjuvant chemotherapy (Inj. Cisplatin – 500 mg) of oral cavity cancer patients treated with radiotherapy



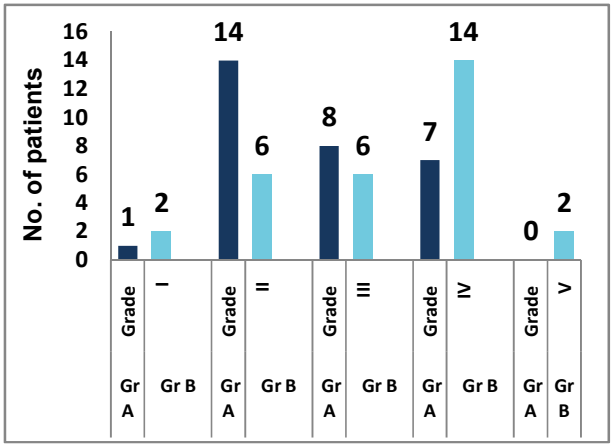
Adjunct weekly chemotherapy (Inj. Cisplatin 500 mg.) was given in more or less same number of patients in both groups. 16 patients from group A and 17 patients in group B were given adjunct weekly chemotherapy along with radiotherapy.

II) Observation of Side effects

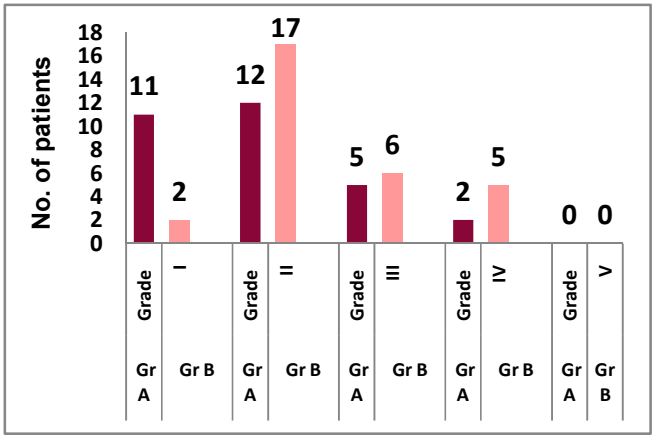
Table 17 – showing gradation of stomatitis in oral cancer patients treated with radiotherapy

Time points	No of patients									
	Group A	Group B	Group A	Group B	Group A	Group B	Group A	Group B	Group A	Group B
	Grade I		Grade II		Grade III		Grade IV		Grade V	
Immediate After RT	1	2	14	6	8	6	7	14	0	2
After 1 month of RT	11	2	12	17	5	6	2	5	0	0
After 3 month of RT	15	6	12	18	2	6	1	0	0	0

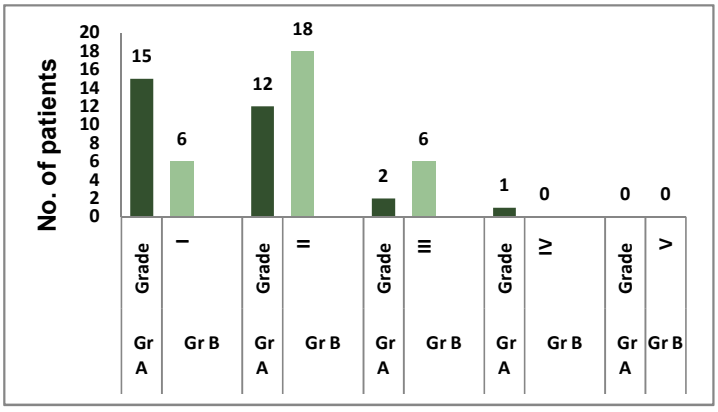
Graph 8A – Graphical representation of gradation of stomatitis in oral cancer patients treated with radiotherapy



Immediately after RT



After 1 month of RT



After 3 months RT

Symptoms were assessed at three time points immediately after completing RT, 1 montha and three months post RT. As RT related symptoms would appear only during the course of RT and continue till certain period after competing RT, they do not exist before RT.

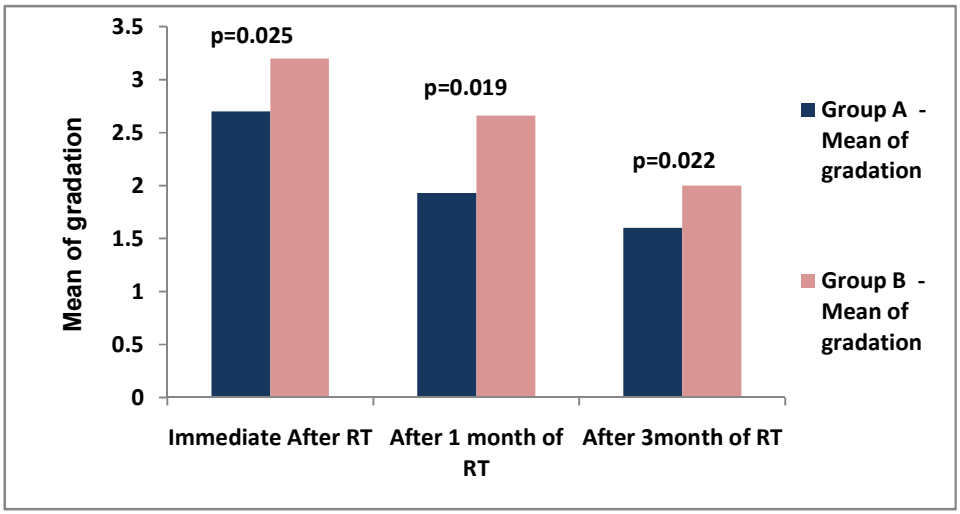
It can be seen that in Group A (Study group), 14 patients had grade II stomatitis immediately at the end of radiotherapy. 11 patients after 1 month of RT and 15 patients after 3 months of RT were free of stomatitis.

In group B (Control group) 14 patients had high grade ie grade IV stomatitis immediately after RT which continued as grade II and III reactions till 3 months after completing RT. In this group 17 patients got grade II reaction after 1 month of RT, 18 patients had grade II reaction after 3 months of RT.

Statistical Table 1 - showing statistical analysis of gradation of stomatitis in oral cancer patients treated with radiotherapy

Stomatitis	Group A Gradation score			Group B Gradation score			Mann-Whitney Z	P
	Median	Mean	Sd	Median	Mean	Sd		
Immediate After RT	2.5	2.70	0.877	4.0	3.27	1.081	2.235	0.025 **Sig**
After 1 month of RT	2.0	1.93	0.907	2.0	2.47	0.860	2.347	0.019 **Sig**
After 3 month of RT	1.50	1.63	0.765	2.0	2.00	0.643	2.288	0.022 **Sig**

Graph 8B – Graphical representation of statistical analysis of gradation of stomatitis in oral cancer patients treated with radiotherapy

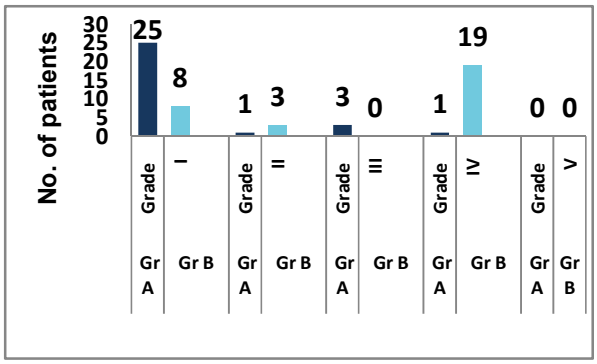


For statistical analysis means of gradation of symptoms at given time points were compared.Statistically significant results were seen in stomatitis in Group A when compared to Group B immediately after RT (p=0.025), one month after RT (p=0.019) and (p=0.022) after three months of RT

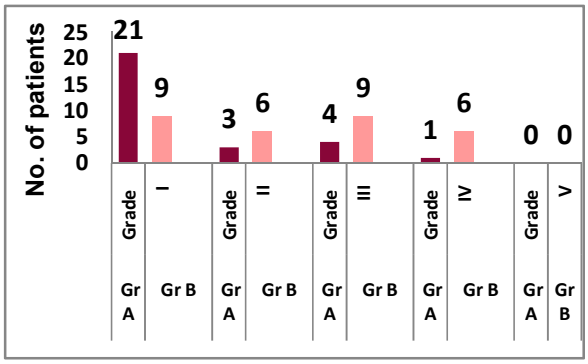
Table 18 – showing gradation of xerostomia in oral cancer patients treated with radiotherapy

Time points	Number of Patients									
	Group A	Group B	Group A	Group B	Group A	Group B	Group A	Group B	Group A	Group B
	Grade I		Grade II		Grade III		Grade IV		Grade V	
Immediate After RT	25	8	1	3	3	0	1	19	0	0
After 1 month of RT	21	9	3	6	4	9	1	6	0	0
After 3 month of RT	22	9	4	8	4	12	0	1	0	0

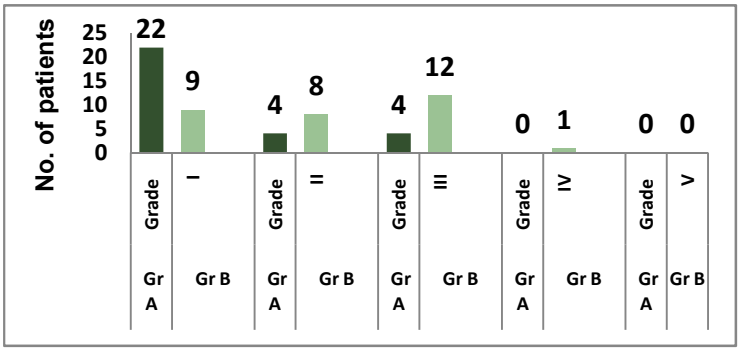
Graph 9A – Graphical representation of gradation of xerostomia in oral cancer patients treated with radiotherapy



Immediately after RT



After 1 month of RT



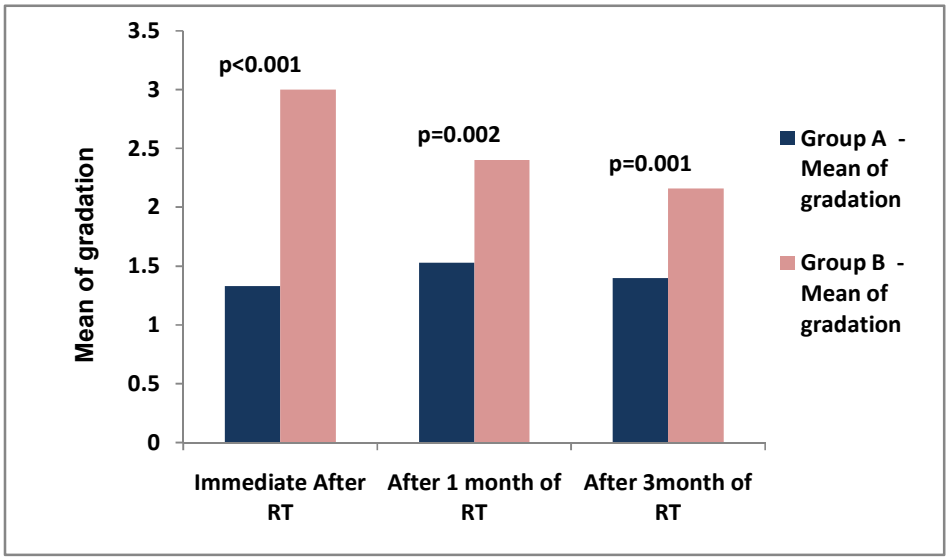
After 3 months RT

In Group A, 25 patients did not suffer from xerostomia when observed immediately at end of radiotherapy. In group B 19 patients suffered high grade ie grade IV xerostomia immediately after RT which continued till 3 months after completing RT in 12 patients.

Statistical Table 2 -showing statistical analysis of gradation of xerostomia in oral cancer patients treated with radiotherapy

Xerostomia	Group A Gradation score			Group B Gradation score			Mann-Whitney Z	P
	Median	Mean	Sd	Median	Mean	Sd		
Immediate After RT	1.0	1.33	0.802	4.0	3.00	1.365	4.755	<0.001 **HS**
After 1 month of RT	1.0	1.53	0.90	2.5	2.40	1.133	3.113	0.002 **Sig**
After 3 month of RT	1.0	1.40	0.724	2.0	2.17	0.913	3.348	0.001 **Sig**

Graph 9B – Graphical representation of statistical analysis of gradation of xerostomia in oral cancer patients treated with radiotherapy

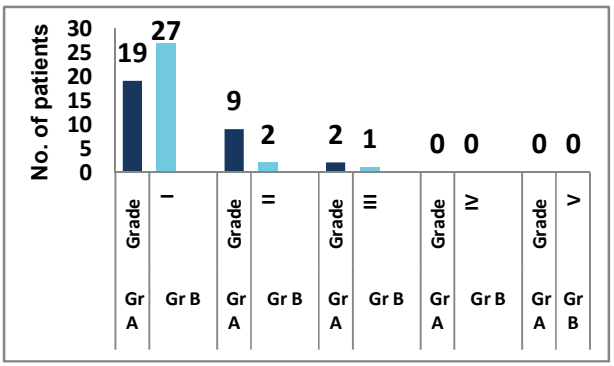


Statistically extremely significant result was obtained in Group A when compared to Group B immediately after RT (p <0.001). One month after RT (p=0.002) and (p=0.001) after three months of RT

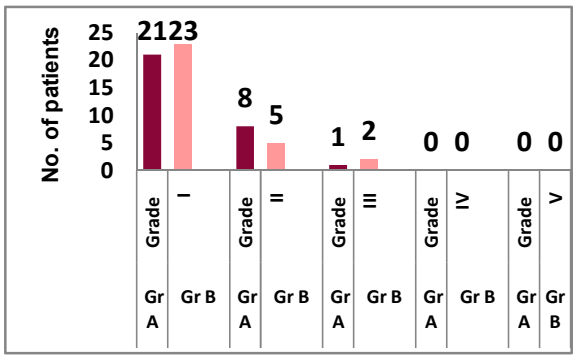
Table 19 – showing gradation of loss of taste in oral cancer patients treated with radiotherapy

	Number of patients									
	Group A	Group B	Group A	Group B	Group A	Group B	Group A	Group B	Group A	Group B
Time points	Grade I		Grade II		Grade III		Grade IV		Grade V	
Immediate After RT	19	27	9	2	2	1	0	0	0	0
After 1 month of RT	21	23	8	5	1	2	0	0	0	0
After 3 month of RT	26	27	4	3	0	0	0	0	0	0

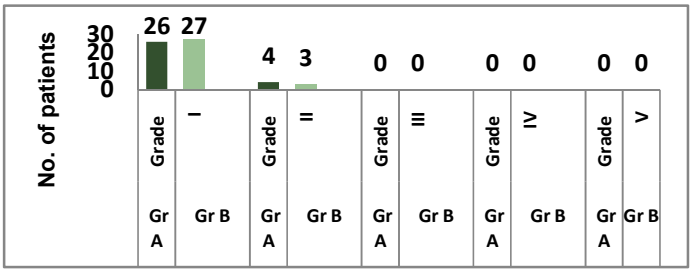
Graph 10A – Graphical representation of gradation of loss of taste in oral cancer patients treated with radiotherapy



Immediately after RT



After 1 month of RT



After 3 months RT

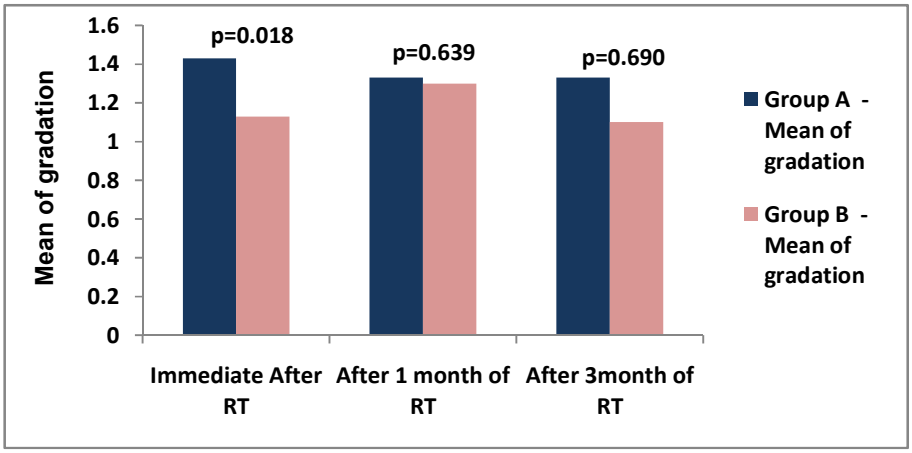
In Group A, 19 patients did not loss of taste at end of radiotherapy. 21 patients after 1 month of RT and 26 patients after 3 months of RT were free from taste disturbance.

In group B, 27 patients were in grade I loss of taste immediately after RT till 3 months of RT.

Statistical Table 3- showing statistical analysis of gradation of loss of Taste in oral cancer patients treated with radiotherapy

Loss of taste	Group A Gradation score			Group B Gradation score			Mann-Whitney Z	P
	Median	Mean	Sd	Median	Mean	Sd		
Immediate After RT	1.0	1.43	0.626	1.0	1.13	0.434	2.357	0.018 **Sig**
After 1 month of RT	1.0	1.33	0.547	1.0	1.30	0.596	0.469	0.639 **NS**
After 3 month of RT	1.0	1.13	0.346	1.0	1.10	0.305	0.399	0.690 **NS**

Graph 10B – Graphical representation of gradation of loss of taste in oral cancer patients treated with radiotherapy

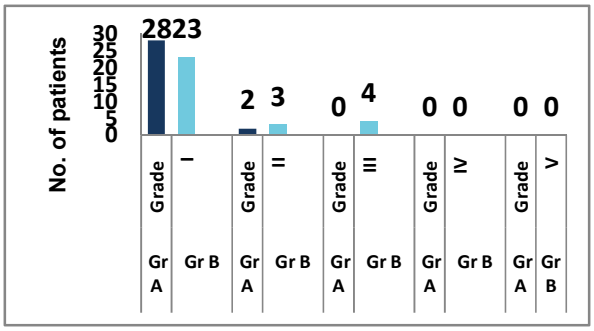


Statistically significant difference is noted in loss of taste in Group B when compared to Group A immediately after RT (p=0.018).

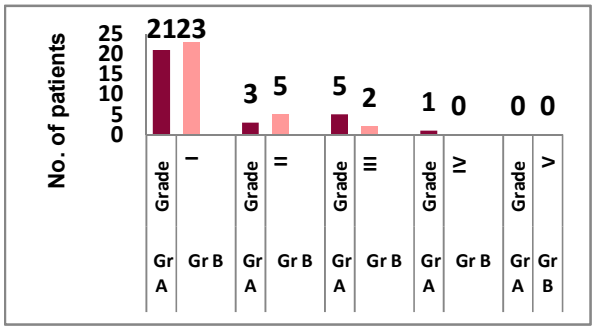
Table 20– showing gradation of excessive salivation in oral cancer patients treated with radiotherapy

Time points	Number of patients									
	Group A	Group B	Group A	Group B	Group A	Group B	Group A	Group B	Group A	Group B
	Grade I		Grade II		Grade III		Grade IV		Grade V	
Immediate After RT	28	23	2	3	0	4	0	0	0	0
After 1 month of RT	21	23	3	5	5	2	1	0	0	0
After 3 month of RT	22	25	4	3	4	2	0	0	0	0

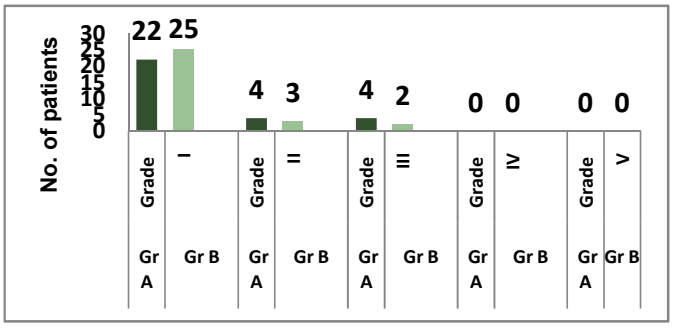
Graph 11A – Graphical representation of gradation of excessive salivation in oral cancer patients treated with radiotherapy



Immediately after RT



After 1 month of RT



After 3 months of RT

There was not much difference in observations in both groups for excessive salivation.

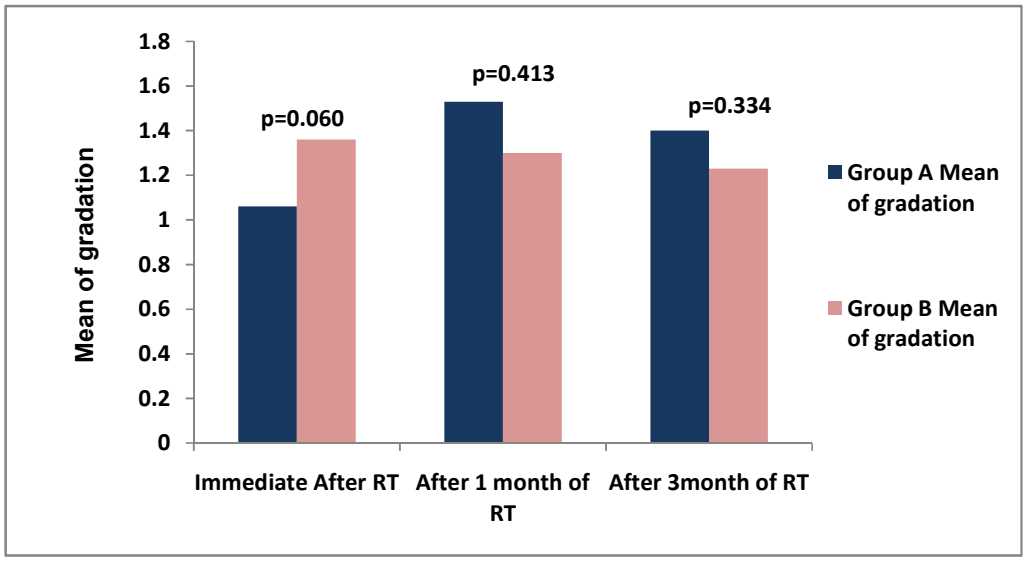
It can be seen that in Group A respectively 28, 21 and 22 patients did not have excessive salivation when observed immediately after completion of RT, one month after RT and 3 months after finishing RT.

In group B respectively 23, 23 and 25 patients did not have excessive salivation when observed immediately after completion of RT, one month after RT and 3 months after finishing RT.

Statistical Table 4 - showing statistical analysis gradation of excessive salivation in oral cancer patients treated with radiotherapy

Excessive Salivation	Group A Gradation score			Group B Gradation score			Mann-Whitney Z	P
	Median	Mean	Sd	Median	Mean	Sd		
Immediate After RT	1.0	1.07	0.254	1.0	1.37	0.718	1.882	0.060 **Sig**
After 1 month of RT	1.0	1.53	0.900	1.0	1.30	0.596	0.819	0.413 **NS**
After 3 month of RT	1.0	1.40	0.724	1.0	1.23	0.568	0.966	0.334 **NS**

Graph 11B – Graphical representation of statistical analysis of gradation of excessive salivation in oral cancer patients treated with radiotherapy

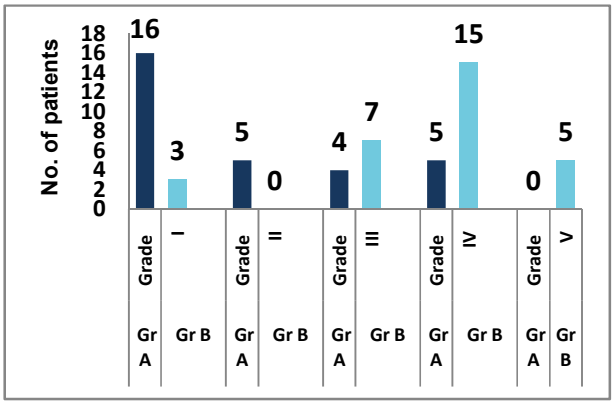


Statistically significant improvement in excessive salivation was noted in Group A when compared to Group B immediately after RT (p=0.06). While statistically no difference was noted in one after RT and 3 month after RT in both groups.

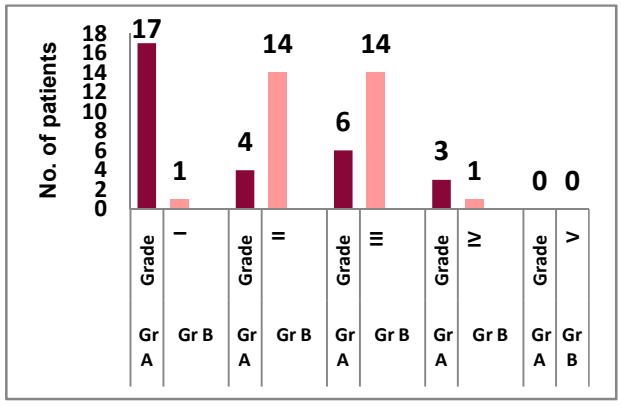
Table 21– showing gradation of trismus in oral cancer patients treated with radiotherapy

Time points	Number of patients									
	Group A	Group B	Group A	Group B	Group A	Group B	Group A	Group B	Group A	Group B
	Grade I		Grade II		Grade III		Grade IV		Grade V	
Immediate After RT	16	3	5	0	4	7	5	15	0	5
After 1 month of RT	17	1	4	14	6	14	3	1	0	0
After 3 month of RT	18	4	6	12	5	13	1	1	0	0

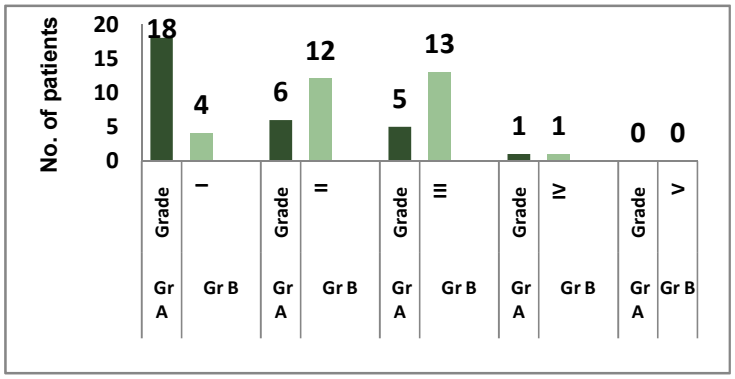
Graph 12A – Graphical representation of gradation of trismus in oral cancer patients treated with radiotherapy



Immediately after RT



After 1 month of RT



After 3 months RT

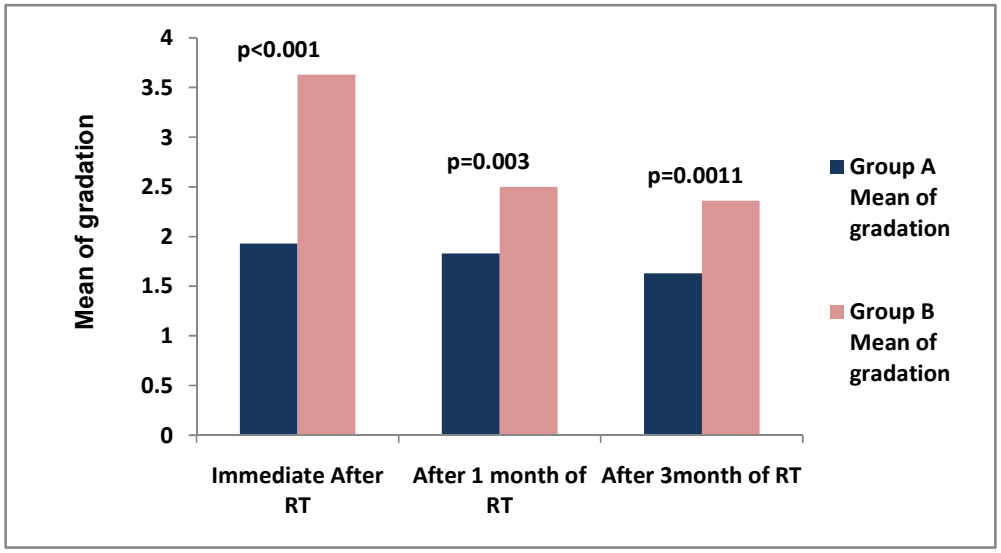
It can be seen that in Group A, 16 patients were free from trismus immediately after end of radiotherapy. 17 patients after 1 month of RT and 18 patients after 3 months of RT.

In group B 15 patients had high grade ie grade IV trismus immediately after RT which continued till 3 months after completion of RT. In this group 28 patients got grade II to III trismus after 1 month of RT and 25 patients had grade II - III trismus after 3 months of RT.

Statistical Table 5 - showing statistical analysis of gradation of trismus in oral cancer patients treated with radiotherapy

Trismus	Group A Gradation score			Group B Gradation score			Mann-Whitney Z	P
	Median	Mean	Sd	Median	Mean	Sd		
Immediate After RT	1.0	1.93	1.172	4.0	3.63	1.098	4.575	<0.001 **HS**
After 1 month of RT	1.0	1.83	1.085	2.5	2.50	0.630	2.931	0.003 **Sig**
After 3 month of RT	1.0	1.63	0.890	2.0	2.37	0.765	3.310	0.001 **Sig**

Graph 12B – Graphical representation of statistical analysis of gradation of trismus in oral cancer patients treated with radiotherapy.

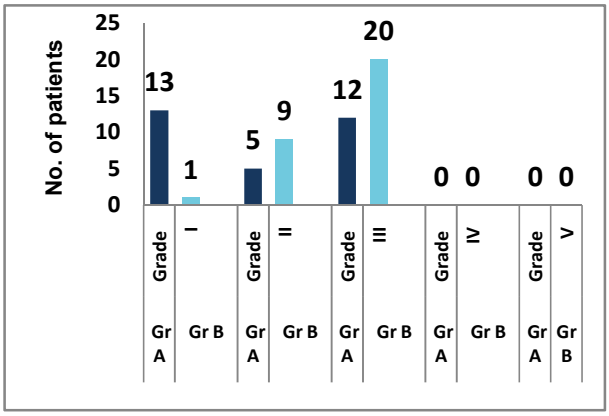


Statistically extremely significant results were noted in Group A when compared to Group B immediately after RT (p<0.001), one month after RT (p=0.003) and (p= 0.0011) after three months of RT.

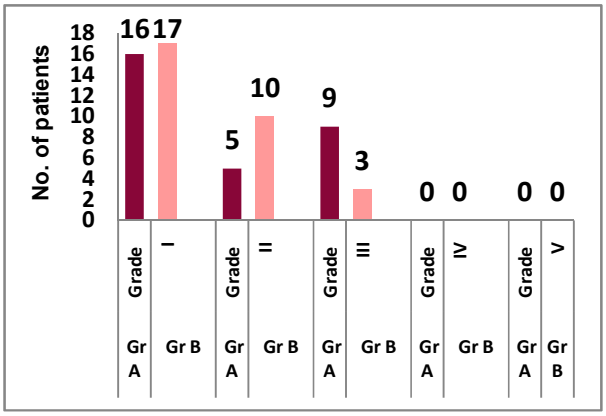
Table 22 – showing gradation of dysphagia in oral cancer patients treated with radiotherapy

	Number of patients									
Time points	Group A	Group B	Group A	Group B	Group A	Group B	Group A	Group B	Group A	Group B
	Grade I		Grade II		Grade III		Grade IV		Grade V	
Immediate After RT	13	1	5	9	12	20	0	0	0	0
After 1 month of RT	16	17	5	10	9	3	0	0	0	0
After 3 month of RT	21	19	5	9	4	3	0	0	0	0

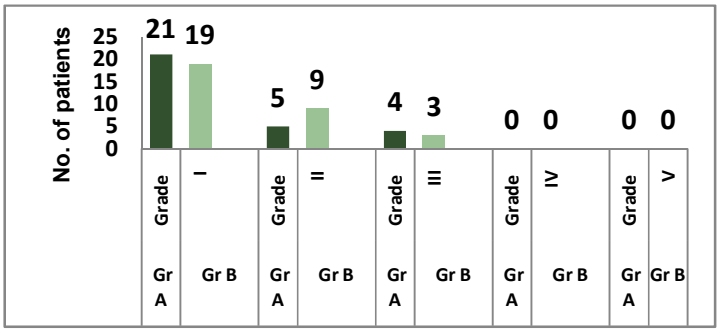
Graph 13A – Graphical representation of gradation of dysphasia in oral cancer patients treated with radiotherapy



Immediately after RT



After 1 month of RT



After 3 months of RT

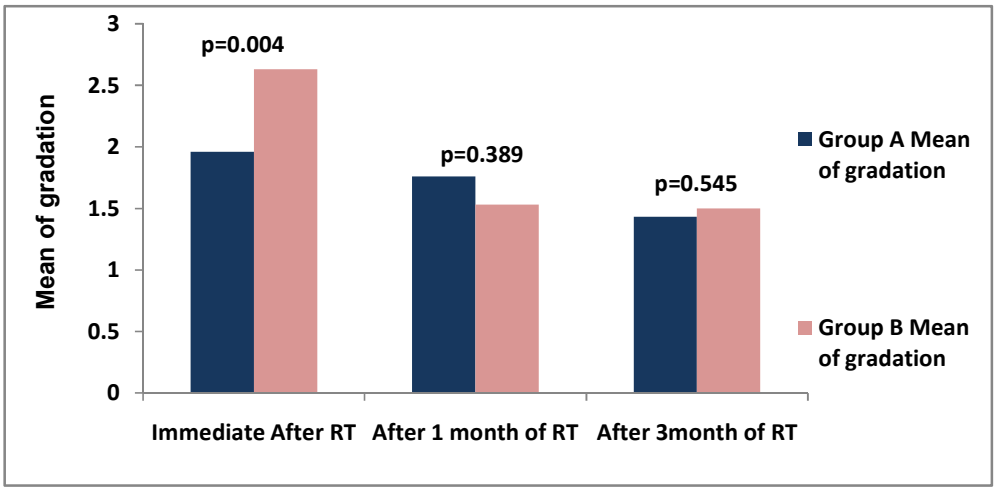
It can be seen that in Group A, 13 patients were free from dysphasia immediately after end of radiotherapy while 20 patients suffered from grade III dysphagia in group B when tested immediately after RT.

Results in both the groups when observed after 1 month of RT and after 3 months of RT were almost same

Statistical Table 6 - showing statistical analysis of gradation of dysphagia in oral cancer patients treated with radiotherapy.

Dysphagia	Group A Gradation score			Group B Gradation score			Mann-Whitney Z	P
	Median	Mean	Sd	Median	Mean	Sd		
Immediate After RT	2.0	1.97	0.928	3.0	2.63	0.556	2.868	0.004 **Sig**
After 1 month of RT	1.0	1.77	0.898	1.0	1.53	0.681	0.862	0.389 **NS**
After 3 month of RT	1.0	1.43	0.728	1.0	1.50	0.682	0.605	0.545 **NS**

Graph 13B – Graphical representation of statistical analysis of gradation of dysphagia in oral cancer patients treated with radiotherapy

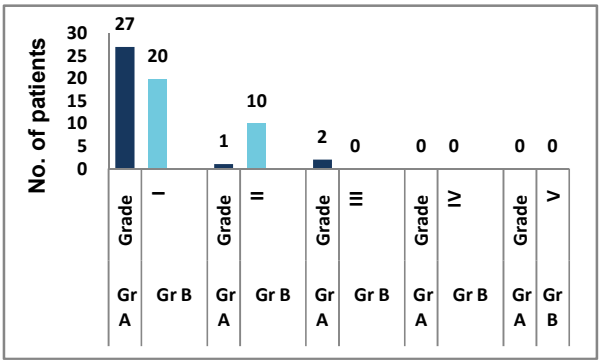


Statistically very significant results were noted in Group A when compared to Group B immediately after RT (p=0.004) while after 3 months of RT observations were not statistically significant in dysphagia.

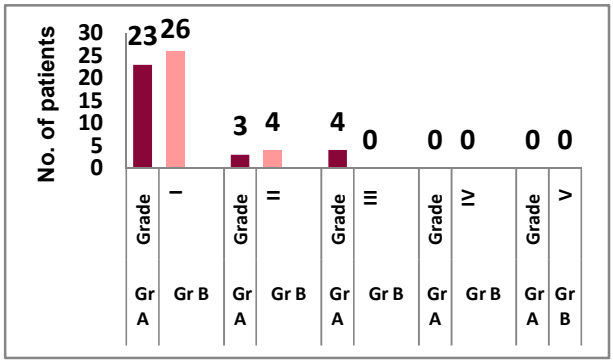
Table 23 – showing gradation of nausea in oral cancer patients treated with radiotherapy

Time points	Group A	Group B	Group A	Group B	Group A	Group B	Group A	Group B	Group A	Group B
	Grade I		Grade II		Grade III		Grade IV		Garde V	
Immediate After RT	27	20	1	10	2	0	0	0	0	0
After 1 month of RT	23	26	3	4	4	0	0	0	0	0
After 3 month of RT	27	28	2	2	1	0	0	0	0	0

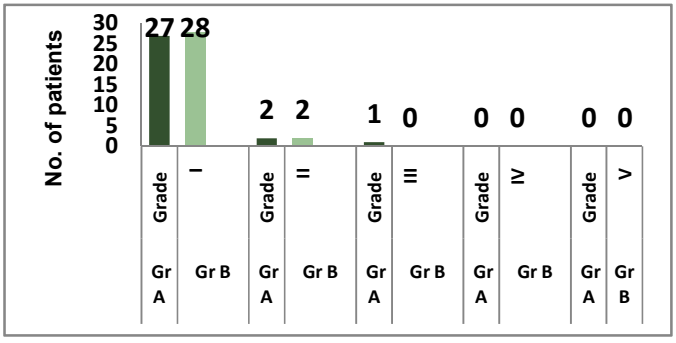
Graph 14A – Graphical representation of gradation of nausea in oral cancer patients treated with radiotherapy



Immediately after RT



After 1 month of RT



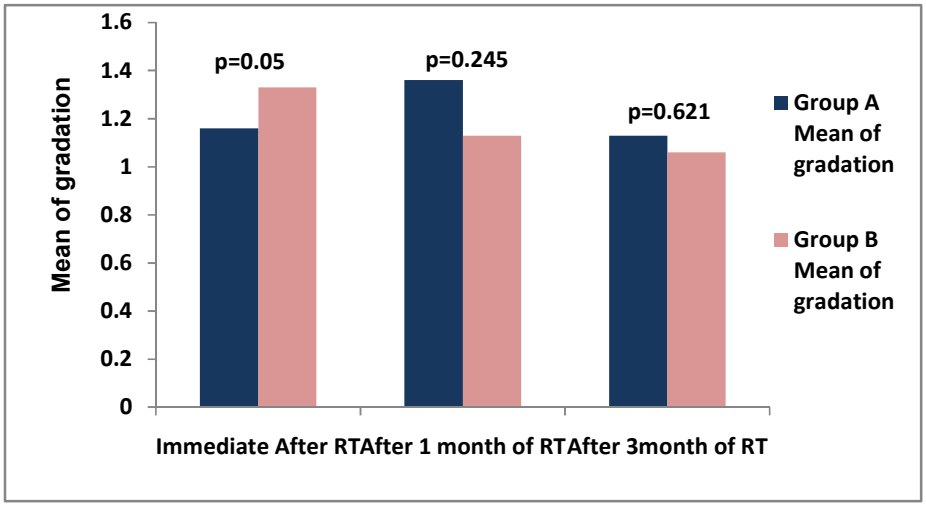
After 3 months of RT

There was no difference in nausea is observed in results of both the groups immediately after RT, after 1 month of RT and after 3 months of RT. 27 and 20 patients respectively did not suffered from nausea in group A and group B after completion of RT. This picture remains same when observed till 3 months of RT.

Statistical Table 7 - showing statistical analysis of gradation of nausea in oral cancer patients treated with radiotherapy

Nausea	Group A Gradation score			Group B Gradation score			Mann-Whitney Z	P
	Median	Mean	Sd	Median	Mean	Sd		
Immediate After RT	1.0	1.17	0.531	1.0	1.33	0.479	1.960	0.05 **NS**
After 1 month of RT	1.0	1.37	0.718	1.0	1.13	0.346	1.163	0.245 **NS**
After 3 month of RT	1.0	1.13	0.434	1.0	1.07	0.254	0.494	0.621 **NS**

Graph 14B – Graphical representation statistical analysis of gradation of nausea in oral cancer patients treated with radiotherapy

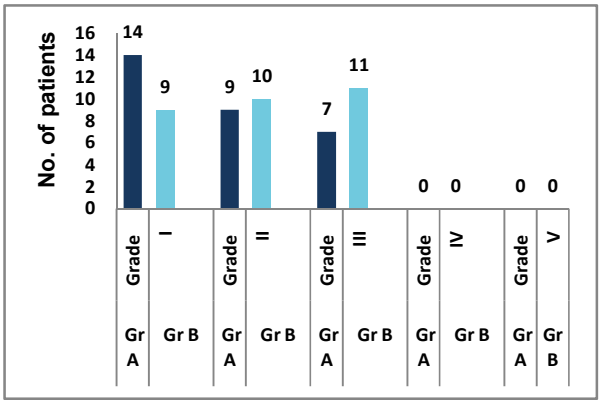


Statistically no difference was found at any time point.

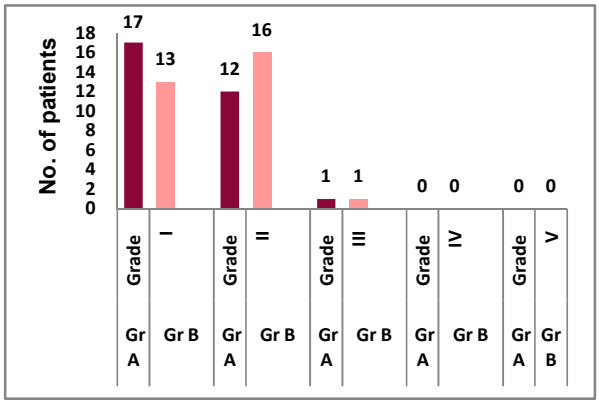
Table 24 – showing gradation of percentage of weight loss in oral cancer patients treated with radiotherapy

Time points	Number of patients									
	Group A	Group B	Group A	Group B	Group A	Group B	Group A	Group B	Group A	Group B
	Grade I		Grade II		Grade III		Grade IV		Grade V	
Immediate After RT	14	9	9	10	7	11	0	0	0	0
After 1 month of RT	17	13	12	16	1	1	0	0	0	0
After 3 month of RT	29	28	1	2	0	0	0	0	0	0

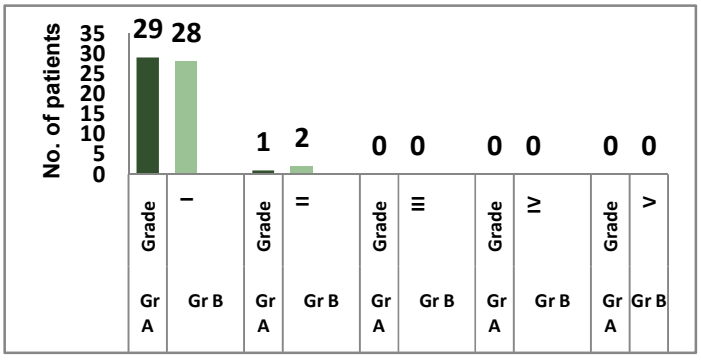
Graph 15A– Graphical representation gradation of percentage of weight loss in oral cancer patients treated with radiotherapy



Immediately after RT



After 1 month of RT



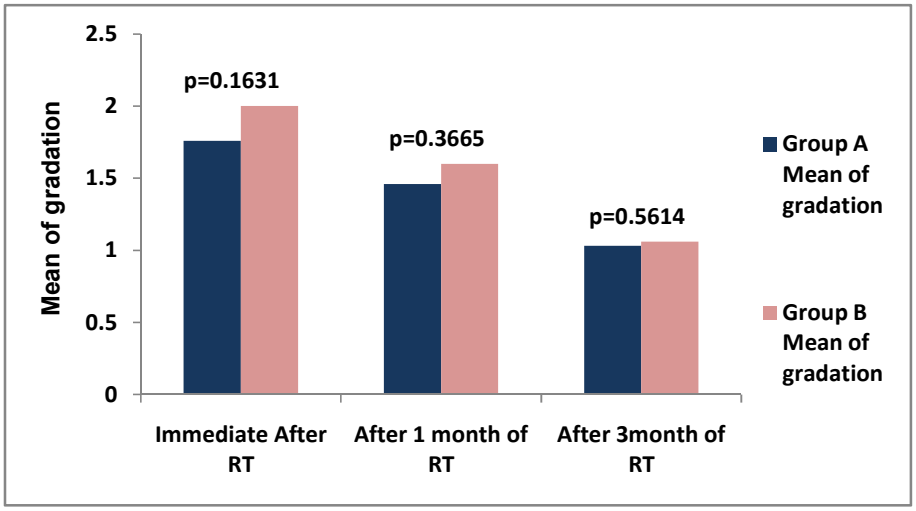
After 3 months RT

There was not much difference noted in weight loss when observed in both the groups immediately after RT, after 1 month of RT and after 3 months of RT. 29 and 28 patients of group A and group B respectively had grade I percentage of weight loss .

Statistical Table 8 - showing statistical analysis of gradation of percentage of weight loss in oral cancer patients treated with radiotherapy

Weight Loss	Group A % weight Loss		Group B % weight Loss		Unpaired t	P
	Mean	Sd	Mean	Sd		
Immediate After RT	1.76	0.81	2.0	0.82	1.413	0.163 **NS**
After 1 month of RT	1.46	0.57	1.6	0.56	0.910	0.366 **NS**
After 3 month of RT	1.03	0.18	1.06	0.25	0.584	0.561 **NS**

Graph 15B– Graphical representation of statistical analysis of gradation of percentage of weight loss in oral cancer patients treated with radiotherapy



Statistically no difference was found in any group at any time point.

III) Observation of karnofsky score

Table 25A – showing change of karnofsky score in oral cancer patients treated with radiotherapy

	Number of patients					
	Group A			Group B		
	Immediate after RT	1 Month after RT	3 Months after RT	Immediate after RT	1 Month after RT	3 Months after RT
Karnofsky Score Improved	6	13	17	0	2	0
No change in Karnofsky Score	23	9	5	9	10	10
Karnofsky Score Not Improved	1	8	8	21	18	18

Graph 16A – Graphical representation of change of karnofsky score in oral cancer patients treated with radiotherapy

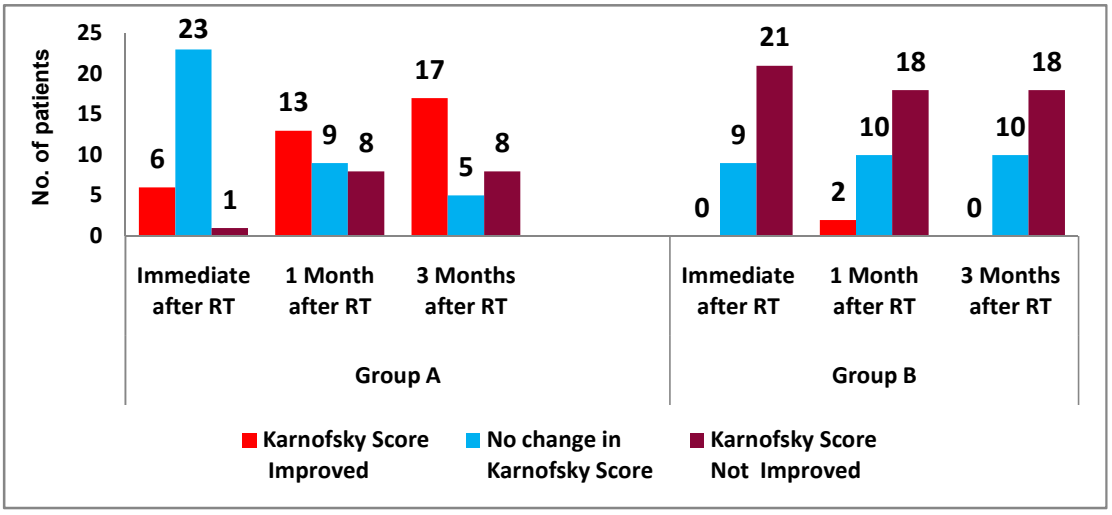
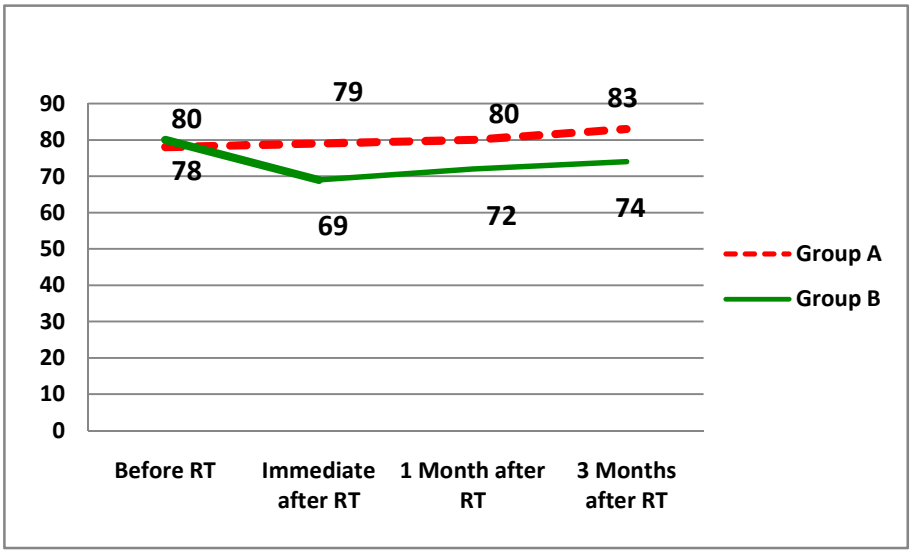


Table 25B – showing mean values depicting karnofsky score in oral cancer patients treated with radiotherapy

Sr. No	Time points	Group A Mean	Group B Mean
1	Before RT	78	80
2	Immediate After RT	79	69
3	After 1 month of RT	80	72
4	After 3 month of RT	83	74

Graph 16B – Graphical representation of mean values depicting karnofsky score in oral cancer patients under radiotherapy



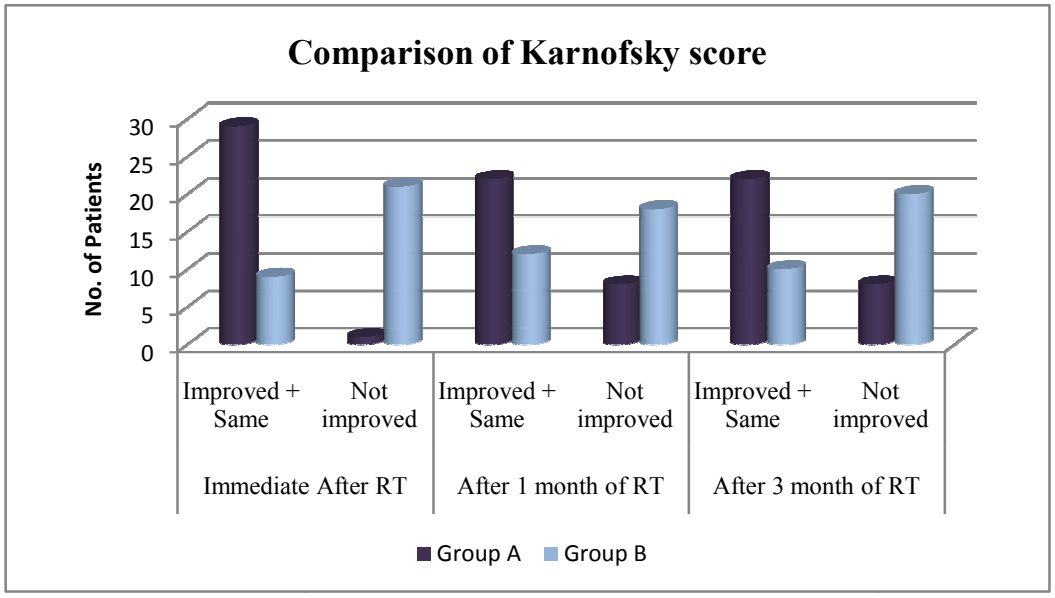
In group A (Study) Karnofsky score was maintained in 23 patients immediately after RT. In 9 patients; 1 month after RT and in 5 patients, 3 months after completing RT. While in control group it was maintained in 9 patients immediately after RT and in 10 patients each after 1 month and after 3 months of completing RT.

When mean values of Functional score were considered, as seen from data in the group A, there was a reduction in karnofsky score from 80 to 79 immediately after RT and then improvement (79 - 80 – 83) was noted after one month and 3 month. On the other hand in group B marked reduction was noted in karnofsky score (78-69) immediately after RT while after that minimum improvement was observed (69-72-74) at one month after RT and three months after RT time points respectively.

Statistical Table 9- showing statistical analysis of stsatus of karnofsky score in oral cancer patients under radiotherapy

Karnofsky score	Group A Karnofsky score		Group B Karnofsky score		Chi square (df=1)	P
	Improved + Maintained	Not improved	Improved + Maintained	Not improved		
Immediate After RT	6+23=29	1	0+9=9	21	25.909	<0.001 **HS**
After 1 month of RT	13+9=22	8	2+10=12	18	5.498	0.019 **Sig**
After 3 month of RT	17+5=22	8	0+10=10	20	8.103	0.004 **Sig**

Graph 16C – Graphical representation of statistical analysis of status of karnofsky score in oral cancer patients under radiotherapy



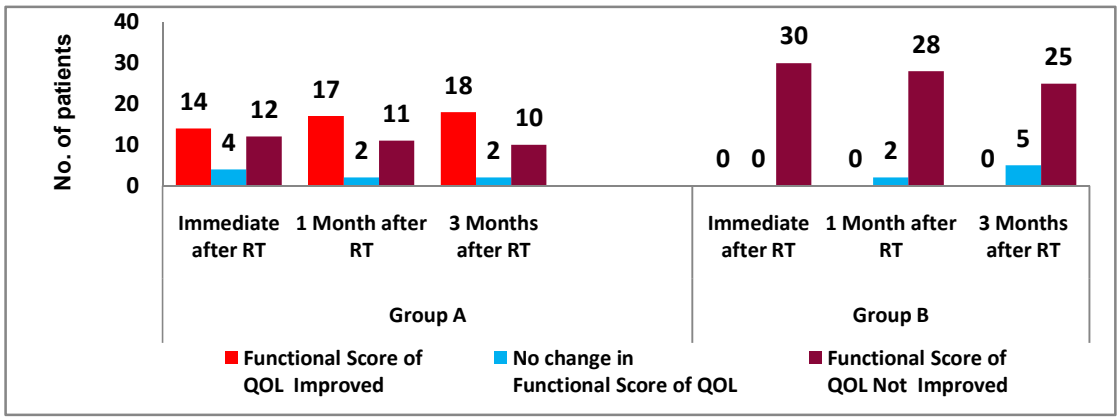
Statistically significant difference was noted in karnofsky score with ($p < 0.001$) at end of RT, ($p=0.019$) at one month of RT and ($p=0.0004$) at 3 months after finishing RT.

IV) Observations of QLQ scores-

Table 26A – showing change in Functional score of quality of life in oral cancer patients under Radiotherapy

	Number of patients					
	Group A			Group B		
	Immediate after RT	1 Month after RT	3 Months after RT	Immediate after RT	1 Month after RT	3 Months after RT
Functional Score of QLQ Improved	14	17	18	0	0	0
No change in Functional Score of QLQ	4	2	2	0	2	5
Functional Score of QLQ Not Improved	12	11	10	30	28	25

Graph 17A – Graphical representation of change in Functional score of quality of life in oral cancer patients under Radiotherapy

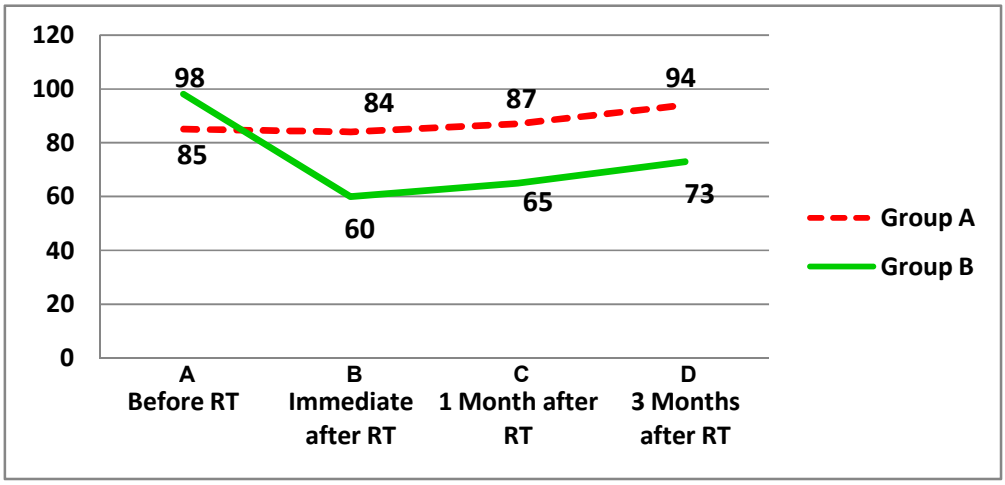


Functional score of QLQ was maintained and improved in more than half patients of group A (18, 19, and 20 respectively), while almost all the patients of group B showed hampered functional score of QLQ (30, 28, 25) respectively.

Table 26B – showing mean values depicting Functional score of QLQ in oral cancer patients under Radiotherapy

Sr. No	Time points	Group A Mean	Group B Mean
1	Before RT	85	98
2	Immediate After RT	84	60
3	After 1 month of RT	87	65
4	After 3 month of RT	94	73

Graph 17B – Graphical representation of mean values depicting Functional score of QLQ under Radiotherapy



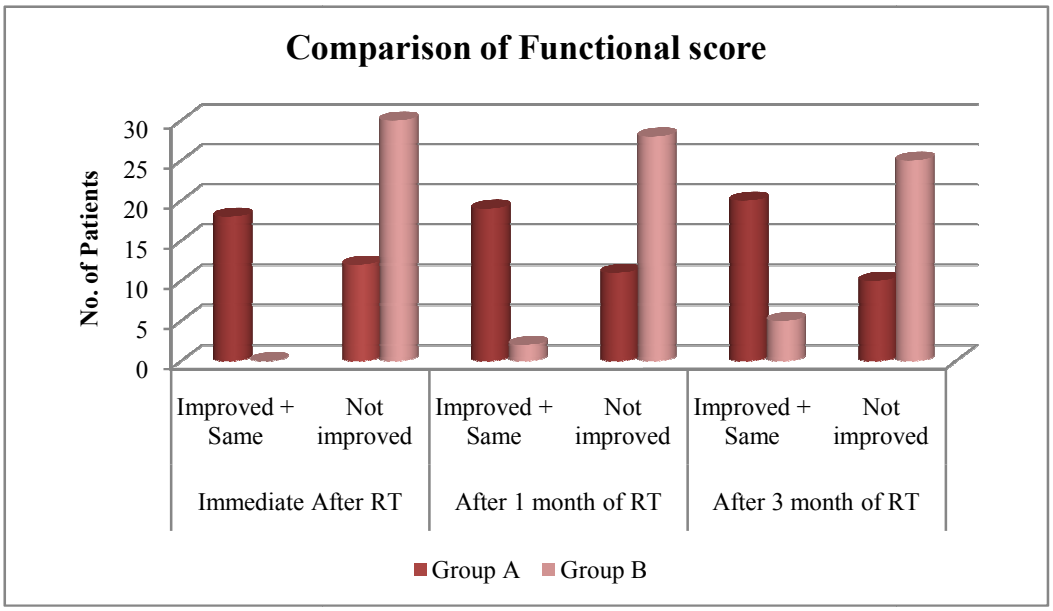
When mean values of Functional score were considered, Study has shown that group A patients had maintenance in the functional score of QLQ (85-84) when observed at end of RT. Improvement in functional score was noted then after (84-87-94) at one month after RT and three months after RT respectively in group A

In group B marked reduction in functional score was noted at the end of RT (98-60). Which was then maintained till 3 months of RT (60-65-73).

Statistical Table 10- showing statistical analysis of status of Functional score of QLQ in oral cancer patients under Radiotherapy

Functional Score	Group A Functional score		Group B Functional score		Chi square (df=1)	P
	Improved + Same	Not improved	Improved + Same	Not improved		
Immediate After RT	14+4=18	12	0	30	22.937	<0.001 **HS**
After 1 month of RT	17+2=19	11	0+2=2	28	18.755	<0.001 **HS**
After 3 month of RT	18+2=20	10	0+5=5	25	13.440	<0.001 **HS**

Graph 17C – Graphical representation statistical analysis Functional score of QLQ in oral cancer patients under Radiotherapy

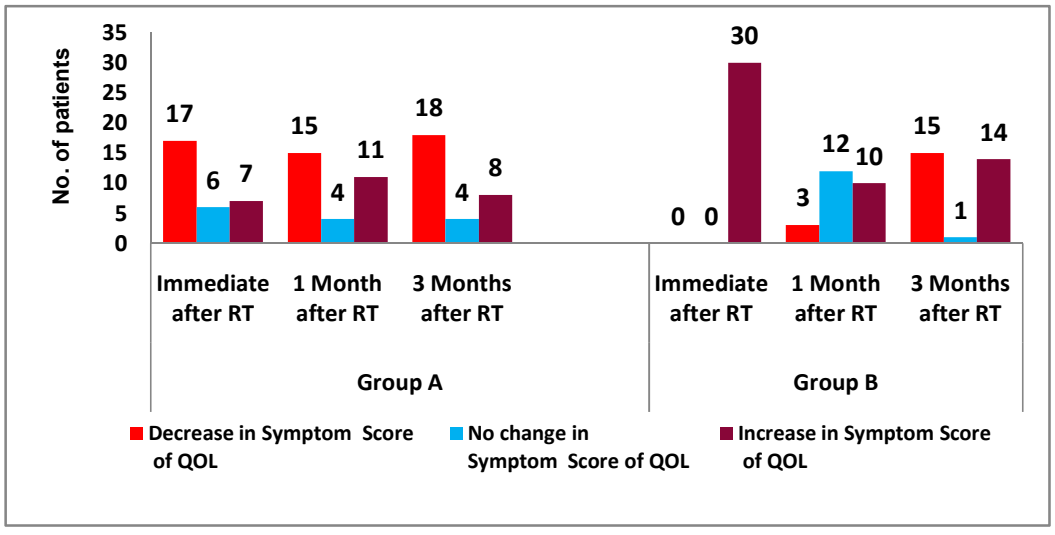


Statistically extremely significant observations were noted at all three time points with $p<0.0001$.

Table 27A – showing change in symptom score of quality of life in oral cancer patients under radiotherapy

	Number of patients					
	Group A			Group B		
	Immediate after RT	1 Month after RT	3 Months after RT	Immediate after RT	1 Month after RT	3 Months after RT
Decrease in Symptom Score of QLQ	17	15	18	0	3	15
No change in Symptom Score of QLQ	6	4	4	0	12	1
Increase in Symptom Score of QLQ	7	11	8	30	10	14

Graph 18A – Graphical representation of change in symptom score of quality of life in oral cancer patients under radiotherapy

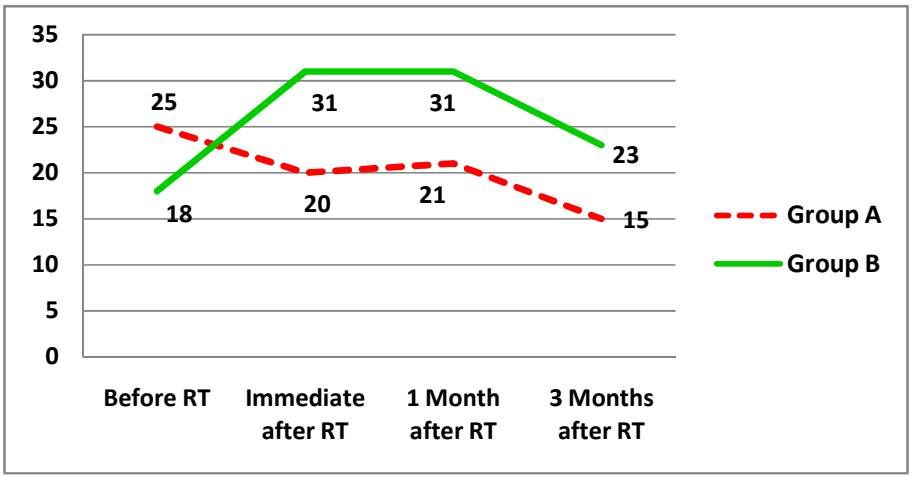


Symptom score of QLQ was maintained and improved in more than half patients of group A (17, 15, and 18 respectively), while all the pts of group B showed raisedsymptoml score of QLQ in 30 patients immediately after RT.

Table 27B – showing mean values depicting symptom score of QLQ in oral cancer patients under radiotherapy

Sr. No	Time points	Group A Mean	Group B Mean
1	Before RT	25	18
2	Immediate After RT	20	31
3	After 1 month of RT	21	31
4	After 3 month of RT	15	23

Graph 18B – Graphical representation of mean values depicting symptom score of QLQ in oral cancer patients under radiotherapy



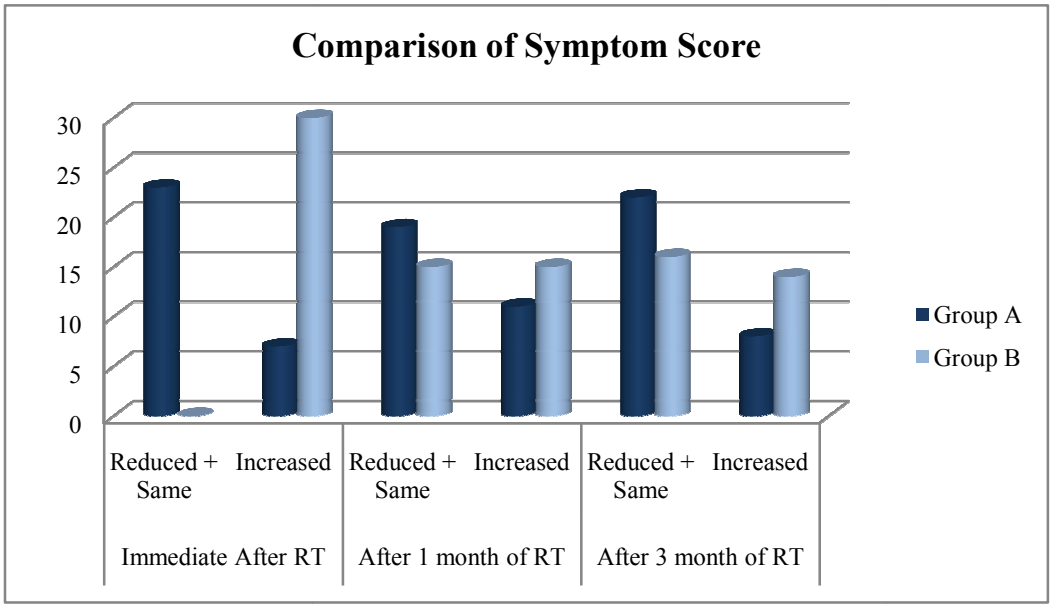
Group A patients had not much difference in the symptom score of QLQ when mean values are calculated (25-20-21-15) respectively at end of RT, at one month after RT and three months after RT.

In group B marked increase in symptoms score is noted (18-31) at the end of RT which remains as it is still one month after RT and then decreased to 23.

Statistical Table 11- showing statistical analysis of symptom score of QLQ in oral cancer patients under radiotherapy

Symptom score	Group A Symptom score		Group B Symptom score		Chi square (df=1)	P
	Reduced + Same	Increased	Reduced + Same	Increased		
Immediate After RT	17+6=23	7	0	30	34.125	<0.001 **HS**
After 1 month of RT	15+4=19	11	3+12=15	15	0.611	0.434 **NS**
After 3 month of RT	18+4=22	8	15+1=16	14	1.794	0.180 **NS**

Graph 18C – Graphical representation statistical analysis symptom score of QLQ in oral cancer patients under Radiotherapy

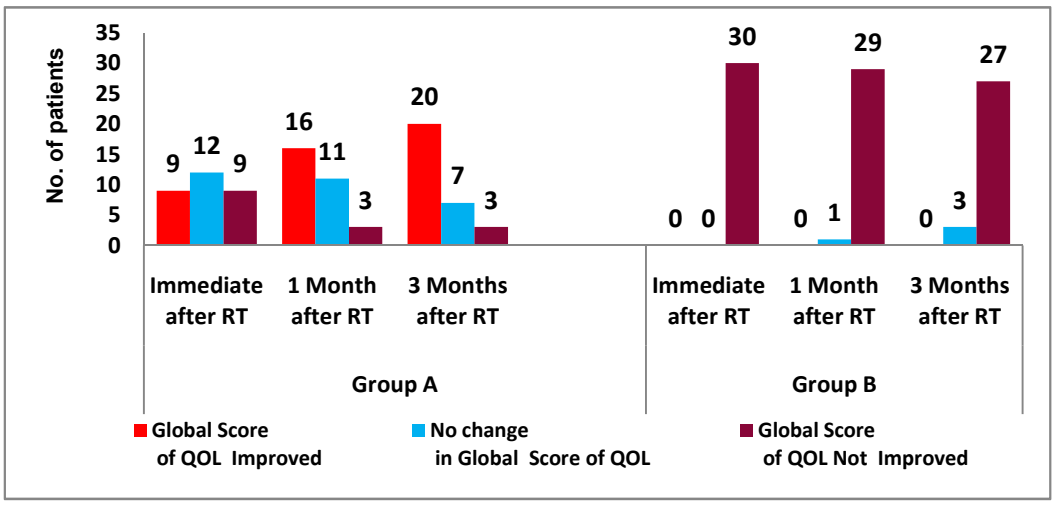


Statistically significant observation were noted immediately after RT (p<0.001)

Table 28A – showing change in Global score of quality of life in oral cancer patients under radiotherapy

	Number of patients					
	Group A			Group B		
	Immediate after RT	1 Month after RT	3 Months after RT	Immediate after RT	1 Month after RT	3 Months after RT
Global Score of QLQ Improved	9	16	20	0	0	0
No change in Global Score of QLQ	12	11	7	0	1	3
Global Score of QLQ Not Improved	9	3	3	30	29	27

Graph 19A – Graphical representation of change in Global score of quality of life in oral cancer patients under radiotherapy

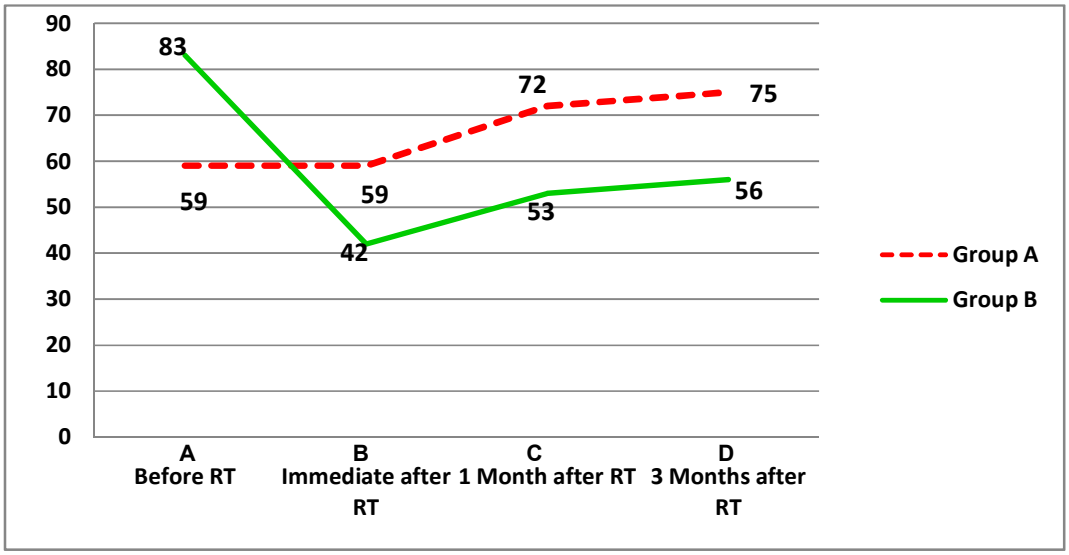


Global score of QLQ was maintained and improved in patients of group A (21, 27, and 27 respectively), while all the pts of group B showed hampered global score of QLQ in all patients immediately after RT till three months of RT.

Table 28B – showing mean values depicting Global score of QLQ in oral cancer patients under radiotherapy

Sr. No	Time points	Group A Mean	Group B Mean
1	Before RT	59	83
2	Immediate After RT	59	42
3	After 1 month of RT	72	53
4	After 3 month of RT	75	56

Graph 19B – Graphical representation of mean values depicting Global score of QLQ in oral cancer patients under radiotherapy



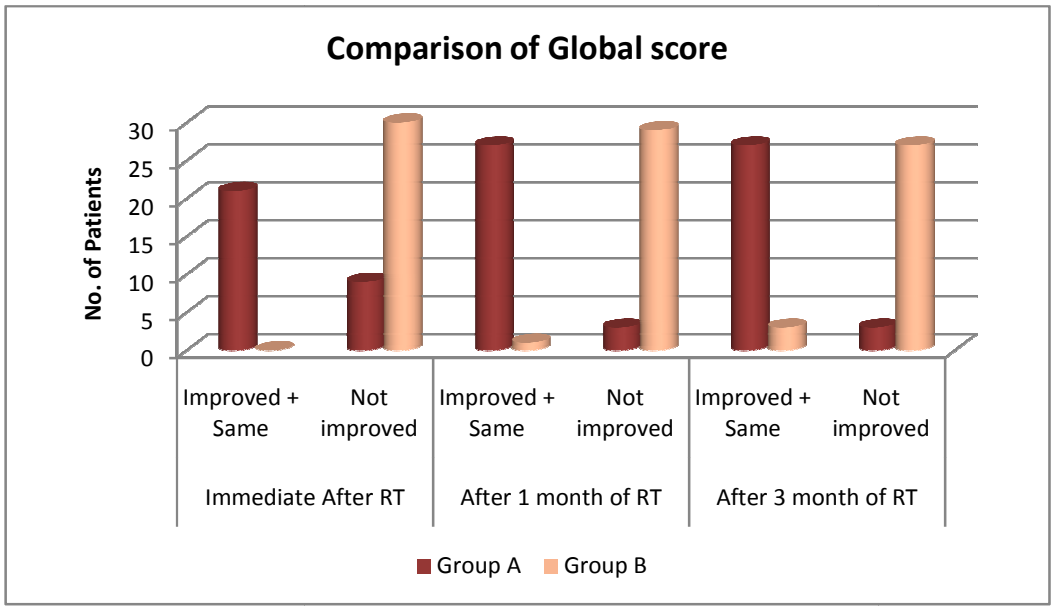
Group A patients had global score of QLQ was on 59 when observed at end of RT. Improvement in global score thereafter is noted (59-72-75) at one month after RT and three months after RT respectively in group A.

In group B marked reduction in global score was noted at the end of RT (82-42) which was then improved (42-53-56) till three months after RT.

Statistical Table 12- showing statistical analysis Global score of QLQ in oral cancer patients under radiotherapy

Global score	Group A Global score		Group B Global score		Chi square (df=1)	P
	Improved + Same	Not improved	Improved + Same	Not improved		
Immediate After RT	9+12=21	9	0	30	29.304	<0.001 **HS**
After 1 month of RT	16+11=27	3	0+1=1	29	41.853	<0.001 **HS**
After 3 month of RT	20+7=27	3	0+3=3	27	35.267	<0.001 **HS**

Graph 19C -Graphical representation statistical analysis Global score of QLQ in oral cancer patients under Radiotherapy

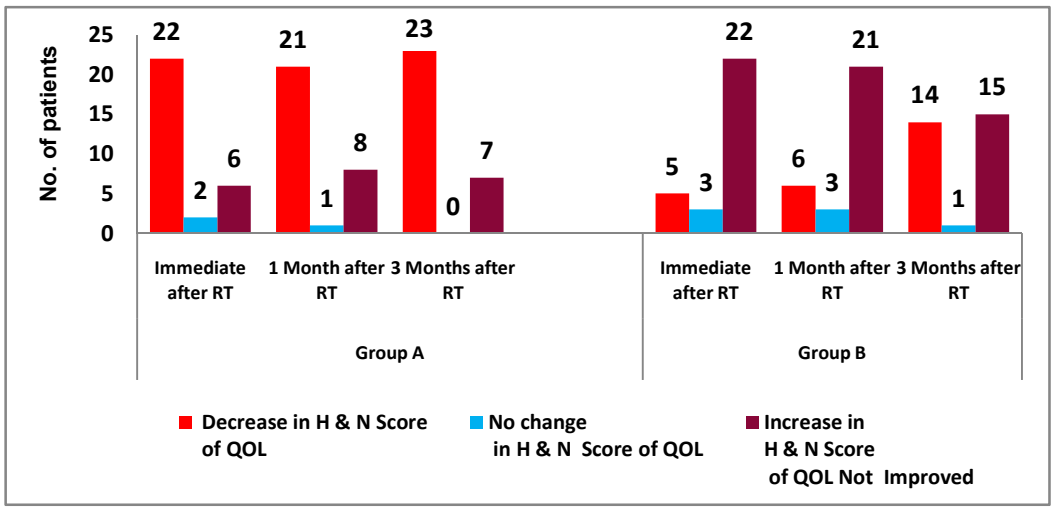


Statistically extremely significant observations were noted at all three time points with p<0.0001.

Table 29A – showing change in H & N symptom score of quality of life in oral cancer patients under Radiotherapy

	Number of patients					
	Group A			Group B		
	Immediate after RT	1 Month after RT	3 Months after RT	Immediate after RT	1 Month after RT	3 Months after RT
Decrease in H & N Score of QLQ	22	21	23	5	6	14
No change in H & N Score of QLQ	2	1	0	3	3	1
Increase in H & N Score of QLQ	6	8	7	22	21	15

Graph 20A – Graphical representation of change in H & N symptom score of quality of life in oral cancer patients under Radiotherapy

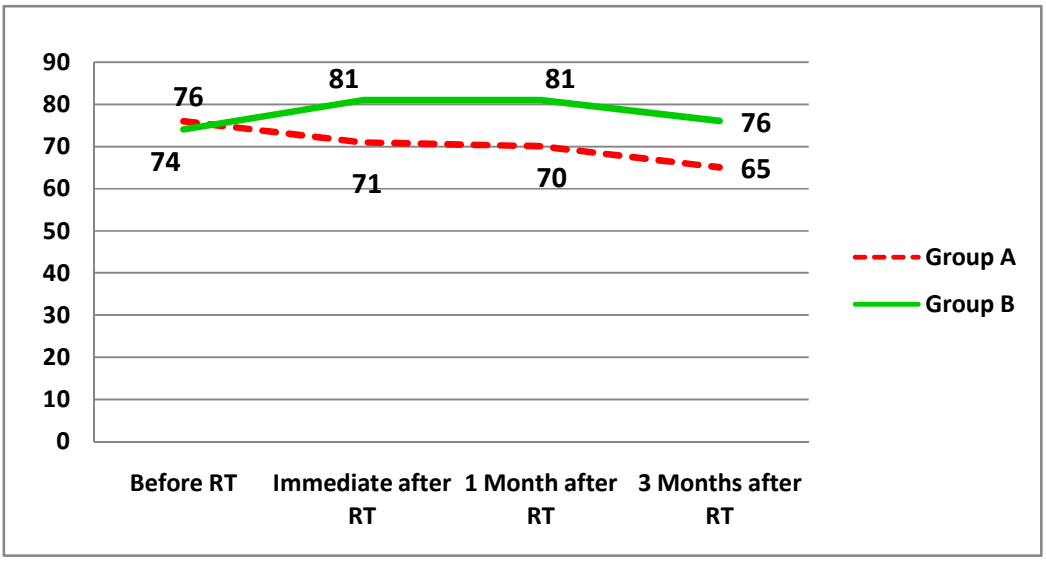


It is observed in H&N symptom score that Head and Neck cancer related symptoms score ie Head and neck related symptoms of 22 patients were improved in group A. While these symptoms are not improved in 22 patients in group B immediately after completing RT. Same patteren had been followed in 21 patients in each group.

Table 29B – showing mean values depicting H & N symptom score of QLQ in oral cancer patients under radiotherapy

Sr. No	Time points	Group A Mean	Group B Mean
1	Before RT	76	74
2	Immediate After RT	71	81
3	After 1 month of RT	70	81
4	After 3 month of RT	65	76

Graph 20B – Graphical representation of mean values depicting H & N symptom score of QLQ in oral cancer patients under radiotherapy



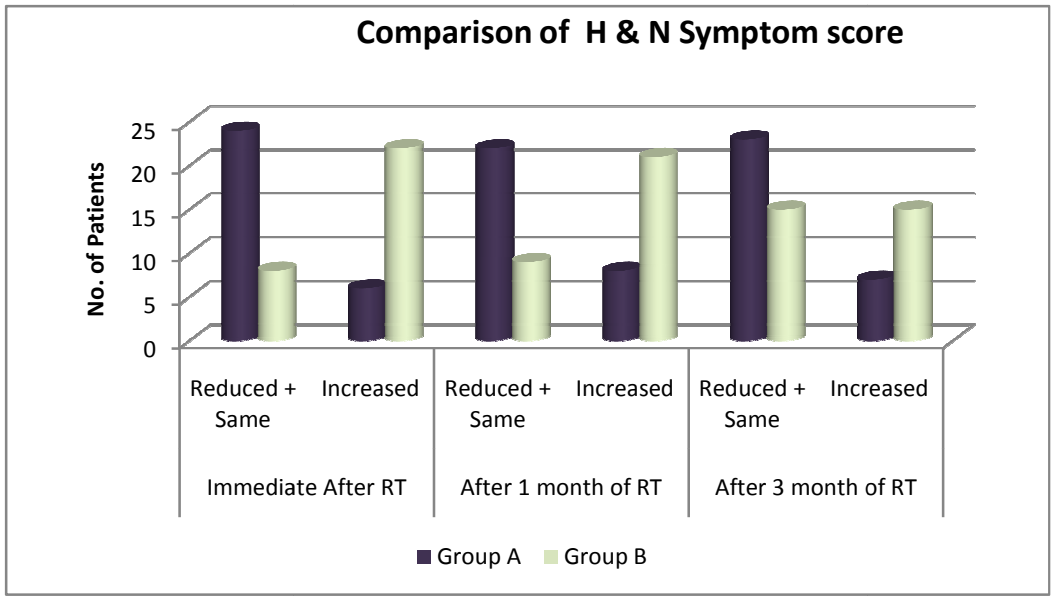
In group A patients, Head and Neck symptom score of QLQ decreased (76-71-70-65) respectively at end of RT, one month after RT and three months after RT.

In group B marked increase is noted in Head and Neck symptom score of QLQ at the end of RT (74-81) which was then decreased to 76 after three months of RT.

Statistical Table 13 - showing statistical analysis Head and Neck symptom score of QLQ in oral cancer patients under radiotherapy

H & N Symptom score	Group A H & N Symptom score		Group B H & N Symptom score		Chi square (df=1)	P
	Reduced + Same	Increased	Reduced + Same	Increased		
Immediate After RT	22+2=24	6	5+3=8	22	15.067	<0.001 **HS**
After 1 month of RT	21+1=22	8	6+3=9	21	9.611	0.002 **Sig**
After 3 month of RT	23+0=23	7	14+1=15	15	3.517	0.061 **NS**

Graph 20C -Graphical representation statistical analysis Head and Neck Symptom score of QLQ in oral cancer patients under Radiotherapy



Statistically extremely significant observations were noted at immediately after RT and 1 month after RT with p<0.0001, p=0.002 respectively.

Table 30 – Showing Summary of Statistical Analysis of symptoms and QLQ scores.

Sr. No		Immediate After RT (B)		After 1 month of RT (C)		After 3 month of RT (D)	
		P Value	Significance	p Value	Significance	p Value	Significance
1	**Stomatitis**	0.025	Significant	0.019	Significant	0.022	Significant
2	**Xerostomia**	< 0.001	Extremely Significant	0.002	Significant	0.001	Significant
3	**Loss of Taste**	0.018	Significant	0.639	Not Significant	0.690	Not Significant
4	**Excessive Salivation**	0.06	Not Significant	0.413	Not Significant	0.334	Not Significant
5	**Trismus**	< 0.001	Extremely Significant	0.003	Very Significant	0.001	Very Significant
6	**Dysphagia**	0.004	Very Significant	0.389	Not Significant	0.545	Not Significant
7	**Nausea**	0.05	Not Significant	0.245	Not Significant	0.0.621	Not Significant
8	**% of Weight Loss**	0.163	Not Significant	0.366	Not Significant	0.561	Not Significant
9	**Karnofsky score**	< 0.0001	Extremely Significant	0.0019	Very Significant	0.0004	Extremely Significant
10	**Functional Score of QLQ**	< 0.0001	Extremely Significant	< 0.0001	Extremely Significant	< 0.0001	Extremely Significant
11	**Symptom score of QLQ**	< 0.0001	Extremely Significant	0.434	not quite significant	0.180	not quite significant
12	**Global Score of QLQ**	< 0.0001	Extremely Significant	< 0.0001	Extremely Significant	< 0.0001	Extremely Significant
13	**Head and neck score of QLQ**	< 0.0001	Extremely Significant	0.002	Significant	0.061	Not Significant

DISCUSSION

I) Discussion on mode of action of combination of Ayurvedic medicines –

Patients from Group A received combination of oral Ayurvedic medicines (RG4) from the begning of radiotherapy and continued till 3 months after completion of Radiotherapy. RG4 protocol was consisting of Mouktikayukta Kamdudha[77], Mauktikyukta praval panchamrut[78], Ananta vati[79] and Yashtimadhu ghrut[80].

Mouktikayukta kamdudha is a herbomineral Ayurvedic medicine containing Guduchi (Tinospora cordifolia) sattva as a herbal content and mineral contents like Shankh bhasma (Conch shell), Shauktik bhasma (Pearl shell), Kapardika bhasma (Cowries), Praval bhasma (Coral), Maouktik bhasma (Mukta) and Gairik (Red Lumber Stone). Guduchi poseses Tikta Kashay Ras and Madhur Vipak. It had Rasayan, Agni deepan, Balya, Dahshamaka, Jwaraghna and Raktashodhak action. It pacifies three Doshas. Guduchi sattava which is the starch based preparation of Guduchi has additional cooling effect. All these properties of Guduchi are beneficial in Pitta dominant, Raktadushtikar and Agnimandya induced side effects of radiotherapy. Its Rasayan action is also beneficial in suppressed immune status in these patients. Gairik posseses Pittashamk properties due to Madhur ras, Madhur vipak and Sheeta Virya. Additionally it has Vishanashak property. Thus it minimizes pitta dominant side effects of radiotherapy like stomatitis, xerostomia etc in oral cavity cancer patients and eliminates toxins accumulated in the process of disease development and radiotherapy. Praval posseses Madhur, Amla, Kashay ras, Madhur Vipak and Sheet Virya. It is Pitta Kapha nashak and posseses Rasayan, Jwarhar, Raktapittanashak and Vishghna action which is beneficial in radiotherapy induced toxicities like stomatitis, xerostomia, excessive salivation, loss of taste and boosting up immunity.

77. Sharma HP Rasa Yoga Sagar Part -1, KrishnadasAyurved Series, pp 260
78. Sharma HP Rasa Yoga Sagar Part -2, KrishnadasAyurved Series, pp 93.
79. Bhavprakash Nighantu by Bhavmishra with Vidyodini Hindi Commentary by Shree Bramha Shankar Mishra and Shree Ruplalji Vaishya, Chaukhamba Sanskrit Samsthan, (2002), 10th Eddition, Nighantu Bhag,pp 65
80. Bhavprakash Nighantu by Bhavmishra with Vidyodini Hindi Commentary by Shree Bramha Shankar Mishra and Shree Ruplalji Vaishya, Chaukhamba Sanskrit Samsthan, (2002), 10th Eddition, Nighantu Bhag,pp 426

Being raktaprasadak it also helps in maintaining hemoglobin levels during the course of radiotherapy. Mouktik bhasma possese Madhur Kashay ras, Madhur Vipak, and Sheet Virya. By these virtues it is Tridoshshamak, Dahanashak and Balya. Radiotherapy induced stomatitis, xerostomia and loss of weight are thus well controlled by administration of Mouktik Bhasma. Combination of Shankh bhasma, Shauktika bhasma and Kaprdika Bhasma is mainly Pachak and Tridoshshamak. Thus it alleviates aruchi and chhardi by improving digestion. Nausea and loss of taste developed during course of radiotherapy is well controlled with this combination. The mineral products of this combination namely Praval, Shankha, Shauktika and Kapardika are mainly aquatic in nature and thus posses Jal mabhut dominance. Most of the contents of this combination are Prithvi and Jala Mahabhuta dominant, thus they reduce the heat (Ushna Guna) in the body. A mineral in the form of Gairik is Prithvi Mahabhut dominant. Hence this combination is beneficial in Tej Mahabhut dominant side effects of radiotherapy according to Vishesh Siddhant [84].

Mouktikayukta praval panchamrut is a combination of Shankh bhasma (Conch shell), Shauktik bhasma (Pearl shell), Kapardika bhasma (Cowries), Praval bhasma (Coral), and Mouktik bhasma (Mukta). Mode of action of these minerals in radiotherapy side effect is already discussed. Praval Panchamrut can be preperaed by triturating it either with Arkakshira or godugdha. As we were expecting cooling effect and pittashamka activity in this study, we had prepared Praval Panchamrut with triturating with Godugdha.

Ananta possese Tikta, Madhur ras, Madhur vipak and Sheet virya due to which it has Pittashamka, Raktprasadak and Dahsghamka properties. It is Tridoshashamak and Visghghna. These properties of ananta are beneficial in Pitta Raktadushtikar side effects of radiotherapy like stomatitis and xerostomia. Due to its Visghghna property it detoxifies accumulated Pitta Rakta dominant doshas during the course of radiotherapy. It minimizes excessive heat in Raktadhatu during radiotherapy.

84. Charak Samhita, Vol.1, Tripathi B (2003) Chaukambha Subharati Prakashan, Varanasi, Sutrasthan 1/44-45,pp 15

Yashtimadhu has Madhur ras, Madhur vipak and Sheet virya. It is Guru and Snigdha in nature. It possesses Vat Pitta Shamak, Dah shamak, Kanthya, Varnya, Sandhaniya and Rasayan properties. Yashtimadhu is used in this study in the form of Sidhha Ghrut which enhances its properties and exhibits soothing effect. In view of these properties Yashtimadhu ghrut is beneficial in minimizing stomatitis, xerostomia and trismus when administered orally as well as used as a local application internally in oral cavity. In these forms Yashtimadhu Ghrut heals mouth ulcers, softens facial muscles which become rigid during course of radiotherapy and imparts soothing effect on throat.

II) Discussion on observations, results and statistical analysis

Discussion on Demographic data and its role in oral cancer patients undergoing radiotherapy.-

Management of radiation induced side effects described above is a perpetual problem in giving radiotherapy in oral cancers. The allopathic modalities of management of side effects are rather peripheral, which include nutritional support, pain control, oral decontamination, palliation of dry mouth, control of bleeding, and cryotherapy. Attempts are also being made to treat patients with keratinocyte growth factor and anti-inflammatory agents[85].

However, the fact remains that there is no definitive medicine to treat side effects of radiation especially in oral cancer. In this respect, the study conducted and data presented here is very useful. The drugs used are non-toxic, easily palatable and not very expensive, and the effect appears to be quite significant. The study was carried out in 2 groups. Group A was study group of 30 patients who have received Ayurvedic treatment (RG4) during RT and thereafter for three months. Group B was the control group of 30 patients who had received radiotherapy as described earlier.

85. Clinical practice guidelines for the prevention and treatment of cancer therapy–induced oral and gastrointestinal mucositis† (2004), Edward B. Rubenstein ,Douglas E. Peterson , Mark Schubert , Dorothy Keefe , Deborah McGuire R.N., Joel Epstein , Linda S. Elting , Philip C. Fox , Catherine Cooksley , Stephen T. Sonis . Cancer Volume 100, Issue S9, pp 2026–2046 http://onlinelibrary.wiley.com/doi/10.1002/cncr.20163/full

Patients diagnosed with oral cavity cancers and underwent radiotherapy are mostly in-between age of 41 – 60 yrs. in both the groups. Male patients are more than female patients (twice in numbers). More than 80 % patients of oral cancer underwent radiotherapy were in lower socioeconomical group. These observations are due to the fact that middle aged males in lower socioeconomical class are more addicted to tobacco in various forms. Though tobacco consumption is also common in middle and upper socio-economical class the percentage of development of oral cavity cancer is comparatively low due to awareness about screening facilities and maintaining oral hyegine.

Tobacco is main concern while considering risk factors in oral cancers. More than 80 percent of patients in both the groups are addicted to either smokeless or smoked tobacco in one or other form. It is found that tobacco when consumed with alcohol can increase the risk of cancer of the oral cavity and their combined use has a multiplicative effect on risk**.** Moreover, those regions of the mouth which are more directly exposed to alcohol or tobacco are more likely to be affected by cancer than other regions. For squamous cell carcinomas alcohol and tobacco also appear to increase risk synergistically.

In our study patients who underwent surgery before radiotherapy are more than those who are directly subjected to radiotherapy depending upon the stage of the disease and age of the patient.

Equal distribution of patients was found in both the groups, treated with or without adjunct chemotherapy. The general impression in practice is that toxicity is enhanced by the use of concurrent chemotherapy. But it should be noted that addition of chemotherapy to radiotherapy has significantly increased the morbidity of treatment as well as the chance of initial tumour response and local control. A statistically significant improvement in survival was found for the simultaneous use of chemotherapy and radiotherapy as per study done by Jay S. Cooper, Thomas F. Pajak, Arlene A. Forastiere etal on postoperative concurrent radiotherapy and chemotherapy for high-risk squamous-cell carcinoma of the head and neck [86]**.**

86. Postoperative Concurrent Radiotherapy and Chemotherapy for High-Risk Squamous-Cell Carcinoma of the Head and Neck,(2004) Jay S. Cooper, Thomas F. Pajak, Arlene A. Forastiere, John Jacobs, Bruce H. Campbell, Scott B. Saxman, Julie A. Kish, Harold E. Kim, Anthony J. Cmelak, Marvin Rotman, Mitchell Machtay, John F. Ensley, K.S. Clifford Chao, Christopher J. Schultz, Nancy Lee, and Karen K. Fu, N Engl J Med; 350, pp1937-1944.

Discussion on adverse effects of radiotherapy in oral cancer patients undergoing radiotherapy -

Stomatitis (Mukhapak) is a significant side effect of radiotherapy when given in oral cavity cancers. Radiotherapy hampers function of bodhak kapha which is present in oral cavity. It produces pitta and rakta dushti and thus induces mukhapaka.

It can be seen that in Group A (Study group) 15 patients had Grade I and II stomatitis immediately at the end of RT while 20 patients from group B (Control group) had grade III and IV stomatitis. It implies grade III and IV reactions were evident in control group patients while I and II reactions were seen in patients treated with adjunct Ayurvedic treatment. This observation statistically supported with significant p value ie p=0.025.

11 patients from group A were free of stomatitis while 2 patients from group B were free of stomatitis when assessed after 1 month of RT. At this time point 17 patients from group B and 12 patients from group A had grade II stomatitis. As radiotherapy side effects like stomatitis are remarkably reduced after completing radiotherapy grade III and IV stomatitis was persistent in very few patients as compared to grade I and II stomatitis. P value of stomatitis after 1 month of RT is also significant ie p= 0.019.

It is a common observation that severity of stomatitis is markedly reduced when observed after 3 months of RT. Our study also followed the same pattern. Thus very few patients suffered from grade III and IV stomatitis at this time point. When stomatitis was assessed 3 months after completing RT, 15 patients from group A were free of stomatitis while 6 patients from group B did not have stomatitis. At this time point 18 patients from group B and 12 patients from group A had grade II stomatitis. P value is also significant at this time point ie p= 0.022.

These observations established the efficacy of Ayurvedic treatment in management of stomatitis (Mukhapaka) which is caused due to pittavrudhi and Raktadushti as a consequence of radiotherapy.

Xerostomia meaning dryness of mouth due to reduced salivation is another common ill-effect of radiotherapy. Bodhak Kapha whose site is Mukha (oral cavity), is responsible

for salivation and thus keeping oral cavity moist. Radiotherapy which produces ushna guna, causes Bodhaka Kapha and Pitta dushti leading to dryness of mouth i.e. xerostomia.

In our study, 25 patients who were treated with adjunct Ayurvedic treatment and 8 patients who were treated with RT alone, did not develop xerostomia immediately after completing RT. On the other hand, 19 patients from control group developed grade IV xerostomia and only 1 patient from study group developed grade IV xerostomia at the end of RT. p value at this time point is thus extremely significant ($p<0.001$) indicating effectiveness of selected Ayurvedic medicines in minimizing ushna guna, pacifying bodhaka kapha and pitta dushti and thus subsiding xerostomia.

Xerostomia is usually a late side-effect of radiotherapy which continues years together after completing RT. In our study when patients were assessed till 3 months, it is observed that number of patients suffering from grade II and III xerostomia were significantly more after 3 months as compared to 1 month in control group. But this difference was not significant in study group, indicating efficacy of selected Ayurvedic medicines in alleviating xerostomia. This observation is also supported by highly significant p value ($p=0.002$), one month after completing RT and significant (0.001), three months after completing RT.

Radiotherapy induced loss of taste in oral cavity cancers is developed due to inactivity of taste buds as per modern medicine. According to Ayurvedic principles, Bodhaka Bapha, whose site is Jivha, is responsible for knowledge of tastes. Radiotherapy which hampers functions of bodhaka Kapha, causes loss of taste.

In our study, selected Ayurvedic medicines were not found to be effective in both groups. Perhaps it may be due to physiological irreversible changes in taste buds after radiotherapy.

Radiotherapy induced excessive salivation is caused due to Aashayapakarshagati of prakupita Vatadosha, which is vitiated due to excessive dryness produced during radiotherapy. Prakupita Vatadosha carries Kaphadosha at oral cavity, producing excessive salivation.

In our study, 28 patients from study group did not develop excessive salivation while 23 patients from control group did not suffer from excessive salivation, immediately after completing RT. At the same time grade III excessive salivation was developed in 4 patients in control group and none of the patients from study group developed grade III excessive salivation.

Radiotherapy induced trismus is developed due to aggravated ruksha and laghuguna of Vatadosha during the course of radiotherapy.

Ayurvedic medicines, mainly Yashtimadhu ghruta (used for oral administration and local application) was effective in alleviating ruksha guna of vatadosha and subsequently maintaining softness of muscles of oral cavity. This process helps to prevent trismus.

This expected mode of action of Ayurvedic medicine was proved in our study. More than half of the patients in study group did not develop trismus at all 3 time points, while half of the patients from control group developed grade IV trismus immediately after completing RT. Statistically extremenly significant results were found at all three time points.

Radiotherapy induced dysphagia is mainly developed during the course of radiotherapy as a consequence of stomatitis. This symptom remains persistent, but with less severity, after completing RT due to xerostomia.

In our study, dysphagia was statistically very significant ($p= 0.004$) immediately after completing RT. This was due to the fact that stomatitis was well controlled by selected Ayurvedic medicines.

Nausea is a less common side-effect of radiotherapy in oral cavity cancers. It is developed mainly due to loss of taste and occasionally due to hampered digestion.

In our study, very few patients from both the groups develop nausea during and after radiotherapy and thus statistically it was not significant.

Weight loss is a frequently occurring side-effect of radiotherapy in oral cavity cancer patients due to inability to take food. It is developed due to stomatitis, trismus, xerostomia, dysphagia and nausea. This symptom is obvious during the course of radiotherapy, while remarkable weight gain is observed within few weeks after completing RT.

In our study weight loss was observed in nearly all patients in both the groups. Thus statistically it was not significant (p=0.16, 0.37 and 0.56) respectively at 3 time points.

Discussion on Karnofsky score and Scores of QoL -

In this study, we assessed the patient's response to treatment in terms of functional ability and global status with the help of QLQ of EORTC and karnofsky scores which are well - accepted methods of analysis of outcome measures.

Karnofsky score for performance status was recorded for assessment of general wellbeing and ability to conduct activities of daily life. The higher score of Karnofsky denotes better ability to carry on normal activity which was recorded in Oxford Textbook of Palliative Medicine[87]**.** As karnofsky score indicates feeling of wellbeing. It commonly shows decreasing trend during the course of RT. As per this trend karnofsky score of most of the patients in control group was not improved during the course of RT and 1 and 3 months after completing RT (21, 18, and 18 respectively). On the other hand karnofsky score was either maintained or improved immediately after RT in study group (23, 6 respectively). Same patteren of karnofsky score is observed when compared on 1 and 3 Months after completing of RT in this group. Our results showed increase in karnofsky score is maintained at the end of radiotherapy while it is steadily increasing after 1 month of RT and after 3 months of RT in group A, indicative of beneficial effects of adjunct oral Ayurvedic medicines. On the other hand, remarkable decrease in karnofsky score is noted in group B patients, during RT and 1 month after RT.

87. http://www.pennmedicine.org/homecare/hcp/elig_worksheets/Karnofsky-Performance-Status.pdf

Karnofsky score shows $p<0.0001$ (extremely significant), $p= 0.0019$ (very significant) and $p= 0.0004$ (extremely significant) when tested immediately after RT, after 1 month of RT and after 3 months of completing RT.

The Quality of Life (QLQ) is assessed on the basis of 3 parameters ie functional score, global score and symptom score as per EORTC QLQ - C30. Symptom score specifying symptoms of head and neck cancer were also noted by QLQ - H & N 35. Functional scale is the sum total of improvement in all ill effects of radiotherapy leading to achieving normal levels of functional ability of the patient, which is end point of assessment of well – being of the patient. It is a numerical score. Increase in the score denotes improvement in general functional activity of the patient. Global score denotes improvement in QLQ as judged by the patient himself. Head and neck symptom score is total score derived from specially designed questionnaire specifically in view of symptoms of oral cancer. Higher score indicates severe symptom gradations. Functional score and Global score of QoL is nornmally hampered after completing RT and this process continues for next few months due to long lasting side effects of RT. In our study decreased functional and global scores were observed in almost all patients in control group, while these parameters are improved or maintained in nearly 2/3 patients of study group. This indicates effectiveness of selective Ayurvedic medicines in boosting immunity due to their rasayan action, decreasing symptomatology and ultimately improving functional ability of patients during and after RT. Functional score and global score were significant at all time points when tested.

Symptom score is the sum total effect of all the symptomatic parameters. Decrease in symptom score indicates well being of patients. In our study symptom score reflected disease related symptoms like pain, trismus etc and symptoms of side effects of radiotherapy like xerostomia, stomatitis. Thus this score is more evident immediately after completing RT. Efficacy of Ayurvedic treatment on management of disease related and radiotherapy side effects related symptoms is proved in our study with the fact that symptom score was not improved in none of the patient in control group immediately after completeing RT, on the other hand it is improved or maintained in 23 patients of group A. This is due to the fact that disease related symptoms and radiotherapy related symptoms were well controlled by combination of radiotherapy and Ayurvedic treatment.

Symptom score shows $p<0.0001$ (Extremely significant), $p= 0.434$ (not quite significant) and $p= 0.051$(not quite significant) when tested immediately after RT, after 1 month of RT and after 3 months of completing RT respectively. This is due to the fact that all radiotherapy side effects in oral cavity cancer are evident during the course of RT and gradually subside within few weeks of completion of RT.

Head and Neck symptom score represents symptoms related to disease and symptom related radiotherapy side effects. It is peculiarity of radiotherapy in oral cavity cancer that the side effects related symptoms are more or less similar to that of disease related symptoms. Thus these symptoms are aggrevated during course of RT. Symptom score of H&N 35 questionnaire represents sum total of both these symptoms. It is noticeable that score of these symptoms is improved (Reduction in total symptoms) in more than 20 patients at all three time points in group A, while H & N is not improved (symptoms agrrevated) in 20, 21 and 15 patients at three time points respectively in group B. This indicates head and cancer related and RT side effects related symptoms were well controlled with combination of RT and Ayurvedic treatment. When Head and neck symptom score is considered it shows decreasing trend in control group patients that is (74-81-81-76) at four time points respectively while it represents decreasing trend in study group (76-71-70-65) at respective time points. This observation is supported by statistical evaluation with extreamely significant $p<0.0001$ (extremely significant) at end of RT, $p= 0.002$ (significant) after 1 month of RT and $p=0.061$ (Not significant) after 3 months of RT.

These findings suggest that all scores of QLQ are also highly significant immediately after RT and for functional score and global score till three months of RT. Assessment of radiation induced symptoms described above was done by clinicians (as per CTC guidelines). As per QLQ guidelines these symptoms were also assessed by patients in their own perspective and recorded as symptom score of QLQ. It was interesting to note that both the assessments matched. All the scores show significant improvement in patients treated with adjunct oral Ayurvedic medicines.

CONCLUSION

a. Combination of Ayurvedic medicines selected in our study was highly effective in management of side-effects of radiotherapy namely stomatitis, xerostomia and trismus, which are commonly developed during the course of radiotherapy and usually persistent for months together in oral cavity cancer patients.

b. Radiotherapy induced loss of taste; excessive salivation and dysphagia were well controlled with study medicines during the course of radiotherapy.

c. Significant improvement in loss of weight and nausea was not observed with adjunct Ayurvedic medicines.

d. Karnofsky score depicting wellbeing and ability to conduct activities of daily life was highly significant in patients treated with adjunct Ayurvedic treatment, when compared with control group in oral Cancer patients undergoing Radiotherapy. This score was significant when assessed during the course of radiotherapy and upto three months after completing radiotherapy.

e. Functional score of quality of life questionnaire (QLQ), which is indicative of functional acivities and global score of QLQ, which is revealing wellbeing from patients perspective, were highly significant in study group when compared with control group and when assessed during the course of radiotherapy as well as upto three months after completing radiotherapy.

f. Sum total of disease related symptoms and radiotherapy induced side effects represented by symptom score of QLQ was remarkably redused in patients treated with adjunct Ayurvedic treatment during the course of radiotherapy.

g. QLQ-H&N35, sumerising symptoms of head and neck cancer and radiotherapy induced side effects in it, when assessed during the course of radiotherapy as well as upto three months after completing radiotherapy, showed significant reduction in both sorts of symptoms in study group.

h. Mauktikyukta Kamdudha and Ananta vati were effective in management of radiotherapy induced stomatitis due to their Pittashamak and Raktaprasadan action. Yashtimadhu ghrut possessing soothing and healing effect was beneficial in the management of stomatitis, xerostomia, trismus and dysphagia, when administered internally and externally. Mauktikayukta Praval panchamrut improved appetite and enhanced digestion which was hampered during the course of radiotherapy. Radiotherapy induced excessive salivation was well controlled by kashay rasa of

Gairik. Well being and quality of life of these patients were maintained or improved due to Rasayan action (Immunomodulatory action) of Guduchi sattva, Yashtimadhu and Ghrut.

SCOPE FOR FURTHER STUDY

It is well known that radiotherapy (RT) induces several side effects such as stomatitis, dysphasia, xerostomia, nausea, trisms, excessive salivation, weight loss and hampers wellbeing and Quality of life of oral cavity cancer patients. These ill-effects are due to immunosuppressive effect of radiotherapy. Above study implies effectiveness of adjunct Ayurvedic treatment in clinical assessment of oral cavity cancer patients treated with radiotherapy. As a further step of this study it is interesting to observe immunological parameters relating the immune status in these patients during and after radiotherapy.

For this pilot study, we enrolled 4 new patients of oral cancer (OC) to investigate if the improvement in the radiation induced symptoms and quality of life in these patients could be related to improvement in the immune status of the patients. The inclusion and exclusion criteria were similar to the clinical study. In addition, two patients included in the study were tobacco chewers showing mild and severe leukoplakia each, without frank malignancy. The leukoplakia patients had tobacco habit for more than 30 years. While OC patients included in the study also chewed tobacco for 12 to 50 years. The Five OC patients received full course of RT along with Ayurvedic medicines. They were observed clinically and assessed for immunological parameters at three time points namely before RT (**a**), immediately after RT (**b**) and 1 month after completion of RT (**c**). Patients included in the study had undergone surgery, and belonged to all stages and grades of the disease.

The following immune parameters were assessed at three time points:

1. Percentage of T and B cells and T cell subsets from peripheral blood mononuclear cells (PBMC) by flow cytometry using antibodies provided by BD Biosciences, San Diego, CA
2. T and B cell proliferation induced by Phytohaemagglutinin (PHA) and Poke Weed mitogen (PWM) respectively, using ^{3}HTdR incorporation assay from Sigma (PHA) and Gibco-BRA (PWM)
3. IgA levels in saliva by ELISA using commercial kits provided by Uscn Life sciences Inc., China in order to assess local immune response

4. Pro-inflammatory (IL-1, IL-6, IL-8, TNF- α) and anti-inflammatory cytokines (IFN-γ and IL-10) in saliva and sera by ELISA using commercial kits provided by BD Biosciences

Conclusion of Pilot Study:

Since the OAM combination used is reported in Ayurvedic literature to boost up immunity, and to reduce inflammation we ventured to study a small group of OC patients treated similarly for their immune status at the same time points. The immune parameters assessed were T cell subsets and B cell counts in PBMCs, and their mitogen induced proliferative responses, salivary IgA levels and serum and salivary levels ofcytokines IL-1, IL-6, IL-8, IL-10, TNF-α and IFN-γ. We also studied the same parameters in one patient each of mild and severe leukoplakia.

Although the data reported here is on a very small sample size of 4 cancer patients and 2 patients with leukoplakia, we have reported some interesting observations.

1. We have sequentially studied immune parameters before, immediately after and one month after completion of RT which would indicate basal level, compared with immediate post RT and one month after recovery of RT-induced inflammation.
2. We have correlated levels of pro-inflammatory cytokines IL-1 and IL-6 with post RT inflammatory response.
3 We have correlated reduced IL-10 responses with increased IFN-γ levels, which is indicative of polarization of immune response towards Th1 type.
4. We have shown the significance of saliva as importantnon-invasive source of bio fluid for analysis of immune parameters especially in OC.
5. We did not find correlation between impairment in immune parameters in leukoplakia parallel with increase in severity of the condition. We feel that improvement of clinical parameters along with immune responses in OC patients could be due to adjunct therapy with oral Ayurvedic medicines given throughout the observation period.

It is however essential to extend this study on a larger number of OC patients and include control group of patients treated with RT alone without additional Ayurvedic medicines, to arrive at definitive conclusion.

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Group A(Study) (A = Before Radiotherapy, B= After Radiotherapy, C=After 1 month of RT,D= After 3 months of RT)

									Stomatitis				Xerostomia				Loss of taste				Excessive Salivation				Trismus				Dysphagia				Nausea			
Sr. No.	**Initials**	**Age**	**Sex**	**HPR Grade**	**History of Addiction**	**Opeartive stutus before RT**	**Adjuvant Chemotherapy taken with RT**	**Socio Economic Status**	**A**	**B**	**C**	**D**	**A**	**B**	**C**	**D**	**A**	**B**	**C**	**D**	**A**	**B**	**C**	**D**	**A**	**B**	**C**	**D**	**A**	**B**	**C**	**D**	**A**	**B**	**C**	**D**
1A	VK	70	M	III	Tobacco	N	N	Middle	2	4	2	2	1	3	2	2	1	3	2	1	1	1	1	1	2	3	2	2	2	3	2	1	1	3	3	1
2A	AP	43	M	I	Tobacco , Alcohol	N	Y	Middle	2	4	2	2	1	3	3	3	1	2	1	1	1	1	1	1	2	3	1	1	2	3	1	1	1	3	1	1
3A	MS	46	M	III	Tobacco	Y	Y	Middle	2	4	2	1	1	4	3	2	1	2	1	1	1	1	1	1	2	3	1	1	2	3	1	1	1	1	1	1
4A	GM	76	M	II	Tobacco , Alcohol	Y	Y	Lower	2	4	3	2	1	1	2	1	1	2	2	1	1	1	1	1	2	3	3	2	2	3	3	1	1	1	1	1
5A	JC	28	F	III	Tobacco , Betal Nut	Y	Y	Lower	2	4	2	2	1	1	1	1	1	2	1	1	1	1	2	2	2	4	1	1	2	3	1	1	1	1	1	1
6A	GD	39	M	I	Tobacco	Y	Y	Middle	2	4	2	2	1	1	1	1	1	2	2	1	1	1	3	3	2	4	3	2	2	3	3	1	1	1	1	1
7A	VT	60	M	II	Tobacco, Smoking, alcohol	Y	Y	Lower	2	4	1	1	1	1	1	1	1	2	1	1	1	1	3	2	2	4	1	1	2	3	1	1	1	1	1	1
8A	VD	75	M	I	Tobacco , Betal Nut	N	N	Lower	2	3	1	1	1	1	1	1	1	2	1	1	1	1	2	1	2	4	1	1	2	3	1	1	1	1	1	1
9A	SP	55	M	II	NIL	Y	N	Upper	2	3	2	1	1	1	1	1	1	1	1	1	1	1	1	1	2	4	4	2	2	3	3	1	1	1	1	1
10A	AM	30	M	III	Tobacco , Alcohol	Y	Y	Lower	2	3	1	1	1	3	3	2	1	2	1	1	1	1	1	1	2	1	1	1	2	3	1	1	1	1	1	1
11A	JS	42	M	II	Tobacco	Y	Y	Lower	2	2	2	2	1	1	3	3	1	1	1	1	1	1	1	1	2	2	4	3	2	2	3	3	1	1	1	1
12A	RM	49	M	III	Tobacco , Alcohol	N	Y	Lower	2	2	2	4	1	1	4	3	1	1	2	2	1	1	1	1	2	2	3	4	2	2	3	3	1	1	3	3
13A	RD	64	M	II	Tobacco, Smoking, alcohol	N	N	Lower	2	3	4	2	1	1	1	1	1	3	1	1	1	1	1	1	2	1	1	1	2	3	1	1	1	1	1	1
14A	SL	28	F	II	NIL	Y	N	Lower	2	3	3	1	1	1	1	1	1	1	1	1	1	2	3	2	2	1	1	1	2	3	1	1	1	1	1	1
15A	SS1	53	M	II	Tobacco , Alcohol	N	Y	Lower	2	3	3	3	1	1	1	1	1	1	2	1	1	2	3	3	2	1	3	3	2	1	3	2	1	1	3	1
16A	RP	59	F	II	Tobacco	Y	N	Lower	2	3	2	2	1	1	1	1	1	1	1	1	1	1	4	3	2	1	1	1	2	1	1	1	1	1	1	1
17A	RL	45	M	II	Tobacco	Y	Y	Middle	2	3	1	2	1	1	1	1	1	1	1	1	1	1	1	1	2	1	1	1	2	1	1	1	1	1	1	1
18A	HT	65	M	II	Tobacco , Alcohol	Y	Y	Lower	2	2	1	1	1	1	1	1	1	1	1	1	1	1	1	1	2	1	1	1	2	1	1	1	1	1	1	1
19A	CS	70	F	II	Betal Nut	Y	Y	Middle	2	2	2	2	1	1	1	1	1	1	1	1	1	1	1	1	2	1	1	1	2	1	1	1	1	1	1	1
20A	VR	65	M	II	Tobacco , Alcohol	Y	Y	Middle	2	2	1	1	1	1	1	1	1	1	1	1	1	1	1	1	2	1	1	1	2	1	1	1	1	1	1	1
21A	MR	40	M	III	Tobacco	Y	N	Lower	2	2	1	2	1	1	1	1	1	1	2	1	1	1	1	1	2	1	3	2	2	1	3	2	1	1	3	1
22A	RG	60	M	II	Tobacco , Alcohol	N	N	Lower	2	2	1	1	1	1	1	1	1	1	1	1	1	1	3	3	2	1	2	1	2	1	2	1	1	1	2	1
23A	SS2	58	F	III	Tobacco	Y	Y	Lower	2	2	4	3	1	2	3	3	1	1	3	2	1	1	1	1	2	2	4	3	2	1	3	3	1	1	1	1
24A	SZ	65	F	I	Tobacco , Betal Nut	Y	N	Lower	2	2	3	1	1	1	1	1	1	1	2	2	1	1	2	2	2	2	3	3	2	2	3	3	1	2	2	2
25A	CG	34	M	II	Tobacco	N	N	Lower	2	2	3	1	1	1	1	1	1	1	1	1	1	1	1	1	2	1	2	3	2	2	2	2	1	1	2	2
26A	ST	65	F	I	Tobacco	N	N	Lower	2	1	2	2	1	1	2	2	1	1	1	1	1	1	1	1	2	2	2	2	2	2	2	2	1	1	1	1
27A	AS	40	F	II	Betal Nut	N	N	Lower	2	2	1	1	1	1	1	1	1	1	1	1	1	1	1	1	2	1	1	1	2	1	1	1	1	1	1	1
28A	BD	50	M	I	Tobacco	Y	N	Middle	2	2	1	1	1	1	1	1	1	1	1	1	1	1	1	1	2	1	1	1	2	1	1	1	1	1	1	1
29A	KG	40	M	I	Tobacco , Alcohol	N	N	Lower	2	2	1	1	1	1	1	1	1	1	1	1	1	1	1	1	2	1	1	1	2	1	1	1	1	1	1	1
30A	DS	79	M	I	Tobacco	N	Y	Middle	2	2	2	1	1	1	1	1	1	2	2	2	1	1	1	1	2	1	1	1	2	1	2	2	1	1	1	1

Group A (Study) (A = Before Radiotherapy, B= After Radiotherapy, C=After 1 month of RT,D= After 3 months of RT)

		Karnofsky score				% of Weight Loss						Functional score of QLQ				Symptom score of QLQ				Global scoreof QLQ				H & N Symptom score of			
Sr. No.	Initials	A	B	C	D	B-A	C-A	D-A	% of weight loss at B	% of weight loss at C	% of weight loss at D	A	B	C	D	A	B	C	D	A	B	C	D	A	B	C	D
1A	VK	80	80	60	70	0	0	0	0	0	0	75.56	100	102.22	102.22	30.77	15.38	12.82	7.69	50	66.67	66.67	100	82	70	60	52
2A	AP	80	80	80	80	0	0	1	0	0	2	84.44	100	102.22	102.22	12.82	5.13	5.13	2.56	58.33	58.33	66.67	66.67	64	60	61	55
3A	MS	70	80	70	80	-3	3	0	-12	11	0	6.67	31.11	31.11	80	48.72	48.72	58.97	17.95	58.33	58.33	66.67	66.67	90	86	90	60
4A	GM	70	80	100	100	4	-2	-4	8	-4	-8	55.56	100	102.22	102.22	30.77	0	-2.56	-2.56	58.33	75	100	100	83	71	60	60
5A	JC	80	80	60	70	8	0	-8	14	0	-14	80	77.78	66.67	71.11	28.21	25.64	33.33	28.21	50	58.33	50	66.67	76	72	80	82
6A	GD	80	90	80	80	1	0	-1	2	0	-2	20	84.44	77.78	88.89	30.77	23.08	30.77	17.95	50	50	50	66.67	82	72	80	60
7A	VT	90	90	100	100	0	-1	1	0	-2	2	68.89	97.78	102.22	106.67	33.33	12.82	2.56	-2.56	58.33	66.67	83.33	83.33	89	66	55	50
8A	VD	90	90	100	100	1	3	-3	2	6	-6	93.33	91.11	80	88.89	15.38	12.82	12.82	12.82	100	100	83.33	83.33	74	70	72	71
9A	SP	90	90	70	80	5	0	-4	8	0	-7	100	100	88.89	88.89	5.13	5.13	17.95	17.95	66.67	66.67	66.67	66.67	63	60	72	72
10A	AM	60	60	60	80	0	0	-1	0	0	-2	77.78	80	80	88.89	30.77	23.08	17.95	17.95	41.67	66.67	66.67	66.67	75	72	70	70
11A	JS	60	60	90	80	6	-2	-4	11	-4	-7	95.56	97.78	102.22	106.67	12.82	7.69	2.56	2.56	66.67	66.67	100	100	66	61	55	56
12A	RM	90	90	80	80	2	0	-2	4	0	-4	95.56	97.78	97.78	102.22	5.13	5.13	2.56	2.56	66.67	66.67	83.33	83.33	62	62	60	60
13A	RD	80	80	60	70	4	6	-10	7	11	-17	60	88.89	75.56	88.89	12.82	20.51	43.59	17.95	33.33	33.33	33.33	50	68	72	80	70
14A	SL	80	80	60	60	4	4	-8	8	9	-17	95.56	95.56	88.89	88.89	10.26	12.82	30.77	17.95	58.33	66.67	50	50	68	73	80	72
15A	SS1	70	70	70	70	4	3	-7	8	6	-13	68.89	75.56	73.33	77.78	41.03	43.59	48.72	43.59	33.33	33.33	33.33	50	96	85	90	84
16A	RP	70	70	70	80	2	0	-2	4	0	-4	113.33	64.44	66.67	77.78	43.59	28.21	43.59	43.59	66.67	58.33	83.33	83.33	98	86	80	81
17A	RL	60	60	80	80	6	-2	-4	18	-7	-12	115.56	88.89	93.33	97.78	23.08	23.08	23.08	23.08	58.33	50	66.67	66.67	86	82	82	82
18A	HT	80	90	100	100	-2	-1	3	-5	-1	6	113.33	95.56	111.11	111.11	17.95	12.82	-7.69	-7.69	66.67	66.67	83.33	83.33	85	75	65	64
19A	CS	80	80	80	80	0	0	0	0	0	0	117.78	51.11	88.89	88.89	53.85	41.03	28.21	17.95	50	41.67	66.67	66.67	102	90	82	70
20A	VR	90	90	90	100	8	-2	-6	17	-5	-13	108.89	95.56	111.11	111.11	5.13	10.26	7.69	7.69	83.33	50	83.33	83.33	62	62	56	56
21A	MR	80	80	70	70	10	0	-10	13	0	-13	113.33	44.44	44.44	88.89	76.92	69.23	69.23	43.59	66.67	58.33	66.67	66.67	102	88	70	65
22A	RG	80	60	50	60	2.5	2.5	-5	4	4	-7	115.56	86.67	77.78	88.89	10.26	17.95	30.77	30.77	66.67	50	50	50	73	80	94	92
23A	SS2	90	90	100	100	8	-4	-3	11	-6	-5	82.22	53.33	88.89	88.89	7.69	35.9	23.08	17.95	66.67	50	100	100	70	85	66	60
24A	SZ	80	80	90	90	0	0.5	2	0	1	4	91.11	93.33	93.33	93.33	12.82	2.56	2.56	2.56	66.67	50	66.67	66.67	60	55	54	52
25A	CG	80	80	90	90	2.5	0	-3	6	0	-6	100	95.56	100	100	7.69	10.26	12.82	-2.56	66.67	50	66.67	66.67	56	60	64	50
26A	ST	80	80	90	90	5	0	-3	9	0	-5	111.11	95.56	111.11	111.11	30.77	2.56	-2.56	-2.56	66.67	75	66.67	66.67	71	56	50	50
27A	AS	70	80	80	80	3	-1	-2	6	-2	-4	80	97.78	95.56	95.56	30.77	7.69	10.26	5.13	25	33.33	100	100	75	58	62	60
28A	BD	60	70	80	80	-1	0	1	-1	0	1	66.67	66.67	62.22	77.78	33.33	33.33	43.59	43.59	66.67	66.67	66.67	66.67	86	80	92	92
29A	KG	90	90	100	100	4	-3	-2	5	-4	-3	66.67	66.67	100	100	33.33	33.33	33.33	33.33	66.67	66.67	100	100	74	75	75	75
30A	DS	90	90	90	90	8	0	-8	15	0	-15	77.78	102.22	102.22	102.22	15.38	0	-2.56	-2.56	50	66.67	100	100	55	50	51	50

Group A (Study) (A = Before Radiotherapy, B= After Radiotherapy, C=After 1 month of RT)

		HB			WBC			RBC			PLATLET			BILIRUBIN			SGOT			SGPT			ALKALINE PH			CREATININE		
Sr. No.	**Initials**	**A**	**B**	**C**	A	B	C	**A**	**B**	**C**	**A**	**B**	**C**	**A**	**B**	**C**	**A**	**B**	**C**	**A**	**B**	**C**	**A**	**B**	**C**	**A**	**B**	**C**
1A	VK	10.3	8.5	8.6	7000	5700	2400	4.65	3.06	3.09	294000	288000	248000	0.4			14.1			13.5			165			1.1		
2A	AP	14.8	13.9	12.9	8100	6600	10300	5	4.99	4.48	243000	210000	197000				39			34						1.06		
3A	MS	13.7	14.1	13.7	7000	9800	7400	4.9	5.2	5.07	245000	294000	343000	0.9			14.54			25.19			103					
4A	GM	11.5	10.8		8400	6700		4.16	3.9		237000	272000																
5A	JC	9.3			5400			4.1			154000			0.26			25			39			105			0.85		
6A	GD	12.6	11.6	12	9100	5400	5800	5.28	4.69	4.92	346000	235000	324000															
7A	VT	9.5	9	7.9	9600	12700	6300	4.45	4.44	x	427000	578000	507000	0.75			34.9			24			167					
8A	VD	11	11.7	11.2	8000	2800	8800	4	3.23	3.68	240000	284000	277000	1.78			12			12			131			1.2		
9A	SP	14.8	13.2		8700	4600		5.7	5.38		315000	355000			0.58			23.86		35	14.49					1.5	0.99	
10A	AM	17.3	15.6		8700	7000		4.99	5.58		292000	247000		0.6			33.9			51			167			0.8		
11A	JS	13.9	12.1		6800	3300		4.98	4.24		362000	199000																
12A	RM	16.1	14.2	12.1	6900	10900	8500	5.19	4.57	4.62	457000	421000	289000	0.53												1.01	1.2	
13A	RD	11.2	11.1	10	10500	6800	9300	4.08	4.04	3.69	100000	120000	312000	0.72	0.5		28.5	29		13.93	19.6		189.3	100.3		0.94	0.83	
14A	SL	14	13.8	13.8	6810	8700	7700	4.51	4.11	4.1	447000	294000	295000										94			0.7		
15A	SS1	11.5	12.3	12..4	8400	9100	6000	4.06	4.49	4.41	381000	482000	385000	0.6			31.2			17.7			153.9			1		
16A	RP	12.4	13	12.3	5000	4800	4100	4.54	4.85	4.78	212000	172000	176000	0.5	0.5	0.57		25.62	19.49		16.1	12.78	195	201	98.5	1.1	0.62	0.99
17A	RL	12.3	11.6		12500	3400		3.87	3.87		192000	163000														1		
18A	HT	15.2	12.3	117.7	17400	6000	5100	4.87	4.48		203000	244000	224000															
19A	CS	10.6	9.4	9.6	5200	3400	4600	3.99	4.14	4.16	189000	213000	217000							17.1						1.3		
20A	VR	14	12.6	9.7	7400	5100	7900	4.69	4.06	4.87	398000	292000	429000	0.59			28.7			24.58						0.75		
21A	MR	11	11.2	11	7100			4.6			189000																	
22A	RG	14.5	11	12.8	8900	12800	8300	5.69	4.36	4.53	265000	255000	313000	0.5	0.61		22.7	21.17		25	12.94		114	174.1		0.8	1..0	0.95
23A	SS2	9	11.2	10.1	3700	4700	3700	3.77	4.31	3.77	415000	276000	418000															
24A	SZ	12.3			8100			4.59			241000						48			44.3			144			0.9	0.8	
25A	CG	11.8	9.5		27100	8800		4.45			442000	364000								142.2						1		
26A	ST	9.1			5300			3.89			232000						20			9			79			0.7		
27A	AS	10	10.5	11	8100			4.5			265000																	
28A	BD	15.8	13.9		12700	7400		4.91	5.27		214000	255000		1.26	0.73		22	34.82		15	39.46		190	71.58		0.8	0.98	
29A	KG	11.3	11.9		7100	5300		5.72	6.09		223000	266000		0.75			19.41			23.08			47.47			1.1		
30A	DS	12.6	12.5	11.7	6200	5600	5800	4.8			335000	357000	218000															

Group B (Control) (A = Before Radiotherapy, B= After Radiotherapy, C=After 1 month of RT,D= After 3 months of RT)

									Stomatitis				Xerostomia				Loss of Taste				Excessive Salivation				Trismus				Dysphagia				Nausea			
Sr. No.	**Initials**	**Age**	**Sex**	**HPR Grade**	**History of Addiction**	**Opearti ve stutus before RT**	**Adjuvant Chemother apy taken with RT**	**Socio Economi c Status**	**A**	**B**	**C**	**D**	**A**	**B**	**C**	**D**	**A**	**B**	**C**	**D**	**A**	**B**	**C**	**D**	**A**	**B**	**C**	**D**	**A**	**B**	**C**	**D**	**A**	**B**	**C**	**D**
1B	DS1	50	M	I	Tobacco , alcohol , Smoking	Y	Y	lower	2	3	3	2	1	4	2	2	1	1	1	1	1	1	1	1	2	3	3	2	2	3	1	1	1	2	1	1
2B	UO	55	F	I	Tobacco, Betal Nut	N	Y	Lower	2	3	3	2	1	4	1	1	1	1	2	1	1	1	2	3	2	3	3	1	2	1	1	1	1	1	1	1
3B	AK	71	M	II	Smoking	Y	Y	Upper	2	2	2	1	1	4	2	2	1	1	1	1	1	1	1	1	2	3	3	2	2	2	1	1	1	2	1	1
4B	MC	40	M	III	Tobacco	Y	N	Lower	2	3	2	2	1	4	2	2	1	1	1	1	1	1	1	1	2	3	3	2	2	2	1	1	1	1	1	1
5B	SM	59	F	III	NIL	Y	N	Upper	2	3	2	2	1	4	2	2	1	1	1	1	1	1	1	1	2	4	3	2	2	2	1	1	1	1	1	1
6B	KS	46	F	II	Tobacco	Y	Y	Middle	2	4	3	2	1	1	1	1	1	1	1	1	1	2	2	2	2	5	2	3	2	3	2	2	1	1	1	1
7B	DP1	77	M	II	Tobacco, Alcohol	Y	N	Middle	2	4	4	3	1	2	3	3	1	1	1	1	1	1	1	1	2	5	2	3	2	3	2	1	1	1	1	1
8B	DP2	62	F	III	NIL	N	N	Middle	2	4	3	3	1	4	3	3	1	2	1	1	1	1	1	1	2	4	3	2	2	3	1	1	1	1	1	1
9B	NM	62	M	III	NIL	N	Y	lower	2	3	2	2	1	4	3	3	1	1	1	1	1	1	1	1	2	4	3	3	2	3	3	3	1	1	1	1
10B	RS	60	F	I	Tobacco	Y	N	Middle	2	4	4	3	1	4	4	3	1	1	2	2	1	1	1	1	2	4	3	3	2	2	2	2	1	1	1	1
11B	SM	50	M	I	Tobacco	N	N	Middle	2	4	3	3	1	4	3	3	1	2	1	1	1	1	1	1	2	4	3	3	2	2	1	1	1	1	1	1
12B	RP	60	M	II	Tobacco, Alcohol	Y	N	lower	2	4	4	2	1	4	3	3	1	1	1	1	1	1	1	1	2	4	3	3	2	3	1	1	1	2	1	1
13B	RJ	63	M	II	Tobacco	Y	Y	Middle	2	1	1	1	1	4	4	3	1	1	1	1	1	1	1	1	2	4	3	2	2	3	2	2	1	1	1	1
14B	CK	55	M	II	Tobacco	Y	Y	Middle	2	4	2	2	1	1	1	1	1	1	1	1	1	2	1	1	2	1	2	1	2	2	2	2	1	1	1	1
15B	RH	38	M	III	Tobacco , smoking	Y	Y	Upper	2	5	2	2	1	2	3	2	1	1	1	1	1	1	1	1	2	1	2	3	2	2	1	1	1	1	1	1
16B	SM	42	M	III	Tobacco, Betal Nut	Y	Y	Upper	2	4	2	2	1	1	1	1	1	1	3	2	1	3	3	3	2	5	2	3	2	3	3	3	1	2	2	2
17B	US	50	M	III	Tobacco , alcohol , Smoking	Y	Y	Upper	2	3	2	2	1	1	1	1	1	1	3	2	1	3	3	1	2	4	2	2	2	3	3	3	1	2	1	1
18B	PD	48	M	I	Tobacco, Alcohol	Y	N	Middle	2	2	3	2	1	4	4	3	1	3	2	1	1	1	1	1	2	4	4	3	2	3	2	2	1	2	2	1
19B	TS	72	F	II	Tobacco, Betal Nut	Y	Y	Middle	2	2	2	1	1	4	3	2	1	1	1	1	1	1	1	1	2	3	3	3	2	3	2	2	1	2	1	1
20B	KD	67	M	III	Tobacco, Betal Nut	Y	N	Middle	2	2	2	2	1	2	3	3	1	1	1	1	1	1	1	1	2	5	2	3	2	2	2	2	1	1	2	2
21B	KC	60	M	I	Tobacco, Alcohol	N	Y	Middle	2	2	2	1	1	4	2	2	1	1	2	1	1	1	1	1	2	3	1	1	2	3	1	1	1	1	1	1
22B	KB	63	F	II	NIL	Y	N	Lower	2	2	2	1	1	4	4	3	1	1	1	1	1	1	1	1	2	3	3	1	2	3	1	1	1	2	1	1
23B	NQ	45	F	II	Tobacco	Y	Y	Lower	2	4	4	3	1	4	4	4	1	1	1	1	1	1	1	1	2	4	2	3	2	3	1	1	1	1	1	1
24B	MM	49	M	II	Tobacco	Y	N	Upper	2	4	2	2	1	1	1	1	1	1	1	1	1	3	2	2	2	4	2	2	2	2	1	1	1	2	1	1
25B	GS	28	F	II	Tobacco	Y	N	lower	2	4	4	3	1	4	2	2	1	1	1	1	1	1	1	1	2	5	2	4	2	3	1	1	1	1	1	1
26B	RG	48	F	III	Tobacco	N	Y	lower	2	4	2	2	1	1	1	1	1	1	2	1	1	1	1	1	2	4	2	2	2	3	2	2	1	1	2	1
27B	DS2	54	M	I	Tobacco , alcohol , Smoking	Y	N	Middle	2	1	1	1	1	1	1	1	1	1	1	1	1	2	2	2	2	4	2	2	2	3	1	1	1	2	1	1
28B	SN	60	F	III	Tobacco	Y	Y	Middle	2	4	2	2	1	4	4	3	1	1	1	1	1	1	1	1	2	4	3	2	2	3	1	1	1	1	1	1
29B	RG	55	F	II	Tobacco, Betal Nut	Y	Y	lower	2	5	2	2	1	1	1	1	1	1	1	1	1	3	2	1	2	1	2	3	2	3	2	2	1	1	1	1
30B	PJ	38	M	III	Smoking	Y	Y	lower	2	4	2	2	1	4	3	3	1	1	1	1	1	1	1	1	2	4	2	2	2	3	1	1	1	1	1	1

Group B (Control) (A = Before Radiotherapy, B= After Radiotherapy, C=After 1 month of RT,D= After 3 months of RT)

		Karnofsky score				% of Weight Loss						Functional score of QLQ				Symptom score of QLQ				Global scoreof QLQ				H & N Symptom score of QLQ			
Sr. No.	**Initials**	**A**	**B**	**C**	**D**	**B-A**	**C-A**	**D-A**	% of weight loss B	% of weight loss C	% of weight loss D	**A**	**B**	**C**	**D**	**A**	**B**	**C**	**D**	**A**	**B**	**C**	**D**	**A**	B	C	D
1B	DS1	80	60	60	70	3	3	1	12	11	5	97.78	60	66.67	75.56	17.95	25.64	25.64	17.95	83.33	50	66.67	66.67	70	76	78	72
2B	UO	80	50	80	80	3	2	1	12	12	5	97.78	88.89	97.78	97.78	17.95	2.56	5.13	-2.56	83.33	50	66.67	83.33	71	68	70	55
3B	AK	80	70	70	70	3	2	1	11	11	5	97.78	48.89	44.44	53.33	17.95	25.64	17.95	10.26	83.33	33.33	50	50	72	80	75	65
4B	MC	80	60	80	80	3	2	2	11	11	6	97.78	48.89	44.44	53.33	17.95	38.46	30.77	23.08	83.33	66.67	83.33	83.33	73	90	88	84
5B	SM	80	70	70	70	2	2	1	7	7	5	97.78	68.89	71.11	80	17.95	12.82	17.95	10.26	83.33	25	33.33	33.33	70	70	70	65
6B	KS	80	70	70	70	2	2	2	8	11	6	97.78	91.11	77.78	86.67	17.95	20.51	30.77	23.08	83.33	8.33	33.33	33.33	71	75	80	76
7B	DP1	80	70	70	70	2	2	1	8	7	5	97.78	68.89	71.11	80	17.95	17.95	17.95	10.26	83.33	50	66.67	83.33	72	73	74	66
8B	DP2	80	70	80	80	2	2	1	7	12	5	97.78	82.22	84.44	93.33	17.95	7.69	17.95	10.26	83.33	50	66.67	66.67	73	70	80	80
9B	NM	80	70	70	70	2	2	1	7	5	3	97.78	13.33	44.44	53.33	17.95	64.1	56.41	48.72	83.33	25	25	25	68	96	92	92
10B	RS	80	60	60	70	3	2	1	11	11	5	97.78	62.22	77.78	86.67	17.95	46.15	43.59	35.9	83.33	33.33	33.33	33.33	70	90	88	85
11B	SM	80	60	70	70	3	2	1	11	11	5	97.78	80	80	88.89	17.95	20.51	17.95	10.26	83.33	50	50	50	70	75	75	64
12B	RP	80	60	60	70	3	2	1	11	7	5	97.78	13.33	22.22	31.11	17.95	64.1	69.23	61.54	83.33	25	33.33	33.33	72	96	102	95
13B	RJ	80	70	70	70	2	1	1	8	4	-2	97.78	15.56	33.33	42.22	17.95	51.28	56.41	48.72	83.33	16.67	33.33	33.33	75	95	100	94
14B	CK	80	70	70	70	2	1	1	8	5	5	97.78	62.22	66.67	75.56	17.95	46.15	43.59	35.9	83.33	33.33	33.33	33.33	76	86	84	84
15B	RH	80	80	80	80	1	1	1	4	5	5	97.78	37.78	37.78	46.67	17.95	35.9	43.59	35.9	83.33	33.33	50	66.67	71	85	90	85
16B	SM	80	80	90	90	1	1	1	4	5	5	97.78	26.67	22.22	31.11	17.95	58.97	56.41	48.72	83.33	50	50	66.67	72	96	96	96
17B	US	80	80	90	90	1	1	1	4	4	4	97.78	22.22	44.44	53.33	17.95	58.97	56.41	48.72	83.33	33.33	66.67	66.67	68	100	96	98
18B	PD	80	60	70	70	2	1	1	8	4	4	97.78	77.78	77.78	86.67	17.95	12.82	17.95	10.26	83.33	50	50	50	80	82	82	80
19B	TS	80	60	80	80	3	2	1	12	7	5	97.78	88.89	97.78	97.78	17.95	10.26	5.13	-2.56	83.33	50	50	50	78	75	75	70
20B	KD	80	60	60	70	3	2	1	12	7	5	97.78	62.22	62.22	71.11	17.95	46.15	43.59	35.9	83.33	33.33	50	50	80	80	80	75
21B	KC	80	80	80	80	1	1	1	4	4	5	97.78	60	66.67	75.56	17.95	25.64	17.95	10.26	83.33	50	50	50	76	76	74	70
22B	KB	80	80	70	70	1	1	1	4	-3	-3	97.78	88.89	88.89	97.78	17.95	2.56	5.13	-2.56	83.33	50	50	66.67	78	66	62	60
23B	NQ	80	80	70	70	1	1	1	4	-3	-3	97.78	48.89	55.56	64.44	17.95	25.64	17.95	10.26	83.33	33.33	50	66.67	80	72	60	58
24B	MM	80	70	70	70	2	2	1	8	5	5	97.78	48.89	55.56	64.44	17.95	38.46	43.59	35.9	83.33	66.67	66.67	66.67	82	86	90	84
25B	GS	80	70	80	80	2	1	1	8	4	2	97.78	73.33	77.78	86.67	17.95	25.64	17.95	10.26	83.33	66.67	66.67	66.67	72	79	72	70
26B	RG	80	60	60	60	3	2	1	11	5	5	97.78	64.44	66.67	75.56	17.95	41.03	43.59	35.9	83.33	41.67	50	50	75	89	88	78
27B	DS2	80	60	60	70	3	2	1	11	5	5	97.78	68.89	66.67	75.56	17.95	41.03	43.59	35.9	83.33	25	66.67	66.67	78	87	90	82
28B	SN	80	80	80	80	1	1	1	4	6	5	97.78	68.89	66.67	75.56	17.95	12.82	17.95	10.26	83.33	25	66.67	66.67	72	68	74	62
29B	RG	80	80	80	80	1	1	1	4	-2	-2	97.78	80	88.89	97.78	17.95	17.95	17.95	10.26	83.33	66.67	66.67	66.67	76	78	78	72
30B	PJ	80	80	80	80	1	1	1	4	-2	-2	97.78	80	88.89	97.78	17.95	17.95	17.95	10.26	83.33	66.67	66.67	66.67	74	75	72	66

Group B (Control) (A = Before Radiotherapy, B= After Radiotherapy, C=After 1 month of RT,D= After 3 months of RT)

		HB			WBC			RBC			PLATLET			BILIRUBIN			SGOT			SGPT			ALKALINE PH			CREATININE		
Sr. No.	**Initials**	**A**	**B**	**C**	A	B	C	**A**	**B**	**C**	**A**	**B**	**C**	**A**	**B**	**C**	**A**	**B**	**C**	**A**	**B**	**C**	**A**	**B**	**C**	**A**	**B**	**C**
1B	DS1	11.9	12.5	10.6	7200	9900	6300	5.83	6.16	5.26	445000	296000	232000	0.8			23			21			123			1.12		
2B	UO	8.8	8.4		6400	3500		3.54	3.16		113000	219000														0.77	1.12	
3B	AK	9.4			4100			3.35			265000			0.5			10			8.8			139			0.8		
4B	MC	13.2	14.8		4800	7000		4.44	5.12		215000	308000		2.1			53			40			74			1.29	1.08	
5B	SM	11.5			4500			5.56																				
6B	KS	11.7			8100			4.44			270000															0.74	0.86	
7B	DP1	14.3			8610			4.43			300000			0.72									58			1		
8B	DP2	9.7	9.3		31100	45700		3.39	3.27		655000	569000														1.1	1	
9B	NM	9.3			6900			3.37			196000															1.2		
10B	RS	12.2			8500			4.75																				
11B	SM	11.9	11.5	12.9	15600	13300	15100	4.27	4.56	4.65	472000	419000	419000	0.6			21			19			122			0.99	1	1
12B	RP	9.8	10.9		7800	4000		4.05	4.15		179000	182000		0.69			53			34.9						1.2	1	
13B	RJ	9.4			6100			4.03			227000			0.6			12.7			6.7			156.9			1.3		
14B	CK	9.2	10.2		11000	7900		3.92	4.57		326000	300000		0.85			28			20			136			1.3		
15B	RH	12.2	11.2		2480	3690		3.89	3.6		320000	322000		0.4												0.79	1	
16B	SM	11.4			4300			4.75			237000																	
17B	US	14			4400			3.89			200000						36			34						1		
18B	PD	12			6000			4.05																				
19B	TS	11.9			8300			5.17			295000															1.26		
20B	KD	10.1			6400			3.66			240000																	
21B	KC	12.3			8500			4.03																				
22B	KB	13.4			6830			4.78			248000			0.55			20.24			17.27					113.13			
23B	NQ	10.2	9.6		17600	9900		3.55	3.17		456000	319000															0.9	
24B	MM	9.5	9.7		15600	3600		2.9			223000	194000																
25B	GS	10			17700			3.93			400000						10			5			78			0.7		
26B	RG	9.3	12.3	11.2	2300	10530	535000	3.16	5.37	2.78	137000	376000	330000				0.3									0.7	0.8	
27B	DS2	14	12.5		9100	4800		4.26	4.58		123000	275000																
28B	SN	13.1	11.5		6330	2500		4.29	4.45		342000	207000														0.88	1	
29B	RG	9.6	9.7		8700	6500		3.87	4.26		338000	352000																
30B	PJ	12.4	12.3	12.5	8700	8600	5600	4.79	4.88	4.87	268000	295000	165000															

PATIENT CONSENT FORM

Title of the Study: 'Role of RG4 (an Ayurvedic formulation) in the management of side-effects of Radiotherapy of oral cavity cancers'

Name of the Participant:

Documentation of the informed consent:

I, ……. have read the information in this form (or it has been read to me). I was free to ask any questions and they have been answered.

1. I have read and understood this consent form and the information provided to me.
2. I have had the consent document explained to me.
3. I have been explained about the nature of the study.
4. My rights and responsibilities have been explained to me by the researcher.
5. I have been explained the researcher of all the treatments I am taking or have taken in the past ……. months including any desi (alternative) treatments.
6. I hereby give permission to the investigators to release the information obtained from me as result of participation in this study ethics committee. I understand that they may inspect my original records.
7. My identity will be kept confidential if my data are publicly presented.
8. I have had my questions answered to my satisfaction.
9. I have decided to be in the research study.

I am aware, that if I have any questions during this study, I should contact at one of the addresses listed above. By signing this consent form, I attest that the information given in this document.

Name and signature / thumb impression of the participant (or legal representative if participant incompetent) :

Name :

Address :

Contact No. :

Email Id :

रुग्ण संमतीपत्रक

अभ्यासक्रमाचे शीर्षक : 'Role of RG4 (an Ayurvedic formulation) in the management of side-effects of Radiotherapy of oral cavity cancers'

रुग्णाचे नाव :

रुग्ण संमतीपत्रक नियम :

मी रुग्ण पत्रकातील सर्व माहिती वाचून किंवा मला वाचून दाखविले आहे.

मी विचारल्या जाणाऱ्या प्रश्नांची उत्तरे देण्यास संमती दर्शवित आहे.

१. मी रुग्ण पत्रकात नमूद केलेली सर्व माहिती वाचली आहे.

२. मला रुग्ण संमती पत्रक समजवून सांगण्यात आले आहे.

३. मला माझे हक्क अभ्यासकाने माहिती करुन दिले आहे.

४. मला अभ्यासाबद्दल माहिती देण्यात आली आहे.

५. मी सध्या घेत असलेल्या सर्व औषधोपचाराची माहिती अभ्यासकाला देत आहे.

६. मी ओळख (Identity) माहिती (Publish) करताना गोपनीय ठेवण्यात यावी.

७. मी माझी उत्तरे समाधानकारकरीत्या देत आहे.

८. मी स्वतः अभ्यासाचा एक भाग होण्यास तयारी दर्शवित आहे.

प्रौढ व्यक्तीसाठी :

रुग्णाचे नाव सही / अंगठा :

नाव :

सही :

दिनांक :

Tilak Maharashtra Vidyapeeth, Pune

The Late Vaidya P.G.Nanal Department of Ayurveda

CASE RECORD FORM

Title - Role of RG4 (an Ayurvedic formulation) in the management of side-effects of Radiotherapy of oral cavity cancers'

Name of Scholar – Vd. Shweta R. Gujar

Name of Guide – Dr. Vineeta V. Deshmukh

Date:

Name of patient: **OPD No. :**

Address:

Contact No. :

Sex: **Occupation:**

Qualification:

Type of Work: **Work Duration:**

Vartaman Vyadhivrutta:

Purvavyadhi

Kulaja itihas - Swakula /Pitrukula /matrukula

Vyasan

Supari / Tambakhu / Vidi / Sigaret / Gutakha / Madhyapan / Others

Praman :

Purva Chikitsa / Purva shastrakarma

Indriyaparikshan

Dnyanendriya -

Karmendriya –

- **Strotas Parikshana-**

1. Pranavaha strotas-

2. Udakvaha strotas-

3. Annavaha strotas

4. Rasavaha strotas

5. Raktavaha strotas

6. Mansavaha strotas

7. Medovaha strotas

8. Asthivaha strotas

9. Majjavaha strotas

10. Sukravaha strotas

11. Aartavaha strotas

12. Purisavaha strotas

13. Mutravaha strotas

14. Swadevaha strotas

- **Nidanpanchak**

1. Hetu

   Aaharaja -

   Viharaja

   Manasik

2. Purvarupa

3. Rupa

4. Upashaya / Anupshaya

5. Samprapti

Chikitsa - Group –A/ Group B

Primary Examination -

B.P. - Pulse - Weight –

Mala – Mutra -

Jivha Parikshan -

Mukha Parikshan -

Ura Parikshan -

Udara Parikshan -

Present signs & symptoms (Symptom / specification / grading / duration)

Sr. No.	Criteria	Day 1	Day 8	Day 15	Day 30	End of Radiation Therapy	After 2 months	After 3 months
1	No. Of Radiation completed till date							
2	No. of Chemotherapy cycles completed till date							
5	Weight							
6	Karnofsky Score							
10	Photo taken / Not Taken							
11	QLQ Taken / 30							
12	QLQ Oragan Specific (HN 35)							
12	Pathological Evaluation							
	Hb							
	WBC							

	RBC							
	Platelet							
	RFT							
	LFT							

		Day 1	Day 8	Day 15	Day 30	End of Radiotherapy	After 2 months	After 3 months
1	Xerostomia							
2	Extensive Salivation							
3	Loss of Taste							
4	Stomatitis							
5	Difficulty in opening of mouth							
6	Dysphasia							
7	trismus							

Signature of Guide **Signature of Student**

Indian Drugs Research Association & Laboratory

561-B, Shivajinagar, Behind Congress Bhavan Lane, Pune - 411 005.
☎ : (020) 25534018 / 25537875 • E-mail : idralpune@gmail.com

Ref. No. _____ Date _____

21-11-2013

Report No. 155

CERTIFICATE OF ANALYSIS
CONFIDENTIAL

Name of the Party	B.S.D.T's Integrated Cancer Treatment and Research Centre, Wagholi.
Your Ref.No.	Your Letter dt.12-11-2013.
Type of the Sample.	Ananta Vati.
Date of Receipt.	13-11-13.
Batch No.	-
Quantity Received.	1 X 10 Tab. Sample Drawn by Party.
Description:	Round Cylindrical Brown Coloured Tablet.
Thin Layer Chromatography:	
Extraction -	Alcoholic Extract.
Mobile Phase -	Chloroform:Methanol (9:1).
Adsorbent used -	Silica Gel $G_{60}F$.
Detection –	
254 nm-	One spot. Rf- 0.87 Blue.
366 nm-	One spot. Rf – 0.61 (Flu.Blue).
Iodine Vapours -	Seven spots. Rf – 0.03, 0.10,0.17,0.26,0.36, 0.61, 0.87.(All Yellow).
Vanillin Sulphuric Acid Reagent.	Five spots. Rf - 0.03,0.17 (Gray),0.61,0.87, 0.96 (Violet).

For I.D.R.A.&L. Pune.

AcDesai

Indian Drugs Research Association & Laboratory

561-B, Shivajinagar, Behind Congress Bhavan Lane, Pune - 411 005.
☎ : (020) 25534018 / 25537875 • E-mail : idralpune@gmail.com

Ref. No. _____ Date _____

Report No. 153 21-11-2013

CERTIFICATE OF ANALYSIS
CONFIDENTIAL

Name of the Party	B.S.D.T's Integrated Cancer Treatment and Research Centre, Wagholi.Pune.
Your Ref.No.	Your Letter dt.12-11-2013.
Type of the Sample.	Praval Panchamrit. (Mouktik Yukta).
Date of Receipt.	13-11-2013.
Batch No.	-
Quantity Received.	1 X 10 Tab.

Sample Drawn by Party.

Description:	Grey coloured round cylindrical Tablet.
Ca % (As is)	42.22 %

ADesai

For I.D.R.A.& L. Pune.

Indian Drugs Research Association & Laboratory

561-B, Shivajinagar, Behind Congress Bhavan Lane, Pune - 411 005.
☎ : (020) 25534018 / 25537875 • E-mail : idralpune@gmail.com

Ref. No. _____ Date _____

21-11-2013

Report No. 152

CERTIFICATE OF ANALYSIS
CONFIDENTIAL

Name of the Party	B.S.D.T's Integrated Cancer Treatment and Research Centre, Wagholi.Pune.
Your Ref.No.	Your Letter dt.12-11-2013.
Type of the Sample.	Kamdudha Rasa.. (Mouktik Yukta).
Date of Receipt.	13-11-2013.
Batch No.	-
Quantity Received.	1 X 10 Tab.

Sample Drawn by Party.

Description:	Brown coloured round cylindrical Tablet.
Ca % (As is)	24.39 %
Fe % (As is)	0.64 %

AeDesai

For I.D.R.A.& L. Pune.

Atharva Yashtimadhu Ghrut

Sr. No.	Test Applied	Remark/ Parameter
1	Description	Yellow colored Ghruta with characteristic odour of Yashtimadhu.
2	Agni Pariksha	Kalka burn without crackling sound when exposed to flame.
3	Fena Pariksha	Foam should disappear over the Ghruta.
4	Varti Pariksha	Kalka becomes harder and rolls in to Varti (Wick).

Atharva Ananta Vati

Sr. No.	Test Applied	Remark/ Parameter
1	Description	Reddish colored, circular, compressed, biconvex, uncoated tablet. Odour, characteristic aromatic.
2	Loss on drying	Not More Than 5 %w/w
3	Average Weight	0.285 – 0.325 gm
4	Diameter	10 – 11 mm
5	Thickness	4-5 mm
6	Hardness	2-4 kg/sq.cm
7	Disintegration Time	NMT 30 min
8	Friability	NMT 1 % w/w

Atharva Praval Panchamrut Ras (Mouktik Yukta)

Sr. No.	Test Applied	Remark/ Parameter
1	Description	Grey colored, circular, compressed, flat, uncoated tablet.
2	Loss on drying	Not More Than 5 %w/w
3	Average Weight	0.275 – 0.325 gm
4	Diameter	8-9 mm
5	Thickness	3-4 mm
6	Hardness	2-5 Kg/Sq.cm
7	Disintegration Time	Not More Than 30 %w/w
8	Friability	Not More Than 1 % w/w

Atharva Kamdudha Vati (Mouktik Yukta)

Sr. No.	Test Applied	Remark/ Parameter
1	Description	Light pink colored, circular, compressed, flat, uncoated tablet.
2	Loss on drying	Not More Than 5 %w/w
3	Average Weight	0.275 – 0.325 gm
4	Diameter	8-9 mm
5	Thickness	3-4 mm
6	Hardness	2-5 Kg/Sq.cm
7	Disintegration Time	Not More Than 30 min
8	Friability	Nor More Than 1 % w/w

EORTC QLQ-C30 (version 3)

We are interested in some things about you and your health. Please answer all of the questions yourself by circling the number that best applies to you. There are no "right" or "wrong" answers. The information that you provide will remain strictly confidential.

Please fill in your initials: ⌊_⌊_⌊_⌊_⌋

Your birthdate (Day, Month, Year): ⌊_⌊_⌊_⌊_⌊_⌊_⌊_⌊_⌋

Today's date (Day, Month, Year): 31 ⌊_⌊_⌊_⌊_⌊_⌊_⌊_⌊_⌋

		Not at All	A Little	Quite a Bit	Very Much
1.	Do you have any trouble doing strenuous activities, like carrying a heavy shopping bag or a suitcase?	1	2	3	4
2.	Do you have any trouble taking a long walk?	1	2	3	4
3.	Do you have any trouble taking a short walk outside of the house?	1	2	3	4
4.	Do you need to stay in bed or a chair during the day?	1	2	3	4
5.	Do you need help with eating, dressing, washing yourself or using the toilet?	1	2	3	4

During the past week:

		Not at All	A Little	Quite a Bit	Very Much
6.	Were you limited in doing either your work or other daily activities?	1	2	3	4
7.	Were you limited in pursuing your hobbies or other leisure time activities?	1	2	3	4
8.	Were you short of breath?	1	2	3	4
9.	Have you had pain?	1	2	3	4
10.	Did you need to rest?	1	2	3	4
11.	Have you had trouble sleeping?	1	2	3	4
12.	Have you felt weak?	1	2	3	4
13.	Have you lacked appetite?	1	2	3	4
14.	Have you felt nauseated?	1	2	3	4
15.	Have you vomited?	1	2	3	4
16.	Have you been constipated?	1	2	3	4

Please go on to the next page

During the past week:	**Not at All**	**A Little**	**Quite a Bit**	**Very Much**
17. Have you had diarrhea?	1	2	3	4
18. Were you tired?	1	2	3	4
19. Did pain interfere with your daily activities?	1	2	3	4
20. Have you had difficulty in concentrating on things, like reading a newspaper or watching television?	1	2	3	4
21. Did you feel tense?	1	2	3	4
22. Did you worry?	1	2	3	4
23. Did you feel irritable?	1	2	3	4
24. Did you feel depressed?	1	2	3	4
25. Have you had difficulty remembering things?	1	2	3	4
26. Has your physical condition or medical treatment interfered with your family life?	1	2	3	4
27. Has your physical condition or medical treatment interfered with your social activities?	1	2	3	4
28. Has your physical condition or medical treatment caused you financial difficulties?	1	2	3	4

For the following questions please circle the number between 1 and 7 that best applies to you

29. How would you rate your overall health during the past week?

1	2	3	4	5	6	7
Very poor						Excellent

30. How would you rate your overall quality of life during the past week?

1	2	3	4	5	6	7
Very poor						Excellent

EORTC QLQ - H&N35

Patients sometimes report that they have the following symptoms or problems. Please indicate the extent to which you have experienced these symptoms or problems during the past week. Please answer by circling the number that best applies to you.

During the past week:		**Not at all**	**A little**	**Quite a bit**	**Very much**
31.	Have you had pain in your mouth?	1	2	3	4
32.	Have you had pain in your jaw?	1	2	3	4
33.	Have you had soreness in your mouth?	1	2	3	4
34.	Have you had a painful throat?	1	2	3	4
35.	Have you had problems swallowing liquids?	1	2	3	4
36.	Have you had problems swallowing pureed food?	1	2	3	4
37.	Have you had problems swallowing solid food?	1	2	3	4
38.	Have you choked when swallowing?	1	2	3	4
39.	Have you had problems with your teeth?	1	2	3	4
40.	Have you had problems opening your mouth wide?	1	2	3	4
41.	Have you had a dry mouth?	1	2	3	4
42.	Have you had sticky saliva?	1	2	3	4
43.	Have you had problems with your sense of smell?	1	2	3	4
44.	Have you had problems with your sense of taste?	1	2	3	4
45.	Have you coughed?	1	2	3	4
46.	Have you been hoarse?	1	2	3	4
47.	Have you felt ill?	1	2	3	4
48.	Has your appearance bothered you?	1	2	3	4

Please go on to the next page

During the past week:		**Not at all**	**A little**	**Quite a bit**	**Very much**
49.	Have you had trouble eating?	1	2	3	4
50.	Have you had trouble eating in front of your family?	1	2	3	4
51.	Have you had trouble eating in front of other people?	1	2	3	4
52.	Have you had trouble enjoying your meals?	1	2	3	4
53.	Have you had trouble talking to other people?	1	2	3	4
54.	Have you had trouble talking on the telephone?	1	2	3	4
55.	Have you had trouble having social contact with your family?	1	2	3	4
56.	Have you had trouble having social contact with friends?	1	2	3	4
57.	Have you had trouble going out in public?	1	2	3	4
58.	Have you had trouble having physical contact with family or friends?	1	2	3	4
59.	Have you felt less interest in sex?	1	2	3	4
60.	Have you felt less sexual enjoyment?	1	2	3	4

During the past week:		**No**	**Yes**
61.	Have you used pain-killers?	1	2
62.	Have you taken any nutritional supplements (excluding vitamins)?	1	2
63.	Have you used a feeding tube?	1	2
64.	Have you lost weight?	1	2
65.	Have you gained weight?	1	2

EORTC QLQ-C30 (version 3)

आपली व आपल्या आरोग्याविषयाची माहिती जाणून घेण्यास आम्ही उत्सुक आहोत. कृपया आपल्याला लागू पडणारी सर्व उत्तरे आपण स्वतः योग्य त्या आकडया भोवती वर्तुळ करून द्यावीत. ही उत्तरे बरोबर अथवा चुक या सदरात मोडत नाहीत. आपण पुरवलेली माहीती अतिशय गुप्त राखली जाईल.

आपल्या नावाची अद्याक्षरेः
जन्मतारीख (दिवस, महिना, वर्ष)ः
आजची तारीख (दिवस, महिना, वर्ष)ः ३१

		अजिबात नाही	थोडा	बराच	खूपच
१.	आपणास कष्टदायक काम करताना काही त्रास होतो का उदा. जड पिशवी किंवा सूटकेस उचलताना?	१	२	३	४
२.	आपणास जास्त लांब चाललयावर काही त्रास होतो का?	१	२	३	४
३.	आपणास घराबाहेर थोडे अंतर चालताना त्रास होतो का?	१	२	३	४
४.	आपणास दिवसभरात खुर्चीत बसून अथवा पलंगावर पडून राहण्याची गरज भासते का?	१	२	३	४
५.	आपणास जेवताना, कपडे घालताना स्नान करताना अथवा शौचादी कामासाठी मदत घ्यावी लागते का?	१	२	३	४

गेल्या आठवडयात

		अजिबात नाही	थोडा	बराच	खूपच
६.	आपले कामकाज अथवा इतर दैनंदिन व्यवहार करण्यावर काही बंधने आली का?	१	२	३	४
७.	आपले छंद पुरवण्यात अथवा फावल्या वेळातील उद्योग करण्यावर काही बंधने आली का?	१	२	३	४
८.	आपणास धाप लागली होती का?	१	२	३	४
९.	आपणास वेदना झाल्या होत्या का?	१	२	३	४
१०.	आपणास विश्रांतीची गरज भासली का?	१	२	३	४
११.	आपणास झोपेचा काही त्रास झाला होता का?	१	२	३	४
१२.	आपणास अशक्तपणा वाटला होता का?	१	२	३	४
१३.	आपली भूक मंदावली होती का?	१	२	३	४

गेल्या आठवडयात	अजिबात नाही	थोडा	बराच	खूपच
१४. आपणास मळमळल्यासारखे वाटले होते का?	१	२	३	४
१५. आपणास उलटया झाल्या होत्या का?	१	२	३	४
१६. आपणास बध्दकोष्ठतेचा त्रास झाला का?	१	२	३	४
१७. आपणास जुलाब झाले होते का?	१	२	३	४
१८. आपणास थकवा जाणवला का?	१	२	३	४
१९. वेदनेमुळे आपल्या दैनीक व्यवहारात अडथळा आला का?	१	२	३	४
२0. आपणास चित्त एकाग्र करणे कठीण गेले होते का, (उदा. पेपर वाचताना किंवा दूरचित्रवाणी बघताना)	१	२	३	४
२१. आपणास मानसिक ताण जाणवला का?	१	२	३	४
२२. आपण काळजी करत होता का?	१	२	३	४
२३. आपली चिडचिड झाली का?	१	२	३	४
२४. आपण उदास होता का?	१	२	३	४
२५. आपणास गोष्टी लक्षात ठेवण्यास त्रास झाला होता का?	१	२	३	४
२६. आपली शारीरिक स्थिती अथवा वैदयकिय उपचार यामुळे आपल्या कौटुंबिक जीवनात काही अडथळे आले का?	१	२	३	४
२७. आपली शारीरिक स्थिती अथवा वैदयकीय उपचार यामुळे आपल्या सामाजीक व्यवहारात काही अडथळे आले का?	१	२	३	४
२८. आपली शारीरिक स्थिती अथवा वैदयकिय उपचार यामुळे आपल्यापूढे आर्थिक अडचणी निर्माण झाल्या आहेत का?	१	२	३	४

खालील प्रश्नांची उत्तरे १ ते ७ पैकी आपल्याला लागू पडणा-या आकडया भोवती वर्तुळ करून द्यावीत.

२९. मागील आठवडयातील आपल्या सर्व साधारण आरोग्याचे मूल्यमापन आपण कसे कराल?

१	२	३	४	५	६	७
अति वाईट.						उत्कृष्ट.

३0. मागील आठवडयातील आपल्या जीवनाच्या दर्जाचे मूल्यमापन आपण कसे कराल?

१	२	३	४	५	६	७
अति वाईट.						उत्कृष्ट.

EORTC QLQ - H&N35

रूग्ण कधी त्यांना खालीलप्रमाणे त्रास होत आहे किंवा खालील लक्षणांपैकी काही लक्षणे दिसत आहे असे सांगत येतात. कृपा करून तुम्हाला खाली दिलेल्या लक्षणापैकी कोणत्या बाबतीत किती त्रास गेल्या आठवडयात झाला ते नमुद करा. ज्या प्रमाणात तुम्हाला त्रास झाला तो दर्शविणा-या आकडयाभोवती वर्तुळ करा

गेल्या आठवडयात	अजिबात नाही	जरासे	बरेच	खूप जास्त
३१. तुमच्या तोंडात दुखत होते का?	१	२	३	४
३२. तुमच्या जबडयात दुखत होते का?	१	२	३	४
३३. तुमचे तोंड आल्यासारखे वाटत होते का?	१	२	३	४
३४. तुमचा घसा दुखत होता का?	१	२	३	४
३५. पातळ पदार्थ गिळायला त्रास होत होता का?	१	२	३	४
३६. वाटून सरसरीत केलेले पदार्थ गिळायला अडचण आली होती का?	१	२	३	४
३७. घन अन्न पदार्थ गिळायला त्रास होत होता का?	१	२	३	४
३८. गिळताना घुसमटल्या सारखे वाटत होते का?	१	२	३	४
३९. तुम्हांला दातांचा काही त्रास झाला होता का?	१	२	३	४
४0. तोंड पूर्ण उघडायला त्रास झाला होता का?	१	२	३	४
४१. तोंड कोरडे पडत होते का?	१	२	३	४
४२. तुमची लाळ चिकट झाली होती का?	१	२	३	४
४३. वास घेण्याच्या क्षमतेमध्ये अडचण आली होती का?	१	२	३	४
४४. चव घेण्याच्या क्षमतेमध्ये अडचण आली होती का?	१	२	३	४
४५. खोकला आला होता का?	१	२	३	४
४६. आवाज घोगरा झाला होता का?	१	२	३	४
४७. तुम्हांला आजारी वाटत होते का?	१	२	३	४
४८. आपण कसे दिसतो याबद्ल चिंता वाटली होती का?	१	२	३	४

पुढील पानावर

गेल्या आठवडयात	अजिबात नाही	जरासे	बरेच	खुप जास्ती
४९. खाताना त्रास झाला होता का?	१	२	३	४
५0. कुटुंबियांसमोर खाताना त्रास झाला होता का?	१	२	३	४
५१. इतर माणसांसमोर खाताना त्रास झाला होता का?	१	२	३	४
५२. जेवणातील आनंद अनुभवताना त्रास वाटला होता का?	१	२	३	४
५३. दुस-यांबरोबर बोलताना त्रास होत होता का?	१	२	३	४
५४. टेलिफोनवर संभाषण करताना त्रास वाटला होता का?	१	२	३	४
५५. कुटुंबीयांबरोबर सामाजिक संबंध ठेवताना त्रास झाला होता का?	१	२	३	४
५६. मित्रमैत्रिणींबरोबर सामाजिक संबंध ठेवताना त्रास झाला होता का?	१	२	३	४
५७. बाहेर समाजात वावरताना त्रास झाला होता का?	१	२	३	४
५८. कुटुंबीयांसमवेत अथवा मित्रमैत्रिणींबरोबर शारिरीक जवळीक करताना काही त्रास वाटला होता का?	१	२	३	४
५९. लैंगिक जीवनातील आकर्षण कमी झाले आहे असे वाटले होते का?	१	२	३	४
६0. शरीर संबंधातील (संभोग) आनंदात कमीपणा आला आहे असे वाटले होते का?	१	२	३	४

गेल्या आठवडयात	नाही	होय
६१. वेदनाशामक गोळयांचा वापर केला होता का?	१	२
६२. (जीवनसत्वे सोडून) दुसरे काही पूरक अन्नघटक घेतले होते का?	१	२
६३. नळीद्वारा जेवण द्यावे लागले होते का?	१	२
६४. तुमचे वजन कमी झाले आहे का?	१	२
६५. तुमचे वजन वाढले आहे का?	१	२