

Incidence of Complications in Head and Neck Cancer Patients Receiving Radical Radiotherapy with or without Chemotherapy - A Hospital based Study

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ABSTRACT

Introduction: The combined modality treatment (chemotherapy and radiation therapy using both conventional and altered fractionation) have produced increases in both disease-free and overall survival rates, although these approaches have produced higher rates of mucosal toxicity, with grade 3 rates ranging from 32% to 84% and grade 4 rates ranging from 0% to 30%. When compared with other toxic effects, these studies have established mucositis as the dose-limiting toxicity.

Material and methods: Patients receiving chemo-radiation in the form of Cis-platinum, Gemcitabine or Paclitaxel alternating with Gemcitabine were enrolled in this study. Patients particulars were noted, a thorough history of the disease was taken. A complete physical examination with assessment of ECOG performance score, oral assessment, Mucositis was determined weekly while the patient was on chemo-radiation or radiation. Results were displayed as mean \pm standard deviation or percentage. The independent sample "t-test" was used to assess group differences for continuous variables.

Results: Neck swelling was the one of the chief complaint in 89 patients of the series. Facial disfigurement was complained by 12 patients, loss of the appetite was observed by 48 patients and 31 were having complaints of the weight loss. 89 patients presented with the complaint of the difficulty in swallowing. Restriction of the movement of tongue was seen in 53 patients.

Conclusion: It was observed in the present study that mucositis was the one of the chief complication. More than 50% of the patients had nutritional deficiencies in the form of anemia and hypo-proteinemia due to oral mucositis.

Keywords: Mucositis, Voice Change, Neck Mass, Metastasis

INTRODUCTION

Cancer of the head and neck is among one of the commonest cancers. They account for one fourth of male and one-tenth of female cancers in India. These are common in regions with high tobacco and alcohol consumption. Tobacco use in various forms, heavy alcohol consumption and poor diet causes over 90% of head and neck cancers. While combined chemotherapy and radiation therapy (using both conventional and altered fractionation) have produced increases in both disease-free and overall survival rates, these approaches have produced higher rates of toxicity, with grade 3 rates ranging from 32% to 84% and grade 4 rates ranging from 0% to 30%. When compared with other toxic effects, these studies have established mucositis as the dose-limiting toxicity.^{1,2-4} Chemo-radiation toxic effects included Grade 3 and 4 mucositis in 88% of patients, cutaneous reaction in 50%, neutropenia in 49%, thrombocytopenia in 12%, and nausea in 5% in a study of 8 year single institutional study carried at University hospital of Cleveland. The mean weight loss was 12% of initial body weight.² Borbosi et al indicated that

quality of life was significantly compromised for patients with mucositis who found eating and drinking difficult and painful. Research also revealed that worsening mucositis was related with a longer stay in hospital thereby increasing treatment cost⁵ When Gemcitabine was given concomitantly with the radiation in head and neck cancer in phase I trial, the rate of mucositis found to be increased.⁶ The Incidence of grade III mucositis increased with the use of paclitaxel as radiosensitiser in studies done. In a multi-institutional study at Germany in 1998, it was noted that more supportive care is demanded when chemotherapy is given concomitantly along with radiotherapy in head and neck cancer patients.⁷

MATERIAL AND METHODS

The study was conducted at Cancer Treatment Hospital, Punjab and is a single center prospective study. A total of 150 Head & neck cancer patients receiving chemoradiation in the form of Cis-platinum, Gemcitabine or Paclitaxel alternating with Gemcitabine were included in the study. A signed informed consent, ECOG performance status = 0-3, no distant metastases (M0) were included in the study. Patient receiving cytoreduction either in the form of neoadjuvant chemotherapy or surgery, thyroid carcinoma patients, distant metastasis were excluded. informed consent forms were obtained from the patients. Patients particulars were noted, a thorough history of the disease. Any history of addiction to smoking, alcohol, opium and tobacco consumption was taken. History of diabetes mellitus was noted. A complete physical examination with assessment of ECOG performance score, oral assessment, primary tumor size and regional lymph nodes was carried out for all the patients in the study. Routine investigations like CBC, RFT, TSP, DSP, CXR-PA view, ECG were noted and ECHO was done where required. Mucositis was determined weekly while the patient was on chemo-radiation or radiation. Results were displayed as mean \pm standard deviation or percentage.

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The independent sample “t-test” was used to assess group differences for continuous variables.

RESULTS

Most of the patients presented with chief complaint of non healing ulcer in the oral cavity along with the neck swelling (96 patients). Neck swelling was the one of the chief complaint in 89 patients of the series. Facial disfigurement was complained by 12 patients, loss of the appetite was observed by 48 patients and 31 were having complaints of the weight loss. 89 patients presented with the complaint of the difficulty in swallowing. Restriction of the movement of tongue was seen in 53 patients (table 1).

Neck nodes were present in 59% patients of the present series (table 2).

62% of the patients in the present series were anemic (<11 gram/decilitre) and 45.33% were having hypo-proteinemia (<6 gram/decilitre). 4.67% of the patients were having raised RFT and another 4.67% were having abnormal ECHO. More than 50% of the patients had nutritional deficiencies in the form of anemia and hypo-proteinemia (table 3).

Most patients were seen with ECOG performance status of 2 and none of the patients were taken with ECOG Performance scale of 4 or 5 (table 4).

Maximum no. of patients are observed in stage II (41.33%), followed by stage III (37.33%) and stage IV (18.67%) (table 5). 124 patients in the study were given concomitant chemotherapy weekly along with the radiation. Chemotherapy used was Cisplatin, Gemcitabine, or Gemcitabine alternate with the paclitaxel. 5 to 8 cycles of weekly chemotherapy was given. 26 patients were treated with radiotherapy alone.

Mean treatment time in all patients was almost same and around 59 days and it was not affected by the chemotherapy used. In radiotherapy alone arm, as radiation dose in range of 68-72 Gy was used so treatment time came almost equal to that in the RT plus chemotherapy arm (table 7).

Hospitalization days were an average 3.269 days for radiotherapy alone arm to a maximum of 4.037 days, in RT plus cis-platinum arm (table 8).

Radiation delay was least in radiotherapy alone arm, with a mean of 1.8 days and maximum in RT plus cis-platinum arm, mean of 2.185 days (table 9).

DISCUSSION

Normally cells of the mouth undergo rapid renewal over 7 to 14 day cycle. Both chemotherapy and radiotherapy interfere

Presenting complaints	No. of patients
Ulceration/nodule in oral cavity	96
Change in voice	14
Neck mass	89
Tonsillar enlargement	18
Difficulty/problem in swallowing	89
Facial disfigurement	12
Difficulty/problem in breathing	35
Decreased appetite	48
Decreased weight	31
Restriction of tongue movement	53

Table-1: Incidence of presenting complaints in the studied series

Association with nodes	No. of patients
Present	89
Absent	61
Total	150

Table-2: Association with nodes in present series

Positive findings	No. of patients
Hb<11gm%	93
Renal function tests raised	7
Abnormal ECHO	7
Hypo-proteinemia	68

Table-3: Biochemical investigation in the studied series

ECOG PS	No. of patients
5	0
4	0
3	36
2	88
1	26

Table-4: ECOG performance status in present series

Stage	No. of patients
Stage I	4
Stage II	62
Stage III	56
Stage IV	28

Table-5: Staging of the patients in series studied

Chemotherapy used	No. of the patients
Cisplatin 35mg/sq.m	27
Gemcitabine 130-150mg/sq.m	41
Paclitaxel alternate with gemcitabine weekly	56
Radiotherapy alone	26

Table-6: Chemotherapy used on weekly basis in the present series

	Treatment time (Days)
RT alone	58.923
RT + Cisplatin	58.778
RT + Gemcitabine	58.609
RT + Paclitaxel/gemcitabine alternate weekly	58.893

Table-7: Mean treatment time

	Hospitalization (Days)
RT alone	3.269
RT + Cisplatin	4.037
RT + Gemcitabine	3.609
RT + Paclitaxel/gemcitabine alternate weekly	3.357

Table-8: Mean days of hospitalization

	Radiation delay (Days)
RT alone	1.807
RT + Cisplatin	2.185
RT + Gemcitabine	1.975
RT + Paclitaxel/gemcitabine alternate weekly	1.946

Table-9: Mean radiation delay

with cellular mitosis and reduce the regenerating ability of oral mucosa. A healthy oral mucosa serves to clear micro organisms and provide a chemical barrier that limits penetration of many compounds into the epithelium.⁸ Oral mucosa is comprised of stratified squamous epithelium that overlies the lamina propria, which consists of fibroblasts and connective tissue, small blood vessels (capillaries), inflammatory cells (macrophages) and extracellular matrix.⁸ The epithelium of the movable mucosa (which makes up the cheeks, inner aspects of the lips, ventral surface of the tongue, floor of the mouth and soft palate) is not keratinized, in contrast to the dorsal tongue, hard palate and gingival mucosa. The most common oral complications related to cancer therapies are mucositis, infection, salivary gland dysfunction, taste dysfunction and pain. These complications can lead to secondary complications such as dehydration, dysgeusia, and malnutrition.⁹⁻¹⁷ In our study the frequency of mucositis was revealed 100% after chemoradiation. Head and neck irradiation can cause a wide spectrum of oral complications. Ulcerative oral mucositis is a virtually universal toxicity resulting from this treatment. Oral mucosa, vasculature, muscle, and bone are irreversibly injured. This can result in xerostomia, rampant dental caries, trismus, soft tissue necrosis, and osteonecrosis. There are clinically significant similarities as well as differences compared with oral mucositis caused by chemotherapy. The most common sites for mucositis include the uvula, labial, buccal and soft palate mucosa, as well as the floor of mouth and ventral surface of tongue.⁹⁻¹² In the present study ulceration/nodules were observed in 96 patients. To counter this acute toxicity, many recommendations had been proposed from time to time. Some were recognized on institutional level and some were widely recognized. Regarding the mucositis, one thing always remain in contention that better understanding of mechanism of mucositis is required to decrease the severity of mucositis. It was also made clear that we can only decrease the severity of mucositis but never zero it. In 1990, Sonis ST, Woods PD, White BA give concept of pretreatment oral assessment.¹⁸ While working in Division of Dentistry, Brigham and Women's Hospital, Boston they noticed that individuals undergoing cancer therapy may be at a risk for a wide variety of oral problems that can significantly affect morbidity and mortality. Pretreatment oral assessment of these patients is an opportunity to identify and eliminate potential sources of sepsis and irritation. While preliminary studies strongly support the efficacy of pretreatment oral screening programs, a number of issues were yet to be addressed relative to patient-related and cost-related outcomes.^{18,19} In the present study complications like change in voice (19), neck mass (89), tonsillar enlargement (18), difficulty in breathing, decreased appetite (48), decreased weight (31), restriction in tongue movement (53) were observed.

CONCLUSION

It was observed in the present study that mucositis was the one of the chief complication. More than 50% of the patients had nutritional deficiencies in the form of anemia and hypoproteinemia due to oral mucositis.

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