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The Comparison of Toxicities between Paclitaxel-Carboplatin Regimen versus Gemcitabine-Carboplatin Regimen as Palliative Chemotherapy for Advanced Non-Small Cell Lung Cancer

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Abstract **Original Research Article**

Introduction: Advanced Non-Small Cell Lung Cancer (NSCLC) is a serious condition characterized by the spread of cancer beyond the lungs, commonly adenocarcinoma and squamous cell carcinoma. Palliative chemotherapy is used to manage advanced NSCLC, focusing on relieving symptoms and improving quality of life rather than curing the disease. Paclitaxel-Carboplatin and Gemcitabine-Carboplatin are commonly used regimens for palliative chemotherapy in advanced NSCLC. Comparing the toxicities of these two regimens is important to determine which one has fewer side effects for patients. ***Aim of the Study:*** The aim of the study was to compare the toxicities of Paclitaxel-Carboplatin and Gemcitabine -Carboplatin as palliative chemotherapy for Advanced Non-Small Cell Lung Cancer. ***Methods:*** This Quasi- Experimental study was conducted at the Department of Medical Oncology, Combined Military Hospital, Dhaka, Bangladesh, the National Institute of Cancer Research & Hospital (NICRH), Mohakhali, Dhaka, Bangladesh, and the Bangabandhu Sheikh Mujib Medical University (BSMMU), Shahbagh, Dhaka, Bangladesh. The study duration 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. ***Result:*** The majority of participants in both Arm-A and Arm-B were in the age group of 51-60 years (40.54% in Arm-A, 43.24% in Arm-B) with an overall mean age of 58.35 years in Arm-A and 57.54 years in Arm-B. An overall male prevalence was observed, with 78.38% of participants in Arm-A and 70.27% in Arm-B being male. The majority of participants had an ECOG status of 1 (45.95% in Arm-A, 59.46% in Arm-B). Risk factors such as smoking and various lung diseases were present among participants, but there was no significant difference between the two arms. After 6 weeks of follow-up, 62.16% of Arm-A and 56.76% of Arm-B had a partial response, with a slightly higher prevalence of progressive disease in Arm-B (10.81%). However, this difference was not statistically significant. Both arms of the study population had similar incidence of nausea and vomiting, diarrhea, thrombocytopenic bleedings, but Arm B had more grade 3/4 febrile neutropenia and grade 2/3 mucositis. Incidence of fatigue/flu-like symptoms was similar in both arms. Other symptoms like skin rash, cardiac toxicity, renal toxicity, alopecia etc. also developed in both arms, but these findings were statistically insignificant. ***Conclusion:*** The study found that both chemotherapy regimens were effective in controlling advanced non-small cell lung cancer and that the Paclitaxel and Carboplatin regimen had lower severity of acute hematological toxicities compared to the Gemcitabine and Carboplatin regimen, which had a higher incidence of leucopenia, neutropenia and thrombocytopenia of various grades. No significant differences in non- hematological toxicities were found between the two regimens.

Keywords: Cancer, Toxicities, Chemotherapy, Paclitaxel, Gemcitabine, Carboplatin, Hematological.

INTRODUCTION

Cancer, a group of diseases characterized by abnormal cell growth, can spread to other parts of the body. One of the most frequently diagnosed cancers is lung cancer, which is also the leading cause of death worldwide [1, 2]. According to GLOBOCAN 2020, lung cancer is the most frequently diagnosed cancer,

with an incidence of 22,06,771 (11.4%) and a mortality rate of 17,96,144 (18%) [3]. In Bangladesh, lung cancer is the 4th most prevalent cancer in both men and women, with an incidence of 12,999 (8.3%) and it is also the 2nd most common cause of cancer-related mortality [3–5]. There are two primary subtypes of lung cancer: small-cell lung cancer (SCLC) and non-small-cell lung cancer (NSCLC). NSCLC accounts for 80-85% of lung cancers [6, 7]. Environmental and lifestyle factors, with cigarette smoking being the most common cause, have been linked to the development of lung cancer [8]. The diagnostic evaluation for NSCLC includes a biopsy or cytology of the primary or metastatic site, which can be done by image guidance or bronchoscopy [9, 10]. The staging workup includes a patient's history, physical examination, imaging studies, and other tests as per the guidelines [8]. The treatment options for NSCLC are determined by the stage, histology, and performance status of the patient [7]. Surgery, radiation therapy, chemotherapy, targeted therapy, and immunotherapy are the different modalities of treatment used for NSCLC [11, 12]. In advanced-stage non-small-cell lung cancer (NSCLC), the mainstay of treatment is chemotherapy. Paclitaxel-Carboplatin and Gemcitabine-Carboplatin are two commonly used chemotherapy regimens for the treatment of advanced NSCLC [13, 14]. Comparing the efficacy of these two regimens through clinical response will help determine which regimen is more effective in treating advanced NSCLC. Another criterion for measuring the effectiveness of a chemotherapy treatment is the number of toxicities, or lack thereof. The side effects or toxicities can vary depending on the type and dose of chemotherapy drugs and the duration of treatment [15, 16]. The present study was focused on comparing the post-operative toxicities between two different chemotherapy treatment methods, Paclitaxel-Carboplatin, and Gemcitabine-Carboplatin. Paclitaxel is a chemotherapeutic medication that works by preventing cancer cell proliferation. Carboplatin is a chemotherapeutic medication used to treat a variety of cancers, including lung cancer. This two-drug combination is successful in treating advanced NSCLC [6, 17, 18]. Another chemotherapy regimen often used to treat advanced non-small cell lung cancer is gemcitabine-carboplatin. Gemcitabine is a chemotherapeutic medication used to treat a variety of cancers, including lung cancer. Carboplatin is a chemotherapeutic medication used to treat a variety of cancers, including lung cancer. This two- drug combination is also beneficial in treating advanced NSCLC [19, 20]. There have been several studies that have compared the efficacy of Paclitaxel-Carboplatin with Gemcitabine-Carboplatin as palliative chemotherapy for advanced NSCLC. But majority of such studies had been focused around the clinical progression of the disease itself, instead of the side-effects and toxicities. The main focus of the present study was the observation and comparison of toxicities between the two treatment methods.

OBJECTIVE

General Objective

- To observe the toxicities of Paclitaxel-Carboplatin as a palliative chemotherapy for Advanced Non-Small Cell Lung Cancer.
- To observe the toxicities of Gemcitabine - Carboplatin as a palliative chemotherapy for Advanced Non-Small Cell Lung Cancer.

Specific Objectives

- To compare the toxicities of Paclitaxel-Carboplatin and Gemcitabine -Carboplatin as palliative chemotherapy for Advanced Non-Small Cell Lung Cancer.

METHODS

This Quasi-Experimental study was conducted at the Department of Medical Oncology, Combined Military Hospital, Dhaka, Bangladesh, the National Institute of Cancer Research & Hospital (NICRH), Mohakhali, Dhaka, Bangladesh, and the Bangabandhu Sheikh Mujib Medical University (BSMMU), Shahbagh, Dhaka, Bangladesh. 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 infusional Paclitaxel–Carboplatin (PC) regimen, and Arm-B having 37 patients being treated with an infusional Gemcitabine-Carboplatin (GC) regimen. The patients were informed about treatment costs, expected response rate, and toxicity of both arms. Informed consent was obtained from the patients prior to data collection. 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. Patients were assessed for acute toxicities during the treatment through weekly investigations and clinical examination by using National Cancer Institute Common Terminology Criteria for Adverse Events (NTC-CTCAE) v 5.0 criteria. T, N, and M staging of the patients was done according to the AJCC 8th edition [21]. 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.
- Patients aged less than 18 years & more than 70 years.
- Very serious co-morbidity like clinically significant CVD.
- Who cannot afford the cost of treatment

RESULTS

Table 1: Sociodemographic characteristics of the study participants

Variables	Arm-A		Arm-B	
	n	%	n	%
Age				
30-40	0	0.00%	1	2.70%
41-50	10	27.03%	8	21.62%
51-60	15	40.54%	16	43.24%
61-70	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.

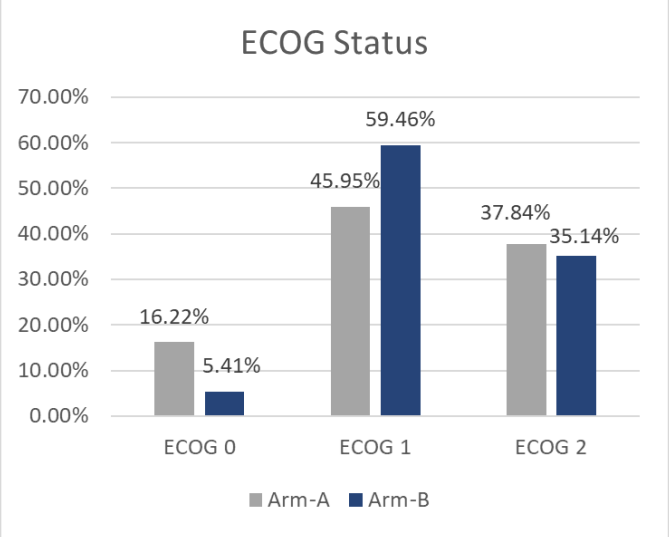

Figure 1: Distribution of participants by ECOG status

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 2: Distribution of patients according to the risk factors

Risk factors		**Arm A (n = 37)**	**Arm B (n = 37)**	**P – value**
Tobacco related	Smoking	28 (75.67%)	26 (70.27%)	0.87
	Jarda	19 (51.35%)	21 (56.75%)	
	Betel Leaf	25 (67.56%)	27 (72.97%)	
Lung disease	COPD	8 (21.62%)	12 (32.43%)	0.63
	Asthma	4 (10.81%)	5 (13.51%)	
	Tuberculosis	6 (16.21%)	4 (10.81%)	
Others Comorbidities	Hypertension or Diabetes Mellitus	14 (37.83%)	16 (43.24%)	0.46
Occupation	Factory Worker	5 (13.51%)	7 (8.91%)	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).

Table 3: Distribution of participants by clinical presentations

Symptoms	**Arm A (n = 37)**	**Arm B (n = 37)**	***P* – value**
Cough	32 (86.48%)	31 (83.78%)	0.49
Dyspnea	11 (29.73%)	17 (45.94%)	0.31
Hemoptysis	10 (27.03%)	06 (16.22%)	0.36
Chest Pain	03 (08.11%)	08 (21.62%)	0.12
Infection	10 (27.02%)	15 (40.54%)	0.21
Hoarseness	03 (08.11%)	02 (05.40%)	0.16
SVCO	05 (13.51%)	07 (18.92%)	0.55
Others (weight loss, loss of appetite, weakness, etc.)	09 (24.32%)	13 (35.14%)	0.6

In terms of clinical symptoms, it was observed that the majority of the patients in Arm A presented with cough (32 out of 37, 86.48%) followed by dyspnea (11 out of 37, 29.73%), whereas patients in Arm B presented with cough (31 out of 37, 83.78%) followed by dyspnea (17 out of 37, 45.94%). The findings were statistically insignificant (p> 0.05).

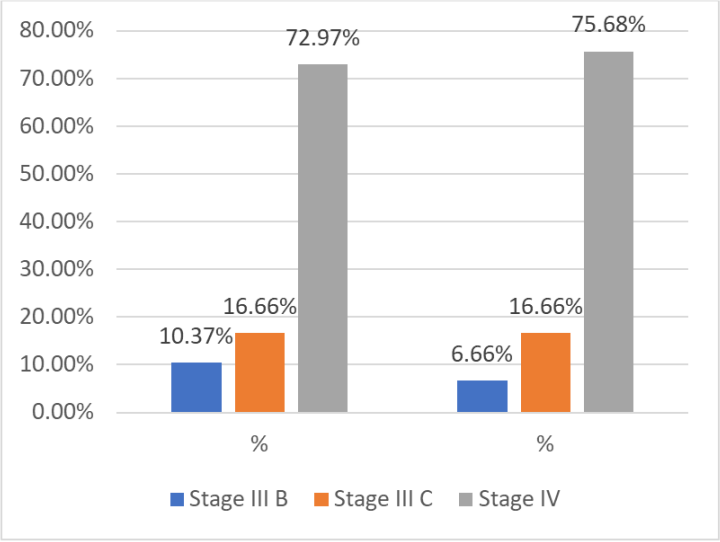

Figure 2: Distribution of participants by stage of the tumor

Among the participants of the present study, the majority of the patient presented with Stage IV disease in both Arms. In Arm A, 10 (27.03%) and 27 (72.97%) patients were in Stage III and IV, whereas 09 (24.32%) 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.

Table 4: Distribution of patients by histopathological type of tumor in percentage

Histopathological Type	Arm A (n=37)	Arm B (n=37)	Overall (n=74)	*P* value
Adenocarcinoma	32 (86.48%)	33 (89.19%)	65 (87.84%)	0.55
Large cell carcinoma	05 (13.51%)	04 (10.81%)	09 (12.16%)	1

Adenocarcinoma was the most commonly observed histopathological type in both arms, with 86.48% prevalence in Arm-A and 89.19% prevalence in Arm-B. overall, the prevalence of adenocarcinoma was 87.84% and for large cell carcinoma, it was 12.16%.

Table 5: Clinical response at 6 weeks of follow-up after completion of chemotherapy

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)	01 (02.70%)	04 (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.

Table 6: Distribution of acute hematological toxicities in both the arms

Hematological toxicities	Arm A (n = 37)	Arm B (n = 37)	P – value
Anemia			
Grade 0	06 (16.21%)	03 (08.10%)	0.05
Grade 1	20 (54.05%)	16 (43.24%)	
Grade 2	08 (21.62%)	12 (32.43%)	
Grade 3	02 (05.40%)	04 (10.81%)	
Grade 4	01 (02.70%)	02 (05.40%)	
Leucopenia			
Grade 0	03 (08.10%)	03 (08.10%)	0.005
Grade 1	15 (40.54%)	06 (16.21%)	
Grade 2	11 (29.72%)	09 (24.32%)	
Grade 3	06 (16.21%)	13 (35.14%)	
Grade 4	02 (05.40%)	06 (16.21%)	
Neutropenia			
Grade 0	03 (08.10%)	03 (08.10%)	0.005
Grade 1	15 (40.54%)	06 (16.21%)	
Grade 2	11 (29.72%)	09 (24.32%)	
Grade 3	06 (16.21%)	10 (35.14%)	
Grade 4	02 (05.40%)	09 (16.21%)	
Thrombocytopenia			
Grade 0	02 (05.40%)	01 (02.70%)	0.01
Grade 1	14 (37.84%)	07 (18.92%)	
Grade 2	12 (32.43%)	09 (24.32%)	
Grade 3	06 (16.21%)	13 (35.13%)	
Grade 4	03 (08.12%)	07 (18.92%)	

It can be seen that none of the patients were spared from anemia. The severity of anemia was higher in Arm B compared to Arm A. 11 (29.73%) patients developed Grade 2 or more anemia in Arm-A, whereas

17 (45.95%) patients in Arm-B. This finding was statistically insignificant between the two arms (p>0.05). Leucopenia of various grades was predominant in both the Arms. It was seen that Grade 3 or more leucopenia was seen in 08 patients (21.61%) vs 19 patients (51.35%) among Arm A and B respectively. The finding was statistically significant (p<0.05). Neutropenia, like leucopenia; of various grades was predominant in both the Arms. It was seen that Grade 3 or more neutropenia was seen in 08 patients (21.61%) vs 19 patients (51.35%) among Arm A and B respectively. The finding was statistically significant (p<0.05). Grade 3 and Grade 4 thrombocytopenia was significantly seen more in Arm B compared to Arm A. 09 (24.33%) patients in Arm A and 20 (54.05%) in Arm B developed Grade 3 and 4 thrombocytopenia. The finding was statistically significant (p<0.05).

Table 7: Distribution of acute non-hematological toxicities observed during Chemotherapy

Toxicities	Arm A (n = 37)	Arm B (n = 37)	P – value
Nausea/vomiting			
Grade 0	04 (10.81%)	07(18.92%)	0.97
Grade 1	21 (56.76%)	18(48.65%)	
Grade 2	11 (29.73%)	10(27.03%)	
Grade 3	01 (02.70%)	02(05.40%)	
Diarrhoea			
Grade 0	24 (64.86%)	22(59.46%)	0.5
Grade 1	10 (27.03%)	11(29.73%)	
Grade 2	03 (08.10%)	04(10.81%)	
Grade 3	-	-	
Bleeding			
Grade 0	25(67.56%)	23(62.16%)	0.6
Grade 1	10(27.02%)	11(29.74%)	
Grade 2	01 (02.70%)	02(05.40%)	
Grade 3	01(02.70%)	01(02.70%)	
Febrile neutropenia			
Grade 0	27(72.98%)	23(62.16%)	0.25
Grade 3	07(18.92%)	10(27.02%)	
Grade 4	03(08.10%)	04(10.82%)	
Mucositis			
Grade 0	25 (67.57%)	23(62.16%)	0.5
Grade 1	09 (24.32%)	10(27.03%)	
Grade 2	02 (05.40%)	04(10.81%)	
Grade 3	01 (2.70%)	-	
Fatigue/Flu like symptoms			
Grade 0	22(59.46%)	21(56.76%)	0.97
Grade 1	08(21.62)	09(24.32%)	
Grade 2	05(13.51)	06(16.22%)	
Grade 3	02(05.40%)	01(02.70%)	
Others			
Grade 0	26(70.28%)	24(64.87%)	0.35
Grade 1	08(21.62)	08(21.62)	
Grade 2	03(08.10)	05(13.51)	
Grade 3	-	-	

Incidence of nausea and vomiting was almost similar on both arms. 11 (29.73%) and 01 (02.70%) patients in Arm A, whereas 10 (27.03%) and 02 (05.40%) patients in Arm B developed grade 2 and grade 3 nausea and vomiting. The finding was statistically insignificant (p= 0.46). The incidence of diarrhoea was also similar in both arms. The incidence was Grade 2 diarrhoea was 03 (08.10%) patients in Arm A, whereas 04(10.81%) in Arm B. The finding was statistically insignificant (p= >0.05). 02(05.40%) patients developed Grade 2/3 thrombocytopenic bleedings in Arm-A & 03(08.10%) patients in Arm-B. The finding was statistically insignificant (p>0.05). Grade 3/4 febrile neutropenia was seen to be more in Arm B than Arm A. 10 (27.02%) patients in Arm A, whereas 14 (37.84%) in Arm B developed grade 3/4 febrile neutropenia respectively. The finding was statistically insignificant (p>0.05). Grade 2/3 mucositis was more in Arm B, 03 (08.10%) and 04(10.81%) respectively. The incidence of grade 2/3 fatigue/flu like symptoms was similar in both arms, 07(18.92%) patients in each arm. Other less common symptoms

like, skin rash, cardiac toxicity, renal toxicity, alopecia etc. also developed in both arms. Overall, the finding was statistically insignificant (p>0.05).

DISCUSSION

The purpose of this study was to compare the toxicities of the Paclitaxel-Carboplatin regimen (Arm-A) and Gemcitabine-Carboplatin regimen (Arm-B) as palliative chemotherapy for advanced Non-Small Cell Lung Cancer (NSCLC). The study population's baseline characteristics were similar in both groups. The mean age of the participants in Arm-A was 58.35 years and 57.54 years in Arm-B, with the bulk of the participants being between the ages of 51 and 60. These findings were consistent with earlier studies, with the bulk of participants being in their fifth or sixth decade of life [22, 23]. Only 19 (25.68 percent) of the 74 patients were female, whereas 55 (74.32 percent) were male. The male- female ratio was 2.89:1. This finding is consistent with other research that has found a higher male predominance [24, 25]. At presentation, the majority of patients in both arms had an ECOG performance score of 1 (47 percent in Arm A and 59 percent in Arm B), with ECOG 2 being the next highest (37 percent in Arm A and 35 percent in Arm B). Several risk variables were examined among the individuals. Tobacco use is widely acknowledged as the primary cause of lung cancer worldwide [26, 27]. In this study, 28 (75.67%) of patients in Arm A and 26 (70.27%) of patients in Arm B smoked. In total, 54 (72.97 percent) of the patients in the research were smokers. Many of the research populations smoked tobacco in various forms, including jarda, gul, and tobacco leaf. However, there were no statistically significant variations in the distribution of risk factors between the two arms. The most prevalent clinical manifestation was cough, which was observed in 86.48 percent of Arm-A and 83.78 percent of Arm-B participants, for a combined frequency of 85.14 percent. The distribution of tumor stage across individuals in both groups was uniform and revealed no significant difference. In both Arms A and B, the most prevalent histologic type was adenocarcinoma. These presentations were similar to the study findings of a phase III study [28]. After the treatment began, all of the individuals had received at least 95 percent of their initial dosage. At the 6-week follow-up after therapy, none of the patients had a full response, however among Arm-A participants, 62.16 percent had a partial response, 35.14 percent had stable disease, and 2.70 percent had advancing disease. In contrast, 56.76 percent of Arm-B individuals had a partial response, 32.43 percent had stable disease, and 10.81 percent had increasing disease. Although Arm-B patients had a higher prevalence of progressing illness, the difference was not statistically significant. This shows that at 6-weeks of follow-up, both treatments were equally effective in treating the condition. In terms of toxicity, the results showed that none of the patients were spared from anemia, but the severity of anemia was higher in Arm B compared to Arm A. 11 (29.73%) patients developed Grade 2 or more anemia in Arm-A, whereas 17 (45.95%) patients in Arm-B. This finding was statistically insignificant between the two arms (p>0.05). Leucopenia and neutropenia of various grades were predominant in both the Arms. It was seen that Grade 3 or more leucopenia and neutropenia was seen in 08 patients (21.61%) vs 19 patients (51.35%) among Arm A and B respectively. The finding was statistically significant (p<0.05) for both leucopenia and neutropenia. Grade 3 and Grade 4 thrombocytopenia was significantly seen more in Arm B compared to Arm A. 09 (24.33%) patients in Arm A and 20 (54.05%) in Arm B developed Grade 3 and 4 thrombocytopenia. The finding was statistically significant (p<0.05). For non-hematological toxicities, nausea/vomiting was seen more in Arm B, but the difference was not statistically significant (p=0.97). Diarrhoea and bleeding were also observed in both arms, but the difference in the incidence and severity of these toxicities were not statistically significant. These findings correlated with those of Gronberg *et al*., [28]. In conclusion, the study found that the Paclitaxel and Carboplatin regimen had lower severity of anemia compared to the Gemcitabine and Carboplatin regimen. However, the Gemcitabine and Carboplatin regimen resulted in a higher incidence of leucopenia, neutropenia, and thrombocytopenia of various grades, which were statistically significant.

Limitations of the Study

The study was conducted 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 study found that both arms of the study population had similar baseline characteristics, with the majority of participants being in the age group of 51-60 years and a higher male prevalence. Risk factors such as smoking and tobacco use were present among the participants, but there was no significant difference in their distribution between the two arms. The study also found that both chemotherapy regimens were effective in controlling the disease, as seen at 6- week follow-up. In terms of toxicities, the Paclitaxel and Carboplatin regimen had lower severity of acute hematological toxicities, while the Gemcitabine and Carboplatin regimen resulted in a higher incidence of leucopenia, neutropenia, and thrombocytopenia of various grades, which were statistically significant. No significant differences in non-hematological toxicities were found between the two regimens.

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Conflict of Interest: None declared.
Ethical Approval: The study was approved by the Institutional Ethics Committee.

RECOMMENDATION

Further long-term randomized studies need to be done with multicenter trials to see survival benefits and late toxicities. Studies with larger sample size could help establish the significant benefit in terms of response.

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