RADIOTHERAPEUTIC EFFECT ON OROPHARYNGEAL FLORA IN HEAD AND NECK CANCER

M. Panduranga Kamath[1], Mahesh Chandra Hegde[2], Suja Sreedharan[3], D. K. Salmi [4], K. Padmanabhan [5]

ABSTRACT : *The effect of radiotherapy on oropharyngeal bacterial and mycotic flora was studied. Thirty five patients were included from whom swabs were taken before and at the end of irradiation. Fifteen controls were included.*

It was found that Streptococcus pneumoniae was significantly decreased at end of irradiation, while there was an increase in Staphylococcus aureus, Pseudomonas, Bacteroides and Candida species. There was no change in culture and sensitivity pattern prior to and after radiotherapy.

Key Words : *Radiotherapy, Oropharyngeal flora, Head and Neck cancer*

INTRODUCTION

Malignancies of head and neck constitute a large percentage of cancer. Most of these are very much advanced at presentation and presents a formidable challenge with regards to management both to the otolaryngologist and head and neck surgeon.

With the continuing advances in the techniques and modalities of radiation therapy a large percentage of head and neck tumors are treated by radiation alone or by a combination of radiation and surgery. As it is less disfiguring and disabling, radiation therapy is usually the more desirable modality of treatment for head and neck cancer, provided of course that there is a choice of therapy.

Among all cancers, head and neck cancer is associated with a severe compromise of immunity and irradiation further depresses the immunologic systems, leading to infections, so much so that post operative sepsis is the leading cause of death in head and neck cancer patients, particularly those previously irradiated (Inagarki et al 1974).

In this work the effect of irradiation on oropharyngeal bacterial and mycotic flora in head and neck cancer patients was studied. This is of utmost importance as most postoperative infections in head and neck have an endogenous source, mainly from the oropharynx (Abu Shara 1993).

MATERIALS AND METHODS

Thirty five patients suffering from head and neck cancer were included in the study. All patients were free from systemic diseases. Dental infection was controlled before irradiation. Only those patients who had not received antibiotics, chemotherapy or cytotoxic drugs were selected. Their ages ranged from 42 to 80, with a sex distribution of 27 males, 8 females. This is summarized in Table I. The distribution of cases is given in Table II .

Aerobic, anaerobic and fungal culture swabs were taken from the tonsillar fossae, prior to commencement of radiotherapy and soon after completion of the full course. For aerobic culture, swabs were subcultured on to blood agar plates and McConkeys media and incubated at 37°C for 24 hours. Following this, the bacterial isolate was identified biochemically and antibiotic sensitivity done. For anaerobic culture, Robertson cooked meat broth was used as transport medium. This medium was then subcultured on to two blood agar plates, one with antibiotics. Both plates were incubated in an anaerobic jar for 48 hours at 37°C. After this period, the growths were identified by the microbiologist. For fungal culture, swabs were introduced into KOH mounts and subcultured on to Sabouraud's media.

Table I : Age and Sex distribution

Age	No. of cases	%	Sex	Number	Percentage
40-50	8	22.4	Male	27	75.6
51-60	16	44.8			
61-70	10	28	Females	8	22.4
71-80	1	2.8			
Total	35			Total	35

[1]H.O.D and Professor in ENT, [2]Associate Professor, [3]Associate Professor, [4]Resident, [5]ENT Surgeon, Kasturba Medical College, Attavar, Mangalore

Table II : Diagnosis Distribution

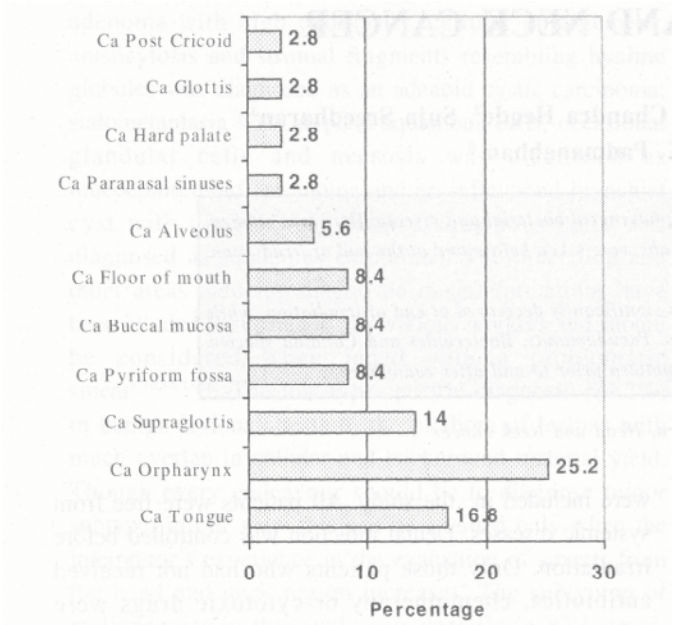


Table III : Histopathology Distribution

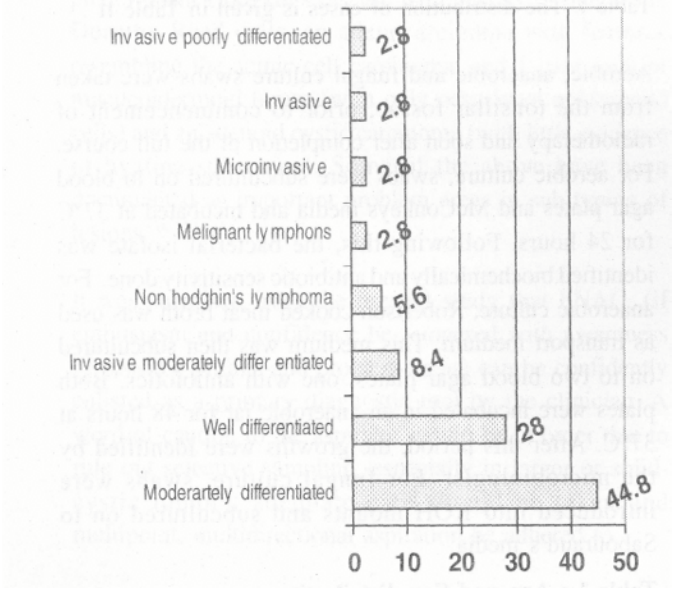
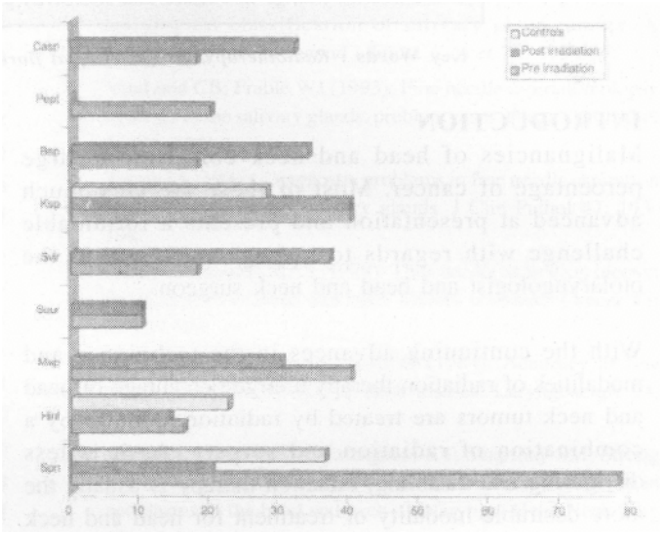


Table IV : Dosage of Radiotherapy

Radiotherapy Total Dose Gy	No. of cases	Percentage
20-30	2	5.6
31-40	6	16.8
41-50	3	8.4
51-60	24	67.2
Total		35

Table V : Distribution of flora



Spn	-	Streptococcus pneumonia
Bsp	-	Bacteroids species
Hinf	-	Haemophilus influenzae
Pept	-	Peptostreptococcus
Msp	-	Moraxella species
Casp	-	Candida species
Saur	-	Staphylococcus aureus
Svir	-	Streptococcus viridans
Ksp	-	Klebsiella species

The changes in distribution pattern of oropharyngeal flora and their antibiotic sensitivity before and after radiotherapy was studied and compared with controls drawn from normal population. Fifteen controls were included in the study. They had an age distribution ranging from 51 to 73 and a male, to female ratio of 3:1.None of the cases had any systemic/locoregional disease or were receiving antibiotics.

Statistical analysis was done using the Chi-square and the Fisher's exact test. The McNemar's test was used in analysis of the matched or paired data.

OBSERVATIONS AND RESULTS

The majority of cases were in the 50 to 60 age group and were males. As per the diagnostic distributions of cases studied, twenty five percent of patients had carcinoma oropharynx, which made up the largest group.

Table VI :Antibiotic Sensitivity Pattern

	Pre-irradiation			Post-irradiation		
Pre-irradiation	gm+	gm-	A	gm+	gm-	A
Ampicillin	12	1	-	0	2	-
Amoxycillin	8	14	-	3	8	1
Cephalosporine	1	-	-	-	-	1
Chloramphenicol	1	20	10	-	20	9
Clindamycin	1	-	4	-	-	5
Cloxacillin	1	-	-	7	-	1
Erythromycin	22	9	6	13	7	-
Gentamycin	2	12	-	2	16	-
Methicillin	1	-	-	-	-	-
Penicillin	23	-	6	15	3	-
Cotrimoxazole	-	17	-	4	14	-
Tetracycline	-	5	6	1	2	-
Ciprofloxacin	22	18	-	13	14	8
Piperacillin	-	3	-	-	1	-
Amikacin	1	5	-	2	2	-
Cefotaxime	26	3	5	6	3	5
Roxithromycin	15	4	5	6	3	1
Ceftriaxone	15	16	1	2	7	1
Netillin	-	-	-	3	-	-
Tobramycin	-	12	1	-	9	-
Ceftazidime	-	4	-	-	5	-

Gm+ gram positive A - anaerobes

Gm - gram negative-As per histopathology of cases 91% of cases were squamous cell carcinomas. Of the 91%, 45% of cases had moderately differentiated squamous cell carcinoma, and 28% had well differentiated squamous cell carcinoma (table III).

67% of cases received a total dose of radiotherapy ranging from 51 to 60 grays in doses of 200cGy per day, 5 days a week. The distribution of total doses of irradiation by Co60 is summarized in Table No:IV. The most common complication of radiation treatment observed was severe mucositis of oral cavity and oropharynx making swabbing extremely difficult in the post irradiation period.

Distribution of flora in the study patients before and after radiotherapy and in controls is given in Table No:V. Commonest organisms isolated in the preirradiation group and controls were Streptococcus pneumoniae (77.1% and 86.7%) and Klebsiella species (40.0% and 66.7%) respectively. The only other organism isolated in controls was Haemophilus influenza. Comparing pre irradiation and control groups, Haemophilus influenzae was significantly decreased in the former group (p=0.01). Streptococcus pneumoniae and Klebsiella species were also decreased, though the difference was not statistically significant. Commonest organisms isolated from post irradiation group were Streptococcus viridans (37.1%), Klebsiella species (37.1%) and Bacteroides species (34.2%).

Comparing the changes in the study group, Streptococcus pneumoniae significantly decreased with irradiation compared to pre irradiation period. (p=0.00l); Moraxella species and Klebsiella also decreased with irradiation but these were not found to be statistically significant. Likewise, although organisms like Staphylococcus aureus, Pseudomonas species, Bacteroides species and Candida species showed marginal increase with irradiation, these were not found to be statistically significant.

Antibiotic sensitivity of gram positive, gram negative and anaerobes were equally distributed among the drugs studied in the preirradiation and postirradiation groups. There was no statistically significant change in the antibiotic sensitivity following radiation. The result is summarized in Table No:VI

DISCUSSION

Advances in the field of chemotherapy, radiotherapy and surgery have resulted in improved survival of cancer patients. Often the life span of these patients are shortened by sepsis complicating these treatment modalities. It has been conclusively proved that about half of cancer deaths was due to infection. Most common causes of sepsis were pneumonia and septicemia caused by gram negative bacilli (Inagarki et al 1974).

Head and neck cancer as such alters the immunological profile of the patient. Previous studies found elevated IgA levels (Katz A.E 1978, Baskis A.M 1979, Mathew D 1980, S.C. Gupta 1981). It was suggested that elevated IgA acts as blocking antibodies to the host immune response. Altered immunological system changes the profile of microbiologic flora both in normal people and in head and neck cancer patients.

Indigenous microflora of the mouth/oropharynx are Viridans streptococci, Fusobacterium, Staphylococcus

epidermidis, Neisseria, Haemophilus species, Staphylococcus aureus, Bacteroides spp., and Branhamella catarrhalis(Alexander W.Cracken and Geoffrey A Lund 1997). Normal flora is altered in head and neck cancer patients as has been borne out by our study which shows that Haemophilus influenzae was significantly reduced in these patients prior to radiation, compared to controls. These patients also grew a wide variety of gram positive, gram negative, aerobic, anaerobic and mycotic pathogens compared to controls where only three pathogens grew. Many studies have reported the effect of radiation on the immunological status of patients receiving radiotherapy. High dose irradiation. of lymphoid tissues reduces the peripheral blood lymphocyte count, irrespective of the fact whether thymus is irradiated or not (Ghossein et.al 1975 and McCredie 1972).

Streptococcus pneumoniae was isolated in 77% cases of cases prior to radiation in this study, while most previous studies isolated Streptococcus viridans (Rohit et.al, Abu Shara et.al). In post irradiation cases, we isolated Streptococcus pneumoniae and Klebsiella as compared to other authors (Rohit et.al 1998, Abu Shara et.al 1993, Rice and Gill 1979) where Staphylococcus aureus and Streptococcus viridans were isolated.

Gram positive organisms were sensitive to penicillin and erythromycin in pre and post irradiation period in our study. Gram negatives were sensitive to chloramphenicol, cotrimoxazoie and ciprofloxacin in pre and post irradiation periods. Anaerobes were sensitive to chloramphenicol in both periods. In our study, we could not find any significant change in the antibiotic sensitivity pattern before and after radiotherapy. Our study indicates a change in oropharyngeal flora with irradiation, although statistical significance could not be demonstrated in most pathogens.

CONCLUSION

Head and neck cancer has an adverse effect on the immune status of the patient. Hence the oropharyngeal flora in these patients can be altered and can consist of abnormal organisms with significantly associated decrease in normal commensals like Haemophilus influenzae and Streptococcus pneumoniae. Radiotherapy further depresses the immune system. This leads to further colonization of oropharynx by pathogens like Bacteroides.The altered oropharyngeal flora however does not have a different antibiotic sensitivity pattern compared to normal flora.

The abnormal flora can cause significant postoperative sepsis in case of postradiotherapy surgical procedures. Hence oropharyngeal swab culture and sensitivity determinations are mandatory in such patients for appropriate antibiotic therapy.

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***Address for Correspondence* :**
Dr. M. Panduranga Kamath
Prof, and H.O.D in E.N.T
KMC, Attavar, Mangalore - 575001