

A Prospective Study of Effect of Cisplatin and Etoposide based Chemotherapy Regimen in End Stage Lung Cancer Patients in A Rural Tertiary Care Hospital

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ABSTRACT

Introduction: Lung cancer is the most common cause of cancer-related deaths in women and men. Small-cell lung cancer constitutes 20% of lung cancers. Non-Small-cell lung carcinoma constitute 80% of all lung cancers. For advanced un-resectable and metastatic lung cancer which are unsuitable for curative treatment options, the standard first-line treatment is palliative chemotherapy. So the study was done to see the clinical improvement with Cisplatin and Etoposide regimen based chemotherapy in end stage lung cancer patients

Material and Methods: 30 patients of end stage lung cancer were taken up for the study. Their KPS scores were calculated and presenting chief complaints mainly in the form of cough, chest pain, dyspnoea and haemoptysis were assessed. The response assessment of patients was done on the above factors after giving 3 cycles of Cisplatin and Etoposide based chemotherapy.

Results: Symptomatically 11 patients (37%) showed Complete response (CR) in at least one symptom. 8 patients (26%) showed Partial Response (PR) in at least one symptom. 8 patients (26%) showed no improvement or worsening in any symptom (SD) and 3 patients (10%) showed worsening in at least one symptom (PD). Change in KPS score post chemotherapy was found to be statistically insignificant ($p=0.344$)

Conclusion: In a rural centre with resource poor patients, this regimen offers a reasonably good cost effective option for management of Lung Cancer mainly as a palliative therapy by improving the quality of life of such patients.

Keywords: Small cell lung cancer (SCLC), Non small cell lung cancer (NSCLC), Cisplatin, Etoposide, KPS score

INTRODUCTION

Treatment options for NSCLC mainly depend on the extent of disease and mainly include: surgery, radiotherapy and chemotherapy in various combinations or alone.¹ Stages I and II and some stage IIIA NSCLC can be cured and surgery is the best treatment option whenever possible.² For stage IIIB disease not amenable to curative treatment and all stage IV disease, treatment is palliative in nature and focus is mainly on increasing survival time, controlling symptoms and maintaining quality of life.³ Palliative treatment options include chemotherapy, radiotherapy and supportive care.⁴ Many studies have concluded that platinum-based chemotherapy regimens are superior to other regimens⁵, SCLC is highly sensitive to chemotherapy. Majority of the patients will initially achieve a complete or good partial response on combination chemotherapy.⁶ The preferred combination is mainly based on the administration feasibility, cost-benefit evaluation and toxicity. Cisplatin and Etoposide based chemotherapy regimen is one of the most commonly used chemotherapy regimens.⁷ Cisplatin is a platinum containing compound and is among the most potent chemotherapy drug and

it damages tumors via induction of apoptosis which is mediated by the activation of various signal transduction pathways.⁸ Etoposide is a semi synthetic derivative of the podophyllotoxins and it inhibits DNA Topoisomerase II, which in turn inhibits DNA synthesis.⁹ Current research aimed to study the clinical improvement with Cisplatin and Etoposide regimen based chemotherapy in stage 3 and stage 4 lung cancer patients.

MATERIAL AND METHODS

The study was conducted in the department of Respiratory Medicine, MMIMSR from May 2014 to July 2015 after getting Approved by the Institute Ethical committee. The sample size was calculated based on the average number of cancer patients admitted per month in ward and 30 patients diagnosed as having stage 3 and stage 4 lung cancer after necessary investigations were included in the study.

Study Criteria

Inclusion criteria

- 1) Patients with stage 3 and stage 4 Lung Cancer

Exclusion Criteria

- 1) Patients with any cardiovascular impairment.
- 2) Patients with any renal and hepatic dysfunction.
- 3) Patients with any neurological disease.
- 4) Patients not giving consent.

Variables to be used

Karnofsky performance score

The Karnofsky score runs from 100 to 0, where 100 is "perfect" health and 0 is death. The practitioners assign performance scores in between standard intervals of 10. This score is named after Dr. David A. Karnofsky in 1949. The primary purpose of it is to evaluate a patient's ability to survive chemotherapy and also to evaluate the response of patient to it.¹⁰

Preparing for Chemotherapy

Before starting chemotherapy complete blood counts of the patient were done and a close watch was kept on TLC as the drugs are immunosuppressive. The renal functions tests were also done as the drugs are nephrotoxic and hence required strict

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monitoring of renal function tests. Patients were adequately hydrated before starting chemotherapy. A total of 2 litres of intravenous fluids mainly Normal saline and DNS were given over 6 hours before starting of chemotherapy. An anti-emetic was also advised prior to start as the chemotherapeutic drugs induce a lot of nausea and vomiting.

Study Sequence

In this study the patients with a suspicion of lung cancer on chest x-ray and clinically were thoroughly evaluated to confirm the diagnosis. After confirming the diagnosis 30 patients of lung cancer in stage 3 and stage 4 were taken up for the study and there KPS scores were calculated and Tumor-related symptoms like chest pain, cough, dyspnoea and haemoptysis were recorded at the start of treatment and after 3 cycles response assessment was done symptomatically and by KPS scores. Symptoms were reassessed following 3 cycles of treatment with patients asked to grade change in symptoms using simple descriptive criteria as follows: (i) complete disappearance of symptoms (CR); (ii) good improvement of symptoms that is more than 50 percent alleviation in symptoms (PR); (iii) minor or no change of symptoms (SD); (iv) Worsening of symptoms (PD). An additional 2 cycles were considered for patients who showed a response (partial/complete). Also in patients developing toxicity to the drugs the chemotherapy was immediately discontinued. There is little benefit in continuing the same regimen in case of no response after 3 cycles. In such cases either best supportive care or switching over to other regimens was considered.

Following chemotherapy regimen was used in the lung cancer patients.

In Non Small Cell Lung Cancer patients- Cisplatin 75mg/m² day 1 and Etoposide 80mg/m² days 1-3 every 21 days for a maximum of 4-6 cycles

In Small Cell Lung Cancer Patients- Cisplatin 80mg/m² day 1 and Etoposide 80mg/m² days 1-3 every 21 days for a maximum of 4-6 cycles

STATISTICAL ANALYSIS

The data collected was entered into Microsoft Excel worksheet. For Quantitative data, Mean and Standard Deviation were calculated. The Qualitative data was expressed in proportions and percentages. Chi Square test and Mc Nemar test was applied for analysis of qualitative data. Minimum 95% confidence interval and p value < 0.05 was considered statistically significant The entire data was analysed using SPSS (Statistical Package for Social Sciences) version 20 (IBM, Chicago, USA).

The symptomatic response post chemotherapy of patients studied has been described in figure 1. Cough was present in 24 patients and the response following chemotherapy was calculated. 8 out of 24 patients showed complete response, whereas 3 patients has partial response. Stable disease is defined as less than 50% improvement in symptom and in our study there were 8 such patients. Progressive disease is characterized by no relief in symptoms, rather deterioration and in our study there were a total of 5 patients with such condition.

In case of chest pain there were a total of 18 patients presenting with it, out of which 5 patients showed complete response, 3 patients showed partial response, stable disease was found in 4 patients and despite treatment 6 patients showed progressive disease.

A total of 20 patients had dyspnoea as the initial presenting complaint, out of which only one patient showed complete response, 4 patients showed partial response, 5 patients showed stable disease and 10 had progressive disease. This poor response of dyspnea to our chemotherapy may be attributed to the underlying copd present in majority of cases.

Hemoptysis is the least common of all the symptoms and the frequency of improvement is maximum of all. 5 patients showed complete response and 5 patients showed partial response, only 2 patients showed no improvement and were considered other options such as bronchial artery embolization.

Table 1 shows response to treatment of each individual histological subtype. As discussed earlier there were a total of 7 patients of adenocarcinoma and out of which 3 patients showed complete response in at least one of the symptom rest. 2 patients had a partial response which is also satisfactory, one patient showed stable disease without showing much response and one patient showed deterioration in symptoms

Squamous cell carcinoma is the most common histological subtype seen and there were a total of 12 patients, response to treatment is almost similar to that seen with that of adenocarcinoma. 5 patients showed complete response in at least one of the symptom and 3 patients showed partial response. No satisfactorily response was seen in 4 patients of which 3 were having stable disease and one patient condition got deteriorated. Adenosquamous histological subtype is the least common of all the subtypes. In our study there were a total of 2 patients and one patient showed complete improvement in at least one symptom and the other one showed partial response.

Small cell carcinoma is the second most commonly seen subtype and there were a total of 9 patients included in the study but the response to treatment is not so satisfactory. Only 2 patients out of 9 showed complete response in at least one of the symptoms and one patient showed partial response, in case of rest 6 patients the results are not satisfactorily of which 5 patients had stable disease and in the other one there was deterioration.

Histological type	Cr	Pr	Sd	Pd	Total
Adenocarcinoma	3	2	1	1	7
Squamous cell carcinoma	5	3	3	1	12
Adeno-squamous carcinoma	1	1	0	0	2
Small cell carcinoma	2	1	5	1	9

Table-1: Response to treatment of each individual histological subtype

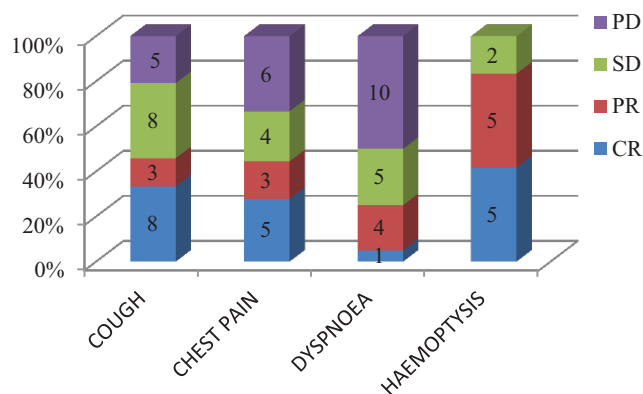


Figure-1: Symptomatic response post chemotherapy of patients studied

In this table 2 the response of patients to chemotherapy in terms of KPS score is shown. Patients were divided into 4 groups as per their KPS score. Those with KPS score ≤ 60 were considered in one single group and their improvement post chemotherapy was evaluated. Total there were 8 patients and none of them showed any improvement in their KPS scoring post chemotherapy. In the Patients with KPS score 70 there was an increase of KPS score seen in 3 patients and 4 patients maintained a same score and 3 patients showed a decline in KPS scores. In Patients with KPS score 80 there was an increase seen in 4 patients and in same number of patients the KPS score remained unchanged. In case of KPS score ≥ 90 all patients had there KPS score unchanged post chemotherapy as already they were in a very good clinical condition and there was no scope for further increase. Results also show that patients with KPS score ≥ 70 show a better response to chemotherapy and there is a greater improvement in quality of life post chemotherapy in such patients. So overall KPS score increased in 7 patients, remained unchanged in 20 patients and decreased in 3 patients. In a total of 30 patients were taken up for the study, at least 11 patients showed Complete Response to at least one symptom (CR). Partial response to at least one symptom was seen in 8 patients (PR) and same number of patients showed stable disease (SD) and at least 3 patients showed deterioration in symptoms (PD) (figure-2).

DISCUSSION

At diagnosis, most of the lung cancer patients have advanced disease and are beyond the possibility of cure. Even though the main treatment intention for these patients is palliative, the beneficial effect of these cytotoxic drugs is documented well. The benefit on survival seems to be closely related to individual patient characteristics, often known as prognostic factors for survival. Some of the common prognostic factors for survival are universal for lung cancer and should be used in the clinical decision-making process. The most important prognostic factors are stage of the disease, Performance Status (Karnofsky scale), and weight loss. However, when palliative treatment is the intention, symptomatic improvement and a better quality-of-life should be the main goals.¹⁰ Oncologic palliation is defined as treatment with surgery, radiotherapy, hormone therapy, chemotherapy or other tumour modulating treatment given as a single modality or combined in patients who cannot be cured. These treatments help in relieving symptoms by reducing tumour burden and may sometimes also prolong life. In addition symptomatic treatment for pain with opioids, 5HT-3 antagonists for emesis is important in lung cancer patients.¹¹ The first-line systemic chemotherapy in the treatment of advanced small cell¹² and non small cell lung cancer¹³ is generally platinum based doublet chemotherapy. The drugs most commonly paired with the platinum agents like cisplatin are gemcitabine, vinorelbine, etoposide, docetaxel, and paclitaxel. The recommendation for treatment duration is that the treatment should not continue beyond 4 to 6 cycles as there is no recorded evidence of improved survival with prolonged treatment and also toxicities increase the longer these drugs are administered. Fumihiro oshita et al in 1994 studied the feasibility of cisplatin based chemotherapy in elderly patients having advanced non small cell lung cancer or small cell lung

Response	KPS score ≤ 60	KPS score 70	KPS score 80	KPS score ≥ 90	Total
Increased	0	3	4	0	7
Unchanged	8	4	4	4	20
Decreased	0	3	0	0	3
Total	8	10	8	4	30

Table-2: response of patients to chemotherapy in terms of kps score

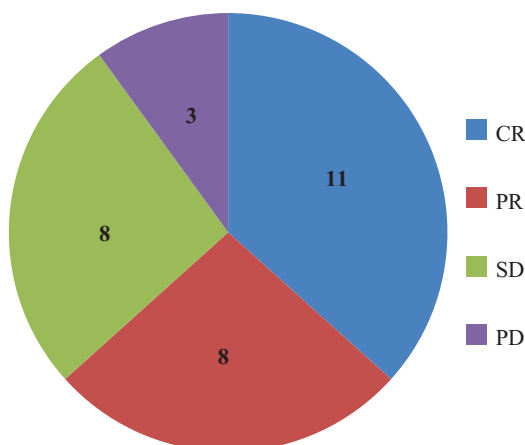


Figure-2: Overall symptomatic response in patients studied

cancer. The results showed that chemotherapy should be given very carefully to elderly patients even if they have normal organ functions and it definitely provides symptomatic relief in most of the patients.¹⁴ In our study also most of the patients were elderly and showed improvement clinically as shown by the increase in their KPS scores post chemotherapy. Kirmani Natukula et al in 2013 conducted a study to check for favourable response of patients to various chemotherapeutic combinations like paclitaxel, gemcitabine, etoposide with platinum based drugs like cisplatin with respect to patient survival in stage 3b and stage 4 non small cell lung cancer and the results showed that following chemotherapy with platinum based agents there was a improvement in overall survival rates and there was a very marginal difference in survival rates among the various chemo regimens evaluated in the study.¹⁵ In our study while giving chemotherapy cisplatin was combined with etoposide as it was easily available and also very economical to the patients. Most of the patients who were a part of our study belonged to poor socioeconomic status and since ours is a rural tertiary hospital availability and cost effectiveness of the drugs was main priority. In our study also most of the patients showed a improvement in survival and quality of life.

CONCLUSION

In our study we found that in a Rural Tertiary Care Centre like ours with resource poor patients who cannot afford even basic investigations and treatment, this regimen offers a reasonably good cost effective option for management of Lung Cancer and improving the quality of life of such patients.

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