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Assessment of Treatment Related Mucositis in Locally Advanced Head and Neck Cancer

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Abstract: ***Oral Mucositis is a common adverse event following radiotherapy and chemotherapy of head and neck cancer. The present study evaluates mucositis in three different treatment arms. Out of 193 consecutive patients of locally advanced cancer of head and neck, 150 complied with the inclusion criteria. 48 patients were included in Arm A i.e. Neoadjuvant Chemotherapy followed by Concurrent chemo-radiotherapy, 55 patients in Arm B i.e. Concurrent Chemo-radiotherapy and 47 patients in Arm C i.e. Radiotherapy alone. In treatment arm A, grade 1, 2 and 3 mucositis occurred in 16.66%, 33.33%, and 50% patients respectively. In treatment arm B, grade 1, 2 and 3 mucositis occurred in 9.09%, 67.27%, and 23.63% respectively. In treatment arm C, grade 1, 2 and 3 mucositis occurred in 10.63%, 63.82%, and 25.53% respectively. Mucositis peaked around week 3 in arm A and B and week 4 in arm C. The severity of mucositis increases with the complexity of treatment and by the addition of simultaneous chemo-radiation, resulting in increased duration and interruption of treatment.***

Keywords: Oral mucositis, locally advanced head and neck cancer

1. Introduction

Worldwide, head and neck cancers account for more than 6 lakhs cancers diagnosed each year.[1] HNCs account for about 20-30% of all cancers in India.[2] Squamous cell carcinoma comprises 90% of all HNCs.[3] Oral mucositis is a major acute adverse effect radiotherapy for HNC. Combined radiotherapy and chemotherapy increase the incidence, duration, and severity of oral mucositis, especially when different combinations of drugs and hyper fractionation are used.[4] Mucositis causes significant pain, ulcers, decreases oral intake, increases debility, infection and affects treatment schedule. As there is a high level of mitotic activity in the mucosa, it is affected severely by radiation and chemotherapy.[5] Present study compare the severity of oral mucositis in HNC patients in 3 arms receiving different modalities of radiotherapy and chemotherapy.

2. Aim & Objectives

1) To compare the severity of mucositis concerning the age, sex, stage (III, IVA) and ECOG score between 3 different treatment arms- A) Neoadjuvant chemotherapy followed by radiation and chemotherapy, B) Concurrent chemo-radiotherapy, C) Radiotherapy alone.
2) Compare time to develop mucositis.

3. Method & Materials

193 consecutive patients of locally advanced, stage III and IVA of head and neck cancer attending outpatient and inpatient department of Radiation-Oncology department at Government Medical College Nagpur between January 2017 to May 2018 were screened. Of which 150 Patients were eligible for study. Patients were assigned into 3 different treatment arm & treated accordingly.

Inclusion criteria

1) Age > 18years and < 65years
2) Biopsy proven carcinoma of head & neck
3) Stage III and IV A
4) ECOG score 0, 1, 2
5) Previous head and neck surgery

Exclusion criteria

1) ECOG score 3 or 4
2) Non-compliant with treatment
3) Distant metastases
4) Previously taken treatment like chemotherapy or radiotherapy

Mucositis was graded according to Radiation Therapy Oncology Group RTOG. Grade I (2^{nd} week) includes erythema having mild pain and requires no analgesic, grade II (3 to 4^{th} week) includes focal areas of desquamation, serosanguinous discharge and requires analgesics, grade III (4 to 5^{th} week) confluent mucositis, severe pain and requires narcotic analgesics and grade IV (5 to 6^{th} week) includes ulceration, necrosis and sometimes bleeding.

4. Treatment Arms

Arm A- Neoadjuvant chemotherapy followed by radiotherapy with concurrent chemo-radiotherapy: In this arm, the patient received neoadjuvant chemotherapy in the form of taxane-based chemotherapy three cycles three weeks apart followed by RT 64.8-66 Gy in 1.8 to 2 Gy per fraction respectively 5 days a week in 7-7.5 weeks.[6],[7],[8],[9]

Arm B- Concurrent Chemo-Radiotherapy. In this arm, the patient received RT 64.8-66 Gy in 1.8 to 2 Gy per fraction respectively 5 days a week in 7-7.5 weeks along with Cisplatin 40 mg/m^2 weekly.[10],[11],[12],[13]

Arm C- Radiotherapy. These patients received 64.8-66 Gy in 1.8 to 2 Gy per fraction, 5 days in 7-7.5 weeks. [14], [15], [16]

Data Analysis

Data were analyzed using software Epi-Info version 7.2. Results were presented in the form of tables & graphs. A chi-square test was used as a test of significance. A p-value of less than 0.05 was considered for significance.

5. Results

Out of 193 patients of stage III and IVA of head and neck cancer 150 patients were eligible for the study. Arm A consists of 48, arm B of 55 and arm C of 47 patients. The demographic characteristics of the study subjects are given in table 1.

Table 1: Showing the demographic characteristics of patients

Patients characteristics	Arm A	Arm B	Arm C	Total	
Number of patients	48	55	47	150	
Sex	M 34 F 14	M 37 F 18	M 25 F 22	M 96 F 54	X^2= 3.61 p=0.16
Mean Age (years)	50 (SD ± 5.92)	40 (SD ± 8.09)	49 (SD ± 7.59)		p<0.01
Stage III IA	 18 30	 31 24	 23 24		X^2=3.67 P=0.15
ECOG score 0 1 2	 4 30 14	 17 19 19	 4 19 24	 25 68 67	 X^2= 18.62, P<0.01

Table 2 and chart 1 are showing the number of subjects in treatment arms A, B, and C developing mucositis grade 1, 2, and 3. There was a significant difference in the occurrence of mucositis in different treatment arms. In treatment arm A, grade 1, 2 and 3 mucositis occurred in 16.66%, 33.33%, and 50% patients respectively. In treatment arm B, grade 1, 2 and 3 mucositis occurred in 9.09%, 67.27%, and 23.63% respectively. In treatment arm C, grade 1, 2 and 3 mucositis occurred in 10.63%, 63.82%, and 25.53% respectively.

Table 2: Table showing the distribution of cases according to mucositis grade in each treatment arm

Mucositis grade	Treatment Arm			Total
	A	B	C	
1	8	5	5	18
2	16	37	30	83
3	24	13	12	49
Total	48	55	47	150

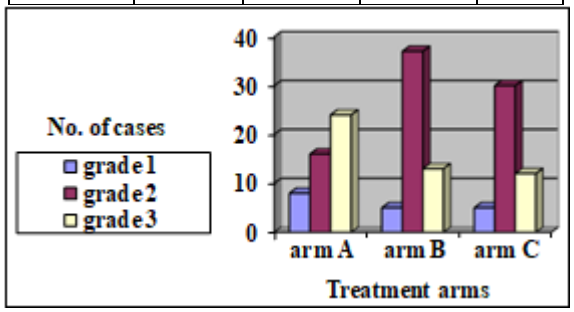
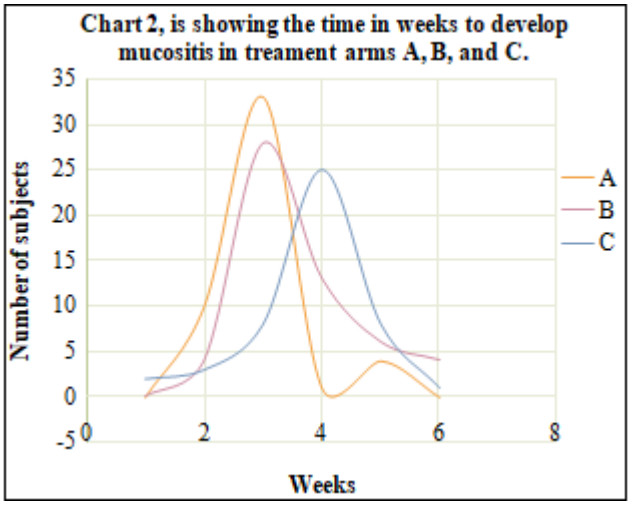


Chart 1: Bar diagram showing distribution of cases according to mucositis grade in each teatment arm

Table 3 and chart 2 are showing the time in weeks to develop mucositis in each treatment arm. Most of the subjects developed mucositis in week 3 in arm A (68.75%), arm B (50.90%) and week 4 in arm C (53.19%) while no subject developed mucositis in week 1 and 6 in arm A and week 1 in arm B.

Table 3: The table is showing time (in weeks) to develop mucositis in each treatment arm

Weeks	Treatment			Total
	A	B	C	
1	0 (0%)	0 (0%)	2 (4.25%)	2
2	10 (20.83%)	4 (7.27%)	3 (6.38%)	17
3	33 (68.75%)	28 (50.90%)	8 (17.02%)	69
4	1 (2.08%)	13 (23.63%)	25 (53.19%)	39
5	4 (8.33%)	6 (10.90%)	8 (17.02%)	18
6	0 (0%)	4 (7.27%)	1 (2.12%)	5
Total	48 (100%)	55 (100%)	47 (100%)	150



6. Discussion

It is well known that the severity of mucositis increases with the increasing dose and duration of chemotherapy and/or radiation. Mucositis causes significant debility in terms of poor oral intake, malnutrition, pain, and infection. There are several treatment regimens for head and neck cancer but there are few studies to compare mucositis among these treatment regimens. Thus, in the current study, we have compared mucositis among three different treatment regimens. Our study shows that there was a significant difference in the occurrence of different grades of mucositis among the treatment regimens. In treatment arm A i.e., neoadjuvant chemotherapy followed by concurrent chemo-radiation there was a higher number of patients with grade 3 mucositis (50%, n=24) while there was a higher number of grade 2 mucositis in arm B i.e., concurrent chemo-radiation (67.27%, n=37) and arm C i.e., radiation (63.82%, n=30). In a study by Garima et al grade III mucositis occurred in 33% patients receiving neoadjuvant chemotherapy followed by accelerated radical radiotherapy, 22% in patients receiving neoadjuvant chemotherapy followed by concomitant conventional radical radiotherapy with carboplatin and 4% in patients receiving neoadjuvant chemotherapy followed by conventional radical radiotherapy.[17]

In a study by Ghoshal et al, the 'Quad Shot' radiation dose schedule was given as 14 Gy/2 days/4 fractions. Mucositis was observed in 8 out of 15 patients in which 6 were grade one and 2 were grade two. None of the patients had grade three mucositides.[18]

Nikam et al found that in the treatment arm with induction chemotherapy followed by concurrent CT-RT, 54% of patients developed mucositis of which grade I, II, III and IV mucositis occurred in 21%, 12%, 17% and 4% of patients respectively. In the treatment arm with only chemoradiotherapy, 56% of patients developed mucositis of which grade I, II, III and IV mucositis noted in 33%, 21%, 2% and 0% of patients.[19]

Also, we have evaluated the time to develop mucositis. The peak number of subjects developing mucositis in neoadjuvant CT followed by concurrent CT-RT and concurrent CT-RT was in week 3 and RT alone was week 4. Thus, it is suggesting that concurrent CT-RT regimens develop early mucositis and RT alone mucositis later. However, as the small sample size is the limitation of the present study, further large studies will be required to confirm the findings.

7. Conclusion

The severity of mucositis increases with the complexity of treatment and by the addition of simultaneous chemo-radiation, resulting in increased duration and interruption of treatment. While simple regimens like radiation alone not only decreases the severity but also reduces the number of patients developing mucositis. Also, concurrent regimens cause early development of mucositis while radiation alone causes late development of mucositis. Prophylactic and symptomatic treatment can improve the compliance.

References

[1] Kowalski LP. Head and neck cancer. BMC Proc 2013;7 Suppl 2:K12.
[PUBMED]
[2] Murthy V, Kundu S, Sahid T, Budrukkar A, Gupta T, Laskar SG, et al. Postoperative radiotherapy in head and neck cancer. Otolaryngol Clin 2012;2:43-5
[3] Vigneswaran N, Williams MD. Epidemiologic trends in head and neck cancer and aids in diagnosis. Oral Maxillofac Surg Clin North Am 2014;26:123-41
[4] Denham JW, Peters LJ, Johansen J, Poulsen M, Lamb DS, Hindley A, et al. Do acute mucosal reacti ons lead to consequenti al late reacti ons in pati ents with head and neck câncer? Radiother Oncol. 1999;52(2):157-64.
[5] Sonis et al. Perspectives in cancer therapy induced mucosal injury. Cancer 2004;100 (9 Suppl): 1995-2005.
[6] Bhushan M. Nikam et al. The effect of induction chemotherapy followed by chemoradiotherapy in advanced head and neck cancer: a prospective study. Int J Res Med Sci. 2014 May;2(2):476-480.
[7] Malik G, Dhull AK, Atri R, Kaushal V. A comparative evaluation of neoadjuvant chemotherapy followed by concomitant chemoradiation versus accelerated radiation therapy versus conventional radiation therapy in a locally advanced head and neck carcinoma. Asian J Oncol 2017;3:59-65.
[8] Delouya G, Clavel S, El-Bared N, Soulières D, Fortin B, et al. (2012) Induction Chemotherapy Followed by Concomitant Chemoradiation in Head and Neck Squamous Cell Carcinoma: A Single Institution Experience. Otolaryngol 1:108. doi:10.4172/2161-119X.1000108
[9] Lin Kong, MD et al. Neoadjuvant Chemotherapy Followed by Concurrent Chemoradiation for Locoregionally Advanced Nasopharyngeal Carcinoma. Interim Results From 2 Prospective Phase 2 Clinical Trials. August 27, 2013 in Wiley Online Library (wileyonlinelibrary.com)DOI: 10.1002/cncr.28324
[10] Jain P, et al. Chemo radiotherapy or neoadjuvent treatment in head and neck cancer. Indian Journal of Cancer | July–September 2008 | Volume 45 | Issue 3
[11] Jeffrey S Tobias et al. chemoradiotherapy for locally advanced head and neck cancer: 10-year follow-up of the UK Head and Neck (UKHAN1) trial. Lancet Oncol. 2009 Sep 9; 10(9): 872-876.
[12] Debabrata Mira et al. Concurrent chemotherapy in advanced head and neck carcinoma – A prospective randomized trial. Bangladesh J Otorhinolaryngol 2011; 17(2): 88-95
[13] Pierre Lavertu et al. Aggressive Concurrent Chemoradiotherapy for Squamous Cell Head and Neck Cancer. An 8-Year Single Institution Experience. Arch Otolaryngol Head Neck Surg 1999;125:142-148
[14] Sushmita Ghoshal, Firuza Patel et al. Palliative radiotherapy in locally advanced head and neck cancer-a prospective trial. Indian Journal of Palliative Care 2004; 10(1): 19-23
[15] Kailash Pandey et al. Palliative Radiotherapy in Locally Advanced Head and Nek Cancer after Failure of Induction Chemotherapy: Comparison of Two Fractionation Schemes. Indian J Palliat Care, 2013 Sep-Dec; 19(3): 139-145
[16] Rajan Paliwal et al. Palliative Hypo-fractionated Radiotherapy in Locally Advanced Head and Neck Cancer with Fixed Neck Nodes. Iran J Cancer Prev 2012; 4:178-82
[17] Malik et al. A comparative evaluation of neoadjuvant chemotherapy followed by concomitant chemoradiation versus accelerated radiation therapy versus conventional radiation therapy in a locally advanced head and neck carcinoma. Asian Journal of Oncology. 2017 Jan-Jun; Vol 3(1): 59-65.
[18] Ghoshal et al. Quad shot: A short but effective schedule for palliative radiation for head and neck carcinoma. 2009; Vol 15(2): 137-140.
[19] Nikam BM et al. The effect of induction chemotherapy followed by chemoradiotherapy in advanced head and neck cancer: a prospective study. Int J Res Med Sci. 2014 May; 2(2):476-480.

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