

Adverse Effects of Anticancer Drugs in A Tertiary Care Hospital in South India

Alapati Yedukondala Rao^{2*}, Naresh Yadav Rasala, Raj Kumar Mandarapu, Bavith Pakeerupalli, Goverdhan Puchchakayala¹

¹Department of Clinical Pharmacy, Vaagdevi College of Pharmacy, Ramnagar, Hanamkonda, Warangal – 506002, Telangana, India.

²Department of Oncology, Kakatiya Medical College, MGM Hospital, Warangal – 506002, Telangana, India.

Abstract

Objective: To study the occurrence and management of adverse effects associated with the use of anticancer drugs in a tertiary care hospital in south India.

Methods: It was a Retrospective, descriptive study. Patients receiving chemotherapy were interviewed for information on type of adverse effects and other pertinent information like demographics, diagnosis, treatment, drugs used to manage the adverse effects were collected from the patients. The data was categorized based on type of cancers, adverse effects and agents used to manage the adverse effects.

Results: Out of the 289 patients included in the study 102 patients were considered of them 78(76.47%) females and 24(23.53%) males, married 84(82.25%) and unmarried 16(15.69%), current smokers 16(15.68%), ex-smokers 14(13.73%), non-smokers 72(70.58%). The common types of cancer diagnosed were oropharyngeal 8(7.84%), colon carcinoma 4(3.92%), stomach carcinoma 14(13.73%), breast cancer 76(74.51%).

Conclusion: Study revealed that all patients receiving cytotoxic drugs suffer one or more AEs. The prevalence of AEs was considerable high inspite of the use of existing premedications. Attempts to minimize the AEs associated with the anticancer drugs should be focused on increasing awareness through educational intervention and development of preventive measures for improved quality of life.

Keywords: Adverse effects, Premedications, Educational intervention, Preventive measures

I. Introduction

Adverse Drug Reaction (ADR) is defined as the response to a medicinal product which is noxious and unintended and which occurs at doses normally used in man for prophylaxis, diagnosis or therapy of disease or for the modification of physiological function^[1]. The science dealing with detecting, assessing and preventing ADRs has been termed "Pharmacovigilance"^[4]. As per the World Health Organisation (WHO), Pharmacovigilance (PV) is defined as the science and activities relating to the detection, assessment, understanding and prevention of adverse drug reactions or any drug-related problems^[1]. Toxic effects of drugs are a major drawback in providing healthcare to patients at a broad range. Toxicity of the drug affects the condition of the patient and also the economic status of the healthcare system^[5]. New pharmaceutical products are evolving in the market at a rapid pace to understand about the drug and to know the safety profile of the drugs and to remove the harmful drugs from the market, Pharmacovigilance program was introduced by the WHO globally^[6].

The National Pharmacovigilance program in India was started in 2010 with objectives of monitoring the safety of the drugs and providing adverse drug reaction database for the Indian population so as to minimize the unwanted consequences caused by the drugs. Pharmacovigilance program mainly focuses on the aspects like early detection of adverse reactions, detection of increase in frequency of known adverse reactions, identification of risk factors and promulgation of information. Pharmacovigilance acts as an early warning for the identification of adverse drug reactions. New processes, both at a regulatory and a scientific level are being developed with an aim of strengthening pharmacovigilance. On a regulatory level, these include conditional approval and risk management plans; on a scientific level, transparency and increased patient involvement are two important elements^[7]. The success of the scheme is dependent upon the vigilance of health care professionals. Scarcity of studies relating to drug safety monitoring in India led us to undertake this study where we tried to evaluate the pattern of ADRs occurring in cancer patients treated with chemotherapy in a tertiary care hospital in South India^[8].

Cancer chemotherapeutic drugs like Cyclophosphamide, 5-fluorouracil, Tamoxifen, Daunorubicin are potent drugs with a high degree of drug toxicity. However the documentation of ADRs to the Pharmacovigilance centre from our hospital was minimal. The reason for poor documentation of ADRs was not clear it might be due to underreporting of ADRs or effective preventive measures being adopted for the patients

receiving chemotherapy. Our study was done on these four drugs to evaluate the adverse drug reaction profile of these drugs as they are most commonly prescribed^[9]. This study was designed to prospectively monitor and analyze the pattern occurrence of ADRs. Our knowledge of adverse drug reactions can be increased by various means including spontaneous reporting, intensive reporting and database studies^[10].

II. Materials And Methods

This is a retrospective, descriptive, case study, this was conducted on patients admitted to medical oncology ward of tertiary hospital after obtaining the approval of the institutional ethics committee. Of 289 patients who received chemotherapy during the study period of 6months, from July to November 31 2015. 102 serial cases developing ADRs were directly collected from the patients, patients of both sexes and all ages diagnosed with cancer and treated with chemotherapy for the same developing one ADR during or after the treatment period were included in the study. Patients who developed ADR due to fresh or blood products infusion, or due to intentional or accidental poisoning and those with a history of drug abuse and intoxication were excluded from the study.

The demographic details of the patients were recorded. Details of the medications prescribed were duly noted. Details regarding occurrence and nature of ADR, suspected drug and outcome were carefully recorded. The severity of repeated reactions was assessed for causality using both WHO causality assessment scale and naranjo scale. The predictability and preventability of the recorded and reported ADRs were assessed using developed criteria for determining predictability of an ADR and modified Schumock and Thornton scales respectively.

The WHO causality assessment scale determines the casual relationship of a suspected drug to the ADR in question and causality is categorized into “certain”, “probable”, “possible”. “Unlikely”, “Conditional/unclassified” and “unassessable/unclassifiable”. Naranjo’s algorithm has 10 objective questions with three options for answers giving scoring 1/0/0/-1/2 which are recorded as yes , no or don’t know. Scores are given accordingly and the causality of the drug can be classified as “definite”, “probable” and “unlikely”. The modified Hartwig and Siegel scale classifies severity of ADR as “mild”, “moderate” or “severe” with various levels, depending on a number of factors like the requirement for change in treatment, duration of hospital stay and the disability produced by the ADR. The developed criteria for determining predictability of an ADR categorizes ADR as “predictable” or “not predictable” based on the incidence rate of reported ADR and history of allergy or previous reaction to the drug. The modified Schumosk and Thornton scale determines the preventability of an ADR and classifies them as “definitely preventable”, “probably preventable” and “not preventable”. The data collected was analyzed with the help of GRAPH PAD PRISM software version 5.0.

Study design

It is a hospital based prospective observational study. The patients will be followed up for a period of one month after they had received the cancer chemotherapeutic drugs.

Inclusion and exclusion criteria

Among the patients receiving chemotherapy, those who developed at least one ADR, were included in the study. The patients who did not show any ADR except alopecia were excluded from the study

Statistical analysis

After collection of data, it will be double entered in Microsoft Excel sheet and validated. One clean datasheet was generated and copied into SPSS (version 16.0). Then the analysis will be done in SPSS (version 16.0).

III. Results

Out of the 289 patients included in the study 102 patients were considered of them 78(76.47%) females and 24(23.53%) males, married 84(82.25%) and unmarried 16(15.69%), current smokers 16(15.68%), ex-smokers 14(13.73%), non-smokers 72(70.58%). The common types of cancer diagnosed were oropharyngeal 8(7.84%), colon carcinoma 4(3.92%), stomach carcinoma 14(13.73%), breast cancer 76(74.51%).

Table 1. Gender distribution among study population.

Male		Female	
No. of cases	Percentage	No. of cases	Percentage
24	23.53%	78	76.47%

Fig 1. Pie diagram showing gender distribution among study population

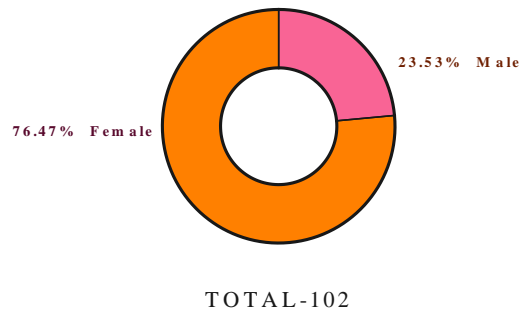


Fig 1. Pie diagram showing gender distribution among study population



Fig 2. Pie diagram showing Subjects who underwent chemotherapy among study population

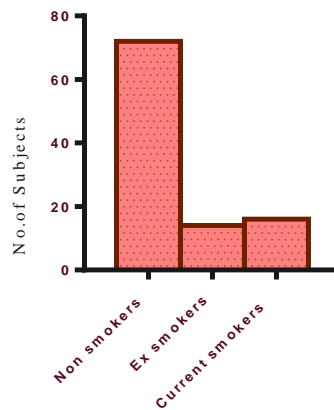


Fig 3. Pie diagram showing Data of Smokers in study population

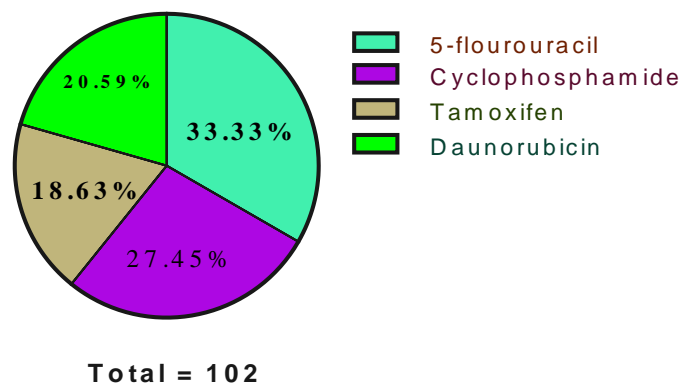


Fig 4. Pie diagram showing Percentage of drugs prescribed in study population

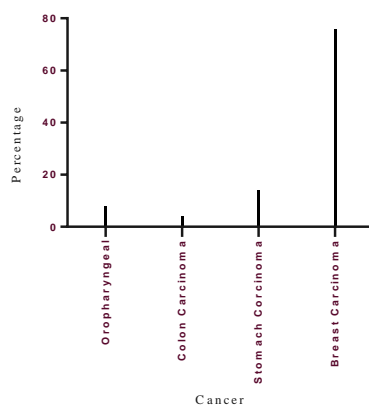


Fig 5. Pie diagram showing Types of cancers in study population

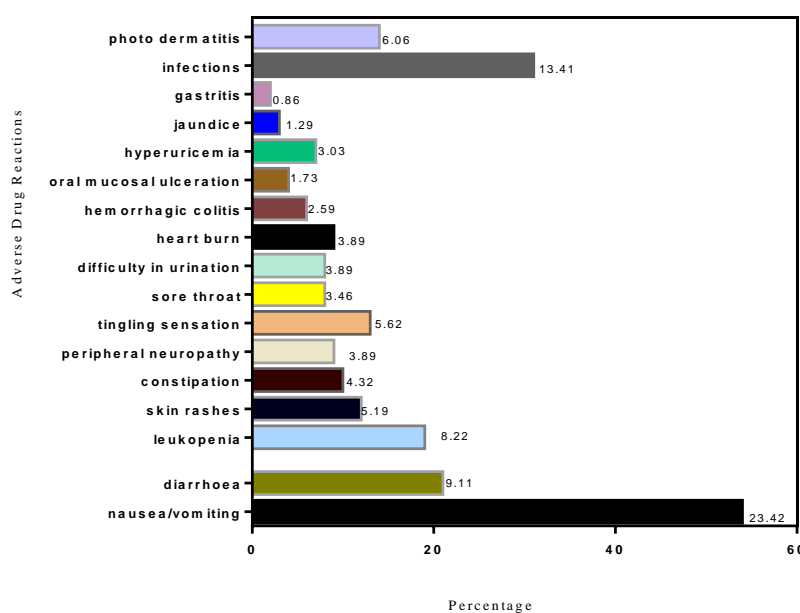


Fig 6. Pie diagram showing Adverse Drug Reactions due to Chemotherapy

Adverse Drug Reaction	Number of drug reactions					
	WHO Causality scale			Naranjo's scale		
	Possible	Probable	Total	Possible	Probable	Total
Nausea/vomiting	54	0	54	54	0	54
Diarrhoea	21	0	21	0	21	21
Infections	2	29	31	0	31	31
Leucopenia	0	19	19	0	19	19
Skin rashes	4	8	12	0	12	12
Constipation	0	10	10	4	6	10
Tingling sensation	13	0	13	12	1	13
Sore throat	2	6	8	0	8	8
Peripheral neuropathy	0	9	9	0	9	9
Difficulty in urination	0	9	9	4	5	9
Haemorrhagic colitis	2	4	6	0	0	6
Oral mucosal ulceration	4	0	4	4	0	4
Heart burn	0	9	9	0	9	9
Jaundice	0	3	3	0	3	3
Gastritis	2	0	2	2	0	2
Hyperuricemia	7	0	7	7	0	7
Photo dermatitis	0	14	14	3	11	14
Total	111	120	231	111	120	231

IV. Discussion

ADRs significantly affect the quality of life, increase hospitalizations and prolong hospital stay increase mortality. Since the anticancer drugs have a lot of adverse drug reactions to document these adverse drug reactions a noble and ethical practice needs accurate documentation and reporting of ADRs^[2]. This documentation serves as a crucial element in explaining the safety and efficacy profile of the drug which helps in decreasing unwanted occurrences of the drug. The current pharmacovigilance study screened suspected ADRs in patients in various malignancies admitted into oncology department. The increased incidence of ADRs in females may be attributed to the alteration occurring in the pharmacokinetics of the drugs due to hormonal changes during different stages of life, like puberty and pregnancy^[3]. Most of the ADRs were reported between the groups 45-55(38%), this is due to decrease metabolic functions and excretory functions leading to accumulation of drugs in the body and thus increasing risk of ADRs. Majority of these cases were non-smokers as reported by Sharma *et al.* Most commonly diagnosed cancers are breast carcinoma (74.51%), stomach carcinoma (13.73%), oropharyngeal (7.84%) and colon carcinoma (3.92%). Commonest ADRs Nausea and vomiting (23.42%) and infections (13.41%) as reported by Sharma *et al.* Cancer chemotherapy damages rapidly dividing cells of bone marrow resulting in myelosuppression thus affecting the white blood cells, platelets and red blood cells. This myelosuppression leads to a lowering of immunity and thus patients on cancer chemotherapy are at a high risk for developing various infections^[4,5].

In this study, most of the reactions showed a similar causality assessment by both WHO causality assessment scale and Naranjo's algorithm except for diarrhoea were assessed as "possible" with lower level of causality by WHO scale, were judged as "probable" with higher level of causality by Naranjo's algorithm. There were no "certain" reactions as re-challenge was not attempted in any of the subjects. The grade of causality remained low due to a number of co-administered drugs^[4].

V. Conclusion

Cancer chemotherapeutic agents have a very high risk of adverse drug reactions where the ADRs should be monitored. Pharmacovigilance offers a great deal in minimizing the ADRs by modifying the dose of the drugs and reduce the economic burden to the patient and to the society. There is a great need in setting up an effective ADR monitoring system in order to increase the quality of the life of the patient.

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