

Drug Utilization Evaluation of Anticancer Drugs in a Tertiary Care Teaching Hospital: a Descriptive Observational Study

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ABSTRACT

Drug Utilization Evaluation (DUE) promotes rational use of drugs. The aim of present study was to conduct DUE of anticancer drugs. Newly diagnosed and/or known case of carcinoma which required treatment with chemotherapy, patients of both sex, and age >18 years were included in the study. Patients diagnosed as having carcinoma that also required surgical intervention, radiotherapy or other modality of management were excluded from the study. WHO core prescribing indicators are used to know about polypharmacy, excessive use of antibiotics, percentage of drugs prescribed by from Essential Drugs List (EDL). Females were commonly affected than males. Patients of age group 41-50 years (mean 52.43, SD \pm 7.77) constituted the highest number, 34% and 13% in rural and urban population respectively. 5-Fluorouracil and Cisplatin are most commonly prescribed anticancer drugs followed by Cyclophosphamide. The most commonly used adjuvant drugs in our study are Diclofenac, B-Complex, Granisetron, Ranitidine, Dexamethasone, Ondansetron, and Mannitol. The cytoprotectant drugs observed in our study are Leucovorin, Mesna and Peg-Filgrastim. Average number of Cytotoxic Drugs per prescription was 1.97. Average number of drugs per prescription was 8.16. Percentage of drugs prescribed from Essential Drugs List (EDL) was 88.4%. Percentage of encounters with an antibiotic prescribed was 54.8%. Polypharmacy, unnecessary antibiotic and injection prescribing were not observed. The percentage of drugs from EDL may be improved.

INTRODUCTION

Cancer is one of the common cause of deaths in India and has profound social and economic consequences, often leading to family impoverishment and societal inequity (Mohandas *et al.*, 2014). According to the WHO, annually people die of cancer in India with prevalence of 500,000, this number is expected to rise to 700,000 by 2015 (IANS, 2014). The global burden of cancer continues to increase largely because of the aging and growth of the world population alongside an increasing adoption of cancer-causing behaviours (Jemal *et al.*, 2011; Takiar *et al.*, 2010), particularly smoking, in economically developing

countries. Drug utilization evaluation (DUE) is system of ongoing, systemic, criteria-based evaluation of drug use that will help ensure that medicines are used appropriately at the individual patient level. Drug utilization is drug or disease specific and can be structured so that it will assess the actual process of prescribing, dispensing or administering a drug (WHO, 2003). Potent cytotoxic drugs like anticancer drugs acts on both cancerous cells and healthy living cells. It makes the healthy living cells vulnerable to the cytotoxic action of anticancer drugs. In this context, DUE of these anticancer drugs was imperative. Irrational use of drugs is a major health problem of present day medical practice. This in turn leads to different consequences including but not limited to ineffective treatment, unnecessary prescription of drugs particularly antimicrobials and injections, development of resistance to antibiotics, adverse effects and economic burden on both patients and society.

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Irrational prescriptions and use of drugs has for long been known to be a feature of health care settings of developing countries, and is characterized by poly pharmacy, excessive use of antibiotics and injections and use of drugs of doubtful efficacy (Igbiks and Joseph, 2012). World Health Organization developed a core prescribing indicators to measure the degree of polypharmacy, the tendency to prescribe drugs by generic name and the overall level of use of antibiotics and injections. The degree to which the prescribing practice conformed to the essential drug list, formulary or standard treatment guideline were also measured by searching for the number of drugs prescribed from essential drug list available (WHO, 1993). Prescribers can only treat patients in a rational way if they have access to an essential drugs list and essential drugs are available on a regular basis (Sunil *et al.*, 2005).

METHODOLOGY

This descriptive study was carried out in chemotherapy ward, government general hospital; Kakinada for duration of 6 months. Total of 150 prescriptions had been reviewed. Newly diagnosed and/or known case of carcinoma which required treatment with chemotherapy, patients of both sex, and age >18 years were included in the study. Patients diagnosed as having carcinoma that also required surgical intervention, radiotherapy or other modality of management were excluded from the study. The data required for present study was noted down from the case sheets of the patients in a data collection form. WHO core prescribing indicators was compiled at the end of the study to know the amount of prescriptions with polypharmacy, percentage of prescriptions with injectables and antibiotics, percentage of drugs prescribed from Essential Drugs list etc. The study was approved by Institutional Ethical Committee. Informed consent was waived since there is no interaction with patients.

RESULTS AND DISCUSSION

Patients of age group 41-50 years (mean 52.43, SD \pm 7.77) constituted the highest number, 34% and 13% in rural and urban population respectively. Similar findings were reported in some studies (Sneha *et al.*, 2015; Mary Rohini *et al.*, 2015; Damodar *et al.*, 2011). The accumulation of age-associated changes in a biochemical process that helps control genes may be responsible for some of the increased risk of cancer seen in older people, according to a National Institutes of Health study. Scientists have known for years that age is a leading risk factor for the development of many types of cancer, but why aging increases cancer risk remains unclear.

Researchers suspect that DNA methylation, or the binding of chemical tags, called methyl groups, onto DNA, may be involved. Methyl groups activate or silence genes, by affecting interactions between DNA and the cell's protein-making machinery. According to the 1994 Surveillance, Epidemiology, and End Results Program of the National Cancer Institute, over 50% of all cancers occur in patients who are older than 65 years of

age. Females were more commonly affected than males. Similar findings were reported in some studies (Kirthi *et al.*, 2014; Kulkarni *et al.*, 2014; Popoola *et al.*, 2013). Males were more commonly affected by cancer when compared to females in some studies (Rathi *et al.*, 2007; Goyal *et al.*, 2014). Gender differences in susceptibility to a disease are a very useful piece of information that can be used to develop a causal hypothesis for the disease, or to define subgroups at highest risk for preventive action. The gender differential in susceptibility can give important clues for the etiology of cancers.

Table 1: Age wise distribution.

S.No.	Age (in years)	Rural	Urban
1	21-30	0	6
2	31-40	9	5
3	41-50	34	13
4	51-60	26	18
5	61-70	16	17
6	71-80	2	2
7	81-90	0	2

Table 2: Gender wise distribution.

S.No.	Gender	Rural	Urban
1	Male	27	31
2	Female	64	28

Table 3: Prescribing pattern of anticancer drugs.

S.No.	Drugs	Male	Female	Total
1	Inj. 5-FU	31	49	80
2	Inj. Cisplatin	39	21	60
3	Inj. Oxaliplatin	5	1	6
4	Inj. Carboplatin	2	8	10
5	Inj. Epirubicin	1	0	1
6	Inj. Acitnomycin D	1	11	12
7	Inj. Doxorubicin	3	33	36
8	Inj. Paclitaxel	11	19	30
9	Inj. Cyclophosphamide	1	38	39
10	Inj. Etoposide	4	1	5
11	Inj. Ifosfamide	0	4	4
12	Inj. Dacarbazine	2	0	2
13	Inj. Vinblastine	1	0	1
14	Inj. Vincristine	1	0	1
15	Inj. Mytomycin C	0	9	9

5-Fluorouracil and Cisplatin are most commonly prescribed anticancer drugs followed by cyclophosphamide. Similar findings were observed in some studies (Mary Rohini *et al.*, 2015; Goyal *et al.*, 2014; Darshan *et al.*, 2014).

The effective prescribing of anticancer drugs is based upon the availability of drugs, cost, tolerance, efficacy, progression of cancer in patient. Recently, many effective anticancer drugs were explored in which the detailed side effect profile and efficacy was not reported. In that context, it is better to use already established drugs which are effective and for which the side effect profile was well known. Of the 21 anticancer drugs listed in hospital formulary, only 15 anticancer drugs were prescribed during study period.

Table 4: List of Cytoprotectant drugs.

S.No.	Drugs	Male	Female	Total
1	Inj. Peg Filgrastim	0	1	1
2	Inj. Leucovorin	6	3	9
3	Inj. Mesna	0	2	2

The cytoprotectant drugs observed in our study are Leucovorin, Mesna and Peg- Filgrastim. Leucovorin is a biochemical modulating agent, chemo protective agent used in combination with 5-FU for treatment of advanced head and neck cancer, esophageal cancer. Filgrastim is a human recombinant granulocyte colony stimulating factor which is used to prevent chemotherapy-induced neutropenia, to increase neutrophil counts, and to prevent infection. Mesna conjugates with acrolein, a nephrotoxic metabolite produced by drugs like Cyclophosphamide, Ifosfamide etc, in urine reducing the incidence of renal toxicity.

Dexrazoxane is not recommended for routine use in breast cancer (BC) in adjuvant setting, or metastatic setting with initial doxorubicin-based chemotherapy. Consider use with metastatic BC and other malignancies, for patients who have received more than 300 mg/m² doxorubicin who may benefit from continued doxorubicin-containing therapy. Cardiac monitoring should continue in patients receiving doxorubicin. Amifostine may be considered for prevention of cisplatin-associated nephrotoxicity, reduction of grade 3 to 4 neutropenia (alternative strategies are reasonable), and to decrease acute and late xerostomia with fractionated radiation therapy alone for head and neck cancer. It is not recommended for protection against thrombocytopenia, prevention of platinum-associated neurotoxicity or ototoxicity or paclitaxel-associated neuropathy, prevention of radiation therapy-associated mucositis in head and neck cancer, or prevention of esophagitis during concurrent chemoradiotherapy for non-small-cell lung cancer (Martee *et al.*, 2009).

Table 5: List of adjuvant drugs.

S.No.	Drugs	Males	Females	Total
1	Tab. Diclofenac	67	83	150
2	Tab. B complex	67	83	150
3	Inj. Tramadol	1	0	1
4	Inj. Mannitol	39	24	63
5	Inj. Mag. Sulphate	37	25	62
6	Inj. Granisetron	67	83	150
7	Inj. Rantidine	67	83	150
8	Inj. Dexamethasone	67	83	150
9	Inj. Ondansetron	4	49	53

The most commonly used adjuvant drugs in our study are Diclofenac, B-Complex, Granisetron, Rantidine, Dexamethasone, Ondansetron and Mannitol. Similar findings were observed in studies (Mary Rohini *et al.*, 2015; Darshan *et al.*, 2014). Mannitol is given along with Furosemide as a palliative therapy (Darshan *et al.*, 2014). With the correct use of antiemetics, Chemotherapy Induced Nausea and Vomiting can be prevented in almost 70% to up to 80% of patients (Jordan *et al.*, 2007). Although not approved as an antiemetic, dexamethasone plays a major role in the

prevention of acute and delayed CINV and is an integral component of almost all antiemetic regimens (Jordan *et al.*, 2007; Grunberg, 2007).

Table 6: WHO Core Drug Prescribing Indicators.

S No	WHO Core Drug Prescribing Indicators	Result
1	Avg. No. of Cytotoxic drugs per Prescription	1.97
2	Avg. No. of drugs per Prescription	8.16
3	Percentage of encounters with an antibiotic prescribed	54.8%
4	Percentage of Encounters with an Cytotoxic Injectable prescribed	100%
5	Percentage of Encounters with an Injectable Prescribed	75.5%
6	Percentage of drugs Prescribed from EDL	88.40%
7	Percentage of drugs Prescribed from WHO Model List	80.70%
8	Percentage of drugs prescribed by generic name	93%

The average number of drugs per prescription was 8.16. Although it may look like polypharmacy, it must be remembered that definition for polypharmacy differs with clinical setting. Adjuvant drugs like anti-emetics corticosteroids etc makes up the prescription volume. Percentage of prescriptions with an antibiotic prescribed was 54.8%. The antibiotic use was limited to any infections caused by the side effects of drugs like blistering of skin, fungal infections etc. Unnecessary antibiotic prescribing was not observed. Percentage of drugs prescribed from EDL was 88.4%.

The drugs are prescribed based on the hospital formulary and are supplied on nonprofit basis by the government. Incontestably, there might be difference in percentage of drugs prescribed from EDL. The percentage of drugs prescribed from list of essential drugs may be improved. Percentage of drugs prescribed by generic name was 93%. Prescribing medicines by generic name has to be encouraged since generic medicines are as effective as brand ones and they cost less which decreases the medical expenditure.

CONCLUSION

5-Fluorouracil and Cisplatin are most commonly prescribed anticancer drugs followed by cyclophosphamide. The cytoprotectant drugs observed in our study are Leucovorin, Mesna and Peg- Filgrastim. The most commonly used adjuvant drugs in our study are Diclofenac, B-Complex, Granisetron, Rantidine, Dexamethasone, Ondansetron and Mannitol. The antibiotic use was limited to any infections caused by the side effects of drugs like blistering of skin, fungal infections etc. Unnecessary antibiotic prescribing was not observed. The percentage of drugs prescribed from list of essential drugs may be improved. Polypharmacy was not observed.

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