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Research Article

DRUG UTILIZATION STUDY IN A RADIOTHERAPY UNIT OF A TERTIARY CARE TEACHING HOSPITAL IN RURAL WEST BENGAL, INDIA

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ABSTRACT

Objective: Drug utilization studies lay special emphasis on the medical social and economic consequences of use of medications in special settings. This study was undertaken to identify the pattern of drugs prescribed frequently among patients attending the radiotherapy department.

Methods: This is a prospective study undertaken between January 1, 2018, and December 31, 2018. Prescriptions and patient records were reviewed and analyzed using the World Health Organization (WHO) indicators for drug utilization studies.

Results: We encountered a total of 618 patients during the study period. Among them, 340 (55.01%) were female. The most common age groups presenting were between 21 and 60 years. Carcinoma breast was the most common type encountered (total cases 181, 29.28%), followed by carcinoma lung (total cases 92, 14.88%), carcinoma cervix, hematological malignancies, carcinoma prostate, and carcinoma rectum. Total number of drugs prescribed was 3008 in total 618 prescriptions making it 4.86 drugs per prescription on average. Among them on average per prescription, 2.82 drugs were cytotoxic drugs (1745 total), whereas 2.04 drugs were supportive or adjunct drugs (1263 total). Among the drugs prescribed, 96.24% were in generic names, 6.95% prescriptions contained antibiotics, and 96.44% (596) prescriptions contained injections. About 85.23% of drugs were prescribed from essential drug list. Average consulting was 8.2 min and dispensing time for adjunct drugs was 4 min on average. On average, 52.42% of patients (324) had complete correct knowledge of the dosage and schedule prescribed. Adverse drug reactions were common, out of 618 patients, 542 (87.7%) experienced ADRs most common being gastrointestinal and dermatological ADRs. The most common implicated drug was cisplatin. Six serious adverse events were encountered.

Conclusions: This study provides a clear picture of drug use in this special clinic in rural Bengal and paves the way for larger and long-term study.

Keywords: Drug utilization study, Anticancer chemotherapy, Generic prescriptions, Prescription.

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INTRODUCTION

Cancer is one of the leading causes of death all over the world. As a matter of fact, it is the second leading cause of death globally. As per global cancer statistics, 18.1 million new cancer cases were diagnosed in 2018 and approximately 9.6 million deaths were estimated due to cancer [1]. At least one in six deaths, worldwide is attributed to cancer. In India, there is an alarming rise of cancer cases [2]. This rise in cancer cases and the eventual rise in mortality may be due to increasing age of the population, population growth, and increasing cancer causing behaviors like smoking. A major problem with cancer is that it not only affects the patient but also affects the families. It puts a huge financial burden that leads to family impoverishment. This is not only due the high cost of chemotherapy or radiation therapy but also due to the utilization of various adjunct drugs such as analgesic or antiemetic drugs.

Many of anticancer drugs depress the immune system considerably making the patient vulnerable to various infections. Hence, antibiotics usage is high in cancer patients. This again leads to further cost and also to antibacterial resistance [3]. Drug utilization evaluation (DUE) is criteria bases systematic study on drug utilization pattern to ensure that the drugs are used appropriately at individual patient level. It can be structured to be drug or disease specific to assess the actual process of drug prescribing, dispensing, and administration. It may be a very useful tool to minimize irrational prescribing and inappropriate use of drugs and can reduce the financial burden considerably not only on the patient but also on the society as a whole [4]. Irrational prescriptions, a major concern of modern health system especially in developing countries, are characterized by though not limited to, polypharmacy, inappropriate use of antibiotics, unnecessary use of injectable drugs, etc. The WHO has developed core prescribing indicators to measure the degree of polypharmacy, the percentage of antibiotics and injectable drugs prescribed, and the overall tendency to prescribe generic drugs. There are other indicators to assess the process of drug dispensing and administration. Considering cancer as a major area of potential drug misutilaztion, it is imperative to conduct DUE on anticancer drug to minimize the inappropriate use of anticancer and other adjunct drugs [5].

Another problem with cancer chemotherapy is the propensity of adverse drug reactions. It is an undesirable consequence of drug use. Adverse reactions though to some extent inevitable are matters of major concern due to their sheer number and impact. They are one of the leading causes of death globally as per epidemiological studies. To control and reduce, the extent of adverse reactions proper monitoring and early reporting of any adverse event is vital [6]. As we know cytotoxic drugs used in cancer chemotherapy not only kill the malignant cells but also have deleterious effects on the normal cells resulting in various adverse reactions. To mitigate these adverse effects, further, treatment becomes necessary along with the extension in hospital stay in severe cases. These all add to already considerable treatment costs leading to more financial burden on the patient and the family. As mentioned earlier, cancer treatment needs the use of myriad of drugs resulting in more adverse effects, drug reactions, and more costs, leading to a vicious cycle ultimately resulting in lack of compliance, discontinuation of treatment, and poor outcome [7].

In our institution and in this part of India, studies looking at drug use among cancer patients and related prevalence of ADRs are scarce and this is more so in a rural set up like ours. Most of the studies we found were conducted in southern part of India. Hence, we undertook a study to evaluate the drug utilization pattern specific to cancer chemotherapy and also the pattern of adverse effects of those drugs.

MATERIALS AND METHODS

This was a prospective and observational study performed at the radiotherapy outpatient department and the adjacent day care center in the department of radiotherapy in a tertiary care teaching hospital in rural West Bengal. The study was undertaken after necessary approval from the Institutional Ethics Committee. The duration of the study was of one year spanning from January 1, 2018, to December 31, 2018. All the patients treated for cancer with chemotherapy only by a consulting oncologist in the radiotherapy outpatient department during that tenure was included in the study.

Data were collected by analyzing the prescriptions and interviewing the patients regarding the treatment. The patient demographic details were collected along with the history of any other disease and relevant medications. Information regarding any adjunctive drugs was also collected from the patient case sheets that those were duly recorded in data collection forms. All data collected from the prescriptions and participants were analyzed using standard tools for descriptive statistics including percentage and average. For analysis, Microsoft Excel Software was used and data were depicted in standard graphical format including bar charts.

The WHO core prescribing indicators were compiled from the collected data. Those indicators were the number of drugs prescribed per encounter, the percentage of encounters with an antibiotic, percentage of drugs prescribed by generic names, percentage of encounters with an injection prescribed, and percentage of drugs prescribed from essential drug list or formulary [4,8]. Other complementary indictors such as average consulting time, average dispensing time, whether the prescriptions complied with the standard treatment guidelines, and percentage of drugs actually dispensed along with the percentage of drugs adequately labeled were noted. We also noted the patients' knowledge of correct dosage.

The data regarding ADRs were either directly collected from the patients or from the reports of laboratory investigations. Detail report regarding the nature of ADR along with the suspected drug, medications required to alleviate the condition, and outcomes was recorded. To assess, the casualty and severity of the ADRs Naranjo's scale and modified Hartwig's severity assessment scale were used, respectively. Naranjo's algorithm used ten questions with according scores and puts the casualty of the drug in one of the classes among definite, probable, possible, and doubtful [9]. Hartwig's scale classifies the severity of the ADR as mild, moderate, or severe depending on various factors such as change in the treatment, hospital stay, and disability incurred [10]. Microsoft excel data sheet was used to collect and analyze the data. Prior permission of Institutional Ethical Committee was obtained and due consent was taken from the patients or their legal representatives.

RESULTS

We encountered 618 patients in the outpatient department of radiotherapy. Among them, 340 (55.01%) were female and 278 (44.98%) were male. Age group distribution showed people among 41–60 years and 20–40 years were most affected, 54.36% and 26.21%, respectively (Fig. 1).

As for the types of cancer, carcinoma breast was the most common type encountered (total cases 181, 29.28%). Carcinoma lung was the second most common after carcinoma breast (total cases 92, 14.88%) followed by carcinoma cervix (total cases 65, 10.51%), hematological malignancies (56, 9.06%), carcinoma prostate (total cases 53, 8.57%), and carcinoma rectum (total cases 48, 7.76%) (Fig. 2).

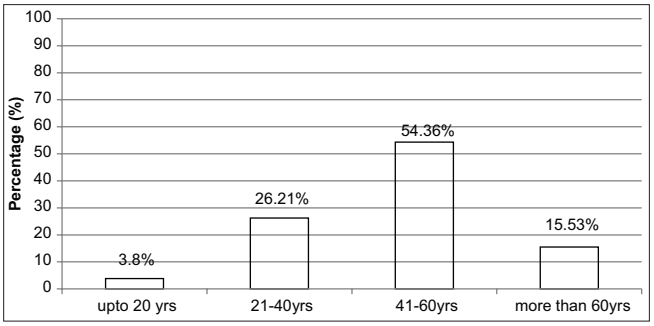

Fig. 1: Age distribution of the patients (n = 618)

Total number of drugs prescribed was 3008 in total 618 prescriptions making it 4.86 drugs per prescription on average. Among them on average per prescription, 2.82 drugs were cytotoxic drugs (1745 total), whereas 2.04 drugs were supportive or adjunct drugs (1263 total). Among the drugs prescribed, 96.24% were in generic names. We encountered 6.95% prescriptions (43 prescriptions) with antibiotics and all prescriptions (100%) contained injectable drugs. About 85.23% of drugs were prescribed from essential drug list.

Analysis of the WHO complementary drug prescribing indicators showed the average consulting time to be 8.2 min, where the dispensing time for adjunct drugs was 4 min on average. About 62% of drugs prescribed were actually dispensed. On average, 52.42% of patients (324) had complete correct knowledge of the dosage and schedule prescribed.

Among the 1745 cytotoxic drugs prescribed, platinum analogues were most commonly prescribed (350 or 27.69% of overall used cytotoxic drugs), among them cisplatin most commonly used (17% of total used cytotoxic drugs). Taxanes (paclitaxel+docetaxel) was the second most common group of drugs used (13.92%) followed by 5FU (13.56%). Majority of patients underwent two cytotoxic drugs combination (56%), where 25.2% of patients needed three or more cytotoxic drugs. Only around 20% of patients underwent anticancer monotherapy. Most common malignancy encountered in our study was carcinoma breast and 5FU and cyclophosphamide were most commonly used drugs in this group of patients. For carcinoma lung platinum, compounds were most commonly used, mostly cisplatin followed by taxanes. For carcinoma cervix platinum, compounds were used most commonly. We encountered significant use of monoclonal antibodies reflecting the free hospital supply of these drugs in our institution. Distribution of anticancer drugs prescribed is shown in Fig. 3.

A total of 1263 drugs were adjunct drugs which were used along with anticancer drugs. Of these, most common was Ondansetron for treatment of anticancer drug induced nausea and vomiting (17.71% of all drugs seen in 533 prescriptions). This was followed by famotidine, proton pump inhibitors, and lactulose – all three drugs for treatment associated adverse effects. Iron/folic acid combination, lorazepam, and paracetamol were among the other significant adjunct drugs used. Fig. 4 shows the distribution of adjunct drugs used in the patients.

Adverse drug reactions were common, out of 618 patients, 542 (87.7%) experienced ADRs. Total number of adverse reactions were 1096 making it 1.77 per patient. Among the adverse reactions, most common were related to gastrointestinal tract (464 in number, 85.6% of total adverse reactions). Among these, 416 were nausea with vomiting, 26 diarrhea, ten mucositis, eight nausea without vomiting, two cases of hematemesis, and two of malena. The second most common system affected was skin with 394 reactions total. Among them alopecia was

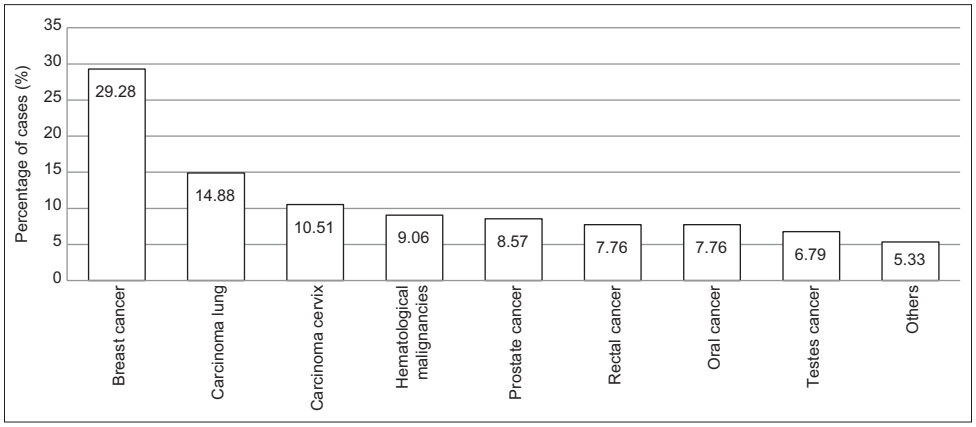

Fig. 2: Distribution of different cancers presenting to the radiotherapy outpatient department for treatment (n = 618)

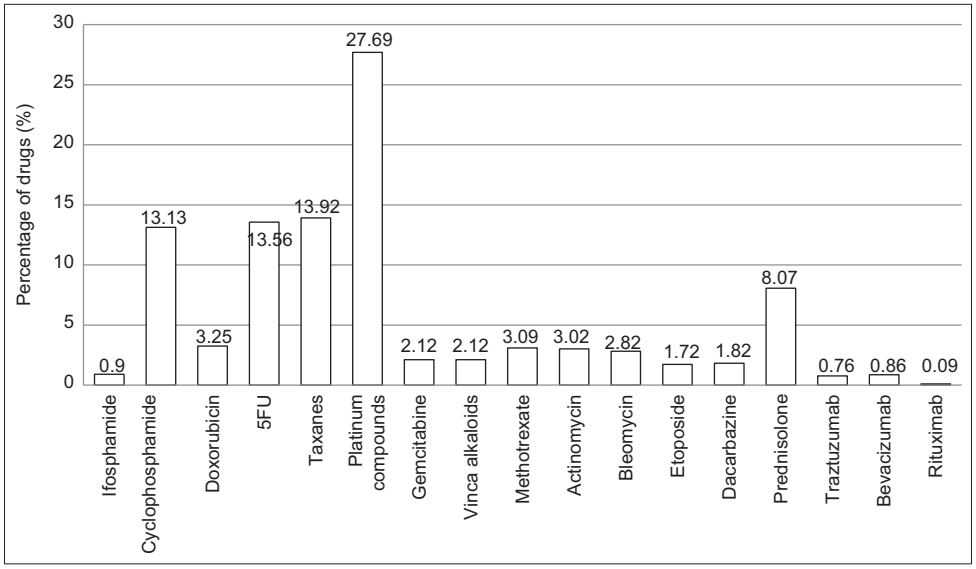

Fig. 3: Percentage distribution of anticancer drugs prescribed. Total 1745 anticancer drugs were prescribed in the 618 prescriptions encountered

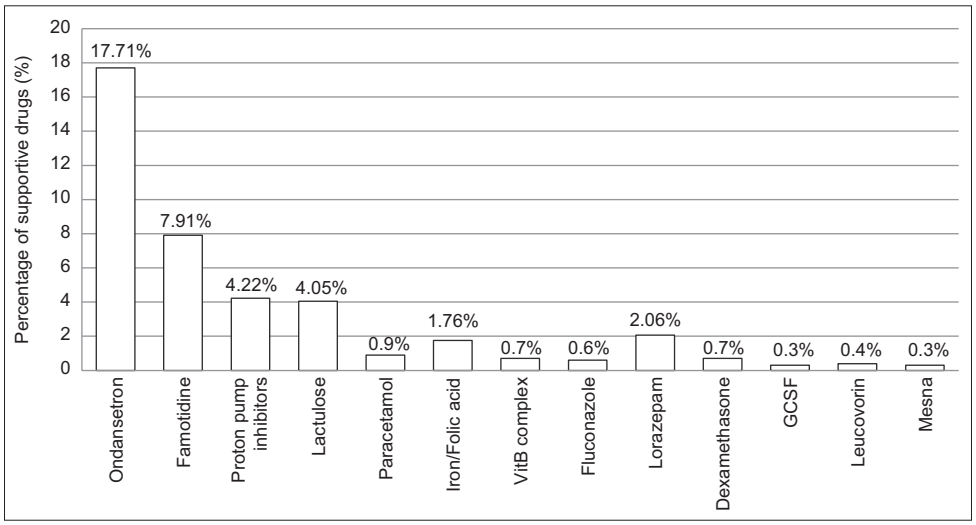

Fig. 4: Distribution of adjunct drugs used in the patients. Total 1263 adjunct drugs were encountered in the 618 prescriptions

most common (202 cases) followed by allergic rash with pruritus (176 cases). Sixteen patients complained of rash without pruritus. Hematological adverse reactions were third most common with 153 cases total with anemia being most common (75 cases) followed by pancytopenia (67 cases). Apart from these, neurological ADRs were also encountered (65 cases).

As for the causality assessment, we found as per Naranjo's algorithm 22.14% (120 cases) of cases were of probable category, whereas 73.24% (397 cases) were of possible category. Among the rest, 3.32% (18 cases) of reactions were definitely caused by the related drug and 1.2% (seven cases) was of doubtful category. Most commonly suspected drug was cisplatin (18.2%) followed by 5 FU (16.5%). Based on Hartwig's severity scale, 96.12% of the ADRs (521 cases) were mild and reversible and 2.8% were of moderate category. We encountered six severe adverse effects (SAE) that required or prolonged admission in the patients.

DISCUSSION

The incidence of cancer in our country is on the rise. Apart from being a severe psychological blow to the family, it also brings huge treatment cost, adverse reactions associated with chemotherapy drugs, and all these further add to the assault on the already injured household economy.

In our study, we have found people from age group 21–60 years being most affected that those are the major earning age groups. A study conducted by Sharma *et al.* [11] also corroborates with this finding. In another study, Dave *et al.* [12] found a slightly more predilection for older age group than what we found in our study. In our study, we found females affected by malignancy more than males which again are corroborated by study done by Sharma *et al.* Another study done by Sneha *et al.* [13] also supports this finding. A study by Siddiqua *et al.* [14] disagrees with this finding, where they found more male preponderance in malignancy in their study. As for the type of cancer, we found breast cancer being the most common followed by carcinoma lung and carcinoma cervix. This finding is in somehow similar to a study conducted by Sunny *et al.* [15], where they found breast carcinoma to be the most common cancer, though gastrointestinal carcinomas were more common than carcinoma cervix or lung. In another study, Ali *et al.* [16] also found breast carcinoma to be the most common cancer in our country.

Total number of drugs prescribe in our study was 3008 in 618 encounters with 4.86 drugs per encounter on average. Although it may look like polypharmacy considering the clinical setting, it may be justified as by definition polypharmacy depends on the clinical setting. Here, apart from cytotoxic drugs, adjunct drugs add to the volume of prescription. We found that 1263 (2.04/prescription) adjunct or supportive drugs prescribed in respect to 1745 (2.82/prescription) cytotxic drugs. A study by Mugada *et al.* [17] found on average 8.16 drugs prescribed per encounter which is higher than we found in our setting. Matthew *et al.* [18] found 9.63 drugs per prescription in their set up.

Among the cytotoxic drugs, platinum compounds were most common used and cisplatin was the commonest among them. Taxanes were the second most common group followed by followed by 5 FU. Majority (56%) of patients had two anticancer drug combinations, where 25.2% of patients needed three or more cytotoxic drugs. Only 20% of patients underwent anticancer monotherapy. Mugada *et al.* [17] found 5 FU to be the most common drug prescribed followed by cisplatin which is in contrast to our finding. Dave *et al.* [12], in their study, found more tendencies toward utilizing three or more anticancer drug combination which is in disagreement with our finding, but they also found cisplatin and 5 FU among the most common anticancer drugs prescribed. Study by Siddiqua *et al.* [14] also found platinum compounds to be most utilized anticancer drugs. Platinum compounds were mostly used for lung and testicular cancers and 5 FU and cyclophosphamide were mostly used for breast carcinoma.

As for adjunct drugs used, we found Ondansetron to be the most common adjunct drug prescribed followed by famotidine reflecting the high frequency of gastrointestinal side effects in case of cancer chemotherapy. Sneha *et al.* [13], in a study of adjunct drug utilization pattern, also have found high utilization of Ondansetron and H2 blockers though the utilization of diclofenac as analgesic/anti-inflammatory was quite high compared to our study, where the major analgesic used was Paracetamol. Mugada *et al.* [17] also found common use of injection Diclofenac as analgesic. This may reflect less inclination toward analgesia in our set up which may be explored further in a different study. Antibiotic utilization was very controlled in our study. Where study by Mugada *et al.* [17] found, 54.8% encounters with antibiotic prescribed; we found that only 6.2 % of prescriptions contained an antibiotic in the first encounter. Although a majority of patients needed antibiotics in the later stages of treatment, still the low percentage of antibiotic prescribed in the first encounter is a welcome trend.

We found that out of 618 patients included in our study 542 experienced ADRs. Total number of adverse reactions was 1096, thus making it 1.77 per patient. The gastrointestinal tract was the most commonly affected followed by dermatological ADRs. Hematological adverse reactions were third most common followed by neurological ADRs. Our finding was similar to those of Poddar *et al.* [19] who also found gastrointestinal and dermatological adverse reactions to be the most common. Similar findings were also found by Sunny *et al.* [15]. Studies by Sharma *et al.* [11] found infection to be the most common adverse effect, whereas Prasad *et al.* [20] found a higher incidence of hematological adverse effects. Demographically females (62.5%) experienced more adverse effects than their male counterparts (37.5%) in our study. Similar findings were obtained by Sunny *et al.* [15] who found females (60.55% of total patients experiencing adverse effects) experiencing more adverse effects.

We found that as per Naranjo'sscale 22.14% of cases were of probable category, whereas 73.24% were of possible category. Most commonly suspected drug was cisplatin followed by 5 FU. This finding is complementary to those of Prasad *et al.* [20] who also find cisplatin to be the most common offending drug though with a higher percentage. Severity wise most of the ADRs were mild, whereas only six cases of SAE were reported.

CONCLUSIONS

Anticancer therapy is mostly done in combination with monotherapy being relatively rare in our set up. Apart from the anticancer drugs, a significant number of adjunct drugs are needed to counter the adverse reactions of chemotherapy. In our study, cisplatin was used in most patients followed by 5 FU. Adverse events were common and the most common adverse effect was nausea explaining the use of Ondansetron as the most commonly prescribed adjunct drug. The drug prescriptions were mostly rational and a high percentage of generic drugs were prescribed. Antibiotic usage was restricted and paracetamol was the most preferred analgesic.

The negative finding from our study included the fact that a significant number of patients lacked the correct knowledge regarding the correct dosage and schedule of the drugs and the dispensing time was also short. This may cause mistakes on the part of the patients or their relatives while taking the prescribed oral drugs at their homes. The study was limited by small sample size, and due to short time period, it was not possible to measure the long-term adverse effects. We plan to endeavor a study involving more number of patients over long time period to overcome this problem.

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AUTHORS' CONTRIBUTIONS

AM: Conceived the study, analyzed the results and prepared the manuscript. TG and SM: Collected data and helped in analysis and final preparation of manuscript.

CONFLICTS OF INTERESTS

None to declare.

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