Research Paper

Volume : 3 | Issue : 1 | January 2014 • ISSN No 2277 - 8179

# Pattern of Adverse Drug Reactions Due to Cancer Chemotherapy in Tertiary Care Teaching Hospital in Gujarat

Medical Science

**KEYWORDS :** Adverse drug reaction, Cancer, Chemotherapy

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## ABSTRACT

*Aim: To assess the pattern of adverse drug reactions in patients receiving cancer chemotherapy.*

*Methods: A prospective, observational study was carried out for duration of twelve months. Clinical and treatment data were collected from patients who underwent cancer chemotherapy during the study period. CDSCO forms were used to record the ADRs. Causality, severity and preventability were assessed by suitable scales.*

*Result: Total of 199 ADRs were noted among 105 patients. Out of them 57(54.29%) were males and 48(45.71%) were females. The most common SOC was gastrointestinal disorders (35.17%). Platinum (54.29%) and antimetabolites(48.71%) were most common drug classes responsible for ADRs. According to WHO causality assessment most of the ADRs were "possible" 78(39.19%). Hartwig and Siegel severity scale shows 53.26% ADRs were "moderate". Shumock and Thornton scale shows 171(85.93%) ADRs were "not preventable".*

*Conclusion: Early detection of drug toxicity helps to treat the patient and modify the doses or the drug regimen to minimize toxic effects.*

**INTRODUCTION:**

Adverse drug reactions (ADRs) constitute a major clinical problem in terms of human suffering and increase healthcare cost[1]. According to WHO an Adverse Drug Reaction (ADR) is defined as "a response to a drug which is noxious & unintended, which occurs at doses normally used in man for prophylaxis, diagnosis or therapy of disease or for modification of physiological function excluding failure to accomplish the intended purpose[2]. A study conducted in USA revealed that adverse drug events extended the hospital stay, increased the cost of hospitalization and nearly two fold increased risk of death[3].

The practice of cancer chemotherapy has changed dramatically as curative treatments have been identified for many previously fatal malignancies and it is employed as part of a multimodal approach to the treatment of many tumours[4]. Most of the adverse effects of cytotoxic drugs are due to effect on rapidly multiplying cells. Many cancers have a lower growth fraction than normal bone marrow, epithelial linings, reticuloendothelial system and gonads. These tissues are particularly affected in a dose depended manner by majority of drugs[5]. The most common side effect of chemotherapy administration is nausea, with or without vomiting. Other common adverse drug reactions (ADRs) are diarrhoea, alopecia, myelosuppression, mucositis, gonadal dysfunction, hyperuricemia, neuropathy, cardiomyopathy, haemorrhagic cystitis, impaired renal function, electrolyte imbalance etc.[6].

A study from south Indian tertiary care teaching hospital has demonstrated that among all ADRs antineoplastic agents were the most common class of drugs causing the ADRs i.e. 21.8%[7]. ADRs can be minimized by adjusting dose intensity of the drugs or by delaying the doses but the regimen and method of administration of some anticancer drugs may play role in development of toxicity [8].

The safety profile study of cancer chemotherapy is not carried out in our hospital till yet, so we decided to conduct this type of study.

**AIMS AND OBJECTIVES:**

**Primary objective:**

To assess the incidence of ADRs of cancer chemotherapeutic drugs.

**Secondary objective:**

1) To assess causality using the offending drugs.
2) To assess severity and preventability of reported ADRs.

**MATERIALS AND METHODS:**

A prospective, observational, epidemiological study was conducted for the study period of twelve months (July 01, 2010 to June 30 2011). The suspected ADR reporting forms prescribed by central drugs standard control organization (CDSCO) were used for collection of ADRs. ADRs were diagnosed by consulting physician and were treated accordingly. Permission from Institutional Ethics Committee was taken.

**Evaluation of data:**

Reported ADRs were analyzed with respect to patient's demographics, nature of the reactions, characteristics of the drugs involved and causality, severity and preventability assessment of the ADRs were done.

**Causality assessment** was done by using WHO causality scale[9] whereby the ADRs were classified into certain, probable, possible and unlikely to be drug induced depending upon the level of association.

**Preventability assessment -** ADRs were categorized into preventable or not preventable using the criteria of Schumock and Thornton[10]

**Severity assessment -** ADRs were classified into mild, moderate and severe reactions using the criteria developed by Hartwig et al[11].

Statistical analysis was done by using Microsoft excel and Graph pad prism.

## RESULTS

Out of 150 patients who were given cancer chemotherapy, 105 (70%) patients developed ADR. Total of 199 ADRs were reported among 105 patients, among them 57 (54.29%) were male and 48(45.71%) were female. The prevalence of ADRs was most common in the age group between 51-60 years 34(32.38%) followed by 41-50 years 22(20.95%) and 61-70 years 21(20%).

The most common type of cancer observed was lung cancer 24(22.86%) followed by breast cancer 19(18.1%) and cervical cancer 10(9.52%) (Figure1).

The suspected anticancer drug classes that cause ADRs are presented in (figure 2). The most common drug class was platinum 57(54.29%) followed by antimetabolites 50(48.71%) and taxanes 31(29.52%). Cisplatin was the most common individual drug responsible for ADR (45%).

Type of treatment given to the cancer patient was classified into three groups. Patients were given either chemotherapy alone (49%) or chemotherapy and radiotherapy (43%) or radiotherapy alone (8%).

Type of chemotherapy given to the cancer patients divided into two classes according to chemotherapy given before surgery i.e. neoadjuvant chemotherapy in (54%), or after surgery i.e. adjuvant chemotherapy in (46%).

The most commonly affected SOC (System Organ Classification) was gastrointestinal disorders (35.17%), followed by blood and lymphatic system disorder (26.63%) **(Table 1)**.

According to WHO causality assessment scale, most of the ADRs were "possible" 78(39.19%) followed by "certain" 66(33.17%) and probable 55(27.64%). As per Hartwig et al severity scale most of the ADRs were moderate 106(53.26%) followed by mild 62(31.16%) and severe 31(15.58%). As per Schumock and Thornton preventability scale majority of ADRs 171(85.93%) were not preventable whereas 28(14.07%) were preventable.

To compensate these ADRs different classes of drugs were used like proton pump inhibitor, antiemetic, antibiotic, $H_2$-receptor blocker, filgrastim, haemetenics, blood transfusion, antispasmodic, antidiarrhoeal etc.

## DISCUSSION

In our study 105(70%) patients developed total 199 ADRs from the total of 150 patients who underwent cancer chemotherapy. This finding is in contrast to study conducted by Mallik S et al[12] which revealed ADRs in 42%. This difference may be due to different medications and different treatment guidelines followed for the treatment of cancer in different set up. In our study 57(54.29%) were male and 48(45.71%) were female this finding is in accordance with study conducted by Mallik S et al[12] (60% male and 40% female) where ADRs were more common in male as compared to female.

In present study the prevalence of ADRs mostly occurred in the age group between 51-60 years 34(32.38%). This finding is in consonance with study conducted by Malliik S et al[12] which showed mean age 57.8 years, while in Poddar et al study[13] prevalence of ADRs was most common in the age group between 41-50 years (26%). In our study the incidence of ADRs among elderly and older adults was significantly higher than other age groups. This may be due to the low metabolizing capacity and reduced excretory functions leading to accumulation of drugs in the body and thus increasing the risk of ADRs[14]. As a result extra precautions should be taken while using chemotherapy in the elderly population.

In our study patients were mostly affected by lung cancer 24(22.86%), breast cancer 19(18.1%) and cervical cancer 10(9.52%) whereas in Poddar et al study[13] patients were mostly affected by breast cancer (20%), leukemia (16%) and cervical cancer (14%). This difference may be due to different group of patients (Age, Gender, Region etc) attending the hospital for the treatment.

The most common anticancer drugs that caused ADRs were platinum 57(54.29%), antimetabolites 50(48.71%) and taxanes 31(29.52%) in current study as compared to antimetabolites (40%), alkylating agents (40%) and antibiotics (20%) in Poddar et al study[13]. The difference observed may be due to different diagnosis of patients in the studies. Cisplatin was the most common individual drug responsible for ADR (45%). This finding is similar to study conducted by Malik et al[12].

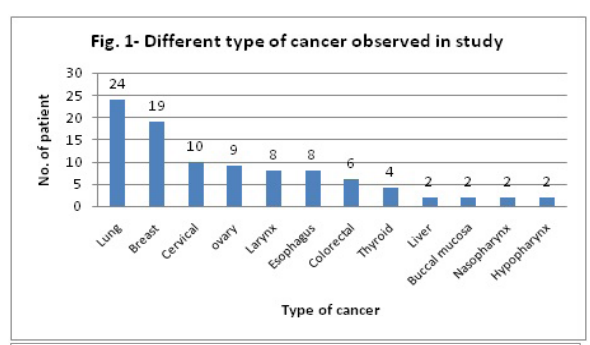
Gastrointestinal Disorders was the most common affected SOC in our study, and vomiting (42%) being the most common individual reaction. This finding is similar to study conducted by Poddar et al[13], Lao et al[15] and Stewart DJ[16].

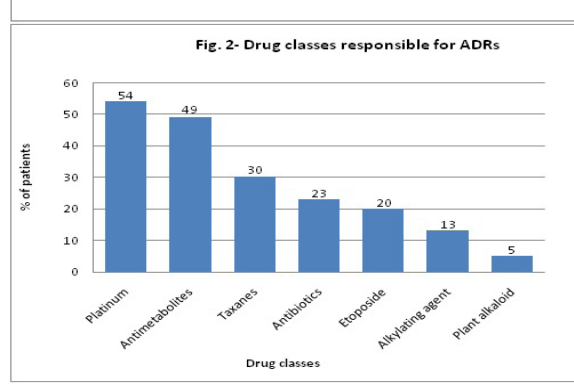
According to WHO causality assessment scale most of the ADRs belonged to category "possible" (39%), followed by "certain" (33%) and "probable" (28%), whereas in Poddar et al study[13] most common ADRs were probable (24%) followed by certain (10%). More ADRs belonged possible category due to use of concomitant radiotherapy along with chemotherapy (43%) in our study.

The use of newer antiemetics agents e.g. ondansetron, aprepitant were used to treat vomiting. However, they have failed to prevent this completely. Neutropenia require sargramostim (Granulocyte-Macrophage Colony-Stimulating factor) or filgrastim (Granulocyte- Colony-Stimulating factor). Thrombocytopenia require oprelvekin (Recombinant human IL-11), or platelet transfusion while anaemia due to chemotherapy can be managed by erythropoietin, haematinics and blood transfusion[17]. Similar pattern of management of ADRs were observed in our study.

## CONCLUSION

The incidence of ADRs (70%) with chemotherapeutic drugs is higher as it has a narrow therapeutic index. ADRs can be minimized by early detection of drug toxicity, modifying the doses or the drug regimen implicating adverse effect. This study provides baseline characteristic of ADRs due to cancer chemotherapy in our institute. Studies covering more patients from different regions are needed to rectify the findings of this study.



Volume : 3 | Issue : 1 | January 2014 • ISSN No 2277 - 8179

**Table: 1: Classification according to system organ class (SOC) and preferred terms (PT) falling under respective SOC using MedDRA 14.0 version English.**

| SOC | Number of ADR reports (%) (n=199) | PT | Number of ADR reports (%) |
|---|---|---|---|
| Gastrointestinal Disorders. | 70(35.17%) | Vomiting | 44(22.11%) |
| | | Stomatitis | 14(7.03%) |
| | | Diarrhoea | 12(6.03%) |
| Blood and Lymphatic system disorders | 53(26.63%) | Bone marrow failure | 38(19.09%) |
| | | Thrombocytopenia | 8(4.02%) |
| | | Anaemia | 7(3.51%) |
| Skin and subcutaneous tissue disorders | 46(23.11%) | Alopecia | 41(20.60%) |
| | | Rash Maculopapular | 3 (1.5%) |
| | | Ecchymosis | 2 (1.00%) |
| Hepatobilliary disorders. | 14(7.03%) | Hepatic function abnormal | 14(7.03%) |
| Renal and urinary tract investigations and urinanalyses | 12(6.03%) | Renal function test abnormal | 12(6.03%) |

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