Assessment of drug utilization pattern in patients undergoing chemotherapy for various types of metastatic cancers in a tertiary care government hospital

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INTRODUCTION

Cancer is one among main causes of morbidity and mortality in developing and developed countries alike.1,2 To add to the present problem, the number of cancer cases and deaths is expected to grow rapidly with populations growth, age, and lifestyle behaviours that increase the risk of cancer. This is more important in low- and middle-income societies as they are in phase of economic transformation, which includes greater mechanization of transport and labour increased exposure and access to international markets and cultural shifts in the roles of women. As a result, many of the lifestyle risk factors, such as tobacco use, physical inactivity, excess bodyweight, and reproductive patterns, which are already prevalent in high-income countries (HIC), and are also becoming increasingly common in LMICs.2 There will be an estimated 18.1 million new cancer cases (17.0 million excluding nonmelanoma skin cancer) and 9.6 million cancer deaths (9.5 million excluding nonmelanoma skin cancer) by 2025. The prescription pattern of anticancer drugs has evolved considerably in recent years because of better understanding of underlying pathophysiology of carcinomas as well as introduction of newer drugs.

ABSTRACT

Background: Cancer is one among main causes of morbidity and mortality in developing and developed countries. The World Cancer Report 2014 of World Health Organization’s (WHO’s) International Agency for Research on Cancer (IARC), states that in 2012 the global incidence of cancer increased to a 14 million new cases, the figure expected to rise to an annual 19.3 million by 2025. The prescription pattern of anticancer drugs has evolved considerably in recent years because of better understanding of underlying pathophysiology of carcinomas as well as introduction of newer drugs.

Methods: It was a hospital-based prospective, cross-sectional study conducted in Department of Oncology, GGH, Kakinada for a period of twelve months from February 2017 to January 2018. A total of 100 patients were enrolled using convenience sampling technique. Patient demographics like age, gender, educational level, employment status, marital status, smoking category, alcohol consumption, stage of cancer was collected. Drug utilization pattern was obtained from inpatient case reports, prescriptions and medication charts used during a chemotherapy cycle.

Results: Among all anticancer drugs, cisplatin and 5-flurouracil were most commonly prescribed followed by Adriamycin. The most commonly used adjuvant drugs were B-complex, diclofenac, granisetron, ranitidine, dexamethasone. Antibiotic use was found to be very limited.

Conclusions: Various anticancer drug prescription patterns are being used for treatment of patient with metastatic cancers. In this study, cisplatin and 5-flurouracil were commonly used. Injudicious antibiotic prescribing was not observed.

Keywords: Drug utilization, Chemotherapy, Metastatic cancer, Antibiotic, Adjuvant drugs
cancer) in 2018. In both sexes combined Lung cancer is the most commonly diagnosed cancer (11.6% of the total cases) and the leading cause of cancer death (18.4% of the total cancer deaths), closely followed by female breast cancer (11.6%), prostate cancer (7.1%), and colorectal cancer (6.1%) for incidence and colorectal cancer (9.2%), stomach cancer (8.2%), and liver cancer (8.2%) for mortality. Lung cancer is the most frequent cancer and the leading cause of cancer death among males, followed by prostate and colorectal cancer (for incidence) and liver and stomach cancer (for mortality). Among females, breast cancer is the most commonly diagnosed cancer and the leading cause of cancer death, followed by colorectal and lung cancer (for incidence), and vice versa (for mortality); cervical cancer ranks fourth for both incidence and mortality.\(^3\)

The prescription pattern of anticancer drugs has evolved considerably in recent years because of better understanding of underlying pathophysiology of carcinomas as well as introduction of newer drugs. Considerable variation in the response rate of individual anticancer drugs, availability of different regimens, and intolerability of combination regimens necessitate observation and evaluation of cancer chemotherapy. Such information will help in optimizing anti-malignancy therapy with improved efficacy and minimal toxicity.\(^3\)

Drug utilization studies (DUS), nowadays, are used as potential tool in the evaluation of healthcare systems. DUS are powerful exploratory tools to ascertain the role of drugs in the society. They create a robust socio-medical and health economic basis for healthcare decision making.\(^4\)

DUS also promotes the rational use of drugs and reduces health care cost. Conducting DUS studies also contribute to reducing healthcare cost and incidence of adverse drug events.\(^5\) Drug utilization research (DUR or DUS) also provides insight into the efficiency of drug use, i.e., whether a certain drug provides value for money. Drug utilization research can thus help to set priorities for the rational allocation of healthcare budgets. WHO suggested DUS are needed in every health care setting.

DUS is a process which is ongoing, authorized and also a process of systematic quality improvement, which is specially designed to review of the drug use and/or patterns of prescription, providing feedback of the results to the clinicians/physicians, development of criteria and standards which gives a description of optimal drug use and promoting appropriate use of the drug via education and other interventions or means.\(^6,7\)

The main aim of DU research is to promote rational use of drugs, which allows prescribing of a well-documented drug in an optimal dose on the right indication, with accurate information and at an affordable and economic price.\(^7\)

**Types of drug use information**

Drug-based information, problem-based information, patient information and prescriber information.\(^7\)

**Sources of drug utilization data**

Computerized databases, pharmacy records, medical practitioner records and health surveys.

**Instruments for data collection on drug utilization**

Patient files and computer registries, home inventories and questionnaires.\(^7\)

It is necessary to realize that inappropriate use of drugs represent a potential hazard to the patients and an unnecessary expense. This necessitates a periodic review of pattern of drug utilization to ensure safe and effective treatment.\(^4\)

A large number of sociocultural factors contribute to the way drugs are being used. Poverty, illiteracy, use of multiple healthcare systems, drug advertising and promotion, sale of prescription drugs without prescription, unbiased drug information are some of the sociocultural factors.\(^4\)

The boost in the marketing of new drugs, wide variations in the pattern of drug prescribing and consumption, increasing concerns regarding the delayed adverse effects, growing concern about the cost of drugs and volume of prescription, all contribute to the rising importance of DUS. These studies focus on the factors related to prescribing, dispensing, administering of medication, its beneficial or adverse effects etc.\(^4\)

DUS can be targeted towards any of the following links in the drug-use chain.\(^4\) The systems and structures surrounding drug use (e.g. how drugs are ordered, delivered and administered in a hospital or health care facility); The process of drug use (e.g. what drugs are used and how they are used and does their use comply with the relevant criteria, guidelines or restrictions); the outcomes of drug use (e.g. efficacy, adverse drug reactions and the use of resources such as drugs, laboratory tests, hospital beds or procedures).

Drugs have to be used rationally, in order to maximize human well-being. Socio-cultural factors also play a major role in the need for DUE (drug utilization evaluation), especially in India. The over-use, misuse and under-use of prescribed drugs are very common.\(^7\)

DUS are the types of vigilant activities that can describe the prescription pattern in a given setup. They also provide feedback on the implementation of the clinical guidelines and the performance of the prescribers. These DUS can be used to compare the situations between two different setups and may be used to measure the impact.
of any interventions taken. They also used as supervisory tools to detect the shortcomings in the performance standards of any individual or health facility. They are the powerful exploratory instruments to ascertain the role of drugs in the society which refers to the marketing, distribution, prescription and use of drugs with special focus on the medical, social and economic consequences.

The main aim of drug utilization research is to facilitate the rational use of drugs in population. WHO specifies drug use indicators (WHO, 1993; Sutharson et al) for adoption in DUS.

### Table 1: Core indicators.

| Indicators                  | Core                                      |
|-----------------------------|-------------------------------------------|
| Prescribing indicators      | Average number of drugs per encounter     |
|                            | Percentage of drugs prescribed by generic name |
|                            | Percentage of encounters with an antibiotic prescribed. |
|                            | Percentage of encounters with an injection prescribed. |
|                            | Percentage of drugs prescribed from essential drug list |
| Patient care indicators     | Average consultation time                  |
|                            | Average dispensing time                    |
|                            | Percentage of drugs actually dispensed     |
|                            | Patients’ knowledge of correct dosage      |
| Facility indicators         | Availability of copy of EDL: by stating yes (or) no |
|                            | Availability of key drugs                  |
| Complementary indicators    | Percentage of patients treated without drugs |
|                            | Average drug cost per encounter            |
|                            | Percentage of drug costs spent on injection |

The anatomical, therapeutic, chemical (ATC) classification system provides global standard for classifying drugs. A technical unit of measurement called defined daily dose (DDD) can be defined as “the assumed average maintenance dose per day for a given drug used for its main indication in adults”. It is recommended by the WHO as the international standard for drug utilization research.

The ATC/DDD system serves as tool for DUS and allows comparison of drug consumption statistics at international and other levels of healthcare. DDD is the assumed average daily dose of a drug prescribed for the drug’s prior indication in the adults. It doesn't give exact picture of the drug consumption but provide a rough estimation of the drug utilization. DDD is not dependent of the dosage form and cost of the drug thus enabling the researchers in the assessment of trends in drug utilization. The aim of calculating DDD is to improve drug usage. The DDD system is a tool for national and international comparison of drug consumption. The defined daily dose is the assumed average maintenance dose per day for a drug used for its main indication in adults.

DUR studies are important not only for policy-making at national level but also for individual patient management. But, in most of the middle or low-income countries the availability of information on drug consumption is inadequate. This information is often lacking on even the broadest measures of drug use like the overall volume of use and total spending on drugs. DUS are conducted to know the current prescribing trends and to evaluate nature, extent and determinants of use. This will help to determine and promote rational use of drugs among population.

**METHODS**

**Ethical considerations**

The study protocol (number: IEC/RMC/2016/177) was approved by the Dr. NTR University of Health Sciences, Vijayawada, Andhra Pradesh and prior permission was also taken from Institutional Ethics Committee of Rangaraya Medical College.

**Study protocol**

The present study was carried out in the Department of Oncology in Government General Hospital at Rangaraya Medical College, Kakinada for a period of twelve months from February 2018 to January 2019. Study was hospital-based prospective, cross-sectional study where the participants who fulfilling the inclusion and exclusion criteria were enrolled.

**Sample size**

The sample size was based on the available number of patients reporting to oncology department and according to the previous year’s medical records and fixed to be 100. We followed convenience sampling while choosing sample for the study. The patients were recruited based on their accessibility, easiness to recruit (convenience sampling).

**Criteria for selection**

**Inclusion criteria**

Inclusion criteria were all metastatic cancer patients receiving chemotherapy, 21-80 years old patients and both male and female patients.
Exclusion criteria

Exclusion criteria were paediatric age group and haematological malignancies.

Data collection

Inpatient case reports, prescription and medication charts were analysed. Patient demographics like age, gender, educational level, employment status, marital status, smoking category, alcohol consumption, stage of cancer is collected from the case sheets of the metastatic cancer patients in oncology ward.

Data was analysed with the help of latest version of SPSS software and Microsoft excel. Demographic data and adverse drug reactions was calculated as percentages and mean average±SD (p=0.05). For age and domains Kruskal-Wallis test was used. For gender and domains Mann-Whitney U test was used. For tumour stage and domains Kruskal-Wallis test was used.

RESULTS

Demographic profile

In the present study Age is divided into 3 subgroups. Most patients (56) observed in 41-60 years subgroup. In gender distribution, among 100 patients, 63 patients are male and 37 patients are female. Education level is more (81%) when compared to uneducated (11%). Unemployed are more (93%). In smoking and drinking category nonsmokers (46%) and non-alcoholics (48%) are more when compared to smokers (32%) and alcoholics (19%).

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Table 2: Demographic parameters and their frequency (n=100).

| Variable          | Frequency | Percentage |
|-------------------|-----------|------------|
| Age in years      |           |            |
| 21-40             | 13        | 13         |
| 41-60             | 56        | 56         |
| 61-80             | 31        | 31         |
| Gender            |           |            |
| Male              | 63        | 63         |
| Female            | 37        | 37         |
| Educational level |           |            |
| Uneducated        | 11        | 11         |
| Less than high school | 8    | 8          |
| High school graduate | 81   | 81         |
| Employment status |           |            |
| Employed          | 7         | 7          |
| Unemployed        | 93        | 93         |
| Smoking category  |           |            |
| Non-smokers       | 46        | 46         |
| Smokers           | 32        | 32         |
| Abstainers        | 22        | 22         |
| Drinking category |           |            |
| Non-alcoholics    | 48        | 48         |
| Alcoholics        | 19        | 19         |
| Abstainers        | 33        | 33         |

Table 3: List of adjuvant drugs in percentage.

| Drugs               | Male | Female | Total |
|---------------------|------|--------|-------|
| Tab. B complex      | 63   | 37     | 100   |
| Tab. diclofenac     | 63   | 37     | 100   |
| Tab. ondansetron    | 37   | 25     | 62    |
| Tab. paracetamol    | 9    | 6      | 15    |
| Tab. doxycycline    | 5    | 3      | 8     |
| Tab. pantoprazole   | 20   | 11     | 31    |
| Tab. fluconazole    | 0    | 3      | 3     |
| Cap. amoxiclav      | 2    | 4      | 6     |
| Tab. iron folic acid| 11   | 32     | 43    |
| Syp. sucralfat      | 4    | 4      | 8     |
| Inj. granisetron    | 63   | 37     | 100   |
| Inj. ranitidine     | 63   | 37     | 100   |
| Inj. dexamethasone  | 54   | 32     | 86    |
| Inj. ondansetron    | 12   | 24     | 36    |
| Inj. paracetamol    | 3    | 1      | 4     |
| Inj. diclofenac     | 19   | 10     | 29    |
| Inj. magnesium sulphate | 28  | 19     | 47    |
| Inj. ethamsylate    | 0    | 1      | 1     |
| Inj. mannitol       | 23   | 15     | 38    |

Among adjuvant drugs B complex, diclofenac, granisetron, ranitidine given to every patient (100%).

Figure 1: Trends in use of anticancer drugs.

In present study most commonly prescribed anti-cancer drug is cisplatin (58%) followed by 5-flourouracil (41%).
DISCUSSION

The main aim of drug utilization study is to facilitate the rational use of drugs in populations. From the individual patient perspective rational use of a drug implies the prescription of a well-documented drug in an optimal dose for right indication, with the correct information and at an affordable price. Without proper knowledge on how drugs are being prescribed and used, it is difficult to start a discussion on the rational drug use and to suggest measures to change prescribing patterns for the better of the patient population. Information about present and past performance of prescribers is the kernel of any drug auditing system.

Drug utilization research was defined by World Health Organization (WHO) in as “the marketing, distribution, prescription and the use of drugs in a society; with special emphasis on the resulting medical, social and economic consequences.” The assessment of drug utilization is important for both the clinical and educational purposes.

In the present study among 100 patients 63% (63) are male and 37% (37) female patients whereas in Mugada et al, study 44.66% (67) are male and 55.33% (83) are female. In Siddiqua et al male population was more, 54% and 46% of patients were found to be females. The main objectives of drug utilization evaluation are identification of the problems in medicine use, analysis of problem, analysis of the consequences of such problem. These objectives differ with different groups of patients, as they seek different alternatives. In present study 21-80 years patients included. Paediatric age group excluded as they are being treated separately and hence only patients above 21 years taken into consideration of this study. Age divided into 3 subgroups. Most patients (56) observed in 41-60 years subgroup.

The major therapeutic class of drugs prescribed for cancer was cytotoxic drugs. These drugs are well-known to cause severe side effects. Cytotoxic drugs have a narrow therapeutic index (TI) and the dosage needed to achieve the therapeutic effect would also cause severe toxic effects.

In present study, most commonly prescribed anti-cancer drug is cisplatin followed by 5-flourouracil and this is inconsistent with the findings of Mugada et al and Kulkarni et al. Cisplatin’s major side effect is nephrotoxicity. Here cisplatin was given as rapid infusions along with nephroprotective agents such as mannitol and magnesium sulphate (MgSO4). Here in this centre cisplatin usually given in combination with 5-flourouracil. Adriamycin usually given in combination with cyclophosphamide and sometimes with dacarbazine. Very rarely adriamycin given as a single agent.

Among adjuvant drugs B complex, diclofenac, granisetron, ranitidine given to every patient. Similar findings were observed in studies by Mugada et al. Nausea and vomiting seen profoundly with chemotherapeutic agents. So granisetron, ondansetron and ranitidine given. More than three fourths of patients (86%) were given dexamethasone. Mannitol and MgSO4 given along with cisplatin. Iron folic acid frequently used (43%) as anaemia is a frequent side effect of cytotoxic drugs. Many of the side effects of the chemotherapy can be managed with adjuvant drugs like anti diarrheals, laxatives, antihistamines, immune-suppressants and gastric protectants.

The effective prescribing of chemotherapeutic drugs is based on the availability of drugs, cost, tolerance, efficacy, progression of cancer in patient. Recently, many effective anticancer drugs were explored. But 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.

Drug use is a complex process since optimal benefits of drug therapy in patient care may not be achieved completely because of under-use, overuse or misuse of these drugs. Inappropriate drug use may also lead to increased cost of medical care, development of antimicrobial resistance, adverse effects and increased patient mortality. Hence, in recent years, DUS have become a potential reliable tool that can be used in the evaluation of health care systems. Drug utilization studies provide an insight into the efficacy and pattern of drug use, and the quality and outcome of use.

Irrational prescriptions and use of drugs for long been known to be a feature of health care setups of developing countries. It is usually characterized by polypharmacy, excessive and irrational use of antibiotics and injections and use of drugs of doubtful efficacy Mugada et al. WHO has developed 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 in health care settings. Data obtained from this drug utilization study could also help in developing educational programs or seminars or symposiums required at healthcare institutes (like teaching hospitals, tertiary care hospitals) to educate the staff about the advantages and disadvantages of the rational use of drugs and healthy prescription habits. This is advantageous from patient end also. The drug utilization and cost distribution should be examined from time to time so as to manage the inventory control in hospital pharmacy.

Limitations

Haematological malignancies not included in present study. The cost component of the drug therapy could not be computed due to unavailability of relevant data. In present study we have not included the drugs taken from outside hospital as the patient does not have knowledge.
about that particular drug. Effect of other treatment modalities like surgery, radiotherapy not taken into consideration. Paediatric malignancies not included in the study. Concomitant malignancies which may affect quality of life also not excluded. Being heterogeneous groups (including several types of cancers), without considering them separately we encountered majority of patients at their different stages of disease progression, so intergroup (within different types of cancer) variations may be present.

Despite the limitations, the current study represents an attempt to understand the drug utilization among metastatic cancer patients.

CONCLUSION

Cisplatin and 5-flourouracil are most commonly prescribed anti-cancer drugs followed by adriamycin. The most commonly used adjuvant drugs in current study are B-complex, diclofenac, granisetron, ranitidine, dexamethasone. The antibiotic use was very limited. Injudicious antibiotic prescribing was not observed.

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