Academic Sciences

International Journal of Pharmacy and Pharmaceutical Sciences

ISSN- 0975-1491 Vol 6, Suppl 2, 2014

Research Article

A STUDY ON THE ADVERSE EFFECTS OF ANTICANCER DRUGS IN AN ONCOLOGY CENTER OF A TERTIARY CARE HOSPITAL

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Received: 12 Dec 2013, Revised and Accepted: 10 Feb 2014

ABSTRACT

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

Methods: It was a single centered, observational study. Patients receiving chemotherapy were interviewed for information on type of adverse effects and the other pertinent information like demographics, diagnosis, treatment, drugs used to manage the adverse effects were collected from the patient's medical records. The data was categorized based on type of cancers, adverse effects and agents used to manage the adverse effects.

Results: Out of the total 130 cases evaluated, 60 (46.2%) were males and 70 (53.8%) were females. The most prevalent cancer among females was found to be breast (40%) and cervical (11.4%) whereas lung (10%) and urinary bladder (8.3%) were common among males. Nausea (48.5%), vomiting (31.5%), decreased appetite (39.2%), alopecia (37.7%), anaemia (35.4%), nail discoloration (30%) were the most frequently reported adverse effects. The premedications commonly used were Ondansetron, Dexamethasone, Aprepitant and proton pump inhibitors individually or in combination.

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

INTRODUCTION

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[1][2], particularly smoking, in economically developing countries.

Different modalities for treatment of cancer includes radiation, surgery, chemotherapy, hormonal therapy, immunotherapy, biologic therapy and cryosurgery[3],[4],[5].

Chemotherapeutic drugs have a narrow therapeutic index and the dosage needed to achieve a therapeutic response usually proves toxic to the body's rapidly proliferating cells. The normal tissues adversely affected by these drugs are those which are rapidly dividing: the bone marrow, gastrointestinal tract and hair follicles. Some agents have other organ specific toxicities. Additionally, some drugs are associated with immediate adverse reactions which are a result of their biochemical nature rather than their action against tumours.Use of cancer chemotherapeutic drugs is associated with several adverse effects (AE) [7] ranging from mild nausea to fatal myelosuppression. During the last decade it has been demonstrated by a number of studies that medicine induced morbidity and mortality is one of the major public health problems[6].

It is well recognised that chemotherapeutic agents are associated with severe adverse effects leading to economic burden and decreased quality of life. There is no extensive published data regarding the adverse effects of anticancer agents in Indian population. The current study was conceived to monitor suspected AEs with anticancer drugs, a therapeutic category prone to AEs, in a focused manner and contribute to the overall knowledge base regarding AEs in the country. The objective of the current study was to study the prevalence of adverse effects associated with the use of anti cancer drugs in a South Indian hospital and their management.

MATERIALS AND METHODS

A prospective, observational, non-interventional study conducted at the Oncology Department, Apollo Hospitals, Jubilee Hills, Hyderabad for period of 6 months after seeking the approval from the ethics committee (SVCP/2012/02). All patient related information was collected as per case record form. Patients of both genders admitted in the cancer hospital and those who were willing to give informed consent were included for the study whereas patients in intensive care units, critical care units and other non selected departments and those with previous history of any disorder or toxicity taking any other drug besides anticancer drug were excluded from the study.

A total of 130 patients receiving chemotherapy were interviewed for information on type of adverse effects and the other pertinent information like demographics, diagnosis, treatment, drugs used to manage the adverse effects were collected from the patient's medical records. The data was categorized based on various parameters. The observed adverse effects were classified into different organ systems and compared with the published literature[8],[9],[10],[11],[12] and package inserts.

RESULTS

Demographics

Among the 130 patients, 60 (46.2%) males and 70 (53.8%) females had suffered from ADRs after receiving cancer chemotherapy. Further classification based on the age and gender revealed that maximum number in females was in the age 41-60 years whereas the highest number in males was seen in >60 years group.

Clinical Diagnosis of the patients

The analysis of our study data revealed that the cancer with highest prevalence as breast (22.3%) followed by esophageal (7.69%), nasopharyngeal (6.92%) and cervical (6.15%). Sub classification based on the gender showed, breast (40%), cervical (11.4%), ovarian (8.6%), and nasopharyngeal (7.1%) as the most the prevalent types in females whereas those in males were lung (10%), urinary bladder (8.3%) and NHL (8.3%) **(Table: 1)**

Further, the most common type of cancer in the age group ≤18 years was ALL (36.36%), 19-40 yrs was nasopharyngeal (17.39%), 40-60 yrs and >60 yrs was breast (36.2% and 13.16% respectively).

Table 1: Types of cancer observed

Type of cancer	No. of females (%)	No. of males (%)
Nasopharyngeal	5 (7.1%)	4 (6.66%)
Colon	3 (4.3%)	3 (5%)
Rectal	3 (4.3%)	2 (3.33%)
AML	2 (2.9%)	4 (6.66%)
Urinary bladder	1 (1.4%)	5 (8.3%)
Non Hodgkin's lymphoma	1 (1.4%)	5 (8.3%)
Breast	28 (40%)	-
Cervical	8 (11.4%)	-
Ovarian	6 (8.6%)	-
Lung	-	6 (10%)
Oesophageal	1 (1.4%)	3 (5%)
Others	11 (15.7%)	28 (46.6%)

Further analysis revealed that the breast cancer had the highest prevalence in females of the age groups 19-40, 41-60 and >60 yrs (23.07%, 48.78% and 33.33% respectively).

Among males, Lung (17.39%) was highest among the age group >60 years. However, ALL (40%) was common among in population ≤18 years.

Chemotherapeutic agents

The commonly prescribed chemotherapeutic agents in our setting were Cisplatin (25.4%), Adriamycin (19.2%), 5- Fluorouracil (18.5%), Cyclophosphamide (18.5%), Paclitaxel (12.3%), Carboplatin (11.5%), and Cytarabine (7.7%).

The most frequent regimens were FAC (5- Fluorouracil + Adriamycin + Cyclophosphamide) accounting for 7.69% of the total prescriptions and AC (Adriamycin + Cyclophosphamide) accounting for 4.61%

Adverse effects

The present study showed that in both males and females, the most affected organ system was GIT (34%, 38%) followed by skin (15%), musculoskeletal (12%, 14%), Heme (10% and 9%) and nervous system (10% and 8%).

The detailed distribution of adverse effects in males and females based on the organ system is depicted in table 2

Table 2: Distribution of Adverse effects based on organ systems

Organ system	Adverse effects (339)	Males (60)	Females (70)
	Nausea	24 (40%)	39(55.7%)
GIT	Vomiting	19 (31.6%)	22 (31.4%)
	Diarrhea	7 (11.6%)	16 (22.8%)
	Constipation	8 (13.3%)	12 (17.1%)
	Abdominal Pain	10 (16.6%)	13 (18.5%)
	Decreased appetite	22 (36.6%)	29 (41.4%)
	Others	25 (41.6%)	40 (57.1%)
	Neutropenia	4 (6.6%)	5 (7.1%)
Heme and lymphatic	Anemia	20 (33.3%)	26 (37.1%)
	Thrombocytopenia	4(6.6%)	8 (11.4%)
	Leukopenia	3(5%)	2(2.8%)
	Bone marrow depression	5 (8.3%)	-
Metabolism and nutritional disorders		7(11.6%)	7(10%)
	Body aches	21 (35 %)	39 (55.7%)
Musculo skeletal and connective	Muscle cramps	3 (5%)	4 (5.7%)
tissue disorders	Muscular weakness	16 (26.6%)	17 (24.2%)
	Weight loss	5 (8.3%)	4 (5.7%)
Nervous disorders		35 (58.3%)	38 (54.2%)
Renal and urinary disorders		10 (16.6%)	13 (18.6%)
	Alopecia	18 (30%)	31 (44.2%)
Skin and subcutaneous tissue	Rash	7 (11.6%)	4 (5.7%)
disorders	Nail discoloration	15 (25%)	24 (34.2%)
	Skin peeling	2 (3.3%)	1 (1.4%)
	Erythema	2 (3.3%)	1 (1.4%)
	Hyper/hypo pigmentation	3 (5%)	3 (4.2%)
	Swollen face	3 (5%)	2 (2.8%)
	Sweating	3 (5%)	1 (1.4%)
	Fever	13 (21.6%)	13 (18.5%)
Infections	Chills	2 (3.3%)	1 (1.4%)
	Fungal infection	10 (16.6%)	6 (8.5%)
Eye disorders		6 (10%)	7 (10%)
Administration site disorders	Extravasation	2 (3.3%)	2 (2.8%)
	Irritation	-	4 (5.7%)
	Pain	3(5%)	4 (5.7%)
	Phlebitis	1 (1.6%)	1(1.4%)

Table 3: Premedications

Antiemetics	No. of prescriptions
Ondansetron 8mg	26
Ondansetron 16mg	54
Dexamethasone 8mg	60
Dexamethasone 16mg	34
Dexamethasone 20mg	7
Palonosetron 0.25mg	37
Aprepitant 125 mg	11

Our analysis showed that 13.6% were on single, 69.5% on two, 15.3% on three and 1.7% on four pre medications.

Ondansetron was used at doses of 8mg and 16mg, of which 8mg was most frequent in patients prescribed with single antiemetic accounting for 50% whereas the use of 16mg was higher in prescriptions containing more than one antiemetic. The dosage of

dexamethasone used in our setting was in the range of4mg - 20mg. Among these, 8mg was the most commonly used individually as well as in combination. Palonosetron 0.25mg was used only in a two drug combination accounting for 16.1% of the total prescriptions. The other antiemetic, aprepitant accounts for only small number of prescriptions of about 8.4%.

Apart from the antiemetics, the other premedications used were Pantoprazole 20mg & 40mg, Ranitidine 150mg and Rabeprazole 20mg. Of these Pantoprazole 40mg was the most frequent accounting for 81% of the total prescriptions.

DISCUSSION

In our study females accounted to more than half of the cases. In our study, it was observed that the populations in the age group 41-60 years were more prone to the development of cancer which is similar to the results obtained from the study conducted by Poddar et al.[13]

A study conducted by S. Mallik [14] on 25 patients treated with chemotherapeutic agents and described the patterns of AEs showed lung cancer (20%) as the most prevalent followed by stomach cancer (16%), breast (12%) and cervical (12%) which was slightly different from our observation.

The commonly prescribed chemotherapeutic agents in our setting were similar to the prescriptions in Kolkata as reported by Amartya De [15]

Nausea and vomiting are one of the most common adverse effects of cancer chemotherapy. A study by Amartya De [15] on 163 patients treated with various chemotherapeutic agents, described the pattern of AEs. Occurrence of nausea, vomiting, alopecia and skin rash had similar frequency in both studies. The frequency of Anorexia (25.4% Vs 1.69%) constipation (15.4% Vs 2.71%), fever (20% Vs 0.34%), headache (20.8% Vs 0.68%) and insomnia (10.8% Vs 0.68%) were much higher in our study. The severity of the adverse effects observed in our study was only mild to moderate requiring no change in the therapy.

The most affected organ systems in both the genders were GIT followed by skin, musculoskeletal, heme & lymphatic and nervous system. However, the study conducted by Guo HJ [17] had slightly different observations, with GIT being the most prominent followed by Heme[16], nervous system and skin.

The use of newer antiemetics agents has significantly decreased the incidence of nausea and vomiting though they have failed to prevent this completely. All the patients received antiemetics prior to the chemotherapy. Ondansetron, Palonosetron, dexamethasone and aprepitant individually or in combination were the commonly prescribed premedications in our setting.

The only high risk emetogenic drug used in our study was Cisplatin. The premedication most commonly prescribed for this drug was ondansetron 16mg and dexamethasone 8mg either individually or in combination. Cyclophosphamide, Carboplatin, Doxorubicin, Epirubicin, Oxaliplatin, Cytarabine and Ifosfamide were the drugs of moderate emetogenicity which have been managed with ondansetron 8mg & 16mg, dexamethasone 4mg, 8mg, 16mg, 20mg, Palonosetron 0.25mg and Aprepitant 125mg.

The overall adverse effects observed in both the genders were similar. However, the effects on GIT and musculoskeletal were higher in females which may be accounted to higher sensitivity in this gender to these effects.

When age group is taken into consideration then elderly patients encountered majority of the AEs. 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 AEs in elderly patients[18]. As a result extra precautions should be taken while using chemotherapy in the elderly population.

Comparison of observed adverse effects with package inserts

The adverse events identified in our study apart from those reported by the package insert for the specific drug include

Cisplatin: Stomach pain, Decreased appetite, Stool discoloration, Anorexia, Weakness and Skin rash

Paclitaxel: Abdominal pain, Leg pain and Nail discoloration

5- Fluorouracil: Abdominal pain, Muscular weakness and Alopecia

Cytarabine: Decreased appetite, **Gemcitabine:** Muscular weakness, **Adriamycin:** Diarrhoea

Anemia is viewed as a relatively common condition in patients with cancer especially those with solid tumours, lymphomas and receiving myelosuppressive chemotherapy. Treatment for CIA is initiated when the haemoglobin level falls below 12mg/dl with oral or IV iron supplements. Blood transfusions are opted in severe cases. The commonly prescribed agents in our setting were ferrous sulphate, folic acid and Vitamin B12

Prophylactic measures such as good oral hygiene, avoidance of spicy, use of mild-flavoured toothpaste and saline-peroxide mouthwashes 3 or 4 times per day were instilled where appropriate for minimizing oral mucositis.

The major limitation of the study was small sample size and inability to distinguish between immediate and delayed adverse events due to difficulty in recall of the AE's by the patient.

CONCLUSION

The Adverse effects associated with the use of anticancer drugs were evaluated during a period of 6 months. The AE prevalence encountered suggest that practically all patients receiving cytotoxic drugs suffer one or more AEs.

Nausea, vomiting, decreased appetite, alopecia, anemia, nail discoloration and anorexia were the most frequently reported adverse effects. Comparison of the observed AEs with the published literature and package inserts did not some new adverse effects.

The prevalence of adverse effects was considerably high inspite of the use of existing premedications. Given the findings of the study, attempts to minimize the adverse effects associated with the anticancer drugs should be focused on increasing the awareness through educational intervention, implement appropriate use of premedications and non pharmacological treatment for improved quality of life.

ACKNOWLEDGEMENTS

We would like to express our thanks to Dr SVSS Prasad, Oncology, staff of Apollo Hospital, Principal and management of Sri Venkateshwara College of Pharmacy.

We are grateful to the most important brave people with cancer in our study for their co-operation.

Conflict of Interest: None

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