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Original Research Article **Medical Oncology**

Treatment Interruption and Hospital Admission in Head and Neck Cancer Patients during Concurrent Chemoradiotherapy with or without Prophylactic Nasogastric Tube Feeding

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Abstract

Background: Worldwide, head and neck cancer (HNC) was the 6th most common cancer in 2020 in all ages and both sexes. In Bangladesh, lip and oral cavity cancer was the 2nd most common cancer in 2020. Up to 60% of HNC patients presents with locally advanced disease. ***Aim and Objective:*** To determine treatment Interruption and hospital admission in head and neck cancer patients during concurrent chemoradiotherapy with or without prophylactic nasogastric tube feeding. ***Materials and Method****:* A quasi-experimental study was performed in Radiation Oncology Department of National Institute of Cancer Research & Hospital from 1st January 2020 to 31st December 2020. A total number of 68 Patients (34 patients in each arm) was included in this study according to inclusion and exclusion criteria by purposive Sampling technique. All patients in Arm A and Arm B were planned for total 66 Gray in 33 daily fractions, 2 Gray per fraction, 1 fraction per day, 5 fractions per week over 6½ weeks and inj. Cisplatin 40mg/m² was given intravenously 2 hours before radiotherapy on 1st day and then weekly. All the information's were recorded in a pre-tested and semi-structured questionnaire. The analysis was done by using independent sample t test for continuous variables and chi-square test for categorical variables and data were presented in tables and graphs. ***Results:*** In this study, mean age was 52.5 ± 8.5 years and male: female ratio was 4.2: 1 among all patients. The Incidence of treatment interruption was significantly lower in Arm A compared with Arm B (29.4% in Arm A and 70.6% in Arm B, *p*-value < 0.05). There were fewer patients who required hospitalization in Arm A (23.5% in Arm A and 55.9% in Arm B) and length of hospital stay was less too (5.3 ± 1.7 in Arm A and 10.0 ± 1.9 in Arm B, *p* value <0.05). There were no significant differences in treatment response and toxicities between the two groups. ***Conclusion:*** Prophylactic nasogastric tube feeding at the beginning of CCRT in head and cancer patients is beneficial in terms of preventing treatment break and reducing hospital admission.

Keywords: Head and neck cancer, prophylactic nasogastric tube, treatment interruption, hospital admission.

INTRODUCTION

Worldwide the incidence of head and neck cancer in 2020 was about 9, 31, 931; which was the 6th most common cancer in both sexes and all ages. Number of HNC death was 4, 67,125 that was about 4.71% of all cancer deaths in both sexes Globocan 2020 [1].

In Bangladesh no reliable data is available on cancer statistic. Some international organizations, journals and local institutes provide discrete data. South Asian Journal Cancer (2013) October- December showed incidence of cancer cases was 2,00,000 per year in Bangladesh. Mouth and oropharynx cancer was the 2nd most common malignancy in male. The 5-years prevalence of oral cavity and pharyngeal cancer was 11.9% in male, 6.5% in female and 8.2% in both sexes.

Globocan showed that in Bangladesh lip and oral cavity cancer was the 2nd most common cancer (8.9%) in both sexes, 3rd in male and 5th in female cancer in 2020. As per World Health Organization (WHO) Cancer Country Profile (2020), in 2019 there were 0.7 public cancer centers and 1.7 radiation oncologists for every 10,000 cancer patients in Bangladesh.

National Institute of Cancer Research & Hospital (NICRH) published Hospital Cancer Registry Report 2015- 2017 which stated that, total 14,044 newly diagnosed cancer patients attended at outpatient department in NICRH in 2017. Among them total head and neck cancer patients were 1,470 (10.5% of total patients) and male patients were 914 (62.17%) and female patients were 556 (37.82%). Among HNC patients the most common site of tumor was the lip and oral cavity-802 (54.56%) followed by hypopharynx-202 (13.74%), oropharynx-188 (12.79%), nasopharynx-39 (2.65%) and larynx-17 (1.16%).

Nearly 60% of head and neck cancer patients presents with locally advanced but non-metastatic disease [2]. Current treatment of locally advanced HNC requires multimodality treatment. Surgery, radiotherapy, and concurrent chemotherapy and radiotherapy (CCRT) have become the standard of care (Sanabria cited in Lewis *et al.,* 2014) [3]. Combined modality therapy is generally recommended for approximately 60% of patients with locally or regionally advanced disease at diagnosis (National Comprehensive Cancer Network NCCN guidelines Version 1.2021). CCRT improves the loco-regional control of advanced stage disease but with increased toxicity that often has negative impact on nutritional status [4]. HNC patients are frequently malnourished at presentation and prior to the beginning of treatment [5]. Adding to the insult, CCRT causes or exacerbates the symptoms, such as alteration or loss of taste, mucositis, xerostomia, fatigue, nausea and vomiting, which consequently worsen the nutritional status [6]. CCRT is associated with a number of detrimental outcomes including increased toxicities, treatment interruptions, hospital admissions, and mortality [7]. Severe dehydration and malnutrition eventually lead to unplanned treatment interruptions and hospitalizations, thereby compromising treatment efficacy [8]. Discontinuation in RT treatment for more than 5 days has been reported in 53% of patients with weight loss > 20% during CRT and complete interruption in 29% of these patients [9].

International guidelines suggest that intensive nutritional counseling (NC) and oral nutritional supplements (ONS) should be used to increase dietary intake and to prevent therapy-associated weight loss and interruption of radiation therapy in patients undergoing radiotherapy or chemoradiotherapy of head and neck areas. Motivation of the patients is needed to maintain appropriate nutrition during treatment of HNC [7]. But this nutritional deficiency cannot be completely prevented by nutritional counseling [9]. International guidelines also suggest that if an obstructing head and neck cancer interferes with swallowing, enteral nutrition (EN) should be delivered by tube. Tube feeding is also suggested if severe local mucositis is expected, which might interfere with swallowing, e.g., in radio-chemotherapy regimens, including radiation of throat. To maintain good nutritional status during treatment enteral nutrition (EN) is required which can be delivered either via a nasogastric tube (NGT) or via percutaneous endoscopic gastrostomy (PEG). Both NGT and PEG are equally effective in maintaining body weight, and data to recommend one application method over the other is insufficient [10]. For patients with diagnosis of head and neck cancer receiving radiotherapy and/or chemoradiotherapy there is no conclusive evidence on which to base recommendations for the optimal method of enteral feeding during treatment and in the post-treatment period (Nugent *et al.,* 2013) [11]. For HNC patients, NGT placement is often preferred due to a low complication rate, less invasiveness, and lower costs compared to PEG [10]. Prophylactic feeding tubes (PFTs) are placed prior treatment in a prediction of significant oral toxicity, whereas reactive feeding tubes (RFTs) are placed later during treatment because of actual toxicity [11]. PFT group may be considered to have low motivation to use their tube as there is no current obvious eating problem, but despite good baseline nutritional and swallowing status, there is strong prediction to develop weight loss and requirement of feeding tube during treatment [12].

Usually patients are supported with oral nutritional supplements and when it is impossible to maintain nutritional requirements enteral feeding is introduced termed as reactive feeding tubes (RFT) [6]. In case of RFT, Patients' oral intake should frequently be monitored to identify timely who is requiring a feeding tube to lower the risk of weight loss, dehydration and treatment interruption. On the other hand, prophylactic feeding tube placement may prevent this [13]. Prophylactic feeding tube placement may prevent the risk of weight loss, dehydration and treatment interruption [13].

The rate of unplanned hospitalizations has important financial and economic implications for the health system [14]. Nutritional support helps in saving the overall health costs by reducing the admissions rate, as the costs of a hospital bed for a day are significantly higher than those for the outpatient management [15]. Moreover, the reduction in hospitalizations may improve the quality of life in these patients.

The purpose of this study was to compare treatment interruption and hospital admission due to nutrition related complications in two feeding tube status groups, one is PFT and another is without PFT in

National Institute of Cancer Research & Hospital. This was the first study regarding a PFT intervention prior to treatment in National Institute of Cancer Research & Hospital.

OBJECTIVES

General Objectives

To determine treatment Interruption and hospital admission in head and neck cancer patients during concurrent chemoradiotherapy with or without prophylactic nasogastric tube feeding.

Specific Objectives

1. To find out the frequency of treatment interruption with prophylactic nasogastric feeding tube (PFT).
2. To compare hospital admission due to nutrition related complications with or without PFT in head and neck cancer patients during concurrent chemoradiotherapy.

METHODOLOGY

Type of study	Quasi-experimental study
Place of study	Department of Radiation Oncology, National Institute of Cancer Research & Hospital (NICRH), Mohakhali, Dhaka.
Study period	1st January 2020 to 31st December 2020 (1 year).
Study population	Patients with histopathologically diagnosed head & neck cancers and selected for concurrent chemoradiotherapy in Radiation Oncology Department, NICRH in between 1st January 2020 to 31st December 2020.
Sampling technique	Purposive sampling technique
Sample size	Total of 68 patients were included in this study and were distributed in two arms (A and B), 34 patients in each arm.

Selection of Patients

Inclusion Criteria

- Histopathologically proven head and neck cancer.
- Squamous cell carcinoma histology.
- Stage III, IVA and IVB.
- Patients selected for CCRT.

Exclusion Criteria

- Carcinoma unknown primary, salivary gland tumor and nasopharyngeal carcinoma were excluded.
- Age less than 18 years or >70 years.
- If diagnosed as severely or moderately malnourished patient who need total parenteral nutrition.
- Patients Eastern Co-operative Oncology Group (ECOG) performance status score >2.
- History of prior chemotherapy or radiotherapy or surgery to the head and neck region.
- Serious uncontrolled concomitant medical illness including heart disease, diabetes mellitus, hypertension or renal disease etc.
- Laboratory criteria for exclusion

Study Procedure

A total 78 patients were selected in NICRH from 1st January 2020 to 31st December 2020. After assessment of eligibility, 10 patients were excluded and a total number of 68 patients were included in the study according to the selection criteria. After selecting the patients, informed written consent (Appendix-III) was taken from each patient before his/her participation in the study. Then history taking, Clinical examination and necessary investigations were done and documented in questionnaire.

Data Collection

Appropriate data were collected by using a preformed questionnaire. Following introducing and informing the study purpose and objectives, an informed written consent was sought from the patient to take part in this study. Data were collected by face to face interview ensuring privacy and confidentiality of the patients. All others required data were collected from available relevant papers.

Data Processing, Analysis and Interpretation

Data were checked and verified. Then it was tabulated in a master sheet. Data were entered into computer and coded. Data categorization and summarization were done. Continuous data were expressed as mean ± standard deviation (SD), whereas, categorical data were expressed with rate, ratio and proportion. Data were presented in tables and graphs. Statistical analysis was done according to the objective of the study by using IBM SPSS (Statistical Package for Social Science) software version 25.0 for windows and graphs by MS Excel 2010.

RESULT

Assessment of Treatment Interruption

Table I: Number of patients with treatment interruption (n = 68).

Trait	Arm A		Arm B		Chi-square value	*p*-value
	n	percentage	n	percentage		
Number of patients with RT break	10	(29.4)	24	(70.6)	11.529	0.001

RT=Radiotherapy

Table II: Duration of treatment interruption.

Trait	Arm A (n=10)		Arm B (n=24)		t value	*p*-value
	Mean	**Standard deviation**	**Mean**	**Standard deviation**		
Duration of RT break	4.1	±0.9	6.7	±1.2	-6.059	<0.001

RT=Radiotherapy

Table II shows that in Arm A 10 patients faced RT break and in Arm B 24 patients faced RT break due acute toxicities which was statistically significant ($p < 0.05$).

Table III shows that mean duration of radiotherapy break was 4.1 ± 0.9 in Arm A and 6.7 ± 1.2 in Arm B. The difference was statistically significant ($p < 0.05$) between two groups.

Table III: Number of patients required hospitalization due to nutrition related complications (n=68)

Trait	**Arm A**		**Arm B**		**χ^2 test**	***P*-value**
	n	**percentage**	**n**	**percentage**		
Number of patients needed hospital admission	8	(23.5%)	19	(55.9%)	7.433	0.006

This table shows that the number of patients required hospitalization due to nutrition related complications was 8 (23.5%) in Arm A and 19 (55.9%) in Arm B (statistically significant $p < 0.05$).

Table IV: Duration of hospital stay and hospital admission related treatment cost.

Trait	**Arm A (n=8)**		**Arm B (n=19)**		**t test**	***p*-value**
	Mean	**Standard deviation**	**Mean**	**Standard deviation**		
Duration of hospital stay (days)	5.3	±1.7	10.0	±1.9	-6.242	<0.001
Hospital Treatment cost (taka)	3352.9	±1039.4	6319.1	±1174.8	-6.509	<0.001

This table shows that Mean length of hospital stay was 5.3 ± 1.7 in Arm A and 10.0 ± 1.9 in Arm B (statistically significant $p < 0.05$).

Hospital admission related treatment cost was significantly more in Arm B (without PFT) in comparison with Arm A (with PFT), (p value < 0.05).

Assessment of Treatment Response

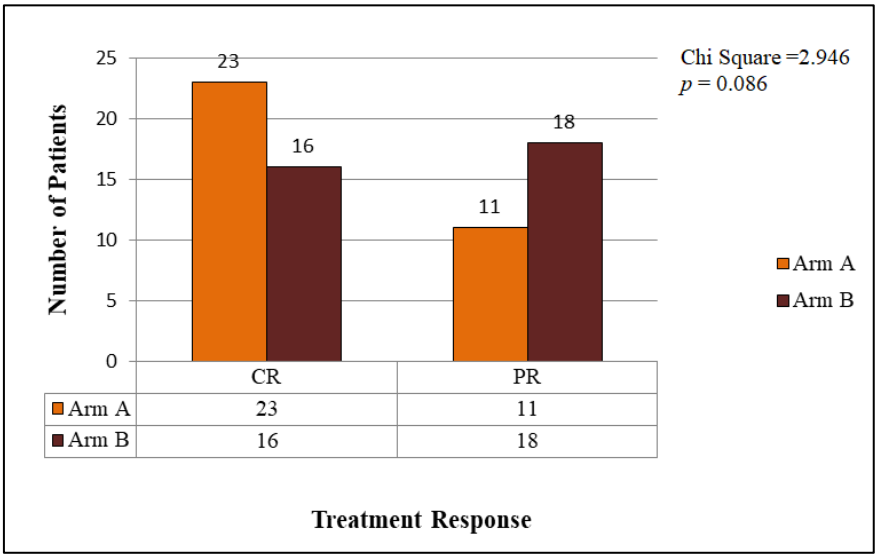

Figure I: Distribution of patients according to treatment response after 12 weeks of end of CCRT (n = 68)
(CR= Complete response, PR= Partial response)

This figure shows that majority of the patients in Arm A had complete response (CR) 23 (67.6%). In Arm B majority of the patients had partial response (PR) 18 (52.9%).

The difference was not statistically significant between two arms (p-value > 0.05).

Table V: Association of treatment response with treatment interruption

Treatment response	Number of patients didn't face treatment interruption		Number of patients faced Treatment interruption		Chi square value	*p*-value
	n	percentage	n	percentage		
CR	28	82.4	11	32.4	17.376	<0.001
PR	6	17.6	23	67.6		

(CR = complete response, PR= partial response was measured after 12 weeks of end of CCRT)

This table shows V (32.4%) patients of Complete response faced treatment interruption during treatment and 23 (67.6%) of partial response patients faced treatment interruption.

The difference is statistically significant ($p < 0.05$).

Toxicities Assessment

Table VI: Distribution of patients according to toxicities (n = 68)

Acute toxicity	Arm A n (%)	Arm B n (%)	Chi-square test	*p*-value
Oral mucositis				
Grade 1	1 (2.9)	2 (5.9)	3.832	0.147
Grade 2	23 (67.6)	15 (44.1)		
Grade 3	10 (14.7)	17 (50)		
Skin toxicity				0.332
Grade 1	17 (50)	11 (32.4)	2.206	
Grade 2	10 (29.4)	13 (38.2)		
Grade 3	7 (20.6)	10 (29.4)		
Dysphagia				
Grade 1	9 (26.5)	7 (20.4)	2.160	0.340
Grade 2	20 (58.8)	17 (50.0)		
Grade 3	5 (14.7)	10 (29.4)		
Xerostomia				
Grade 1	7 (20.6)	6 (17.6)	1.446	0.485
Garde 2	25 (73.5)	23 (67.6)		
Grade 3	2 (5.9)	5 (14.7)		
Nausea/vomiting				
Absent	8 (23.5)	4 (11.8)	2.451	0.294
Grade 1	17 (50)	16 (47)		
Grade 2	9 (26.5)	14 (41.2)		
Toxicities	**Arm A**	**Arm B**	**Chi-square value**	***p*-value**
Anemia				
Absent	3 (8.8)	1 (2.9)	7.293	0.063
Grade 1	18 (52.9)	9 (26.5)		
Grade 2	10 (29.4)	19 (55.9)		
Grade 3	3 (8.5)	5 (14.7)		
Neutropenia				
Absent	22 (64.7)	19 (55.9)		
Grade 1	12 (35.3)	15 (44.1)	0.553	0.621
Thrombocytopenia			0.541	0.624
Absent	21 (61.8)	18 (52.9)		
Grade 1	13 (38.2)	16 (47.1)		
Serum creatinine change	17 (50)	22 (64.7)	0.063	1.000
Absent	13 (38.3)	12 (35.3)		
Grade 1				

This table shows that oral mucositis, skin toxicities, dysphagia and xerostomia were developed in both arms. None of our study patient's developed grade 4 toxicity. These toxicities in both arms were almost same and the differences were not statistically significant ($p > 0.05$).

Nausea/ vomiting, neutropenia, thrombocytopenia and nephrotoxicity were mild in both arms. The differences were not statistically significant ($p > 0.05$) between two arms.

DISCUSSION

Multimodalities treatments are the standard care of locally advanced head and neck cancer patients but treatment break and hospital admission is the main concern.

In this study, 10 (29.4%) patients in Arm A and 24 (70.6%) patients in Arm B underwent treatment interruption due to severe acute toxicities which include oral mucositis, dysphagia, skin toxicity, xerostomia and weight loss. Mean duration of RT break was 4.1 ± 0.9 in Arm A and 6.7 ± 1.2 in Arm B. Weekly chemotherapy was held during radiotherapy break and restarted with radiotherapy. The difference between two groups was statistically significant. Treatment interruption produces unwanted machine occupancy. In a low resource country like ours unwanted machine occupancy produces radiotherapy delay of scheduled patients. Assenat *et al.,* (2011) conducted a retrospective study, where they found 49.6% patients underwent treatment interruption because of side effects [15]. The mean duration was 4.8 days per patient. Interruption, duration of interruption for toxicities and cumulative duration of treatment interruption for toxicity were significantly lower in pPEG group.

In this study, Arm B (without PFT) patients had significantly more hospital admissions during the treatment period compared to the Arm A (with PFT). Number of patients required hospital admissions was 8 (23.5%) in Arm A and 19 (55.9%) in Arm B. Mean length of hospital stay was 5.3 ± 1.7 in Arm A and 10.0 ± 1.9 in Arm B. The difference was statistically significant in both arms (p value < 0.05). No patient in both arms needed parenteral nutrition. Paccagnella *et al.,* (2010) conducted a retrospective study where number of patients was 66 (n = 66) [9]. They found CG (control group) patients had significantly more unplanned hospital admissions during the treatment period compared with the NG (nasogastric tube) (p < 0.05). Hughes *et al.,* (2012) also found significantly less hospital admission in prophylactic group [14].

In Royal Brisbane and women's Hospital, Hughes *et al.,* (2013) conducted a retrospective cohort study [14]. In health cost analysis evaluating average hospital stay, unexpected admissions and gastrostomy insertion-related costs found significant when compared between intervention and control arm [15]. My results also showed duration of hospital stay and hospital admission related treatment costs were significantly lower in PFT arm (Arm A). Patients in Arm A had significantly less mean hospital stay which translated into substantial cost saving for my institutions.

Treatment response assessment by RECIST criteria after 12 weeks of end of CCRT showed in Arm A, Complete Response (CR) was 23 (67.6%) and Partial Response (PR) was 11 (32.4%) and in Arm B, CR was 16 (47.1%) and PR was 18 (52.9%). Though treatment response assessment was not one of the objectives of the study, it can be seen from data that it was clinically significant but statistically not significant (p-value 0.086). Treatment response was further analyzed to determine the association with treatment interruptions. There was significant association between treatment interruption and treatment response. From above discussion it found that treatment response is indirectly associated with prophylactic nasogastric tube feeding.

Oral mucositis, skin toxicities, dysphagia and xerostomia were developed in both arms and were severe at the end of CCRT. None of my study patient developed grade 4 toxicity. These toxicities in both Arm A and Arm B were almost same and the differences were not statistically significant (p > 0.05).

Nausea, vomiting, anemia, neutropenia, thrombocytopenia and nephrotoxicity were mild in both arms and the differences were not statistically significant (p-value > 0.05). Anemia was higher in Arm B. Grade 1 anemia developed among 18 (52.9%) patients in Arm A and 9 (26.5%) in Arm B and grade 2 anemia developed in 10 (29.4%) patients in Arm A and 19 (55.9%) patients in Arm B. It was clinically significant but statistically not significant (p value 0.063).

CONCLUSIONS

This study results suggest that prophylactic nasogastric tube feeding at the beginning of CCRT in head and neck cancer patients is beneficial in terms of preventing treatment break and reducing hospital admission. Nutritional interventions including regular nutritious food according to diet chart and nasogastric tube management as per instructions is the prerequisite for maintaining good nutritional status.

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