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Assessment of Oral Mucositis among Patients Undergoing Radiotherapy for Head and Neck Cancer: An Audit

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ABSTRACT

Background

Radiation-induced oral mucositis is one of the major ionizing radiation toxicities and normal tissue injuries resulting from radiotherapy. It occurs in up to 80% of head and neck cancer irradiated patients, reaching up to 100% in patients with altered fractionation.

Objective

To assess the grade of Radiation induced oral mucositis as per World Health Organization grading system among post-radiotherapy patients of Head and Neck cancer.

Method

World Health Organization grading for oral mucositis was done in patients reporting to Department of Radiation oncology for radiotherapy at BP Koirala Memorial Cancer Hospital, Bharatpur. A total of 71 patients in 1 month duration were included.

Result

Grade 2 mucositis was most common, 52.11% followed by grade 1 (22.5%), grade 3 (18.3%) and grade 4 (7.04%). There were no post-radiotherapy patients who presented without mucositis.

Conclusion

Radiation induced oral mucositis is a common adverse reaction of radiotherapy. With increase in dose and duration of radiotherapy, grade of mucositis was increasing.

KEY WORDS

Head and neck cancer, Mucositis, Radiotherapy

INTRODUCTION

Radiation-induced oral Mucositis (RIOM) is one of the major ionizing radiation toxicities and tissue injuries resulting from radiotherapy.[1] RIOM was first described in 1980 as an adverse effect of radiotherapy (RT) in cancer patients.[2] RIOM is a tissue injury lasting between 7 and 98 days, which start as an acute inflammation of oral mucosa, tongue, and pharynx after RT exposure.[1,3] RIOM occurs in up to 80% of head and neck cancer irradiated patients, reaching up to 100% in patients with altered fractionation in head and neck cancer.[4] Many risk factors have been identified for RIOM including concomitant chemotherapy (CT), poor oral hygiene, below average nutritional stratus, lack of antibiotic use at early stage mucositis, and smoking.[5,6]

RIOM challenges radiation oncologists from many aspects, such as radiation dose limitations, changes in dose fractionation, and negative effects on patients' quality of life.[1] The major clinical consequences of RIOM include hospital admission, extended hospitalization for total parenteral nutrition, intravenous (IV) analgesia and antibiotics. Sixty-two percent of patients require hospitalization, and 70% of patients with grade 3-4 oral mucositis (OM) require feeding tube insertion. Reduction or cessation of cancer treatment occurs in 35% of patients due to the developed dose-limiting toxicity.[7,8]

Thus the aim of this audit was to assess the grade of RIOM as per WHO grading system among post-RT patients of Head and Neck cancer and observe the general trend in management of mucositis.

METHODS

A cross-sectional hospital based audit, conducted in the Head and Neck cancer patients reporting to Department of Radiation oncology for RT.

Place of study: BP Koirala Memorial Cancer Hospital, Bharatpur,

Duration of study: 1 month (11th March - 10th April 2018)

Sample size: 71

Methods of Data Collection:

Procedures and schedules

• Oral screening was done with the help of torch light and tongue depressor in all patients with head and neck cancer, receiving the last fraction of calculated dose of RT.

• Self-designed pro-forma was filled and WHO grading of RIOM was done based on oral screening and patient's ease of having solid or liquid diet.

• WHO grading of RIOM

Grade 0: No change

Grade 1: Soreness or erythema

Grade 2: Erythema, ulcers, can eat solids

Grade 3: Ulcers, require liquid diet only

Grade 4: Alimentation not possible

Patient consent: written informed consent was taken

Population/Participant's selection criteria

I. Inclusion criteria:

All patients who were receiving the last fraction of their calculated dose of RT for head and neck cancer were included.

II. Exclusion criteria:

Patients who had just begun or were in the course of RT were excluded.

Data Management and Statistical Analysis

Data handling:

The data collected was entered in Microsoft Excel Sheet.

Statistical methods used:

Descriptive statistics was calculated.

Calculation of the sample size:

All patients with head and neck cancer, reporting to Department of Radiation oncology for last fraction of calculated dose of RT, in 1 month time were included.

RESULTS

The total of 71 patients (54 Male and 17 Female) receiving last fraction of calculated dose of RT for Head and Neck cancer were included in the audit. The mean age of patient was 52.4 years (Age range: 25-74 years).

WHO grade 2 mucositis was most common, 52.11% followed by grade 1 (22.5%), grade 3 (18.3%) and grade 4 (7.04%). Comparing the general trend of radiation dosage, patients having grade 2 mucositis were receiving 18-35#, grade 1 mucositis were receiving 12-28$^{\#}$, grade 3 mucositis were receiving 28-35# and grade 4 mucositis receiving 30-35$^{\#}$ of RT. We can observe that with the increase in grade of mucositis the dose and hence the duration of RT was increasing. Each fraction consisted of 2 Gray of radiation.

Of the total patients included, 67.6% had oral cancer. This was followed by Oropharyngeal cancer (14.08%), laryngeal cancer (8.45%), Salivary gland cancer (5.63%) and Nasal cavity and paranasal sinus cancer (4.22%). Of the total oral cancer cases, carcinoma gingivobuccal sulcus was highest (47.9%) followed by carcinoma tongue (35.4%).

Stage IV presentation of Head and Neck cancer was most common, 43.66% followed by stage III (36.61%). Except for Salivary glands all cases had histopathological diagnosis of Squamous cell carcinoma (SCC). Adenoid Cystic Carcinoma (ACC), Mucoepidermoid Carcinoma (MC) and Carcinoma ex Pleomorphic Adenoma (Ca ex PA) were the various histopathological diagnoses for salivary gland tumors.

The general trend observed in management of mucositis was, grade 1 cases were advised to apply honey locally and for grade 2 cases, 2% lignocaine gel topical application was added. Grade 3 cases were managed with topical application of honey, 2% lignocaine gel and 0.2% Chlorhexidine (CHX) mouthwash. Nasogastric feeding tube was inserted for grade 4 cases with topical application of honey, 2% lignocaine gel, 0.2% CHX mouthwash and Oro-T (Himalayan) mouthwash.

The summary of the result findings is tabulated in Table 1.

Table 1. Summary of result findings

SN	Regions in Head and Neck		Diagnosis	Number of cases (n),%	TNM stage				Grade of Mucositis (WHO), Number of fractions of radiotherapy				Total
					I	II	III	IV	1	2	3	4	
1	Oral cavity	GBS	SCC	23 (R: 18, L: 5), 47.9%	0	2	5	16	6 (12-28#)	10 (18-30#)	6 (30-35#)	1 (32#)	23
		Tongue	SCC	17 (R: 10, L:7), 35.4%	1	3	7	6	5 (10-22#)	10 (25-30#)	1 (28#)	1 (30#)	17
		Buccal Mucosa	SCC	6 (R: 3, L:3), 12.5%	0	1	4	1	0	6 (22#)	0	0	6
		Lower lip	SCC	1, 2.08%	0	1	0	0	1 (22#)	0	0	0	1
		Maxilla	SCC	1, 2.08%	0	1	0	0	0	1 (30#)	0	0	1
Total, Oral cavity				48, 67.60%	1, 2.08%	8, 16.66%	16, 33.33%	23, 47.91%	12, 25%	27, 56.25%	7, 14.58%	2, 4.16%	48
2	Oropharynx		SCC	10, 14.08%	0	2	3	5	2 (23#)	3 (30-35#)	3 (35#)	2 (35#)	10
3	Larynx		SCC	6, 8.45%	0	0	4	2	0	3 (25-35#)	3 (30-35#)	0	6
4	Salivary glands		ACC, MC, Ca ex PA	4, 5.63%	1	1	1	1	1 (23#)	3 (30#)	0	0	4
5	Nasal cavity and paranasal sinuses		SCC	3, 4.22%	0	1	2	0	1 (23#)	1 (35#)	0	1 (35#)	3
Total				71, 100%	2, 2.81%	12, 16.90%	26, 36.61%	31, 43.66%	16, 22.5%	37, 52.11%	13, 18.30%	5, 7.04%	71
SN	**Regions in Head and Neck**		**Diagnosis**	**Number of cases(n),%**	**TNM stage**				**Grade of Mucositis (WHO), Number of fractions of radiotherapy**				**Tota**
					I	II	III	IV	1	2	3	4	
1	Oral cavity	GBS	SCC	23 (R: 18, L: 5), 47.9%	0	2	5	16	6 (12-28#)	10 (18-30#)	6 (30-35#)	1 (32#)	23
		Tongue	SCC	17 (R: 10, L:7), 35.4%	1	3	7	6	5 (10-22#)	10 (25-30#)	1 (28#)	1 (30#)	17
		Buccal Mucosa	SCC	6 (R: 3, L: 3), 12.5%	0	1	4	1	0	6 (22#)	0	0	6
		Lower lip	SCC	1, 2.08%	0	1	0	0	1 (22#)	0	0	0	1
		Maxilla	SCC	1, 2.08%	0	1	0	0	0	1 (30#)	0	0	1
Total, Oral cavity				48, 67.60%	1, 2.08%	8, 16.66%	16, 33.33%	23, 47.91%	12, 25%	27, 56.25%	7, 14.58%	2, 4.16%	48
2	Oropharynx		SCC	10, 14.08%	0	2	3	5	2 (23#)	3 (30-35#)	3 (35#)	2 (35#)	10
3	Larynx		SCC	6, 8.45%	0	0	4	2	0	3 (25-35#)	3 (30-35#)	0	6
4	Salivary glands		ACC, MC, Ca ex PA	4, 5.63%	1	1	1	1	1 (23#)	3 (30#)	0	0	4
5	Nasal cavity and paranasal sinuses		SCC	3, 4.22%	0	1	2	0	1 (23#)	1 (35#)	0	1 (35#)	3
Total				71, 100%	2, 2.81%	12, 16.90%	26, 36.61%	31, 43.66%	16, 22.5%	37, 52.11%	13, 18.30%	5, 7.04%	71

GBS: Gingivo-Buccal Sulcus, SCC: Squamous Cell Carcinoma, ACC: Adenoid Cystic Carcinoma, MC: Mucoepidermoid Carcinoma, Ca ex PA: Carcinoma ex Pleomorphic Adenoma, R: Right, L: Left, #: Fraction

DISCUSSION

Complications associated with RT can be direct, caused by toxic action of treatment agents on the proliferative mucosal lining of the mouth or indirect, the result of hemopoeitic shut down.[9-12] The earliest signs and symptoms of OM include erythema and edema, a burning sensation, and an increased sensitivity to hot or spicy food.[11,13]

In our audit, WHO grade 2 mucositis was most common, 52.11% followed by grade 1 (22.5%), grade 3 (18.3%) and grade 4 (7.04%). However, in contrast to our finding RIOM of grade 3 and 4 have been recorded in 56-63% of head and neck cancer patients.[1,4,7,14] The possible reason behind could be the concurrent use of CT in these population, while it was not the same in our case. Also the more number of patients receiving higher doses of RT for longer duration could have resulted in higher grade of RIOM. This also proves the fact that, there is direct relation between total dose, dose per fraction, number of fraction and total duration of RT and the grade of RIOM.[2,3,5,7,8,12-14] Based on these facts, our inference i.e., with the increase in dose and duration of RT, generally the grade of mucositis also increases, holds true.

Among various Head and Neck cancer, the prevalence of oral cancer was highest, 67.6% in our audit. Similar prevalence of oral cancer was recorded in various studies in South East Asia.[15-17] The major risk factor for oral cancer is amount and duration of tobacco use in various forms such as smoking and smokeless tobacco.[15] Use of smokeless tobacco has been linked with risk of oral cancer. Smokeless tobacco contains carcinogenic agents like tobacco-specific nitrosamines (TSNAs), polonium, formaldehyde, cadmium, lead, and benzopyrene. Besides these, food habit oral hygiene, alcohol drinking and life style etc. are other risk factors for oral cancer.[18]

In our audit, the patients with Head and Neck cancer presented more commonly at stage IV (43.66%) followed by stage III (36.61%). The late stage presentation clearly highlights lack of knowledge and awareness regarding oral health issues, the risk factors for oral cancer and the signs and symptoms of oral potentially malignant disorders and oral cancer. An oral health awareness programs about the role of habits in the development of oral cancer, its complication and benefits of detecting this disease at early stage needs to be implemented by the policy makers, institutions and hospitals for better patient outcome.[19]

Honey, 2% lignocaine gel, 0.2% CHX mouthwash and Oro-T (Himalayan) mouthwash were the various measures used for management of mucositis in our audit. However, presented below is the summary of different agents used in the treatment of mucositis with definite benefit, doubtful benefit and no benefit.[20]

• Agents with definite benefit for prevention/treatment of RIOM/level of evidence (should be used):

1. Benzydamine mouthwash to prevent OM without concomitant CT (Level-I).

2. Low level laser therapy (wavelength around 632.8 nm) to prevent OM in patients undergoing RT, without concomitant CT (Level-III).

3. 2% morphine mouthwash may be effective to treat pain due to OM (Level-III)

• Agents with doubtful benefit for prevention/treatment of RIOM/level of evidence (may be used)

1. CHX mouthwash for prevention of OM (Level-III)

2. Misoprostol mouthwash for prevention of OM (Level-III)

3. Oral pilocarpine for prevention of OM (Level-III)

4. Palifermin-keratinocyte growth factor (Level-III)

5. Systemic zinc supplements administered orally may be of benefit to prevent OM (Level-III)

6. L-glutamine for prevention of OM (Level-III)

• Agents with No benefit for prevention/treatment of RIOM/level of evidence (should not be used)

1. PTA (polymyxin, tobramycin, amphotericin B) and BCoG (bacitracin, clotrimazole, gentamicin) antimicrobial lozenges and PTA paste prevent OM (Level-II)

2. Antimicrobial mouthwash to prevent OM (Level-II)

3. Sucralfate mouthwash to prevent oral mucositis in patients receiving concomitant CT (Level-II)

4. Sucralfate mouthwash to treat OM in patients receiving RT(Level-II)

5. Pentoxifylline for prevention of OM (Level-III)

RIOM is a self-limiting tissue injury. It is a dose-limiting toxicity in most of Head and Neck cancer patients. This is an era in mucositis research.[7] Currently, there are numerous prevention and treatment strategies for RIOM. Several other promising agents are in clinical development that eventually may be approved for the management of this debilitating condition. Future studies should evaluate if agents that work by different mechanisms can be used in combination for greater clinical effectiveness.[6]

CONCLUSION

RIOM is a common adverse reaction often limiting the efficacy of radiation by increasing treatment breaks. Adequate oral prophylaxis and holistic treatment approach may reduce the severity of RIOM and improve compliance to radiation which may translate in better disease control and survival. Reducing the morbidity of OM helps to avoid unwanted dose reductions or unscheduled breaks in cancer therapy and thus improve outcome of cancer therapy together with improvement in oral health related quality of life.

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