ORIGINAL RESEARCH PAPER
Volume - 14 | Issue - 05 | May - 2025 | PRINT ISSN No. 2277 - 8179 | DOI : 10.36106/ijsr
INTERNATIONAL JOURNAL OF SCIENTIFIC RESEARCH

A PROSPECTIVE INTERVENTIONAL STUDY COMPARING DEFINITIVE CHEMORADIATION WITH AND WITHOUT INDUCTION CHEMOTHERAPY IN LOCALLY ADVANCED INOPERABLE NON SMALL CELL LUNG CARCINOMA

Oncology/Radiotherapy

Dr. Rameshwaram Sharma Senior Professor, Department Of Radiation Oncology SMS Medical College Jaipur

Dr. Priyanka Gupta Senior Resident, Department Of Radiation Oncology SMS Medical College Jaipur

Dr. Vishakha Sharma* Senior Resident Department Of Radiation Oncology SMS Medical College Jaipur *Corresponding Author

Dr. Shivani Gupta Professor, Department Of Radiation Oncology SMS Medical College Jaipur

ABSTRACT

Introduction: The present prospective study has been proposed to compare Induction chemotherapy (Paclitaxel and Carboplatin) two cycle followed by concurrent Chemoradiation through IMRT to Chemoradiation with paclitaxel and carboplatin. Toxicity profile and locoregional control was studied. **Aim & Objectives-** To compare acute toxicity and local control in both arms. **Methodology:** 82 NSCLC patients were randomized into Study and Control arm. In Study arm, 2 cycles IC given before CTRT and in Control arm CTRT was given alone. Acute toxicities and Locoregional response was compared. **Results:** Among 82 patients, male (80.1%), Smokers (85.5%) were predominant. Overall response was higher in Control Arm at 3 months but statistically non-significant. Acute toxicities in both the arms were comparable and similar. **Statistical Analysis:** Chi Square test was applied for statistical analysis whereas p-value <0.05 was taken as statistically significant. **Summary:** Our study indicated that IC with CTRT has a high overall response rate as compared to control arm. Acute haematological, lung, skin, pharynx and esophagus toxicity were similar in both arms. Number of patients with progressive disease was also less in study arm compared to control arm. In short, the study arm is feasible and it showed more efficacy than the standard arm.

KEYWORDS

CTRT, Induction Chemotherapy, Non-Small Cell lung Carcinoma

INTRODUCTION

According to GLOBOCON 2020- In India, lung cancer constitutes 5.5 % of new cases and 7.8 % of cancer related deaths in both gender(4). In India Carcinoma lung is the second most common cancer among males and sixth most common among females.(1)

The number of cigarettes smoked per day and duration correlates with risk for carcinoma. Uranium miners and nuclear plant workers are also have an increased risk because of exposure to radioactive particulate mass (2). Cumulated exposure of ambient air pollution, like emissions rich in various polycyclic aromatic hydrocarbon compounds could be one of the risk factor of lung cancer (3).

Treatment of NSCLC consists of Surgery, Radiotherapy, and systemic therapy.For locally advanced disease, radiotherapy combined with chemotherapy is used.

Induction therapy has potential benefits, like earlier treatment of micro metastatic disease, an increased likelihood of patients receiving the planned regimen, & down staging of disease before local therapy etc. Concurrent chemotherapy appears to increase locoregional control.

The present prospective study is to compare induction chemotherapy (Paclitaxel 175mg/m2 and Carboplatin by AUC-6 I.V.) two cycles at 21 days interval followed by concurrent chemoradiotherapy with paclitaxel 50mg/m2 and carboplatin by AUC-2 i.v on weekly basis to chemoradiotherapy with paclitaxel and carboplatin with respect to treatment outcomes like toxicity profile and locoregional control. The Primary Objective was to evaluate the proportion of Acute toxicities like gastrointestinal, haematological and lung toxicities and Secondary Objective was to evaluate compliance & locoregional response by use of RECIST 1.1 Criteria

Methodology

Patient Selection And Randomisation: This study is done in Department Of Radiation Oncology, SMS Medical College Jaipur. 41 cases in each group was calculated at 95% confidence and 80% power to predict the expected difference of 29% in proportion of no upper GI toxicity in study arm and control arm. Randomization done based on chit in box method with replacement.

Inclusion Criteria

1. Histopathologically confirmed NSCLC
2. Aged= 18 – 70 years
3. ECOG PS= 0 to 2
4. Inoperable STAGE III disease.
5. Patients giving consent.

Exclusion Criteria

1. Systemic co-morbities /pregnant /lactating.
2. Double malignancy.
3. Previously treated with any modalities like surgery, radiotherapy, chemotherapy for lung cancer.
4. Operable lesions.

Study Design: 41 patients in Arm A (Study Arm) received 2 cycles of induction chemotherapy given every 21 days before CTRT. 41 patients in Arm B (Control Arm) received CTRT alone.

Radiotherapy Technique- For both arms patients received 60Gy in 30 fractions radiation dose at 2Gy/fraction at five fractions per week from Monday to Friday per week for 6 weeks once in a day with weekly chemotherapy paclitaxel and carboplatin.

All patients were treated on ELEKTA Versa HD model multi energy Linea Accelerator by IMRT technique. Target Volumes were contoured according to the RTOG lung cancer atlas guidelines.

The treatment was planned with a goal of 100% volume of PTV to be covered by 95% isodose line. Data collected included the volume of PTV receiving atleast 95% and 90% of prescribed dose(V95 and V90) and also dose delivered to 90% of the volume of PTV (D90%) from the DVH.

Toxicity Assessment-

Acute Gastro-intestinal Toxicity- radiation induced esophagitis assessed by symptomatic evaluation and graded by RTOG Grading.
Acute lung toxicity assessed and graded by RTOG Grading.
Acute haematological toxicity and skin toxicity was also assessed.

Local Control Assessment-

Response to treatment and local control was assessed by CECT thorax after 2 cycles of Induction Chemotherapy and 3 & 6 months of completion of Chemoradiation, with the help of RECIST 1.1 Criteria.

Observation During Radiotherapy

All patients were examined once in 3 week during Induction Chemotherapy in study group and weekly during chemoradiation treatment in both arms.

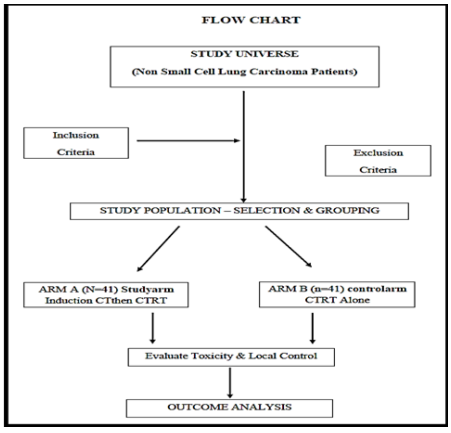

Fig.1 Flow chart

Statistical Analysis

Quantitative data was expressed in means with standard deviation and qualitative data was expressed in percentage proportions. Significance of difference in means of 2 groups was inferred with Unpaired T test. Significance of difference in proportions in two groups was inferred with Chi square test.

P value < 0.05 is taken as statistically significant.

The data collected were analysed by using Chi square test for correlation

RESULTS:

Demographic Analysis (Table 1): 82 patients were randomized into two arms.84.1% were male, with a mean age of diagnosis were (59.29 ± 8.30) years in Arm A and (61.66 ± 8.33) years in Arm B.

Toxicity Assessment During Induction Chemotherapy: In study arm during NACT (n=41), nausea & vomiting (5 %), neutropenia (14%) and anaemia (2.4%) appeared as grade 2 acute toxicity. 41 patients in each arm were started on CTRT. All patients successfully completed CTRT.

Toxicity Assessment During Chemoradiation (Table 2): During CTRT, numerically more grade 2 non haematological toxicities were seen in arm A as compared to arm B (statistically not significant except dysphagia). Grade 2 & 3 dysphagia was seen in 12 patients & 0 patients respectively in Study group, whereas in Control group 2 patients had grade 2 dysphagia and 1 patient had grade 3 dysphagia, which was statistically significant (P-value 0.046).

Response Assessment: The radiological response rates after 3 months of treatment follow up revealed that complete response was achieved in 29.26% and 24.29% patients in Study and Control group respectively. The partial response rates were 39.02% and 34.14% in Study and Control group respectively. Both were not found to be statistically significant (p>0.05). Progressive disease was seen in 5 and 7 patients in Study and control group respectively, whereas stable disease was seen in 8 and 10 patients in Study and Control group respectively.

At 6 months follow up period, complete response was achieved in 39.02% patients in Study and 27.8% patients in Control. The partial response rates were 31.7% in Study group and 36.58% in Control group. Loco-regional control was better in study arm as compared to control arm.

Table 1 Demographic Analysis

Table 1 Demographic analysis			
Category	**Total - 82**		**p-value**
	Arm A 41	**Arm B** 41	
Age	59.29 ± 8.30	61.66 ± 8.33	
Male	32	37	
Female	9	4	0.22
Smoker	34	37	
Non-smoker	7	4	0.82
Adenocarcinoma	20	18	
Squamous cell carcinoma	21	23	0.82
PS0	4	6	
PS1	20	17	
PS2	17	18	0.71
T1	0	0	
T2	5	6	
T3	17	20	
T4	19	15	0.80
N0	2	1	
N1	9	11	
N2	19	18	
N3	11	11	1.00

P<0.05 - Significant

Table 2 Toxicity

Table-2 Toxicity			
	Arm A	**Arm B**	**p-value**
RTOG Lung toxicity			
Grade 1	6	6	
Grade 2	7	5	
Grade 3	4	4	0.90
RTOG GIT toxicity			
Grade 1	19	17	
Grade 2	12	2	
Grade 3	0	1	**0.04**
RTOG Skin toxicity			
Grade 1	25	22	
Grade 2	6	6	
Grade 3	1	2	0.79
Hematological Toxicity			
Anaemia			
Grade 1	6	3	
Grade 2	3	5	
Grade 3	2	3	0.42
Neutropenia			
Grade 1	8	4	
Grade 2	8	11	
Grade 3	2	5	0.22
Thrombocytopenia			
Grade 1	11	5	
Grade 2	7	9	
Grade 3	2	5	0.15

P<0.05 – Significant

DISCUSSION:

This study has shown better patient's compliance, complete response and comparable toxicity profile with Induction chemotherapy followed by chemoradiation but not statistically significant. Initial Cancer and Leukemia Group B 39801 trial, showed no survival benefit by addition of chemotherapy. Survival differences were not statistically significant (P = .3), with a median survival on control arm of 12 months versus 14 months on study arm and a 2-year survival of 29% and 31% (5).

In our Study also, there are comparable severity of toxicities in both the arms. Retrospective comparison done by Eugene H Huang et al. (6) inferred that IC was the most significant factor affecting overall survival.Locoregional control was not significantly different between the two group as in our study. In a similar study done by Hui Luo et al. showed that there was significant benefit of 5-year OS with induction chemotherapy plus CCRT compared to CTRT alone. Treatment-related toxicity was similar between the 2 group (36)

The 70% overall response achieved in our study is comparable to those achieved by Pritam K Sardar et al.(7).They showed there were no significant differences in results between two arms. Response at 6 months was similar for all patients in our study(70.7% vs 66.7%)in study arm and(68.2% vs 60.9%) in control arm as compared to their study.

CONCLUSION:

Our study has shown better patient's compliance, complete response and comparable toxicity profile with Induction chemotherapy arm. CRR was better achieved in study arm compared to control arm that indicates important role of induction chemotherapy in advanced stage NSCLC. Acute toxicities were more frequently present in study group but comparable and manageable.. The combination of paclitaxel and carboplatin is feasible in advanced NSCLC patients. In conclusion, the results of our study indicate that induction chemotherapy with paclitaxel and carboplatin added to standard chemoradiation is feasible, better & encouraging in terms of local control with manageable toxicities.

REFERENCES-

1. Jacques Ferlay, Murielle Colombet, Isabelle Soerjomataram, Donald M.Parkin, Marion Piñeros, ArianaZnaor, Freddie Bray, Cancer statistics for the year 2020: An overview, International Journal of Cancer,10.1002/ijc.33588, 0, 0,(2021).
2. Boffetta P. Epidemiology of environmental and occupational cancer. Oncogene 2004;23(38):6392–
3. Kunzli N, Tager IB. Air pollution: from lung to heart. Swiss Med Wkly 2005;135(47 48):697–702. [PubMed: 16511705] 6403. [PubMed: 15322513]
4. Hwang SJ, Cheng LS, Lozano G, Amos CI, Gu X, Strong LC. Lung cancer risk in germline p53 mutation carriers: association between an inherited cancer predisposition, cigarette smoking, and cancer risk. Hum Genet 2003 Aug;113(3):238–243. [PubMed: 12802680]Epub 2003 Jun 11
5. Vokes EE, Herndon JE II, Crawford J, et al: Randomized phase II study of cisplatin with gemcitabine or paclitaxel or vinorelbine as induction chemotherapy followed by concomitant chemoradiotherapy for stage IIIB non– small-cell lung cancer: Cancer and Leukemia Group B study 9431. J Clin Oncol 20:4191-4198, 2002
6. Huang EH, Liao Z, Cox JD, Guerrero TM, Chang JY, Jeter M, Borghero Y, Wei X, Fossella F, Herbst RS, Blumenschein GR Jr, Moran C, Allen PK, Komaki R. Comparison of outcomes for patients with unresectable, locally advanced non-small-cell lung cancer treated with induction chemotherapy followed by concurrent chemoradiation vs. concurrent chemoradiation alone. Int J RadiatOncolBiol Phys. 2007 Jul 1;68(3):779-85.
7. Sardar PK, Shenoi LR. A prospective study comparing induction chemotherapy followed by chemoradiation versus chemoradiation alone in stage III non-small cell lung cancer. Int J Med Res Rev. 2020;8(1):76-85.