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Original Research Article

Comparison of response and toxicity of induction chemotherapy with cisplatin and 5-fluorouracil versus cisplatin and paclitaxel followed by concurrent chemoradiotherapy in advanced head and neck cancer

Towhidul Islam[1]*, S. M. Nazmul Alam[2], M. Fazle Robbi[3]

[1]Department of Oncology, Kurmitola General Hospital, Dhaka, Bangladesh
[2]Department of Oncology, Sheikh Hasina Medical College Hospital, Tangail, Bangladesh
[3]Department of Oncology, Chattogram Medical College Hospital, Chattogram, Bangladesh

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***Correspondence:**
Dr. Towhidul Islam,
E-mail: towhidulslam.infinity1@gmail.com

ABSTRACT

Background: Head and neck cancer poses a prevalent oncological challenge in Bangladesh, often diagnosed in advanced stages. Standard treatment for inoperable cases involves concurrent chemo-radiotherapy, but induction chemotherapy has shown significant benefits. This study aimed to compare the response and toxicity of induction chemotherapy with cisplatin and 5-fluorouracil versus cisplatin and paclitaxel followed by concurrent chemo-radiotherapy in advanced head and neck cancer.
Methods: From January 2019 to June 2020, a multicenter study enrolled 150 cases with inoperable squamous cell carcinomas in the head and neck. Ethical approval was obtained from Bangabandhu Sheikh Mujib Medical University. Divided into two arms, Arm A had 75 patients receiving cisplatin and 5-fluorouracil, while Arm B had 75 patients receiving cisplatin and paclitaxel for three cycles.
Results: After 24 weeks of treatment, complete response rates were 53.33% in Arm A and 56.0% in Arm B, with partial response rates of 29.33% and 32.0% respectively. Overall response was 82.66% in Arm A and 88.0% in Arm B, showing no statistically significant difference ($p>0.05$). Arm A exhibited more anemia, oral mucositis, skin toxicity, and hand-foot syndrome, while Arm B had higher neuropathy. Hematological and non-hematologic toxicities during concurrent chemo-radiotherapy were similar in both arms.
Conclusions: Induction chemotherapy with cisplatin and paclitaxel, followed by concurrent chemo-radiotherapy, is equally effective as induction chemotherapy with cisplatin and 5-fluorouracil, followed by concurrent chemo-radiotherapy, in treating advanced head and neck squamous cell carcinoma. However, the former regimen demonstrates significantly fewer toxicities, indicating a safer treatment option.

Keywords: Advanced head and neck cancer, Cisplatin 5-fluorouracil, Induction chemotherapy, Paclitaxel, Toxicity

INTRODUCTION

Non-communicable diseases (NCDs) are responsible for the majority of global deaths, with cancer expected to rank as the leading cause of death and a significant barrier to increasing life expectancy worldwide in the 21st century.[1] "Head and Neck Cancer" includes malignant tumors originating from the upper aero-digestive tract, primarily squamous cell carcinoma (about 90%). Cancers of the brain, eye, esophagus, thyroid gland, scalp, skin, muscles, and bones of the head and neck are not usually classified as head and neck cancers.[2] Among head and neck cancers, new cases and deaths in lip and oral cavity were 3,54,864 (2.20%) and 1,77,384 (2.01%), in the larynx were 1,77,422

(1.10%) and 94,771 (1.07%), in nasopharynx were 129,079 (0.8%) and 72,987 (0.83%), in oropharynx were 92,887 (0.58%) and 51,005 (0.58%), and in hypopharynx were 80,608 (0.50%) and 34,984 (0.40%), respectively.[3] Bangladesh, the 8th most populous country globally with 164,670 thousand people, has 13 to 15 lakh cancer patients.[4,5] According to the Bangladesh Bureau of Statistics, cancer is the sixth leading cause of death, with 60% of patients succumbing within five years of diagnosis.[6] In Bangladesh in 2018, the total number of new cancer cases was 0.15 million, with 0.108 million cancer-related deaths. New cases and deaths in Lip and oral cavity were 13,401 (10.24%) and 8,570 (8.97%), in Hypopharynx were 7,099 (5.42%) and 2,176 (2.28%), in Larynx were 4,996 (3.82%) and 2,787 (2.92%), and in Oropharynx were 3,667 (2.80%) and 3,210 (3.36%) respectively.[7] Tongue cancer in males (2.4%, 148 cases) and laryngeal cancer (1.8%, 109 cases) were among the top five malignancies. In females, cheek and buccal mucosa cancers numbered 140, ranking as the 6th most common malignancy.[8] The epidemiology of head and neck cancer is significantly influenced by exposure to environmental agents, particularly tobacco and alcohol. Smoking or chewing tobacco leaves poses a strong causal relationship with oral cavity cancer, with smoking identified as an independent risk factor in 80% to 90% of patients.[9] In cases where surgery is impractical due to anatomical constraints or medical co- morbidities, radiotherapy and chemotherapy become preferred treatment options.[10] Typically, early-stage head and neck cancer are managed with a single modality (surgery or radiotherapy), while advanced disease often necessitates multimodality therapy.[11] However, recent randomized trials have demonstrated the superior efficacy of induction chemotherapy regimens incorporating paclitaxel, particularly in terms of loco-regional control and safety.[12]

The aim of the study was to compare the response and toxicity of induction chemotherapy with cisplatin and 5-fluorouracil versus cisplatin and paclitaxel followed by concurrent chemo-radiotherapy in advanced head and neck cancer.

METHODS

This multicenter quasi-experimental study, conducted from January 2019 to June 2020, enrolled 150 cases with biopsy-proven advanced (inoperable) squamous cell carcinomas in the head and neck region. Ethical approval was obtained from the ethical committee of Bangabandhu Sheikh Mujib Medical University.

The cases were divided into two arms: Arm A, consisting of 75 patients undergoing induction chemotherapy with cisplatin and 5-fluorouracil, and Arm B, with 75 patients undergoing induction chemotherapy with cisplatin and paclitaxel. The study employed a convenient purposive sampling technique for sample selection, ensuring proper written consent from all participants before data collection.

Inclusion criteria

Inclusion criteria comprised individuals aged 18 to 70, Eastern Co-operative Oncology Group (ECOG) performance status score above 2, both sexes and stages III and IVA/IVB of head and neck carcinoma, specifically squamous cell carcinoma, with inoperable cases.

Exclusion criteria

Exclusion criteria included a history of prior chemotherapy or radiotherapy to the head and neck, initial surgery, double primaries, severe comorbidities (heart disease, uncontrolled diabetes, hypertension, hepatic or renal disease), pregnancy or lactation, and distant metastasis.

Demographic and clinical information was recorded, and data were processed, analyzed, and disseminated using MS Office and SPSS version 23.0 as needed.

RESULTS

In this study, the majority of patients in both Arm A (70.7%) and Arm B (73.3%) had the primary site located in the larynx. The study indicates that the percentage of patients with stage III disease is higher in Arm A, while stage IV disease is higher in Arm B. In the second follow-up, complete response was observed in 38 (50.67%) patients in Arm A and 40 (53.33%) patients in Arm B. Partial response was observed in 28 (37.33%) and 29 (38.67%) in Arm A and Arm B respectively. Stable disease (SD) was observed in 6 (8.0%) patients in Arm A and 4 (5.33%) patients in Arm B. Progressive disease (PD) was observed in 3 (4.0%) and (2.67%) patients in Arm A and Arm B respectively. There was no statistically significant difference between the two groups ($p>0.05$). In the third follow-up, complete response was observed in 40 (53.33%) patients in Arm A and 42 (56.0%) patients in Arm B. Partial response was observed in 22 (29.33%) and 24 (32.0%) patients in Arm A and Arm B respectively. Stable disease was observed in 8 (10.67%) patients in Arm A and 6 (8.0%) patients in Arm B. Progressive disease was observed in 5 (6.67%) and 3 (4.0%) patients in Arm A and Arm B respectively. There was no statistically significant difference between the two groups ($p>0.05$). In stage III disease, both Arm A and B showed complete responses in 30 (40.0%) patients. There was partial response in 3 (4.0%) patients in Arm A and 4 (5.33%) patients in Arm B. No statistically significant difference was found between the two groups ($p>0.05$).

In stage IVA disease, complete response was observed in 9 (12.0%) and 10 (13.33%) patients in Arm A and Arm B respectively. There was partial response in 11 (14.67%) patients in Arm A and 10 (13.33%) patients in Arm B. No statistically significant difference was found between the two groups ($p>0.05$). In stage IVB disease, complete response was observed in 1 (1.33%) and 2 (2.67%) patients in Arm A and Arm B respectively. There was partial

response in 8 (10.67%) patients in Arm A and 10 (13.33%) patients in Arm B. No statistically significant difference was found between the two groups (p>0.05).

During the induction chemotherapy period, 22 (29.33%) and 4 (5.33%) patients in Arm A, and 16 (21.33%) and 2 (2.67%) patients in Arm B developed grade 2 and 3 anemia, respectively. This difference was statistically significant (p<0.05). In the same period, 14 (18.67%) and 8 (10.67%) patients in Arm A, and 16 (21.33%) and 10 (13.33%) patients in Arm B developed grade 2 and 3 neutropenia, respectively. This difference was not statistically significant (p>0.05).

During the concurrent chemo-radiotherapy period, 12 (16.0%) and 4 (5.33%) patients in Arm A, and 10 (13.33%) and 3 (4.0%) patients in Arm B developed grade 1 and 2 neutropenia, respectively. This difference was not statistically significant (p>0.05). During the induction chemotherapy period, 1 (1.33%) patient in Arm A and 3 (4.0%) patients in Arm B developed febrile neutropenia, with no statistically significant difference (p>0.05). Thrombocytopenia observed during treatment showed no statistically significant difference (p>0.05). During the induction chemotherapy period, 10 (13.33%) and 8 (10.67%) patients in Arm A, and 18 (24.0%) and 16 (21.33%) patients in Arm B developed grade 1 and 2 neuropathy, respectively. This difference was statistically significant (p<0.05). During the induction chemotherapy period, 4 (5.33%) and 2 (2.67%) patients in Arm A, and 3 (4.0%) and 1 (1.33%) patient in Arm B developed grade 1 and 2 nephropathy, respectively. This difference was not statistically significant (p>0.05). During the induction chemotherapy period, 20 (26.67%) and 9 (12.0%) patients in Arm A, and 16 (21.33%) and 3 (4.0%) patients in Arm B developed grade 2 and 3 oral mucositis, respectively. This difference was statistically significant (p<0.05).

Additionally, during the induction chemotherapy period, 26 (34.67%) and 12 (16.0%) patients in Arm A developed grade 1 and 2 skin toxicity, respectively, while no patients in Arm B developed skin toxicity. This difference was also statistically significant (p<0.05). Grade 1 and 2 skin toxicities were observed in 50 (66.67%) and 17 (22.67%) patients in Arm A, and 47 (62.67%) and 24 (32.0%) patients in Arm B, respectively. Grade 1 and grade 2 mucous membrane toxicities were observed in 55 (73.33%) and 6 (8.0%) patients in Arm A, and 53 (70.67%) and 2 (2.67%) patients in Arm B, respectively. Grade 1 and grade 2 dysphagia were observed in 30 (40.0%) and 13 (17.33%) patients in Arm A, and 32 (42.67%) and 11 (14.67%) patients in Arm B, respectively. Grade 1 and grade 2 xerostomia were observed in 25 (33.33%) and 30 (40.0%) patients in Arm A, and 26 (34.67%) and 28 (37.33%) patients in Arm B, respectively.

Table 1: Distribution of patients according to clinical characteristics in both arm A and B (n=150).

	Arm A (n=75) N (%)	Arm B (n=75) N (%)	t - value	P value
Age range (years)				
18-29	0	0		
30-39	2 (2.67)	1 (1.33)		
40-49	6 (8)	10 (13.3)	0.483	0.629
50-59	40 (53.33)	45 (60)		
60-69	27 (36)	19 (25.33)		
Mean±SD (years)	56.067±6.632	55.533±6.876		
Gender				
Male	53 (70.67)	53 (70.67)	-	0.723
Female	22 (29.33)	22 (29.33)		
Economic status				
Upper class	3 (4.0)	1 (1.33)		
Middle class	16 (21.33)	14 (18.67)	-	0.530
Lower class	56 (74.67)	60 (80.0)		
Performance status				
ECOG 1	50 (66.67)	53 (70.67)		
ECOG 2	13 (17.33)	11 (14.67)	-	0.862
ECOG 0	12 (16)	11 (14.67)		
Sites of primary tumors				
Oral cavity	8 (10.7)	6 (8.0)		
Oropharynx	5 (6.7)	8 (10.7)		
Nasopharynx	6 (8.0)	4 (5.3)	-	0.806
Larynx	53 (70.7)	55 (73.3)		
Hypopharynx	3 (4.0)	2 (2.7)		
Staging				
Stage III	37 (49.33)	36 (48.0)	-	1.0

Continued.

	Arm A (n=75) N (%)	Arm B (n=75) N (%)	t - value	P value
Stage IVA	22 (29.33)	23 (30.67)		
Stage IVB	16 (21.33)	16 (21.33)		
Histopathological grading				
Well differentiated	17 (22.67)	17 (22.67)		
Moderately differentiated	42 (56.0)	44 (58.67)	-	0.926
Poorly differentiated	16 (21.33)	14 (18.67)		
Risk factors				
Smoking	60 (80.0)	56 (74.7)	-	0.435
Betel Leaf chewing	19 (25.3)	23 (30.7)	-	0.467
Tobacco leaf	17 (22.7)	21 (28.0)	-	0.453
Gul	2 (2.7)	1 (1.3)	-	0.560
Multiple	19 (25.3)	23 (30.7)	-	0.467
None	3 (4.0)	3 (4.0)	-	1.0
Presenting complaints				
Oral mass	13 (17.3)	14 (18.7)		
Oral ulcer	13 (17.3)	14 (18.7)		
Pain	46 (61.3)	36 (48.0)		
Hoarseness of voice	5 (6.7)	12 (16.0)		
Difficulty in deglutition	61 (81.33)	65 (86.67)		
Painful deglutition	5 (6.7)	8 (10.7)	-	-
Difficulty in taking food	6 (8.0)	4 (5.3)		
Epistaxis	8 (10.7)	6 (8.0)		
Neck node swelling	45 (60.0)	48 (64.0)		
Shortness of breath	6 (8.0)	12 (16.0)		
Weight loss	46 (61.3)	36 (48.0)		

Table 2: Clinical response after completion of treatment for patients in both arm A and arm B (n=150).

Clinical response					
Follow up	**Clinical response**	**Arm A (n=75) N (%)**	**Arm B (n=75) N (%)**	**Chi-square value**	**P value**
1st Follow up	Complete response (CR)	36 (48.0)	38 (50.67)	0.107	0.744
	Partial response (PR)	39 (52.0)	37 (49.33)		
2nd Follow up	Complete response (CR)	38 (50.67)	40 (53.33)	0.669	0.881
	Partial response (PR)	28 (37.33)	29 (38.67)		
	Stable disease (SD)	6 (8.0)	4 (5.33)		
	Progressive disease (PD)	3 (4.0)	2 (2.67)		
3rd Follow up	Complete response (CR)	40 (53.33)	42 (56.0)	0.921	0.820
	Partial response (PR)	22 (29.33)	24 (32.0)		
	Stable disease (SD)	8 (10.67)	6 (8.0)		
	Progressive disease (PD)	5 (6.67)	3 (4.0)		

Table 3: Post treatment clinical response according to the stages and grades of disease in both arm A and arm B (n=150).

	Response	Arm A (n=75) n (%)	Arm B (n=75) n (%)	P value
TNM stage				
Stage III	CR	30 (40.0)	30 (40.0)	0.888*
	PR	3 (4.0)	4 (5.33)	
	SD	3 (4.0)	1 (1.33)	
	PD	1 (1.33)	1 (1.33)	
Stage IVA	CR	9 (12.0)	10 (13.33)	1.0*
	PR	11 (14.67)	10 (13.33)	

Continued.

	Response	Arm A (n=75) n (%)	Arm B (n=75) n (%)	P value
	SD	1 (1.33)	2 (2.67)	
	PD	1 (1.33)	1 (1.33)	
Stage IVB	CR	1 (1.33)	2 (2.67)	0.738*
	PR	8 (10.67)	10 (13.33)	
	SD	4 (5.33)	3 (4.0)	
	PD	3 (4.0)	1 (1.33)	
Histopathological grading				
Grade I	CR	4 (5.33)	3 (4.0)	0.816*
	PR	8 (10.67)	10 (13.33)	
	SD	5 (6.67)	4 (5.33)	
Grade II	CR	28 (37.33)	32 (42.67)	0.874*
	PR	9 (12.0)	9 (12.0)	
	SD	3 (4.0)	2 (2.67)	
	PD	2 (2.67)	1 (1.33)	
Grade III	CR	8 (10.67)	7 (9.33)	1.0*
	PR	5 (6.67)	5 (6.67)	
	PD	3 (4.0)	2 (2.67)	

*Fisher's Exact test

Table 4: Distribution of toxicities in patients during induction chemotherapy period in both arm A and arm B (n=150).

Toxicity in induction chemotherapy period					
Toxicity	**Grade**	**Arm A (n=75) N (%)**	**Arm B (n=75) N (%)**	**Chi-square value**	**P value**
Anemia	Grade 1	48 (64.0)	46 (61.33)	-	0.012*
	Grade 2	22 (29.33)	16 (21.33)		
	Grade 3	4 (5.33)	2 (2.67)		
Neutropenia	Grade 1	28 (37.33)	30 (40.0)	1.243	0.743
	Grade 2	14 (18.67)	16 (21.33)		
	Grade 3	8 (10.67)	10 (13.33)		
Febrile neutropenia	Grade 3	1 (1.33)	3 (4.0)	-	0.620*
Thrombocytopenia	Grade 1	2 (2.67)	1 (1.33)	-	1.0*
Neuropathy	Grade 1	10 (13.33)	18 (24.0)	7.565	0.023
	Grade 2	8 (10.67)	16 (21.33)		
Nephropathy	Grade 1	4 (5.33)	3 (4.0)	-	0.788*
	Grade 2	2 (2.67)	1 (1.33)		
Oral mucositis	Grade 1	26 (34.67)	18 (24.0)	-	0.015
	Grade 2	20 (26.67)	16 (21.33)		
	Grade 3	9 (12.0)	3 (4.0)		
Hand foot syndrome	Grade 1	5 (6.67)	0	-	0.028*
	Grade 2	1 (1.33)	0		
Skin toxicity	Grade 1	26 (34.67)	1 (1.33)	47.481	0
	Grade 2	12 (16.0)	0		
Nausea	Grade 1	18 (24.0)	14 (18.67)	-	0.715*
	Grade 2	14 (18.67)	12 (16.0)		
	Grade 3	1 (1.33)	2 (2.67)		
Vomiting	Grade 1	12 (16.0)	8 (10.67)	3.171	0.205
	Grade 2	10 (13.33)	5 (6.67)		
Diarrhea	Grade 1	12 (16.0)	10 (13.33)	1.214	0.750
	Grade 2	8 (10.67)	6 (8.0)		
	Grade 3	6 (8.0)	4 (5.33)		

*Fisher's Exact test

Table 5: Distribution of toxicities in patients during concurrent chemo-radiotherapy period in both arm A and arm B (n=150).

Toxicity in concurrent chemo-radiotherapy period					
	Grade	**Arm A (n=75) N (%)**	**Arm B (n=75) N (%)**	**Chi-square value**	**P value**
Acute toxicity					
Dysphagia	Grade 1	34 (45.33)	32 (42.67)	-	0.928*
	Grade 2	20 (26.67)	18 (24.0)		
	Grade 3	2 (2.67)	2 (2.67)		
Xerostomia	Grade 1	26 (34.67)	24 (32.0)	0.552	0.759
	Grade 2	8 (10.67)	6 (8.0)		
Late toxicity					
Skin	Grade 1	15 (20.0)	14 (18.67)	0.665	0.717
	Grade 2	11 (14.67)	8 (10.67)		
Mucous membrane	Grade 1	10 (13.33)	12 (16.0)	1.003	0.606
	Grade 2	6 (8.0)	9 (12.0)		
Dysphagia	Grade 1	18 (24.0)	16 (21.33)	0.470	0.791
	Grade 2	12 (16.0)	10 (13.33)		
Xerostomia	Grade 1	14 (18.67)	12 (16.0)	0.694	0.707
	Grade 2	6 (8.0)	4 (5.33)		

*Fisher's Exact test

DISCUSSION

Induction chemotherapy before concurrent chemo-radiotherapy has been shown to increase the complete response rate, progression-free survival, and loco-regional control.[13] In this study, the mean age of patients in Arm A and Arm B was 56.067±6.632 years and 55.533±6.876 years, respectively, with an age range of 30-70 years, consistent with findings in.[14] The primary site for the majority of patients was the larynx, with 108 (72.0%) patients suffering from carcinoma larynx and 14 (9.33%) patients from carcinoma oral cavity. Oropharynx, nasopharynx, and hypo-pharynx were the primary sites for 13 (8.67%), 10 (6.67%), and 5 (3.33%) patients, respectively. In this study, patients with stage III disease were higher in Arm A, and patients with stage IV disease were higher in Arm B. Considering histological differentiation, more than two-thirds of the patients presented with grade 1 (well-differentiated) and grade 2 (moderately differentiated) tumors, while grade 3 (poorly differentiated) tumors were observed in less than one-third of the patients. After induction chemotherapy, partial response was observed in 70 (93.33%) patients in Arm A and 71 (94.67%) patients in Arm B. All patients with partial response remained inoperable. Following induction chemotherapy, all patients received concurrent chemo-radiotherapy, and toxicities related to chemotherapy and concurrent chemo-radiotherapy were closely observed and managed accordingly. The second follow-up was conducted at 12 weeks after completion of treatment in this study. Complete response was observed in 38 (50.67%) patients in Arm A and 40 (53.33%) patients in Arm B. Partial response was observed in 28 (37.33%) and 29 (38.67%) patients in Arm A and Arm B, respectively. There were stable diseases in 6 (8.0%) patients in Arm A and 4 (5.33%) patients in Arm B. Progressive disease was observed in 3 (4.0%) and 2 (2.67%) patients in Arm A and Arm B, respectively. No statistically significant result was found between the two groups ($p>0.05$). In the third follow-up, complete response was observed in 40 (53.33%) patients in Arm A and 42 (56.0%) patients in Arm B. Partial response was observed in 22 (29.33%) and 24 (32.0%) patients in Arm A and Arm B, respectively. The overall response was 82.66% in Arm A and 88.0% in Arm B. This result correlates with and, where the overall response rate was 80.0% and 81.6%, respectively.[15,16] There were stable diseases in 5 (6.67%) patients in Arm A and 5 (6.67%) patients in Arm B. Progressive diseases were observed in 18 (24.0%) and 17 (22.67%) patients in Arm A and Arm B, respectively. No statistically significant result was found between the two groups ($p>0.05$). Patients were assessed weekly for treatment response and toxicities during the induction chemotherapy period, concurrent chemo-radiotherapy period, and follow-ups. During the induction chemotherapy period, anemia was observed more in Arm A than in Arm B. Specifically, 22 (29.33%) and 4 (5.33%) patients in Arm A, and 16 (21.33%) and 2 (2.67%) patients in Arm B developed grade 2 and 3 anemia, respectively. This difference was statistically significant ($p<0.05$), consistent with (6.5%) and (1.7%).[17,18] Grade 1 anemia patients were carefully observed, and blood transfusions were administered to grade 2 and 3 patients in the transfusion medicine department. During the induction chemotherapy period, neutropenia was observed more in Arm B than in Arm A. Specifically, 14 (18.67%) and 8 (10.67%) patients in Arm A, and 16 (21.33%) and 10 (13.33%) patients in Arm B developed grade 2 and 3 neutropenia, respectively. This difference was not statistically significant ($p>0.05$). Grade 1 neutropenia patients were carefully observed, and Inj. G-CSF was administered daily to grade 2 and 3 patients until the absolute neutrophil count rose to more

than 1500/cmm. All these patients were closely monitored for the development of febrile neutropenia. During the induction chemotherapy period, neuropathy was observed more in Arm B than in Arm A. Specifically, 10 (13.33%) and 8 (10.67%) patients in Arm A, and 18 (24.0%) and 16 (21.33%) patients in Arm B developed grade 1 and 2 neuropathy, respectively. This difference was statistically significant ($p<0.05$), correlating with (17%) and (11%).[15,16] A combination medication of Vit B1+ B6+ B12 as neural nourishment and Cap. pregabalin as a pain modulator were administered. Additionally, during the induction chemotherapy period, 20 (26.67%) and 9 (12.0%) patients in Arm A, and 16 (21.33%) and 3 (4.0%) patients in Arm B developed grade 2 and 3 oral mucositis, respectively. This difference was also statistically significant ($p<0.05$). This correlates with (4.0%) and (11.2%).[19,20] During the concurrent chemo-radiotherapy period, 12 (16%) and 2 (2.67%) patients in Arm A, and 14 (18.67%) and 1 (1.33%) patient in Arm B developed grade 2 and 3 oral mucositis, respectively. This difference was not statistically significant ($p>0.05$). Additionally, during the induction chemotherapy period, 5 (6.67%) and 1 (1.33%) patient in Arm A developed grade 1 and 2 hand-foot syndrome, respectively. This difference was statistically significant ($p<0.05$), and these patients were treated with appropriate medications and advice. During the concurrent chemo-radiotherapy period, 16 (21.33%) and 3 (4.0%) patients in Arm A, and 18 (24.0%) and 2 (2.67%) patients in Arm B developed grade 2 and 3 skin toxicity, respectively. This difference was not statistically significant ($p>0.05$). Additionally, during the concurrent chemo- radiotherapy period, 20 (26.67%) and 2 (2.67%) patients in Arm A, and 18 (24.0%) and 2 (2.67%) patients in Arm B developed grade 2 and 3 dysphagia, respectively. This difference was not statistically significant ($p>0.05$).

This study has some limitations. The non-randomized quasi-experimental study faced challenges in preventing selection bias. The short study period limited the assessment of late toxicities and survival data. A constrained sample size hindered the accuracy of clinical outcomes. The study's scope was confined to two hospitals in Dhaka city, limiting the representation of the entire head and neck cancer scenario in Bangladesh. Non-homogeneous primary sites added complexity. Additionally, delays in starting concurrent chemo-radiotherapy and follow-ups were encountered due to the COVID-19 pandemic.

CONCLUSION

Based on the findings of this study, it can be concluded that induction chemotherapy with cisplatin and paclitaxel followed by concurrent chemo-radiotherapy is equally effective but less toxic and more convenient in terms of toxicity compared to induction chemotherapy with cisplatin and 5-fluorouracil followed by concurrent chemo- radiotherapy in advanced (inoperable) squamous cell carcinoma in the head and neck region.

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