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Evaluation Of Clinical Response And Toxicities Of Cisplatin Plus Etoposide Versus Paclitaxel Plus Carboplatin In The Treatment Of Advanced Small Cell Lung Carcinoma

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Abstract
Background: *Small cell lung cancer (SCLC) is a major cause of cancer deaths and accounts for 20% to 25% of all lung cancer[1]. It follows a more rapid clinical course than non-small-cell lung cancer. In contrast to non-small-cell lung cancer, however, small-cell lung cancer is very sensitive to cytotoxic agents and radiation therapy[2].*
Material And Methods: *This Quasi-experimental prospective study done in the oncology department of different hospital in Dhaka to evaluate the clinical response and toxicities between Cisplatin plus Etoposide Versus Paclitaxel plus Carboplatin in the treatment of advanced Small cell lung carcinoma.*
Result: A total of 60 patients with histologically confirmed small cell lung cancer with advanced stage were selected for the study upon fulfillment of inclusion and exclusion criteria. Patients with Karnofsky performance scale status score below 60 were excluded and age range of patients for the study considered between 30 to 70 years with any sex. Besides the debilitating co-morbidity including severe heart disease, uncontrolled diabetes mellitus or hypertension were also excluded to avoid confounding effect. Thirty of the patients were allocated with Cisplatin-Etoposide based regimen and was leveled as arm-A and another 30 were allocated with Paclitaxel-Carboplatin basedt regimen and leveled as Arm-B.
Following chest examination, both the arms had not significant (p>.05) baseline parameters. In the two arms CxR (P/A and lateral view) findings; presence of ' lesion' (Radio opaque shadow), side, zone and size of the lesions were found to be statistically indifferent (p>.05). Besides these, Performance status was also statistically insignificant (p>.05).
To compared the toxicities, nausea & vomiting were found to be more in arm-A (p>.05) and diarrhea was found to be more in arm-B (p>.05) in several cycles. Sensory neuropathy was found to be only in arm-B and hearing loss was found to be only in arm-A to occur rarely among study subjects. In the initial cycles of treatment only a patient developed hypersensitivity reaction in arm-B, Patient in both the treatment arms were not statistically significant to comparing Haemoglobin, platelet and WBC count during treatment (p>.05).
To assessment of symptoms (cough, haemoptysis, chest pain, and breathlessness), after 2nd cycle of chemotherapy, cough and breathlessness were relived better in arm-B (p>.05) and after 4th cycle of chemotherapy, cough, chest pain and breathlessness were relived better in arm-B than arm-A (p>.05). During follow-up period cough and haemoptysis were found to be relived better in arm-B than arm-A (p>.05).
To compared the responses in terms of relieving clinical signs (palpable supraclavicular lymph node, abnormal percussion, abnormal vocal resonance and added sound), after 2nd cycle of chemotherapy, abnormal vocal resonance and added sound found to be relieved better in arm-B and after 4th cycle, all signs were relived better in arm-B than arm-A (p>.05). During follow-up period arm-B showed superior response in terms of relieved of signs than arm-A (p>.05).
To followed radiological evaluation, regarding patient' s response in terms CxR (P/A view) finding during chemotherapy, assessed after 2nd and 4th cycle chemotherapy, regression of tumour were found to be significantly more in arm-B than arm-A (p>.05). Response to tumour regression revealed by CxR (P/A view) finding during follow up period, arm-B showed superior response than arm-A (p>.05).
Over the five assessment period (after 2nd and 4th of chemotherapy and at three follow-up), trend analysis on tumour regression (CxR P/A view) showed steady decline over the treatment period and follow up. Treatment arm ' B' showed steeper decline in comparison to treatment arm-A. Over all, treatment arm-B showed better response on regression of tumour in comparison to treatment arm-A.

Conclusion: *Combination chemotherapy (two to more drugs) is more effective than single agents chemotherapy in the treatment of Small cell lung carcinoma. This study was to observe and to compare the clinical response and toxicities of two chemotherapy schedules (cisplatin-etoposide vs paclitaxel-Carboplatin) for patients with advanced small cell lung cancer. It is to be concluded that Paclitaxel Plus Carboplatin based chemotherapy schedule showed better response in advanced Small cell lung Carcinoma.*

Keywords: *Small cell lung carcinoma, Cisplatin, Etoposide, Paclitaxel, Carboplatin*

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I. Introduction

Lung cancer is the most common visceral malignancy, accounting for roughly one third of all cancer deaths, and it is the most common cause of cancer-related death in both men and women[2]. It is responsible for 31% of cancer-related deaths in men and 25% in women[3]. The number of cases with lung cancer is equally divided among developed and developing countries. Lung cancer is a disease of the middle-aged and elderly: 90% of cases occur between the ages of 40 and 80. The male : female ratio is 5:1[5].

Exact incidence of lung cancer in Bangladesh is yet not known. However, from a study done by Kamaluddin M et al in 2006 at NICRH (National Institute of Cancer Research and Hospital), the incidence of lung cancer was noted 20.64%[6].

Lung cancer is predominantly a disease of smokers. 80% of lung cancer occurs in active or former smokers, and an additional 5% of cases are estimated to occur as a consequence of passive exposure to tobacco smoke[2].

Chemotherapy is the treatment of choice for small cell lung cancer. Combination chemotherapy (two to four drugs) is more effective than single agents in obtaining complete, though usually temporary, remissions, and in prolonging survival. Overall (complete and partial) response rates of 75-90% can be achieved. A balance has to be struck between the toxicity and clinical benefit of chemotherapy.

My study was to observe and to compare the response to treatment and early toxicities of two chemotherapy schedules (cisplatin-etoposide vs Paclitaxel-Carboplatin)for patients with small cell lung cancer. So, far our knowledge goes, no substantial works has been carried out in this area in Bangladesh. This study will hopefully open a new horizon in the field of oncology.

II. Objectives Of The Study

General objectives: To compare the clinical outcome of cisplatin plus etoposide based chemotherapy regimen and paclitaxel plus Carboplatin with based chemotherapy regimen in the treatment of advanced small cell lung cancers.

Specific Objectives:

a. To assess the response of cisplatin-etoposide and Paclitaxel-Carboplatin based chemotherapy regimen in the treatment of advanced small cell lung cancers.
b. To identify the toxicities of cisplatin-etoposide and Paclitaxel-Carboplatin based chemotherapy regimens in the treatment of advanced small cell lung cancers.
c. To determine the socio-demographic difference of the patients suffering from small cell lung cancers.

III. Methodology

This Quasi-experimental prospective study was done from 1st January 2016 to 31st December 2016 in the Department of oncology, Bangabandhu Sheikh Mujib Medical University (BSMMU), Dhaka; in the Department of Radiotherapy, Dhaka Medical College Hospital (DMCH), Dhaka and in National Institute of Cancer Research and Hospital (NICRH), Dhaka. Histologically confirmed advanced small cell lung Cancer (SCLC) patients attended above mentioned places and also satisfied the eligibility and ineligibility criteria.

Patients were enrolled in the study by following criteria: Histologic or cytologic diagnosis of small cell lung cancerwith advanced disease without visceral or skeletal metastasis. Any sex, age 30-70 years. Kernofsky performance scale (KPS) ≥60. No previous history of chemotherapy or radiotherapy.

Patients were not enrolled in the study by following criteria: Patients with uncontrolled infection. Serious concomitant medical illness, including severe heart disease, uncontrolled diabetes mellitus or hypertension. Major surgery within 3 weeks. Pregnancy or location. Prisoners.

Each patient was interviewed and their particulars and history were documented according to prescribed data sheet. Clinical examination and necessary investigation were done. Selected patients were evaluated properly before treatment. Findings of observation were recorded on a structured close-ended interview schedule. 60 patients enrolled in the study and divided in to two arm-A an darm-B (30 patients in each arm). Diagnosed patients of small cell lung cancer were selected purposively and every odd number of patients

in arm-A and every even number of patients in arm-B were selected. Then each arm case was selected by simple random sampling technique.

Treatment Plan:

Arm-A	Arm-B
a. Inj. Cisplatin 80 mg/m^2 i.v. (1hr inf.) for day 1 and b. Inj. Etoposide 100 mg/m^2 i.v. (2hrs inf.) for day 1-3. Repeated every 3 weeks for a total of 5 cycles.	a. Inj. Paclitaxel 175 mg/m^2 i.v. (3 hrs inf.) for day 1. Repeated every 3 weeks for a total of 5 cycles. b.Inj. Carboplatin AUC 5 i.v.(30 min inf.) for day 1 and

Patient assessment: Assessment during treatment:

a. Tumour regression: Response was assessed by chest x-ray (P/A and lateral view). Pretreatment tumour size (cm) was compared with the tumour size (cm) after 01 weeks of 2nd and 4th cycle of chemotherapy.
b. Relief of symptoms and signs: Complaints of cough, haemoptysis, chest pain & breathlessness were taken as parameter of symptoms and findings of palpable supraclavicular lymph node, abnormal percussion, abnormal vocal resonance and added sound were taken as parameter of signs. Improvement of symptoms and signs were assessed 01 weeks after 2nd and 4th cycle of chemotherapy and compared with the pretreatment condition.
c. Toxicities reporting: The Toxicity of treatment evaluated according to common toxicity criteria (CTC Version 2.0 DCTD, NIC, NIH, DHHS March, 1998). Toxicities assessed 02 weeks after each cycle of chemotherapy.

Assessment during follow up:

a. After completion of treatment patients was carefully supervised to attain first follow up two weeks after end of treatment.
b. They advised to come four weekly for subsequent two follow up.
c. At each follow up chest radiograph was taken and tumour response, improvement of symptoms & signs and toxicities due to treatment were evaluated.
d. Other related investigations were done.

IV. Result:

All response was evaluated in the light of WHO response criteria (attached here in Appendix VI).

Table 01: Distribution of the patients by Nausea during chemotherapy

Nausea	Subject				Total		P value
	Group A		Group B				
	No	%	No	%	No	%	
After 1st chemotherapy	n=30		n=30		n=60		
None	21	70.0	29	96.7	50	83.3	.034
1 episode in 24 hrs.	9	30.0	1	3.3	10	16.3	
After 2nd chemotherapy	n=30		n=30		n=60		
None	9	30.0	28	93.3	37	61.7	0.001
1 episode in 24 hrs.	21	70.0	2	06.7	17	38.3	
After 3rd chemotherapy	n=30		n=30		n=60		
None	6	20.0	20	66.7	26	43.3	0.039
1 episode in 24 hrs.	21	70.0	9	30.0	30	50.0	
2-5 episodes in 24 hrs.	3	10.0	1	3.3	4	6.7	
After 4th chemotherapy	n=30		n=29		n=59		
None	6	20.0	21	70.0	27	45.7	0.025
1 episode in 24 hrs.	20	66.7	9	30.0	28	47.6	
2-5 episodes in 24 hrs.	4	13.3	0	0.0	4	6.7	
After 5th chemotherapy	n=30		n=29		n=59		
None	7	23.3	17	56.7	23	40.0	0.012
1 episode in 24 hrs.	20	66.7	13	43.3	33	55.0	
2-5 episodes in 24 hrs.	3	10.0	0	0	3	5.5	

P value generated through chi square test *Fissure exact test was considered

Table 01 shows that distribution of the respondents by nausea following treatment. On average nausea is prevalent in both the arm. Although it is generally seen more in arm A, the difference is found to be significant throughout the course of treatment ($p < .05$).

Table 02: Distribution of the patients by Vomiting during chemotherapy

Vomiting	Group A		Group B		Total		P value
	No	%	No	%	No	%	
After 1st chemotherapy	n=30		n=30		n=60		
None	20	66.7	28	93.3	48	80.0	0.001
1 episode in 24 hrs.	8	26.7	1	3.3	9	15.0	
2-5 episodes in 24 hrs.	2	6.7	1	3.3	3	5.0	
After 2nd chemotherapy	n=30		n=30		n=60		
None	2	6.7	20	66.7	22	36.7	0.002
1 episode in 24 hrs.	14	46.7	7	23.3	21	35.0	
2-5 episodes in 24 hrs.	14	46.7	3	10.0	17	28.3	
After 3rd chemotherapy	n=30		n=30		n=60		
None	1	3.3	13	43.3	14	23.3	0.027
1 episode in 24 hrs.	19	63.3	10	33.3	29	48.3	
2-5 episodes in 24 hrs.	10	33.3	7	23.3	17	28.3	
After 4th chemotherapy	n=30		n=29		n=59		
None	9	30.0	12	41.4	21	35.6	0.004
1 episode in 24 hrs.	16	53.3	16	55.2	32	54.2	
2-5 episodes in 24 hrs.	5	16.7	2	6.9	7	11.9	
After 5th chemotherapy	n=30		n=29		n=59		
None	15	50.0	19	65.5	34	57.6	0.176
1 episode in 24 hrs.	12	40.0	10	34.5	22	37.3	
2-5 episodes in 24 hrs.	3	10.0	0	0.0	3	5.1	

P value generated through chi square test *Fissure exact test was considered

Table 02 shows the distribution of the respondents by incidence of vomiting following treatment. On average vomiting is equally prevalent in both the treatment arm after 5th cycle of chemotherapy (P >.05), statistically significant difference exists in the two treatment arm after in first 4 cycle of chemotherapy, where vomiting was found to be more in arm A than arm B (p <.05).

Table 03: Distribution of the patients by toxicity (Diarrhea) during chemotherapy

Diarrhea	Group A		Group B		Total		P value
	No	%	No	%	No	%	
After 1st chemotherapy	n=30		n=30		n=60		
None	25	83.3	20	66.7	45	75.0	0.011
<4 stool/day	5	16.7	6	20.0	11	18.3	
4-6 stools/day	0	0.0	4	13.3	4	6.7	
After 2nd chemotherapy	n=30		n=30		n=60		
None	20	66.7	26	86.7	46	76.7	0.042
<4 stool/day	8	26.7	4	13.3	12	20.0	
4-6 stools/day	2	6.7	0	0.0	2	3.3	
After 3rd chemotherapy	n=30		n=30		n=60		
None	14	46.7	18	60.0	32	53.3	0.089
<4 stool/day	12	40.0	12	40.0	24	40.0	
4-6 stools/day	4	13.3	0	0.0	4	6.7	
After 4th chemotherapy	n=30		n=29		n=59		
None	3	10.0	8	27.6	11	18.6	0.039
<4 stool/day	10	33.3	12	41.4	22	37.3	
4-6 stools/day	17	56.7	9	31.0	26	44.1	
After 5th chemotherapy	n=30		n=29		n=59		
None	20	66.7	10	34.5	30	50.8	0.004
<4 stool/day	2	6.7	4	13.8	6	10.2	
4-6 stools/day	8	26.7	16	55.2	24	40.7	

P value generated through chi square test *Fissure exact test was considered

Table 03 shows the distribution of the respondents by diarrhea following treatment. Diarrhea was seen more in arm B than arm A after all the chemotherapy (p <.05) except after 3rd cycle (p >.05).

Table 04: Distribution of the patients by toxicity (Alopecia) during chemotherapy

Diarrhea	Group A		Group B		Total		P value
	No	%	No	%	No	%	
After 1st chemotherapy	n=30		n=30		n=60		
None	30	100.0	30	100.0	60	100.0	NA
After 2nd chemotherapy			n=30		n=60		
None	29	96.7	26	86.7	55	91.7	0.048
Thinning or patchy	1	3.3	4	13.3	5	8.3	
After 3rd chemotherapy	n=30		n=30		n=60		
Thinning or patchy	25	83.3	22	73.3	47	78.3	0.189
complete	5	16.7	8	26.7	13	21.7	

After 4th chemotherapy	n=30		n=29		n=59		
Thinning or patchy	26	86.7	22	75.9	48	81.4	0.029
complete	6	20.0	7	24.1	13	22.0	
After 5th chemotherapy	n=30		n=29		n=59		
		73.3		69.0		71.2	0.044
Thinning or patchy	8	26.7	6	20.7	14	23.7	
complete	22	0.0	23	10.3	45	25.1	

P value generated through chi square test *Fissure exact test was considered

Table 04 shows the distribution of the patients by Alopecia during chemotherapy. Alopecia was found to be equally Prevalent in both the arms in 1st and 3rd chemotherapy. The difference in prevalence of alopecia was found after 2nd, 3rd, 4th and 5th chemotherapy where the patients of arm B found to have more alopecia (p<.05).

Table 05: Distribution of the patients by Haemoglobin during chemotherapy

Haemoglobin (gm/dl)	Subject						P value
	Group A		Group B		Total		
	No	%	No	%	No	%	
After 1st cycle	n=30		n=30		n=60		
WNL	30	100	30	100	60	100	NA
After 2nd cycle	n=30		n=30		n=60		
WNL	30	100	30	96.7	60	95.0	.082
10.0-LLN gm/dl	2	6.7	1	3.3	3	5.0	
After 3rd cycle	n=30		n=30		n=30		
WNL	26	86.7	26	86.7	52	86.7	1.00
10.0-LLN gm/dl	4	13.3	4	13.3	8	13.3	
After 4th cycle	n=30		n=29		n=59		
WNL	28	93.3	27	93.1	55	93.2	0.89
10.0-LLN gm/dl	2	6.7	2	6.9	4	6.8	
After 5th cycle	n=30		n=29		n=59		
WNL	26	86.7	28	96.6	59	94.9	.350
10.0-LLN gm/dl	4	13.3	1	3.4	3	5.1	

P value generated through chi square test *Fissure exact test was considered

Table 05 shows the distribution of the patients by Haemoglobin percentage during chemotherapy. In both the treatment arm incidence of anaemia is similar. Statistical test failed to reveal any significant statistical difference between the groups (p>.05).

Table 06: Distribution of the patients by WBC count during chemotherapy

WBC (counts/µl)	Subject				Total		P value
	Group A		Group B				
	No	%	No	%	No	%	
After 1st cycle	n=30		n=30		n=30		
WNL	30	100	30	100	60	100	NA
After 2nd cycle	n=30		n=30		n=30		
WNL	29	96.7	28	93.7	60	95.0	.640
3000-LLN /µl	1	3.3	2	6.6	3	5.0	
After 3rd cycle	n=30		n=30		n=30		
WNL	29	96.7	29	96.7	58	96.7	1.00
3000-LLN /µl	1	3.3	1	3.3	2	3.3	
After 4th cycle	n=30		n=29		n=59		
WNL	28	93.3	27	93.1	28	93.3	.047
3000-LLN /µl	2	6.7	2	6.9	2	6.7	
After 5th cycle	n=30		n=29		n=59		
WNL	26	93.3	27	90.0	55	86.4	.025
3000-LLN /µl	4	13.3	1	3.4	5	8.5	
2000-3000LLN /µl	2	6.7	1	3.4	3	5.1	

P value generated through chi square test *Fissure exact test was considered

Table 06 shows the distribution of the patients by WBC count during chemotherapy. In both the treatment arm the count was found to be similar throughout the treatment. Statistical test failed to reveal any significant statistical difference between the groups (p>.05) after 1st, 2nd and 3rd cycle. Significant difference was found at last two chemotherapy. Arm A suffered significantly more neutropaenia in last two cycle than arm B (p<.01).

Table 07: Distribution of the patients by Platelet during chemotherapy

WBC (counts/µl)	Subject				Total		P value
	Group A		Group B				
	No	%	No	%	No	%	
After 1st cycle	n=30		n=30		n=30		
WNL	30	100	30	100	60	100	NA
After 2nd cycle	n=30		n=30		n=30		
WNL	30	100	30	100	60	100	NA
After 3rd cycle	n=30		n=30		n=30		
WNL	30	100	30	100	60	100	NA
After 4th cycle	n=30		n=29		n=59		
WNL	29	96.7	29	100	58	98.1	NA
75000-LLN /µl	1	3.3	0	0	1	1.7	
After 5th cycle	n=30		n=29		n=59		
WNL	26	93.3	28	94.6	54	91.5	.002
75000-LLN /µl	4	13.3	1	3.4	5	8.5	

P value generated through chi square test *Fissure exact test was considered

Table 07 shows the distribution of the patients by platelet count during chemotherapy. In both the treatment arm the count was found to be indifferent in the 1st to 4th cycle of the treatment. Statistical test failed to reveal any significant statistical difference between the groups (p>.05). After the 5th cycle arm-A showed grater toxicity on platelet.

Table 08: Distribution of the patients by Symptomatic response during follow-up

3rd follow-up	Subject				Total		P value
	Group A		Group B				
	No	%	No	%	No	%	
Cough	n=28		n=29		n=57		
Completely relived	16	57.1	22	75.9	38	66.7	
Partially relived	8	28.6	7	24.1	15	26.3	0.026
Stable disease	4	14.3	0	0.0	4	7.0	
Progressive disease							
Haemoptysis	n=20		n=17		n=57		
Completely relived	12	60	13	76.5	25	67.6	0.003
Stable disease	8	40	4	23.5	12	32.4	
Progressive disease							
Chest pain	n=28		n=29		n=57		
Completely relived	13	44.8	16	55.2	29	50.0	
Partially relived	10	34.5	13	44.8	23	39.7	0.022
Stable disease	6	20.7	0	0.0	6	10.3	
Progressive disease							
Breathlessness	n=28		n=29		n=57		
Completely relived	13	44.8	16	55.2	29	50.0	
Partially relived	10	34.5	13	44.8	23	39.7	0.016
Stable disease	6	20.7	0	0.0	6	10.3	

P value generated through chi square test *Fissure exact test was considered

Table 08 shows the distribution of the patients by Symptomatic response of chemotherapy assessed at 3rd follow-up. The differences in alleviation of cough (p<.05). Chest pain (p<.05), Haemoptysis (p<.05) and Breathlessness (p<.05) was found to be significantly different, at the 3rd follow-up, Arm B showed significantly better response in alleviating the symptoms.

Table 09: Distribution of the patients by chest X-ray during chemotherapy

	Group A (n=30)		Group B (n=30)		Total (n=60)		P value
	No	%	No	%	No	%	
After 2nd cycle of CT							
Chest X-ray	n=30		n=30		n=60		
Completely relived	0	0.0	5	16.7	5	8.3	NA
Stable disease	30	100	25	83.3	55	91.7	
After 4th cycle of CT							
Chest X-ray	n=30		n=29		n=59		
Completely relived	3	10.0	16	55.2	19	50	.027
Partially relived	10	33.3	13	44.8	23	39.7	

Stable disease	17	56.7	0	0.0	17	10.3

P value generated through chi square test *Fissure exact test was considered

Table 09 shows the distribution of the patients by chest X-ray during chemotherapy assessed at 2nd and 4th cycle of chemotherapy. At 4th cycle of chemotherapy the difference in Response was evident in chest X-ray (p<.05), however after 2nd cycle of chemotherapy due to suboptimal data consideration statistical evidence could not be obtained.

V. Discussion

Treatment decisions in malignancy require an appraisal at the patient' s tumor along with some of the patient factor like age, general condition, Co-morbidity, Habits & life style, Occupation etc. In the current study effort were made to keep the factors homogeneous across two comparing arms. In arm A 20% were aged below 50 years, 50% aged between 50-60 years and 30% were aged above 60 years. In arm B 23.3% was aged below 50 years, 43.3% aged between 50-60 years and 33.3% were aged above 60 years. The age distribution was statistically insignificant (P>.05). The two comparing groups were also statistically indifferent in terms of income and place and place of residence (P>.05).

Small-cell lung cancer (SCLC) is related to cigarette smoking hence history and dose was also assessed s smoker, in both the group proportion of smoker was indifferent and among the smoker in both the group average consumption was also found to be insignificant (P>.05).

Combination chemotherapy with cisplatinum plus etoposide is the present standard for treating patients with SCLC. However, this treatment can be too toxic for many patients with SCLC, especially those who have a compromised performance status or who are older. For example, despite a response rate of 59% and a median survival of 9 months, Larive et al observed a significant toxicity profile, as high incidences of grade 3 and 4 neutropenia (59%), febrile neutropenia (15%), and toxic death (9%) were seen when patients older than 70 years were treated with carboplatin plus etoposide. Moreover, Quoix et al[12] used a similar dosing regimen and also found this combination to produce a substantial RR (58%), but grade 3 and 4 neutropenia (57%), febrile neutropenia (16%), and toxic death (3%) were again evident.

Carboplatin has demonstrated significant single-agent activity in SCLC and has been the cornerstone for most combination regiments[13]. Paclitaxel, if given before a platinum agent such as cisplatin or carboplatin, has been shown to intensify the cell-killing effects of DNA damage[14], and a protective or stimulatory effect on platelets has also been observed with weekly paclitaxel administration[15]. Chemotherapy treatment with paclitaxel and carboplatin is usually effective for four to six cycles, dosing ranges of 135 mg/m^2 to 200 mg/m^2 for paclitaxel and AUC of 5 to 7 for carboplatin are typically administered, and, in most cases, treatment is given once every 3 weeks[14]. Two recently published SCLC studies in which this typical regimen was followed and paclitaxel, carboplatin, and an additional agent were administered (one used ifosfamide, the other etoposide) showed wubstantial RRs of 71% and 74%, respectively[16]. However, both studies had notable incidences of grade 4 neutropenia and documented toxic deaths. Weekly paclitaxel has been shown to be more tolerable than every-3-weeks paclitaxel31, and minimizing toxicity is particularly important in the group of patients chosen for this trial. Because SCLC is primarily a disease of older individuals, and this population typically cannot be treated with the same doses and schedules as younger, more fit patients, alternative combinations and dosing schemes need to be evaluated.

Toxicity of the both treatment regimen was assessed based on standard assessment protocol. On average nausea and vomiting were prevalent in both the arm and generally seen more in arm A, the difference is found to be significant throughout the course of treatment (P<.05). Diarrhoea was seen more in arm B than arm A after all the chemotherapy (P>.05) except after 3rd cycle of chemotherapy (P>.05). Alopecia was found to be indifferent in both the arms in 1st and 3rd chemotherapy. The difference of alopecia was found after 2nd, 3rd, 4th and 5th chemotherapy where the patients of arm B found to more alopecia (P>.05).

In both the treatment arm incidence of anaemia was insignificant. Statistical test failed to reveal any significant statistical difference between the two arms (P>.05). In both the treatment arm, the WBC count was found to be indifferent (P>.05) after 1st, 2nd and 3rd cycle. Significant difference was appeared at the last two cycles. Arm A had highly significantly for neutropenia in last two cycle than arm B (P<.01). In both the treatment arms, the Platelet count was found to be insignificant after 1st to 4th cycle of the treatment and after the 5th cycle arm-A showed grater toxicity on platelet.

First key Response parameters of concern were the alleviation of presenting symptoms with which patient sought medical care, that might influence patient' s compliance to and confidence on the treatment regimen. In the present study At the assessment after 2nd and 4th cycle of chemotherapy, treatment arm B showed better response in terms of relieved of Cough (P<.01), Haemoptysis (P<.05), Chest pain (P<.05) and Breathlessness (P<.05).

Comparison of relieved of symptoms across the two treatment arms revealed that, Over the 5 point assessment, treatment arm B demonstrated clearly superior Response over treatment arm A except in haemoptysis where both arm seems to respond well.

Chest radiography was the key assessment indicators of lung cancer. The difference in Response of treatment between arm A and arm B was not significant after 2nd cycle but became significant after 4th cycle of chemotherapy and during the follow-up period where arm-B showed better tumour regression than arm-A ($p<.05$). Over the 5 assessment points, treatment arm B demonstrated clearly superior Response in terms of radiographic assessment of chest.

VI. Conclusion

Chemotherapy is the treatment of choice for small cell lung cancer. Combination chemotherapy (two to more drugs) is more effective than single agents chemotherapy. Overall (complete and partial) response rates of 75-90% can be achieved. This study was to observe and to compare the response to treatment and early toxicities of two chemotherapy schedules (Cisplatin-Etoposide vs paclitaxel-Carboplatin) for patients with advanced small cell lung cancer.In this study it is to be found that Paclitaxel Plus Carboplatin based chemotherapy showed better response. So, far our knowledge goes, no substantial works has been carried out in this area in Bangladesh. This study will hopefully open a new horizon in the field of oncology.

References

[1]. Perez CA, Brady LW, Halperin EC, Schmidt-Ullrich RK, editors. Principles and Practice of Radiation Oncology. 6th ed. Philadelphia, USA: Lippincort-Raven publisher;2013.

[2]. Casciato DA, Agha ME, Albert SR, et al. Manual of Clinical Oncology. 7th ed. Philadelphia, USA: Lippincort Williams and Wilkins; 2012. P.222.

[3]. Rubin P, Bakemeier RF, Basil J, et al. Clinical Oncology: A Multidisciplinary Approach for Physicians and sutdents. 9th ed. Philadelphia, USA: W.B. Saunders Company;2001. P.8.

[4]. Abeloff MD, Armitage JO, Niederhuber JE, Kastan MB, Mckenna WG, editors. Clinical Oncology. 3rd ed. Philadelphia, USA: Elsevier Inc; 2004.p.1655.

[5]. Bomford CK, Kunkler HI, Hancock BW. Walter and Miller' s Walter Textbook of Radiotherapy. 7th ed. Edinburgh, London: Churchill Livingstone. 2012. p.421-423.

[6]. Kamaluddin M, Baki MO, Hossain AFM, et al. Management of Non small cell lung Cancer (NSCLC)- A Review. Ban Can Reports 2006;31(1):21.

[7]. Hoang T, Schiller JH. Carcinoma of the lung. In: Skeel RT, editor. Handbook of Cancer Chemotherapy. 6th ed. Philadelphia, USA: Lippincott Williams and Wilkins; 20

[8]. E Ihde DC, Pass HI, Glatstein E. Small cell lung cancer. In: Devita VT Jr, Hellman S, Rosenberg SA, editors. Cancer: Principles and Practice of Oncology. 7th ed. Philadelphia: Lippincott Williams and Wilkins; 2005. pp.

[9]. Gridelli C, Manzione I, Perrone F, et al. Carboplatin plus paclitaxel in extensive small cell lung cancer: a multicentre phase 2 study. B J C 2001;84:38-41.

[10]. Larive S, Bombaron P, Riou R, et al. Carboplatin-etoposide combination in small cell lung cancer patients older than 70 years: A Phase II trial. Lung Cancer 2002;35:1-7.

[11]. Quoix E, Breton JL, Daniel C, et al. Etoposide phosphate with carboplatin in the treatment of elderly patients with small-cell lung cancer: A phase II study. Ann Oncol 2001;12:957-62.

[12]. Smith IE, Evans BD. Carboplatin (JMB) as a single agent and in combination in the treatment of small cell lung cancer. Cancer Treat Rev 1985;12:73-75.

[13]. Parker RJ, Dabholkar MD, Lee KB, et al. Taxol effect on cisplatin sensitivity and cisplatin cellular accumulation in human ovarian cancer cells. J Nati Cancer Inst Monogr 1993;15:83-88.

[14]. Kakolyris S, Mavroudis D, Tsavaris N, et al. Paclitaxel in combination with carboplatin as salvage treatment in refractory small-cell lung cancer (SCLC): A multicenter phase II study. Ann Oncol 2001;12:193-97.

[15]. Hainsworth JD, Hopkins LG, Thomas M, et al. Paclitaxel, carboplatin, and extended-schedule oral etoposide for small-cell lung cancer. Oncology 1998;12:31-35.

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