ORIGINAL ARTICLE

Radiation Induced Oral Mucositis and its Co-Relation with the Lifestyle of Cancer Patients: A Prospective Study

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ABSTRACT

Background: Radiation induced oral mucositis (RIOM) develops to some degree in all patients receiving radiation therapy to patients with head and neck cancer.

Materials and Methods: Head and neck cancer (HNC) patients attending the dental clinic during their treatment were recruited. Patients diagnosed histopathologicaly, in the stages between I to IV, had radiation between 20 - 50 Gray (Gy) with or without chemotherapy were included. Treatment types were surgery, radiotherapy (RT) with or without concurrent chemotherapy (CT). A questionnaire was prepared to collect the information regarding age, sex, type of treatment with radiation dose, unilateral/bilateral, mucositis grade, and oral hygiene. Patients were considered as past smokers, or non- smokers. Use of alcohol consumption was also documented.

Results: 106 HNC patients with mucositis and 100 HNC patients without mucositis (non-mucositis group) were analysed. Association of RIOM with alcohol users was; odds ratio (OR)= 9.9 (Confidence Interval (CI)-4.9-20.3), in smokers OR=11.6, (CI 5.7-23.9), in chewable tobacco users OR = 12.7 (CI 6.5-24.8), patients receiving radiation dose with >/=20 Gray the OR was 6.8, (CI 2.5-18.5), and in brushing OR was 0.27, (CI 0.12-0.62)

Conclusion: Knowing past tobacco use history of patients suffering from head and neck cancer will require closer dental follow-up during treatment with radiation, as they are more likely to develop RIOM.

Key Words: Oral mucositis, chemotherapy, radiation therapy

INTRODUCTION

Although modern-day radiotherapy techniques have progressed in leaps and bounds, yet radiation induced oral mucositis still remains a matter of concern for the patient and physician alike. "Radiation Induced Oral Mucositis" or, RIOM in short is a term first used in 1980.[1] It is a radiation–induced toxicity that starts about seven days of starting radiotherapy and continues for approximately ninety days. It is one of the major radiation induced toxicity injuring the normal tissues.[2] Patients with RIOM suffer from pain, altered nutritional status resulting in weight loss, superadded fungal infection as well as a compromised quality of life, and thereby at times, altering the treatment plan.[3] With the addition of concomitant chemotherapy, the oral toxicity due to radiation therapy is further aggravated. RIOM is known to occur due to poor oral hygiene, below average nutritional status, smoking and alcohol consumption, and due to some genetic factors to name a few.[4] Though, the exact pathophysiology of RIOM is yet to be understood, studies suggest that it consists of five stages: initiation stage (Stage I), primary damage and signal amplification (Stage II and III), ulcer (Stage IV), and healing (Stage V).[5] Histologically RIOM is thought to be due to damage to the basal epithelial cells of the oral mucosa during chemotherapy and radiation therapy, yet, the actual pathogenesis is more complex, involving generation of damaging oxygen reactive species, activation of transcription factors e.g. nuclear factor and inflammatory pathway namely cyclo-oxygenase pathway along with the regulation of pro inflammatory cytokines like necrosed tumour factor etc..[6]

It may be helpful to study whether there is a co-relation of RIOM with the life style of the cancer patients in terms of smoking and alcohol consumption habits prior to the start of the cancer treatment.

AIM AND OBJECTIVE

Purpose of this study was to conduct a study to find out the co-relation of RIOM in patients undergoing radiotherapy for head and neck cancers (with/ or without concomitant chemotherapy) in relation to age, sex, habit of alcohol consumption, smoking and non-smoking status. Effects of basic oral care intervention have also been studied to update evidence-based practice guidelines for preventing and treating RIOM in cancer patients undergoing radio and chemotherapy along with other factors.

MATERIAL AND METHODS

This study has been approved by the Institutional Ethics Committee. All patients who were diagnosed histologically and attended the dental clinic of tertiary cancer centre during their cancer treatment, with aero-digestive tract carcinoma, patients in stages between I to IV, received radiation between 20 - 50 Gray (Gy) were prospectively included in this study. Patients with distant metastasis were excluded.

A questionnaire was prepared to collect the information regarding age, sex, total treatment dose, unilateral/bilateral, mucositis grade, and oral hygiene. Patients were considered as smokers or chewable tobacco users, if they were consuming till the diagnosis or less than one year before diagnosis (past smokers).

OM was calibrated under WHO grade and also according to CTCAE both clinically and on functional scales. Patience were evaluated on clinical basis along with a questionnaire on their diet, lifestyle, systemic disease and the grades of OM are evaluated through clinical oral assessments etc [2,5,7,8]. A written consent of the participant was taken on an ethical format regarding their participation in the study. Descriptive statistics is presented in this study. Chi square test was done for significance and $P<0.05$ is considered as significant value.

RESULTS

A total of 106 HNC patients with mucositis with mean age 54.0 ±10.9 (SD) and 100 HNC patients without mucositis (non-mucositis) with mean age 52.4 ±10.0 (SD) were included in the study. We made an attempt to evaluate the association between muscositis and non-mucositis with different parameters such as alcohols consumption, tobacco habits (smoking, chewable and both together), periodontitis, radiation dose, brushing and gender.

The prevalence of mucositis is found higher among the individuals with alcohol consumption habit i.e. 57.5% compared to individuals with non-mucositis (12.0%) and is found individuals with alcohol consumption habit were carrying a statistically significant 10-fold risk (OR = 9.9, P<0.0001, 95%CI 4.9-20.3) of developing mucositis during the chemotherapy and radiotherapy treatment among the HNC patients.

Table 1: Association of oral mucositis with life style and treatment factors

Variables	Non-mucositis	Mucositis	Odds ratio	P value	95.0% CI	
					Lower	Upper
Alcohol						
No	88(88.0%)	45(42.5%0	1(Ref)			
Yes	12(12.0%)	61(57.5%)	9.941	<0.0001	4.86	20.333
Smoking						
No	88(88.0%)	41(38.7%)	1(Ref)			
Yes	12(12.0%)	65(61.3%)	11.626	<0.0001	5.666	23.854
Chewable tobacco						
No	82(82.0%	28(26.4%)	1(Ref)			
Yes	18(18.0%0	78(73.6%)	12.69	<0.0001	6.504	24.76
Smoking + Chewable tobacco						
No	89(89.0%)	47(44.3%)	1(Ref)			
Yes	11(11.0%0	59(55.7%)	10.157	<0.0001	4.873	21.167
Brushing						
No	8(8.0%)	26(24.5%)	1(Ref)			
Yes	92(92.0%)	80(75.5%)	0.268	0.002	0.115	0.624
Periodontitis						
No	98(98.0%)	47(44.8%)	1(Ref)			
Yes	2(2.0%)	58(55.2%)	60.468	<0.0001	14.158	258.262
Radiation dose (Gy)						
<20	95(95.0%)	78(73.7%)	1(Ref)			
>/=20	5(5.0%)	28(26.9%)	6.8	<0.0001	2.5	18.5
Gender						
Female	14(14.0%)	19(17.9%)	1(Ref)			
Male	86(86.0%)	87(82.1%)	0.745	0.444	0.351	1.581

Smoking is significantly prevalent among individuals with mucositis (61.3%) compared to 12.0% in non-mucositis. Smokers have a 12-fold risk of developing mucositis (OR=11.6, P<0.0001, 95%, CI 5.7-23.9) compared to non-smoker during the treatment (Table 1).

The individuals with chewable tobacco habit have a statistically significant risk of 13 times (OR = 12.7, 95%, P<0.0001, CI 6.5-24.8) of developing mucositis than non-chewer individuals. It is observed that among the study individuals with mucositis, 73.6% have a chewing tobacco habit (Table 1).

From the study we found that 55.7% individuals who have developed mucositis during the treatment have a tendency of using both smoking and chewable tobacco products and is found carrying 10 times (OR-4.9, P<0.0001, 95%CI 4.9-21.2) statistically significant risk than those who did not use both.

Brushing is found to be significantly reducing the risk of developing mucositis by 73% (OR= 0.27, P=0.002, 95%CI 0.12-0.62) among the HNC patients. 92.0% of individuals who have a regular brushing habit did not develop mucositis during the treatment periodontitis as shown on table 1.

Periodontitis is highly significantly increasing the risk of developing mucositis, it is observed that those with periodontitis have a 60 times high risk of developing mucositis among HNC patients (P<0.0001, OR=60.5, 95%CI 14.2-258.3). The prevalence of periodontitis among the HNC patients those with mucositis 55.2% compared to 2.0% only those without mucositis.

Radiation dose is also found to be highly associated with developing of mucositis. Radiation dose with >/=20 Gray is observed as significantly elevated the risk of developing mucositis (P<0.0001, OR= 6.8, 95%CI 2.5-18.5). It is observed that gender plays an important role in developing mucositis, Males are found to have a decreasing risk (P=0.444, OR = 0.745, 95%CI 0.4-1.9) than their female counterparts.

DISCUSSION

RION is common side effect in patients receiving radiation for head and neck cancers. Other oral side effects are loose teeth, loss of taste, hyposalivation, caries, trismus, osteoradionecrosis and periodontal diseases. [3,5,9] RIOM is known to occur due to poor oral hygiene, below average nutritional status, lack of antibiotics used at early stage of OM[2,3], smoking and alcohol consumption, and genetic factors. Some patients even develop depression due to RIOM.[8] The risk of depression increases with patients at a young age, among females, hypo salivation, decreased BMI, decreased leukocyte count, poor renal function with elevated serum creatinine level.[10,11] The higher grades of mucositis is observed in patients receiving altered fractionation radiotherapy than the patients receiving conventional radiotherapy.[7,10]

The basic oral care protocol is usually followed before initiating the treatment and during the cancer therapy. The maintenance of oral hygiene, use of oral rinse such as either normal saline water or a mixture of sodium bicarbonate and salt in water are normally considered for maintaining the oral flora during the treatment phase. Study reveals that severe RIOM can be prevented by instituting effective prophylactic treatment. Standard oral care alone is insufficient for patients with head and neck squamous cell carcinoma receiving post-operative definitive radiotherapy with or without chemotherapy.[12]

From the present study, it is evident that risk of RIOM is more in males, having the habits of smoking and alcohol consumption, with increase in dose of radiation. Smoking increases the toxicity, thus increases the risk of mucositis of grade 2 and 3. In comparison to smokers, non-smokers develop less RIOM. It was also found that RIOM increases with age, poor oral hygiene, malnourishment, and vitamin deficiency too.[13] RIOM results in pain, hypo salivation, xerostomia with difficulty in chewing and loss of appetite thus significantly reduces intake of food which enhances weight loss and decreases survival in the entire cohort. [14,15] This decreases oral manifestation which results in decrease in dose of radiation.

A limitation of the present study is the absence of data on co-morbid conditions like uncontrolled diabetes and immune-deficiency status of patients undergoing treatment and which could have influenced in the development of RIOM.

CONCLUSION

In conclusion, patients with head and neck cancers with past alcohol use, past smokers with and without chewable tobacco and receiving radiation dose >/=20 Gy had significant risk of developing oral mucositis, and brushing of teeth was protective factor. Thus, understanding past tobacco use history of patients suffering from head and neck cancer will require closer dental follow-up during treatment with radiation, as they are more likely to develop RIOM.

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