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Comparison of Compliance and Treatment Delay Between Paclitaxel and Carboplatin Regimen Versus Gemcitabine and Carboplatin Regimen as Palliative Chemotherapy for Advanced Non-Small Cell Lung Cancer: A Quasi-Experimental Study

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ABSTRACT

Background: Advanced non-small cell lung cancer (NSCLC) remains a challenging disease with a poor prognosis, and palliative chemotherapy is a common treatment option. The choice of chemotherapy regimen is influenced by several factors, including efficacy, toxicity, and treatment experience. The paclitaxel and carboplatin regimen and the gemcitabine and carboplatin regimen are two commonly used chemotherapy regimens for advanced NSCLC. However, there is limited evidence comparing the compliance and treatment delay between these two regimens. This study aims to compare the compliance and treatment delay of paclitaxel and carboplatin versus gemcitabine and carboplatin as palliative chemotherapy for advanced NSCLC. **Methodology:** This Quasi-Experimental study was conducted at the Department of Clinical Oncology, Bangabandhu Sheikh Mujib Medical University (BSMMU) and the National Institute of Cancer Research & Hospital (NICRH), Dhaka, Bangladesh. The duration of the study was 10 months, from January 2022 to October 2022. During this period, a total of 74 participants were divided into two equal groups, Arm-A receiving the Paclitaxel-Carboplatin treatment regimen, and Arm-B receiving the Gemcitabine-Carboplatin treatment regimen. **Results:** The mean age was 58.35 years in Paclitaxel-Carboplatin (PC) and 57.54 years in Gemcitabine-Carboplatin (GC). The mean weight was 52.56 kg in PC and 53.86 kg in GC. The mean height was 165.53 cm in PC and 163.81 cm in GC. Over 40% of participants from both regimens were 51-60 years old and the majority were male. The majority of participants from both regimens were literate. 45.95% of PC and 59.46% of GC had ECOG status 1, 37.84% of PC and 35.14% of GC had ECOG status 2, and 16.22% of PC and 5.41% of GC had ECOG status 0. 75.67% of PC and 70.27% of GC were smokers. After 3 cycles of chemotherapy, 48.64% of PC and 43.24% of GC had partial response, 45.95% of PC and 56.76% of GC had stable disease, and none had complete response. 81.08% of PC and 59.46% of GC completed therapy within the expected time. The mean number of cycles was 5.73 in PC and 5.40 in GC. 6 weeks after treatment, 62.16% of PC and 56.76% of GC had partial response, 35.14% of PC and 32.43% of GC had stable disease, and 2.70% of PC and 10.81% of GC had progressive disease. **Conclusion:** The present study observed that both Paclitaxel-Carboplatin and Gemcitabine-Carboplatin regimens have similar treatment response rate without any significant difference or treatment delay. However, in terms of compliance to treatment, it was observed that treatment compliance was significantly higher among patients treated with Paclitaxel-Carboplatin, and also had a significantly lower need for supportive care. In conclusion, the results suggest that the PC regimen may be a better option for patients with regards to treatment compliance and outcome.

Keywords: *Compliance, Treatment, Cancer, Paclitaxel, Gemcitabine, Chemotherapy*

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INTRODUCTION

Cancer, a category of disorders marked by abnormal cell proliferation, has the potential to spread to other sections of the body. Lung cancer is one of the most often diagnosed cancers and the leading cause of death worldwide. [1,2] Accordingto GLOBOCAN 2020, the most common cancer is lung cancer, with an incidence of 22,06,771 (11.4%) and a

mortality rate of 17,96,144. (18%). [3]Lung cancer is the fourth most common cancer in both men and women in Bangladesh, with an incidence of 12,999 (8.3%), and it is also the second leading cause of cancer-related mortality.[3-5]Lung cancer is classified into two types: small-cell lung cancer (SCLC) and non-small-cell lung cancer (NSCLC) (NSCLC). NSCLC accounts for 80-85% of all lung cancers.[6,7]Environmental and lifestyle factors, the most frequent of which is cigarette smoking, have been related to the development of lung cancer.[8]A biopsy or cytology of the primary or metastatic location, performed under imaging guidance or bronchoscopy, is part of the diagnostic evaluation for NSCLC.[9,10]According to the standards, the staging workup comprises a patient's history, physical examination, imaging scans, and other diagnostics.[8]The therapy options for NSCLC are dependent by the patient's stage, histology, and performance status. The many treatment options for NSCLC include surgery, radiation therapy, chemotherapy, targeted therapy, and immunotherapy. [11,12] Chemotherapy is the backbone of treatment in advanced-stage non-small-cell lung cancer (NSCLC). Paclitaxel-Carboplatin and Gemcitabine-Carboplatin are two chemotherapy regimens routinely used to treat advanced NSCLC. [13,14] Using clinical response to compare the efficacy of these two regimens can assist discover which regimen is more effective in treating advanced NSCLC. Another element that can aid in comparing the two regimens is the patients' level of compliance with the two regimens, as well as the time between treatments. The compliance level and treatment delay of chemotherapy regimens are important factors in determining the success of treatment. Compliance refers to the extent to which patients follow the prescribed treatment regimen, while treatment delay refers to the time between the start of treatment and the onset of its effects.[15] In developing countries, where access to medical treatment is often limited, compliance and treatment delay can be significant challenges in the management of NSCLC.[16] The current quasi-experimental study was carried out to assess the compliance and treatment delay between the Paclitaxel and Carboplatin regimen and the Gemcitabine and Carboplatin regimen.

OBJECTIVE

General Objective:

- To observe the compliance rate of and treatment delay of paclitaxel-carboplatin as a palliative chemotherapy for advanced non-small cell lung cancer
- To observe the compliance rate of and treatment delay of gemcitabine -carboplatin as a palliative chemotherapy for advanced non-small cell lung cancerz

Specific Objectives:

- To compare the compliance level and treatment delay of paclitaxel-carboplatin and gemcitabine -carboplatin as palliative chemotherapy for advanced non-small cell lung cancer

METHODOLOGY

This Quasi-Experimental study was conducted at the Department of Clinical Oncology, Bangabandhu Sheikh Mujib Medical University (BSMMU), and the National Institute of Cancer Research & Hospital (NICRH), Dhaka, Bangladesh. The duration of the study duration was 10 months, from January 2022 to October 2022. During this period, a total of 74 participants were selected through purposive sampling from the patients with clinically and histologically proven advanced-stage, inoperable non-squamous non-small cell lung cancer following the inclusion and exclusion criteria. The patients were divided into two equal groups or Arms, Arm-A having 37 patients being treated with in fusional Paclitaxel-Carboplatin (PC) regimen, and Arm-B having 37 patients being treated with an in fusional Gemcitabine-Carboplatin (GC) regimen. The patients were informed about treatment costs, expected response rate, and toxicity of both arms. Prior to data collection, Informed consent was obtained from the patients. All patients had a baseline complete blood count, biochemical evaluation, creatinine clearance rate (CCR), and cardiac evaluation, inclusive of an ECG and 2D ECHO before the start of treatment. CT scan 6 weeks' post-treatment was done as and when required. Treatment response evaluation was done using RECIST criteria during chemotherapy as a mid-cycle evaluation and then at 6 weeks of completion of chemotherapy. A semi-structured Data collection form was used as the research instrument. Data collection methods included interviews, oral histories, observations, and investigation records. Statistical analysis of the collected data was performed using SPSS Software.

Inclusion Criteria

- Clinically diagnosed and histopathologically or cytologically proven previously untreated non-squamous non-small cell carcinoma of the lung.
- Advanced stage disease, AJCC stage IIIB to IV diseases (TNM- T1-2N3, T3-4N2, Any T, Any N, M1a or M1b).
- Patients who had given consent to participate in the study.

Exclusion Criteria

- Those who are not willing to take part in this study.
- Patients with a history of prior chemotherapy or radiotherapy.
- Initial surgery (excluding diagnostic biopsy) of the primary site.

- Patients with double primaries or previous primaries.
- Pregnant or lactating woman.
- Patients with ECOG performance status of more than two.
- Age of patients less than 18& more than 70 years.
- Very serious co-morbidity like clinically significant CVD.
- Who cannot afford the cost of treatment?

RESULTS

Table 1: Baseline characteristics of the study population. (N=74)

Variables	Arm-A(n=37)	Arm-B(n=37)
Age (Years)	58.35 ±9.62	57.54 ±8.61
Weight (kg)	52.56±10.17	53.86±7.64
Height (cm)	165.53±3.60	163.81±4.78

Among the participants of the present study, the mean age was 58.35 years in Arm-A and 57.54 years in Arm B. The mean weight was 52.56 kg among Arm A and 53.86 kg among Arm B participants. The mean height was slightly higher among Arm A participants at 165.53 cm, and among Arm-B it was 163.81 cm.

Table 2: Sociodemographic characteristics of the study participants. (N=74)

Variables	Arm-A (n-37)		Arm-B(n-37)	
	n	%	n	%
Age				
30-40 yrs.	0	0.00%	1	2.70%
41-50 yrs.	10	27.03%	8	21.63%
51-60 yrs.	15	40.54%	16	43.24%
61-70 yrs.	12	32.43%	12	32.43%
Mean Age	58.35 ±9.62		57.54 ±8.61	
Gender				
Male	29	78.38%	26	70.27%
Female	8	21.62%	11	29.73%
Educational Status				
Illiterate	3	8.11%	2	5.41%
Literate	34	91.89%	35	94.59%

In terms of age, the majority of the participants from both groups had been from the age group of 51-60 years (40.54% in Arm-A, 43.24% in Arm-B). An overall male prevalence was observed among the participants, with 78.38% male in Arm-A and 70.27% male in Arm-B. In terms of educational status, 8.11% of Arm-A and 5.41% of Arm-B had been illiterate, while 91.89% of Arm-B and 94.59% of Arm-B had been literate.

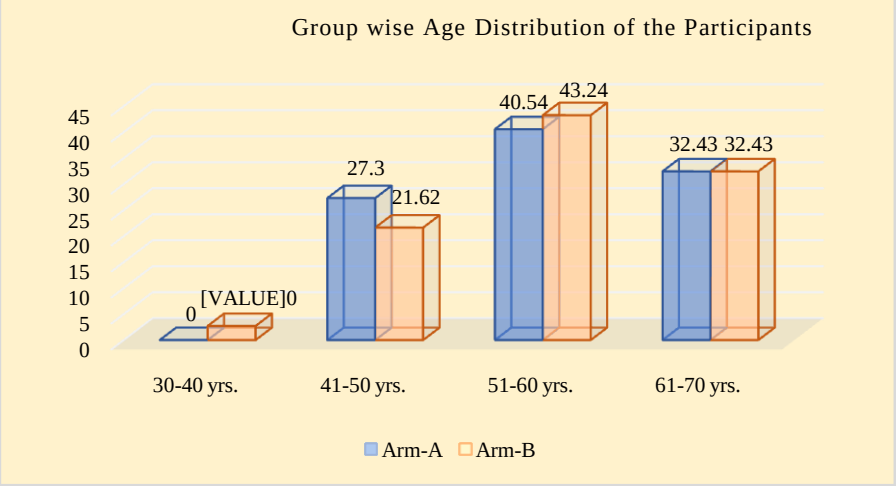

Figure 1: Bar chart showed Arm wiseparticipants byage (N=74).

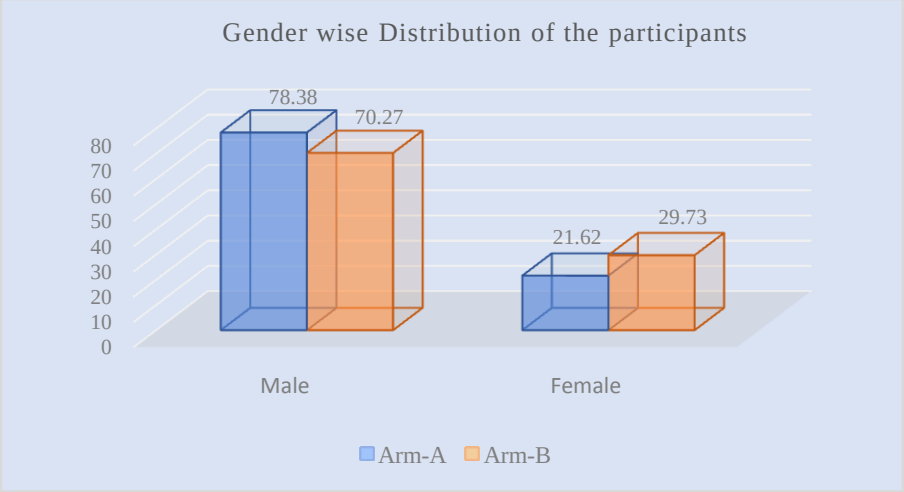

Figure 2: Bar chart showed Arm wise participants by gender (N=74).

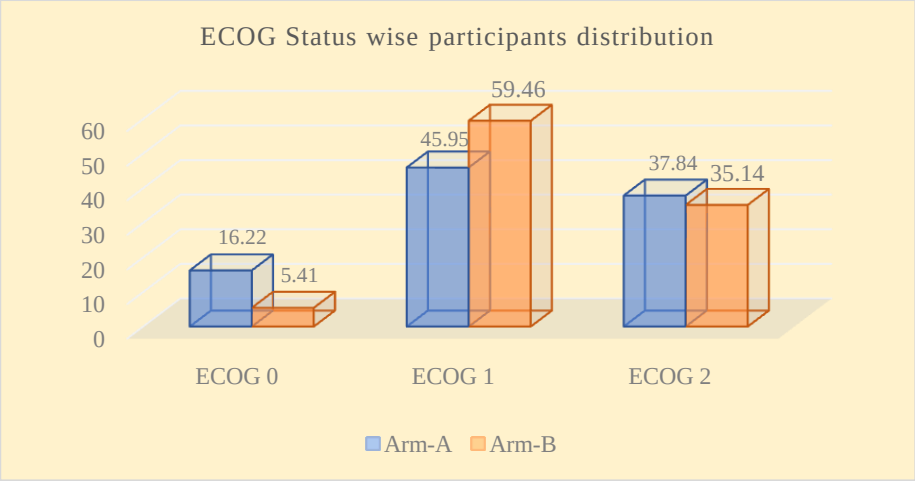

Figure 3: Bar Chart showed Arm wise participants by ECOG Status (N=74).

At baseline, the ECOG status of a majority of the participants was ECOG 1. 45.95% of Arm-A and 59.46% of Arm-B had ECOG status 1, while 37.84% of Arm-A and 35.14% of Arm-B had ECOG status 2. 16.22% of Arm-A, but only 5.41% of Arm-B had ECOG status 0

Table 3: Distribution of patients according to the risk factors. (N=74)

Risk factors		Arm-A (n=37)		Arm-B (n=37)		P-Value
		n	%	n	%	
Tobacco related	Smoking	28	75.68%	26	70.27%	0.87
	Jarda	19	51.35%	21	56.76%	
	Betel Leaf	25	67.57%	27	72.97%	
Lung disease	COPD	8	21.62%	12	32.43%	0.63
	Asthma	4	10.81%	5	13.51%	
	Tuberculosis	6	16.22%	4	10.81%	
Other Comorbidities	Hypertension or Diabetes Mellitus	14	37.84%	16	43.24%	0.46
Occupation	Factory Worker	5	13.51%	7	18.92%	0.14
	Firewood user	12	32.43%	8	21.62%	

In terms of risk factors, various risk factors were identified among both Arms. 28 (75.67%) patients in Arm A and 26 (70.27%) patients in Arm B were smokers. A good number of patients were also associated with various lung diseases such as COPD, Asthma, TB, etc., in both arms. The findings were statistically insignificant (p> 0.05).

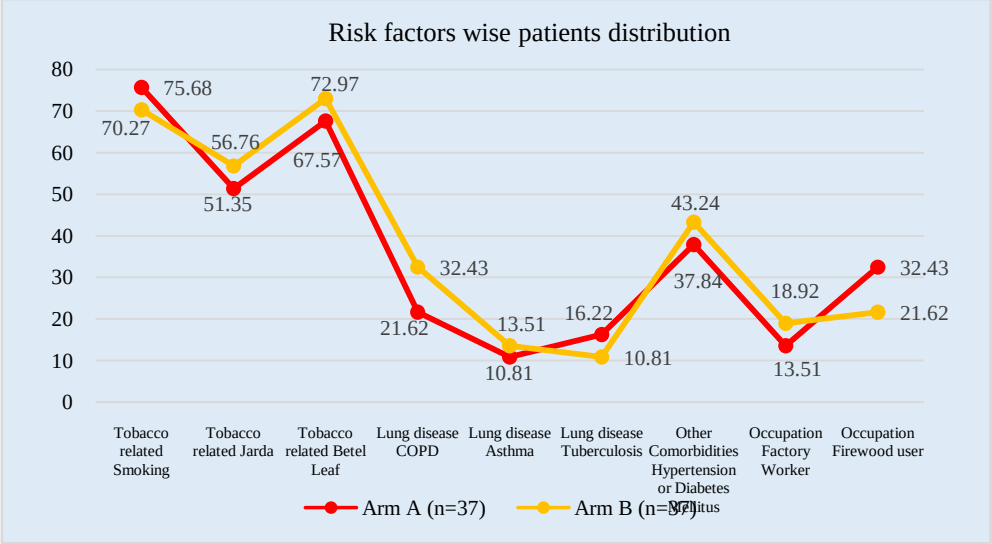

Figure 4: Line chart showed Arm wiseparticipants by risk factors (N=74).

Table 4: Distribution of participants by stage of tumor. (N=74)

Stage of Tumor	Arm-A		Arm-B	
	n	%	n	%
Stage III B	4	10.37%	2	6.66%
Stage III C	6	16.66%	6	17.66%
Stage IV	27	72.97%	28	75.68%

Among the participants of the present study, the majority of the patient presented with Stage IV disease in both Arms. In Arm A, 6(16.66%) and 27(72.97%) patients were in Stage III and IV, whereas 6(17.66%) and 28(75.68%) patients were in Stage III and IV respectively in Arm B. The finding was statistically insignificant (p> 0.05) which shows that there was a uniform distribution of the cases

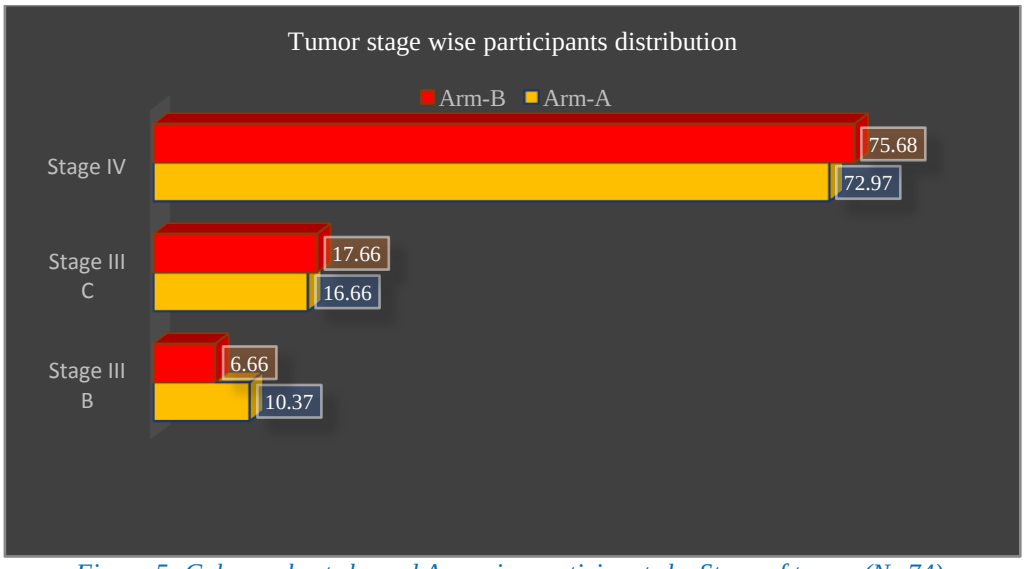

Figure 5: Column chart showed Arm wise participants by Stage of tumor (N=74).

Table 5: Mid-term evaluation after completion of 3rd cycle of chemotherapy. (N=74)

Response	Arm A	Arm B	P-value
	(n=37)	(n=37)	
Complete response (CR)	0(0%)	0(0%)	0.75
Partial response(PR)	18(48.95%)	16(43.24%)	
Stable disease(SD)	19(51.05%)	21(56.76%)	

After 3 cycles of chemotherapy had been completed for all participants, an evaluation of disease response was observed. None of the patients had any complete response in either Arm. 48.95% of Arm A and 43.24% of Arm-B had a partial response, while 51.05% of ArmA and 56.76% of Arm-B participants had stable disease. There was no statistically significant difference between the response rate of both arms.

Table 6: Distribution of patients according to treatment compliance and delay. (N=74)

Variables	Arm A (n=37)		Arm B (n=37)		P-Value
	n	%	n	%	
Chemotherapy Completed within time	30	81.08%	22	59.46%	0.02
Mean No. of chemotherapy cycles	5.73		5.4		-
Chemotherapy Completed without dose reduction	30	81.08%	22	59.46%	0.02
Chemotherapy Cycles					
4 cycles	3	8.11%	7	18.92%	0.02
5 cycles	4	10.81%	8	21.62%	
6 cycles	30	81.08%	22	59.46%	
Other Variables					
Blood transfusion	10	27.03%	19	51.35%	0.035
Platelet transfusion	2	5.41%	8	21.62%	0.025
Use of growth factor	4	10.81%	11	29.73%	0.03

Total 30(81.08%) patients in Arm A and 22(59.46%) patients in Arm B completed the therapy within the expected time, without dose reduction. Mean number of cycles was 5.73 for Arm-A& 5.40 for Arm-B. However, 7(18.92%) patients in Arm A and 15(40.54%) patients in Arm B had delay in completing therapy with further dose reduction. The need for supportive treatment like, blood and platelet transfusions, use of growth factors etc. were lower in Arm-A. Overall, the difference in result was statistically significant.

Table 7: Clinical response at 6 weeks of follow-up after completion of chemotherapy. (N=74)

Clinical Response	Arm A (n=37)	Arm B (n=37)	P-Value
Complete response (CR)	0(0%)	0 (0%)	0.6
Partial response (PR)	23(62.16%)	21(56.76%)	
Stable disease (SD)	13(35.14%)	12(32.43%)	
Progressive disease (PD)	1(02.70%)	4(10.81%)	

After 6 weeks following the completion of treatment, none of the patients had a complete response, but the partial response rate had increased compared to before. Among Arm-A participants, 62.16% had a partial response, 35.14% had stable disease, and 2.70% had progressive disease. On the other hand, among Arm-B participants, 56.76% had a partial response, 32.43% had stable disease and 10.81% had progressive disease. Although the prevalence of progressive disease was higher among Arm-B participants, this difference was not statistically significant.

DISCUSSION

The present study aimed to compare the clinical compliance and treatment delay between Paclitaxel-Carboplatin regimen (Arm-A) and Gemcitabine-Carboplatin regimen (Arm B) as palliative chemotherapy for advanced Non-Small Cell Lung Cancer (NSCLC).In terms of baseline characteristics, both arms had a similar mean age (58.35%) years in Arm A and (57.54%) years in Arm B), with the majority of participants being from the 51-60 year's age group. The majority of participants were male, with slightly more in Arm A (78.38%) than Arm B (70. 27%).This distribution of participants among the older age group, as well as the higher male prevalence, was similar to the findings of other previous studies. [17-20] Most participants in both arms were literate (91.89% in Arm A, 94.59% in Arm B).In terms of ECOG status, the majority of participants in both arms were ECOG 1(45.95% in Arm A, 59.46% in Arm B), with fewer having ECOG status 0 in Arm A (16.22%) compared to Arm B (5.41%). Multiple risk factors were analyzed among the participants. Smoking is globally recognized as the leading cause of lung cancer [21,22]. In this study, 28(75.67%) patients in Arm A and 26(70.27%) patients in Arm B were smokers. So, in the total study population, 54(72.97%) patients were smokers. Many of the study populations also used tobacco in different forms, such as jarda, gul, and tobacco leaf.In terms of the stage of the tumor, the majority of the participants in both arms presented with Stage IV disease, with no significant difference between the two arms ($p>0.05$). To understand the treatment delay between the two treatment regimens, mid-term evaluation was done after completion of the 3rd cycle of chemotherapy, which did not show any complete response in either arm. The prevalence of partial response and stable disease was similar among both arms, with slightly higher incidence of stable disease among Arm-B patients, which was statistically non-significant. In

terms of compliance, it was observed that the mean number of cycles was 5.73 & 5.40 in Arm A & Arm B respectively. A significantly higher number of patients in Arm A had completed the full cycle of chemotherapy (81.08%) compared to Arm B patients (59.46%). This compliance rate was similar to the findings of Bjorn et al. [23] Similarly, a significantly higher number of participants from Arm A had also completed chemotherapy without any dosage reduction. In terms of number of cycles, 81.08% of the Arm A participants had completed 6 cycles of treatment, while only 59.46% had done so in Arm B. This difference was also statistically significant ($p<0.05$). The present study findings also showed that the need for supportive treatment like blood transfusions, platelet transfusions, and the use of growth factors were significantly lower among Arm A patients. The study also observed that at the clinical response at 6-weeks of follow-up after completion of chemotherapy, none of the patients had a complete response, but the partial response rate had increased compared to before. Among Arm A participants, 62.16% had partial response, 35.14% had stable disease, and 2.70% had progressive disease. On the other hand, among Arm B participants, 56.76% had partial response, 32.43% had stable disease and 10.81% had progressive disease. Although the prevalence of progressive disease was higher among Arm B participants, this difference was not statistically significant. This suggests that both regimens were similarly effective in controlling the disease at 6-weeks of follow-up. These findings were also supported by multiple other studies and clinical trials. [24-28]

LIMITATIONS OF THE STUDY

The study was conducted in a single hospital with a small sample size. So, the results may not represent the whole community. It was a non-randomized quasi-experimental study, so selection bias is present. Due to the short study period, the overall survival of the patients in the long term was not possible.

CONCLUSION

The baseline characteristics were similar for both arms, with a majority of older male participants and ECOG status 1. Compliance was higher in Arm A, with a significantly higher number of patients completing the full cycle of chemotherapy without any dosage reduction. At 6 weeks of follow-up after completion of chemotherapy, both regimens were similarly effective in controlling the disease, with a higher prevalence of partial response in Arm-A and stable disease in Arm B. These findings suggest that both regimens can be considered as options for palliative chemotherapy in advanced NSCLC, but with a higher compliance rate in Arm A.

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