ORIGINAL ARTICLE

Oropharyngeal Flora Changes in Patients with Head and Neck Malignancy Post Radiotherapy

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Summary

Radiotherapy has been recognized as a valuable modality of treatment in the management of head and neck cancers. It can have a direct bactericidal effect on the normal flora of the oropharynx. The objective of this study is to determine the changes in the oropharyngeal flora after external beam radiation. This prospective non randomized control study was performed to aid in identification of organisms involved in sepsis, as well as aid in choosing appropriate antibiotics for surgical procedures in irradiated patient.

Forty patients with various head and neck malignancy and thirty control patients were selected. Oropharyngeal swabs were taken prior to radiotherapy, at the end and one month after radiotherapy. A single swab was taken from the control group. A full bacteriological analysis was performed.

There was a statistically significant decrease in Alpha Hemolytic Streptococci and Neisseria species post radiotherapy. B Proteus and Candida Albicans showed a statistical significant increase in patients with head and neck cancer post radiotherapy. These changes remained even one month after radiotherapy.

Key Words: Oropharyngeal flora, Radiotherapy, Head and Neck malignancy

Introduction

Normal flora refers to the population of microbial associates inhabiting the internal and external surfaces of healthy conventional humans. Synonymous terms include indigenous flora and microbial associates. A multitude of bacteria, fungi, protozoa and other microbials are represented among the normal flora of most humans. The principal group of normal flora in the oropharynx consists of Streptococci Viridans (alpha-hemolytic streptococci), Staphylococci, Neisseria species, Haemophilus species, and Branhamella catarrhalis[1]. Unusual organisms may also be found in cases of local disease or in generally debilitated patients; and among these are Candida Albicans, B.proteus, E.coli, Pseudomonas and Klebsiella species. Some of these bacteria which are considered normal flora have pathogenic potential.

Various exogenous influences may profoundly affect the delicate balance between the host and the normal flora. Race[2], occupation [3] and cancer[4] have each been shown to influence the composition of the normal flora. Patients with cancers have a depression in the immunological system. Even more in patients with squamous cell carcinoma of the head and neck who have a T cell deficiency[5]. Radiotherapy can have a direct bactericidal effect on the normal flora of the oropharynx. This can lead to an overgrowth of pathogenic organism not indigenous to this site[6]. It also has other effects that might influence the bacterial

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flora. The histological changes in irradiated tissue are well known. These changes alter tissue metabolism by altering the available nutrients[7]. It can also alter salivary secretion by making it more acidic and mucoid. If the environment is altered, it is possible that the bacterial population will also be altered.

Materials and Methods

Forty patients with various head and neck malignancy were included in this study. The patients were selected on attendance at the ENT clinic University Hospital Kuala Lumpur. All these patients were free from systemic disease. Patients who had received prior chemotherapy or radiotherapy were excluded from this study. There were also screened to be free from any dental infection. The control group consisted of thirty staff from the ENT ward and the Radiotherapy unit. The study group consisted of twenty females and ten males, ages ranging from twenty-two to fifty two. All the subjects in the control group were free from pharyngitis, dental problems, diabetes or any other debilitating disease.

The patients selected were subjected to external beam radiotherapy from a linear accelerator with a dose ranging from 50 to 70 Grays. Oropharyngeal swabs were taken before the start of radiotherapy, at the end and one month after radiotherapy. For the control group a single swab was taken. The swabs were taken by the same person from the same site i.e. the posterior pharyngeal wall in all patients as well as the control group. A full bacteriological study was performed for all these swabs.

Verbal permission was obtained from each patient for taking the oropharyngeal swab for bacteriological study.

Comparison was made between pre and end irradiation (Table II), Pre irradiation and control (Table IV), and after irradiation which is one month after radiotherapy (Table III). The data obtained were categorical data as such chi square and Fisher's exact test were used.

Results

A. Distribution of Cases

The majority of cases in this study consist of patients with nasopharyngeal carcinoma making up 62% of the total cases. The next most common cases in this study were are carcinoma of the tongue and carcinoma of the larynx making 10% of the total cases. The distribution of the other cases selected for this study is shown in Table I.

B. Microbiological Results

It was found that alpha haemolytic streptococci had significantly reduced at the end of irradiation when compared to pre irradiation patients (Table II). In comparison between controls and pre irradiation patients there is also a significant reduction in alpha hemolytic streptococci in pre irradiation patients ($p<0.05$), as shown in Table IV. However, when we compared the results between after irradiation and end irradiation group, there was a no significant increase in the after irradiation group (Table III). Neisseria species too had similar results as alpha hemolytic streptococci in being significantly reduced in patients at the end of irradiation without any significant increase one month after irradiation.

B Proteus was one of the important pathogenic bacteria isolated. There was a significant increase in B Proteus in patients at the end of irradiation when compared to pre irradiation ($p<0.05$) (Table II). It also increased one month after irradiation as shown in Table III. However, there was no significant difference in the number of patients with B Proteus between the control group and the pre irradiation group.

The pre irradiation group.

The number of patients with Candida Albicans increased at the end of irradiation. This increase was significant with a p value < 0.05 as shown in Table II. However there was no difference in the number of patients with Candida Albicans in the pre-irradiation group and the control group (Table IV). There was also no difference in the number of patients with Candida Albicans when compared at the end of irradiation and one month after (Table III).

Other organism found in this study such as Staphylococcus Aureus, H.influenzae and Pseudomonas, did not show any difference between the control group and the selected patients. There was also no significant increase at the end of irradiation as well as one month after. (Table IV, Table II and Table III respectively).

Table I: Distribution of Case Study Patients

Diagnosis	Total
Carcinoma. Buccal Mucosa	3
Nasopharyngeal carcinoma	25
Carcinoma. Tongue	4
Carcinoma. Larynx	4
Carcinoma. Palate	1
Carcinoma. Tonsil	1
Post Cricoid Carcinoma	1
TOTAL	**40**

Table II: Distribution of Different Organisms at Pre and End of Irradiation

Organism		P+	P-	Total	P value
alpha hemolytic	**E+**	12	7	19	
streptococci	**E-**	16	5	21	p<0.05 *
	Total	28	12	40	
Neisseria species	**E+**	12	7	19	
	E-	16	5	21	p<0.05 *
	Total	28	12	40	
Proteus	**E+**	2	4	6	
	E-	2	32	34	p<0.05 *
	Total	4	36	40	
Klebsiella	**E+**	1	3	4	
Pneumonia	**E-**	2	34	36	p>0.05
	Total	3	37	40	
Staph. Aureus	**E+**	0	1	1	
	E-	2	37	39	p>0.05
	Total	2	38	40	
H.Influenzae	**E+**	0	2	2	
	E-	1	37	38	p>0.05
	Total	1	39	40	
Candida Albicans	**E+**	1	6	7	
	E-	0	33	33	p<0.05 *
	Total	1	39	40	
Pseudomonas	**E+**	0	1	1	
	E-	1	38	39	p>0.05
	Total	1	39	40	

P+: Present Prior to Irradiation **P-**: Absent Prior to Irradiation :
E+: Present at the End of Irradiation **E-**: Absent at the End of Irradiation

* Significant

Table III: Distribution of Different Organisms at End and After Irradiation

Organism		E+	E-	Total	P value
alpha hemolytic	**F+**	15	8	23	
Streptococci	**F-**	3	14	17	p>0.05
	Total	18	22	40	
Neisseria species	**F+**	15	8	23	
	F-	3	14	17	p>0.05
	Total	18	22	40	
Proteus	**F+**	5	4	9	
	F-	1	30	31	p>0.05
	Total	6	34	40	
Klebsiella	**F+**	2	0	2	
Pneumonia	**F-**	2	36	38	p>0.05
	Total	4	36	40	
Staph.aureus	**F+**	0	0	0	
	F-	1	39	40	p>0.05
	Total	1	39	40	
H.influenzae	**F+**	0	0	0	
	F-	2	38	40	p>0.05
	Total	2	38	40	
Candida albicans	**F+**	6	1	7	
	F-	1	32	33	p>0.05
	Total	7	33	40	
Pseudomonas	**F+**	0	0	0	
	F-	1	39	40	p>0.05
	Total	1	39	40	

E+: Present at the End of Irradiation **E-**: Absent at the End of Irradiation
F+: Present One Month after Irradiation **F-**: Absent One Month after Irradiation

Table IV: Distribution of Different Organisms at Pre-irradiation and in Control Group

Organism	Control	Pre irradiation	P value
alpha haemolytic streptococci	28/30	28/40	p<0.05 *
Neisseria species	28	28	p<0.05 *
Proteus	1	4	p>0.05
Klebsiella	0	3	p>0.05
Staph. Aureus	1	2	p>0.05
H.influenzae	0	1	p>0.05
Candida Albicans	0	1	p>0.05
Pseudomonas	0	1	p>0.05

* Significant

Discussion

Nasopharyngeal carcinoma formed the majority of the cases in this study. This is attributed to the fact that university hospital is the tertiary referral centre for patients with nasopharyngeal carcinoma. This also correlated to the fact that the majority of patients in this study were ethnically Chinese i.e. 52%. It as been known that the incidence of nasopharyngeal carcinoma is higher among the Chinese population[8].

Alpha hemolytic streptococci and Neisseria species are considered normal flora especially when found as a mixed growth in University Hospital. In comparison between the control group and the pre irradiated group i.e. patients with head and neck cancer (Table IV), there appears to be a significant reduction of the normal flora in patients with head and neck cancers. As mentioned earlier, patients with head and neck cancers are immunologically depressed[6]. This results in an over growth of pathogenic organism.

At the end of irradiation there was a further significant reduction in the normal flora i.e. Alpha streptococci and Neisseria species when compared to pre irradiation. This was also found in other studies [6,9] radiotherapy tends to suppress normal flora either by its direct bactericidal action or by its indirect effect. It causes an alteration in the local environment of the oropharynx thus resulting in a change in the flora.

The significant decrease in Neisseria species in relation to the irradiation was also found by Llory[10]. This could be explained by the delicate nature of the organism which could be killed in a short time if exposed to heat or unfavorable conditions.

B Proteus is one of the important pathogenic organisms which showed a significant increase at the end of irradiation. This finding was also in keeping with other studies[6, 9]. This is an important finding as it provides us with a possible organism in cases of sepsis in irradiated patients. Specific antibiotic prophylaxis in relation to B Proteus can be selected for any operative procedure intended for post irradiated patients.

There was a significant increase in patients with Candida Albicans at the end of irradiation when compared with the pre irradiated group. This was also found by Martin et al [11] and Rice and Gi11[6] Bodey[12] found that fungal infections increased in cancer patients after wide use of new modalities of radiotherapy. McCormick[13] explained this was due to a decrease in blood supply, malnutrition and loss of anatomical barriers. Kapoor et al[14] found that the immunological system was depressed after radiotherapy and this can result in an infection.

Oropharyngeal swabs were taken one month after irradiation to study the delayed effects of irradiation on oropharyngeal flora. In this study there were no significant changes between the flora found at the end of irradiation and one month after irradiation. This shows that the changes in the flora were directly related to effects of irradiation on the oropharyngeal area, which are prolonged.

From the results above, it is quite evident that irradiation has a marked effect on the bacterial flora. Heimdahl A and Nord CE[15] explained in their study, that suppression of indigenous flora can result in new colonization of pathogenic organism. Patients who are severely immunocompromised by disease may be infected by colonizing microorganism.

Nosocomial infections are a major problem in intensive care patients. Kerver et al[16] studied the effect of colonization and infection in surgical intensive care patients. They found an increase in oropharyngeal colonization with gram negative aerobic organism. The overall mortality in his study was 25.6%, bacteraemia with aerobic gram negative microorganism being the cause of death in 7 patients.

Wound infections are the main cause of post-surgical morbidity in head and neck surgery as found by Penel N et al[17]. They arise with an especially immunocompromised predisposition and mainly involve oropharyngeal flora bacteria.

Intractable post-operative infection in previously irradiated patients is one of the most difficult surgical problems. >From this study we can conclude that irradiation has a marked effect on the oropharyngeal flora. It causes a suppression of the normal flora as well as causing an increase in pathogenic organism. This increase in pathogenic organism may play a role in post-operative infections in these patients.

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