e-ISSN: 0975-5160, p-ISSN: 2820-2651

Available online on www.ijtpr.com

International Journal of Toxicological and Pharmacological Research 2023; 13(5); 165-172

Original Research Article

Prescribing Pattern and Safety Profile of Anticancer Drugs in Carcinoma Lung in Tertiary Care Teaching Hospital, Haldwani

Prashant Kumar[1], Bhavana Srivastava[2], Reena Bhardwaj[3], Nirdosh Kumar Pant[4], Neeraj Rajdan[5], Jalaj Gaur[6]

[1]Junior Resident 3, Department of Pharmacology, Government Medical College, Haldwani, Uttarakhand, India

[2]Professor and Head, Department of Pharmacology, Government Medical College, Haldwani, Uttarakhand, India

[3]Professor, Department of Pharmacology, Government Medical College, Haldwani, Uttarakhand, India

[4]Professor, Department of Radiation Oncology, Government Medical College, Haldwani, Uttarakhand, India

[5]Assistant Professor, Department of Pharmacology, Government Medical College, Haldwani, Uttarakhand, India

[6]Assistant Professor, Department of Radiation Oncology, Government Medical College, Haldwani, Uttarakhand, India

Received: 15-03-2023 / Revised: 30-03-2023 / Accepted: 30-04-2023

Corresponding author: Dr Jalaj Gaur

Conflict of interest: Nil

Abstract

Introduction: Cancer is most common cause of morbidity and mortality in world, Lung carcinoma second most commonly diagnosed cancer in men. It is multifactorial, most common cause is smoking.

Objective: This study was conducted to evaluate prescription pattern and adverse drug reactions (ADR) of Anti cancer drugs in Carcinoma Lung patients.

Material and Methods: An observational, prospective, open label hospital based study of 114 patients, from January 2021 to September 2022. All cases of diagnosed lung carcinoma patients coming to Radiation Oncology OPD of Swami Ram Cancer Institute, Haldwani, Uttarakhand. All the reported ADRs were analyzed using WHO-UMC and Naranjo causality assessment scale and Schumock and Thornton preventability scale.

Results: In our present study of 114, male: female was 3:1, majority in age group of. 50-70. Most patients were Smokers (73.7%). Commonly prescribed drug were Platinum coordination complexes, Taxanes, Topoisomerase 2 inhibitor, Folate antagonist, Pyrimidine antagonist, Nitrogen mustard, Antibiotics. Most common ADR were nausea & vomiting, generalized weakness, anaemia and thrombocytopenia. It was observed that 9.6% had Certain, 79.8% had Possible and 10.5% of the patients had Probable Causality Assessments according to WHO-UMC scale.

Conclusion: Lung carcinoma is more common in males then females. Smoking being a major cause. Squamous cell carcinoma was most common followed by small cell carcinoma.

Keywords: Lung Carcinoma, Smoking, Adverse Drug Reaction (ADR).

Introduction

Lung carcinoma is second most commonly diagnosed cancers and the leading cause of cancer-related deaths worldwide with an estimated 2 million new cases and 1·79 million deaths per year.[1] It is multifactorial, most common cause of lung carcinoma is smoking [2,3], other causes are environmental like exposure to second hand smoke, asbestos[3], radon gas, arsenic, hormonal therapy in women with estrogen[3], genetic causes in non-smokers. Among non-smokers it is more common in females as compared to males.[3] [4] Repeated exposure to cigarette smoke leads to dysplasia of lung epithelium leading to genetic mutations and affecting protein synthesis, which in turn disrupts the cell cycle and promotes carcinogenesis.

Various studies are conducted in various parts of world and in India utilizing only a small group of population in their area and their studies cannot be generalized to other places due to availability of specific drug activities and treatment modalities. There is no data available in kumaun region regarding the prescribing pattern and ADR of anticancer drugs especially in carcinoma lung. Therefore this present study will be undertaken to investigate the prescribing pattern and adverse reaction of anticancer drugs in Swami Ram Cancer Institute and Department of Pharmacology, Government Medical College, Haldwani, Uttarakhand.

Materials and Methods

This study was an Observational, prospective, open labelled hospital based study. The study was carried out from January 2021 to September 2022. After taking the approval from Institutional Ethical Committee of Government Medical College and Swami Ram Cancer Institute, Haldwani. Patients were recruited in Swami Ram Cancer Institute and Department of Pharmacology, Government Medical College, Haldwani, Uttarakhand. Written informed consent was obtained from the patients. Data was collected from drug prescription form of the carcinoma lung patient.

Inclusion criteria

1. All patients with old and recent diagnosis of lung cancer coming to OPD in Swami Ram Cancer Institute and Department of Pharmacology, Government Medical College, Haldwani, Uttarakhand, consenting to be a part of the study were enrolled in the study.
2. Age 18 years and above, prescribed with at least one anticancer drug.

Exclusion criteria

1. Brain metastasis.
2. Active infection.
3. Peripheral neuropathy.
4. Inadequate liver function prior to cancer chemotherapy.
5. Pregnant and lactating women.
6. History of any other cancer.
7. Congestive cardiac failure and recent myocardial infarction.

All patients were followed up and ADR monitoring was done in follow ups i.e. on day 0, 21and day 42. All the reported ADRs were analyzed using WHO-UMC and Naranjo causality assessment scale and Schumock and Thornton preventability scale.

Outcome and measure

Overall response rate by the patient in improvement of symptoms

Collected data was coded appropriately, entered in Microsoft Excel (MS Excel) spreadsheet and later checked for any possible errors in SPSS (Statistical Package For Social Studies) for Windows version 21.0. Analysis was also carried out using same software. Categorical data was presented as percentage (%).

Observation and results

In our study out of 114 subjects, male: female 3:1 . Most cases were common in age group 50-70 constituting 74.5% cases in males and 68.4% cases in female. Majority of patients 55.9% were from Haldwani and adjoining area.

Table 1: Distribution of patients according to age and sex

Age (Years)	Number (n=114)	Percentage (%)	Sex			
			Female		Male	
			Number (n=114)	Percentage (%)	Number (n=114)	Percentage (%)
40 – 50	8	7.0%	6	21.4%	10	11.6%
50 – 60	44	38.6%	12	42.9%	36	41.9%
60 – 70	34	29.8%	6	21.4%	28	32.6%
70 – 80	26	22.8%	4	14.3%	10	11.6%
80 – 90	2	1.8%	0	0.0%	2	2.3%
Total	114	100%	28	100.0%	86	100.0%
Mean±SD	61.14 ± 8.902		58.29 ± 10.52		62.07 ± 8.16	
Min–Max	42 – 85		42 – 75		44 – 85	
Median (Q1 - Q3)	60(55.75 - 69.25)		56 (51 - 65)		60 (58 -70)	

Out of 114 study participants majority of patients were male(75%). Most patients in our study were in age group 50-70, males (74.5%), females (68.4%).

Table 2: Distribution of patients according to smoking history

Distribution According to Smoking History	Number (n=114)	Percentage %
Smoker	84	73.7%
Non – Smoker	30	26.3%
Total	114	100%

Smoking being most common cause of lung carcinoma, in our study majority 73.7% of patients were smokers.

Table 3: Distribution according to type of cancer

Distribution According to Diagnosis	Percentage %
Adenocarcinoma	24.6%
Small cell carcinoma	35.0%
Adenoid cystic carcinoma	2.0%
Squamous cell carcinoma	38.6%
Total	100%

Among lung carcinoma squamous cell (non small cell) was most common followed by small cell carcinoma least common was adenoid cystic carcinoma.

Prescribing pattern of anticancer drugs according to type of cancer

Anti-cancer drugs are prescribed according to pathological type of cancer. Different cancer have different drug regimen as first and second line drugs for management as polytherapy or combination therapy. Most drugs are prescribed intravenously, few drugs are prescribed orally. Commonly prescribed drug in our study belong to platinum coordination complexes (cisplatin, carboplatin), taxanes (paclitaxel, docetaxel), topoisomerase 2 inhibitor (etoposide both tablet and

i.v), folate antagonist (methotrexate, pemetrexed), pyrimidine antagonist (gemcitabine), nitrogen mustard (cyclophosphamide), antibiotics (actinomycin D).[9] Cancer treatment requires adjuvant therapy like radiotherapy and surgery along with chemotherapy for complete eradication.

Commonly used combination therapy for lung carcinoma

Table 4: Distribution of drug combination used as first line drug therapy according to type of cancer

Type of cancer	Drug therapy	Percentage %
Small cell	Cisplatin and etoposide	32.5%
Squamous cell	Paclitaxel and carboplatin	30.7%
	Paclitaxel+Cisplatin	9.6%
Adeno carcinoma	Carboplatin +paclitaxel	13.2%
	Gemcitabine+Carboplatin	11.4%
	Pemetrexed +Carboplatin	7.0%
	Cisplatin + paclitaxel	6.1%
	Cisplatin +Pemetrexed	2.6%
Adenoid cystic	Carboplatin+Gemcitabine	0.9%
	Paclitaxel+Carboplatin	0.9%

Among first line paclitaxel was most common used in 78.07% followed by carboplatin used in 72.8%, cisplatin in 50.87%, etoposide 32.45%, gemcitabine 12.28%, Pemetrexed 9.64% patients.

Table 5: Distribution of drugs commonly used in second line therapy

Second line therapy	Percentage %
Carboplatin	39.47%
Docetaxel	27.19%
Paclitaxel	6.14%
Gemcitabine	6.14%
Etoposide	3.50%

Among second line carboplatin was most common used in 39.47%, followed by docetaxel in 27.19%, paclitaxel 6.14%, gemcitabine 6.14%, etoposide 3.50%.

Table 6: Distribution according to poly/single drug therapy

Distribution According to Single/Polytherapy	Percentage %
Single	5.3%
Polytherapy	93.9%

In our study 93.9% patients were prescribed polytherapy

Table 7: Distribution of drug commonly used as concomitant therapy

Adjuvant drug	Percentage %
Ondensatron	100%
Dexamethasone	90%
Ranitidine	85.1%
Mannitol	82.5%
Tramadol	35%

Among concomitant drug most common drug used was Ondensatron almost in 100% cases followed by Dexamethasone 90% for chemotherapy induced nausea and vomiting, Ranitidine

85.1%, Mannitol 82.5% in patients having chemotherapy with platinum group of drugs. Among pain killer Tramadol 35%was most commonly prescribed.

Table 8: Distribution of adjuvant therapy

Adjuvant therapy	Percentage %
Radiotherapy	91.2%
Surgery	8.8%

In our study among adjuvant therapy majority (91.2%) of the patients had radiotherapy while (8.8%) of the patients had surgery.

Cancer drugs cause several adverse effect as they affect normal cells along with cancer cells also. Most common adverse drug reaction noted in our study

Table 9: Distribution of commonly observed ADR

Day of chemotherapy	Symptoms	Percentage %
Day 0	Nausea , vomiting	99.1%
	Fatigue	81.6%
Day 21	Generalized weakness	44.7%
	Decreased appetite	42.1%
	Nausea ,vomiting	40.4%
Day 42	Generalized weakness	65.8%
	Anaemia	36.85
	Thrombocytopenia	28.9%
	Pancytopenia	17.5%

During first and second chemotherapy GIT and generalized symptoms were most common, on subsequent chemotherapy(day 42) patient develop hematological symptoms

Table 10: Distribution according to WHO UMC Causality Assessment Scale

Causality Assessments	Percentage %
Certain	10.5%
Possible	79.8%
Probable	9.6%
Total	100%

According to WHO UMC causalty scale majority of cases in our study were possible

Discussion

In our study in terms of gender prevalence out of 114 study participants majority of patients were male(75%)rest were female which was similar with the study by Vijay M. Motghare, Nikhil H. Dhargawe, *et al*. where majority of the patients were also males (73.05%)[5] Most patients in our study were in age group 50-70, males (74.5%), females (68.4%).(Table1) Smoking being most common cause of lung carcinoma, in our study majority 73.7% of patients were smokers.(Table 2)

In our study majority of patients had squamous carcinoma (38.6%) (non-small cell) followed by small cell cancer (35%), adenocarcinoma (24.6%) patients, adenoid cystic carcinoma (2%). (Table 3), this was in contrast to study by A Mohan *et al*. where adenocarcinoma was the most common type (34%), followed by squamous cell carcinoma (28.6%) and small cell lung carcinoma (16.1%).[6]

Commonly prescribed drug in our study belong to platinum coordination complexes

(cisplatin, carboplatin), taxanes (paclitaxel, docetaxel), topoisomerase 2 inhibitor (etoposide both tablet and i.v), folate antagonist (methotrexate, pemetrexed), pyrimidine antagonist (gemcitabine), nitrogen mustard (cyclophosphamide), antibiotics (actinomycin D). Most of drugs are prescribed IV few drugs like etoposide and methotrexate were also prescribed orally. Most patients were prescribed drugs as combination therapy/ polytherapy.

Most common prescribed regimen first line drug in Squamous cell carcinoma were Paclitaxel + Carboplatin(30.7%), Paclitaxel + Cisplatin(9.6%).(Table 4)

Most common prescribed regimen first line drug in small cell lung carcinoma were Cisplatin + Etoposide (32.5%).(Table 4) consistent with study done by Stein Sundstrom *et al*.[7].

Most common prescribed regimen first line drug in Adenocarcinoma were Carboplatin + Paclitaxel (13.2%), Gemcitabine + Carboplatin (11.4%), Cisplatin + Paclitaxel (6.1%), Pemetrexed + Carboplatin (7%), Cisplatin + Pemetrexed (2.6%). (Table 4)

Most common prescribed drug regimen in Adenoid cystic carcinoma drug regimen. Paclitaxel + Carboplatin (0.9%) and Carboplatin + Gemcitabine (0.9%).(Table 4)

Among second line therapy carboplatin was most common used in 39.47%, followed by docetaxel in 27.19%, paclitaxel 6.14%, gemcitabine 6.14%, etoposide 3.50%.(Table 5)

In our present study only 5.3% of the patients were given single drug therapy while maximum proportion 93.9% of the patients were given poly drug therapy or combination therapy. (Table 6)

Among first line drugs Paclitaxel was most common used in 78.07% followed by Carboplatin used in 72.8%, Cisplatin in 50.87%, Etoposide 32.45%, Gemcitabine 12.28%, Pemetrexed 9.64% of patients.

Among second line Carboplatin was most common used in 39.47%, followed by Docetaxel in 27.19%, Paclitaxel 6.14%, Gemcitabine 6.14%, Etoposide 3.50%, Actinomycin D and Cyclophosphamide 1.75%, tab Etoposide 1.75%.

In our study most common drugs used were Platinum coordinating complexes and Taxanes, in contrast to our study Manichavasagam *et al* (2017) observed that Alkylating agents and Antimetabolites were the mostly used anticancer drug.[8]

Among adjuvants drugs all patients were prescribed with Ondensatron 100%, Dexamethasone 90%, Ranitidine 85.1%, Mannitol 82% and Tramadol 35.5%.(Table 7),

It was observed that 99% of the patients were prescribed drugs according to NLEM, WHO drug list while 1% of the patients were not prescribed according to NLEM, WHO drug list. Most common adjuvant therapy in our study was radiotherapy followed by surgery (Table 8),

Cancer drugs cause several adverse effects as they also affect normal dividing cells. Majority of adverse effects nausea, vomiting, generalized weakness occurs immediately, some effects hematological have late presentation after few days or on subsequent chemotherapy.

In our study patient were assessed on day 0,21,42 days of chemotherapy. On day 0 most common ADR were related to GIT and generalized weakness. On day 21 and 42 patient mostly present with hematological symptoms such as anaemia, neutropenia, pancytopenia and thrombocytopenia.[9]. (Table 9). Hematological ADR develop on continued therapy takes time to manifest were more common around 3 cycle of chemotherapy most of which were managed by blood transfusion, fresh frozen plasma, and platelet transfusion.

All the reported ADRs were analyzed using WHO-UMC and Naranjo causality assessment

scale and Schumock and Thornton preventability scale. In our present study it was observed that 9.6% of the patients had Certain, 79.8% of the patients had Possible and 10.5% of the patients had Probable Causality Assessments according to WHO-UMC scale. (Table 10)

According to modified Hartwig & Seigel's severity assessment scale mild level 1 ADR was maximum due to Carboplatin 38(95%), Gemicitabine 13(92%) and least due to Docetaxel 13(65%). While mild level 2ADR was maximum due to Cisplatin 25(74%) and least due to Carboplatin 1(3%). On the other hand moderate level 3 ADR was maximum with Cyclophosphamide 1 (50%) and Pemetrexed 1(33%) followed by level 4 maximum due to Cisplatin 9(26%) followed by Paclitaxel 2(5%).

To assess preventability of ADR, Schumock & Thorton preventability scale applied to all reported ADR. Carboplatin 38(95%), Gemicitabine 13(92%), Paclitaxel 35(80%), Cisplatin 25(74%) & Docetaxel 13(65%) caused majority of probably preventable ADRs. On the other hand only Cisplatin 9(26%) & Paclitaxel 2(5%) caused majority of non-preventable ADRs also.

In a study by D Chakraborty As per WHO-UMC causality assessment, study revealed that most of the ADRs were under 'possible' category (90.02%)[10]. The remaining ADRs (9.98%) were under 'probable' category. In consistent with our finding Chopra *et al*. Causality assessment revealed that 80% of the ADRs were possible[11]. On contrary to our study Amartya De reported 85.28% were probable, 12.88% were possible and about 1.84% were certain ADRs.[12]

Conclusion

The present study concludes that incidence of cancer increases with increasing age. Most patients were in age group 50-70. Prevalence of cancer is more in males then in females. More common in smokers. Squamous cell carcinoma was most common followed by small cell carcinoma. Anticancer drugs are prescribed more commonly in combination as polytherapy is more common because of synergistic action.

Among prescribed anti cancer drugs platinum compounds is most commonly prescribed followed by taxanes. On initial therapy most common ADR were related to GIT which decreases on subsequent chemotherapy. In our present study it was observed that 79.8% of the patients had Possible Causality Assessments according to WHO-UMC scale. Modalities of treatment include chemotherapy, radiation therapy and surgery. So early diagnosis and treatment will limit morbidity and mortality in patients and prolong survival.

References

1. Boone CW, Kelloff GJ, Malone WE. Identification of candidate cancer chemoprotective agents and their evaluation in animal models and human clinical trials a review. cancer research. 1990; 50(1);2-9.
2. Cagle PT, Allen TC, Oslen RJ,. Lung cancer biomarkers: present status and future development s. Arch.Pathol.Lab. Med2013 Sep;137(9):1191-8.
3. Zang EA, Wynder EL.Differences in lung cancer risk between men and women; in examination of evidence. J Natl Cancer Inst. 1996;88(3-4):183-192.
4. Noronha V, Dikshit R, Rout N, Joshi A, Pramesh CS, George K, Agarwal JP, Munshi A, Prabhash K. Epidemiology of lung cancer in india. Focus on difference between non-smokers and smokers: A single centre experience. Indian Journal of Cancer. 2012 July; 49(1):74-81.
5. Vijay M. Motghare, Nikhil H. Dhargawe, Chaitali S. Bajait, Vijay Mahobia, AK Diwan. Study of prescription patterns and adverse drug reaction monitoring in patients of oral cavity malignancies attending radiotherapy department in a tertiary care teaching institute. Dept. of

Radiotherapy, Govt. Medical College, Nagpur, Maharashtra, 2017, 10.18231/23939087.2017.0010.
6. Mohan Anant; Garg Avneet; Gupta Aditi; Sahu Satyaranjan; Choudhari Chandrashekhar; Vashistha, Vishal, Clinical profile of lung cancer in North IndiaA 10-year analysis of 1862 patients from a tertiary care center Lung India; 2020 May–Jun; 37(3):190-197.
7. Stein Sundstrom, Roy M. Bremnes, Stein Kaasa, Ulf Aasebø, Reidulv Hatlevoll, Ragnar Dahle..Cisplatin and Etoposide Regimen Is Superior to Cyclophosphamide, Epirubicin, and Vincristine Regimen in Small-Cell Lung Cancer: Results From a Randomized Phase III Trial With 5 Years' Follow-Up. J Clin Oncol. 2002 Dec 15;20(24):4665-72.
8. Manichavasagam M, *et al*. Prescribing Pattern of Anticancer Drugs in a Medical Oncology Department of a Tertiary Care Teaching Hospital. Ann Med Health Sci Res. 2017; 7: 1-3.
9. The effects of cancer chemotherapeutic agents on normal hematopoietic precursor cells: a review. Cancer Res. 1976 Jun; 36(6):1853-82.
10. D Chakraborty, R Kale, L Das, M Das, S Kirde. Pharmacovigilance Study of Anticancer Drugs in a Tertiary Care Rural Hospital in Central India. Biomed Pharmacol J. 21 June;14(2): 597-606.
11. Chopra D, Rehan HS, Sharma V, Mishra R. Chemotherapy-induced adverse drug reactions in oncology patients: A prospective observational survey. Indian J Med Paediatr Oncol. 2016; 37(1):42–6.
12. De A. Sriram S, Ghasemi A, Ramasamy R, Devi M, Monitoring of Suspected Adverse Drug Reactions in Oncology Unit of an Urban Multispeciality Teaching Hospital. Int J Res Pharm Biomed Sci. 2010;1(2):1-32.