EUROPEAN JOURNAL OF BIOMEDICAL AND PHARMACEUTICAL SCIENCES

http://www.ejbps.com

ISSN 2349-8870
Volume: 6
Issue: 1
444-447
Year: 2019

ADVERSE DRUG REACTIONS DUE TO CANCER CHEMOTHERAPY IN A TERTIARY CARE TEACHING HOSPITAL.

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Article Received on 06/11/2018 **Article Revised on 27/11/2018** **Article Accepted on 17/12/2018**

ABSTRACT

Introduction: An adverse drug reaction (ADR) is defined by WHO as 'Any response to a drug which is noxious, unintended and occurs at doses used in man for prophylaxis, diagnosis or therapy'. ADRs linked with cancer chemotherapy deserve analysis on their severity and preventability. The result would generate awareness among health care professionals and avoid their recurrence. We have done a prospective observational study intended to analyze the pattern of ADRs to Anticancer agents in cancer patients of a tertiary care hospital. **Methods:** A total of 474 cancer patients were monitored for suspected ADRs during the course of chemotherapy from June 2015 to July 2017. Clinical events were recorded and analyzed with regard to the demographics and drug details of the patients. **Results:** The ADRs commonly encountered included nausea, vomiting, constipation, alopecia and hematological changes. Cisplatin, cyclophosphamide, paclitaxel and 5-FU were used for the treatment of commonly found cancers in this region affecting the lungs, esophagus and lymphomas. Naranjo's causality assessment showed 1.7% possible (score 4) and 98.3% probable (score 5–6). A total of 85.3% of ADRs were preventable reactions such as nausea, vomiting and constipation. **Conclusions:** This study stresses the role of active monitoring as an important tool for early detection, assessment and timely management of ADRs in patients undergoing cancer chemotherapy. The observed ADRs were preventable although ADRs such as hiccough, anemia, neutropenia and alopecia were not preventable.

KEYWORDS: adverse drug reactions, cancer chemotherapy, premedications.

INTRODUCTION

The World Health Organization (WHO) defines pharmacovigilance as the science and activities relating to the detection, assessment, understanding and prevention of adverse effects or any other medicine-related problem.[1] Adverse drug reactions are considered as an important cause of human suffering, hospitalization, increased health care costs and even death. Chemotherapy is employed as part of a multimodal approach to the treatment of many tumors and it has been revolutionized with the advent of newer drugs.[2]

Review of literature

The magnitude of adverse drug reactions (ADRs) endured by oncology patients is colossal making them almost synonymous with the treatment. Epidemiological research performed in the Australia shows 11% of ADRs in Australian Hospitals were associated with antineoplastic drugs and immunosuppressive drugs with antineoplastic drugs being the most common agents responsible for medication-related hospitalizations.[3, 4]

Justification for the study

The practice of cancer medicine has changed dramatically nowadays with treatment available for many previously fatal malignancies. Adjuvant chemotherapy has proven to extend life and prevent disease recurrence. Despite these therapeutic successes, many of the antineoplastic drugs possess narrow therapeutic index and a greater potential for causing adverse effects such as nausea/vomiting, neutropenia/anemia/ pancytopenia, alopecia, constipation/diarrhea, and fatigue/tiredness.[5] Therefore knowledge about the specific pattern of adverse drug reactions helps in better prescription writing, early

diagnosis of adverse drug reactions, of the drug to prevent morbidity and mortality.

AIMS AND OBJECTIVES

To study the clinical spectrum, causality, severity and outcome of cancer chemotherapy adverse drug reactions.

Study Design

Retrospective cross-sectional observational study.

Inclusion Criteria

Cancer chemotherapy adverse drug reactions collected in the CDSCO's ADR reporting form by the Adverse Drug reaction monitoring centre, Coimbatore Medical College and hospital, Coimbatore from June 2015 to July 2017 will be included. Oncology department of Coimbatore Medical College and hospital, Coimbatore will be included in this study, which has enormous potential of the adverse drug reactions.

Exclusion Criteria

Cancer chemotherapy adverse drug reactions collected in the CDSCO's ADR reporting form with incomplete history or difficulties in communication of adverse reactions will be excluded from the study.

Study period

3 months.

METHODOLOGY

Eligible patients with Cancer chemotherapy adverse drug reactions will be included

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Demographic details, medication details, details of CADR, causality, seriousness and outcome will be recorded from the ADR reporting form

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Data will be entered in excel sheet for statistical analysis

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Results will be discussed & Conclusion will be arrived.

Risks and Benefits

There is no extra risk involved in this study, because this study is an observational study to collect only data.

The study is beneficial as it provides the drugs causing adverse drug reaction and morphological pattern of CADR. It also gives the importance of strengthening pharmacovigilance center which requires early detection, evaluation and monitoring of ADR to reduce harm to the patient and to improve public health.

Outcome measures

This study analysis of ADRs associated with the cancer chemotherapy in a hospital setup gives an insight regarding the causality, severity and preventability of the identified ADRs. It may also create awareness among the treating physicians that can prevent further occurrence of similar ADRs in the same patient**.**

Statistical Analysis

Descriptive statistics will be used for data analysis and results will be expressed as percentages.

RESULTS

A total of 474 patients who were receiving cancer chemotherapy participated in our study. The mean age group of the study population was 52.71±10.14 years. In our study, patients who manifested with any type of ADRs were included and analyzed. The ADRs were seen more in male participants which accounted for 63.71% (n=302) than in female participants which accounted for 36.29% (n=172). Among the ADRs encountered, the most common were gastrointestinal adverse reactions such as break- through and delayed onset vomiting almost seen in all cases, in our study in 456 cases (96.20%), itching (n=16), rash (n=4) and fever (n=3). Thrombocytopenia (n=3) was the most common hematological reactions that were recorded. Apart from these reactions palpitation with chest pain was seen in 4 patients, while hand foot syndrome and pleural effusion was seen in a single case. Dermatological manifestation like discoloration of skin was seen in 5 patients. Malena with GI bleed was seen in two patients.

The commonly used drugs for chemotherapy in our patients was cisplatin which was used in 256 cases either single drug or in combination with cyclophosphamide, paclitaxel and 5-FU for the treatment of cancers common in this region such as those that affect the lungs, esophagus and lymphomas. Carboplatin, oxaliplatin, docetaxel and doxorubicin were the other drugs used for the treatment of cancers of the breast, cervix, ovary, uterus, stomach, rectum and colon; Etoposide, Adriamycin, Dacarbazine, geftinib and rituximab are also used in few cases.

Causality and severity assessment

The ADRs were analyzed for causality assessment with the Naranjo scale among which 1.7% were possible (score 4) and 98.3 % were probable (score 5–6) reactions in association with the suspected drugs. The assessment of the severity of adverse reactions by using the Hartwig scale showed that 87.4% were mild (level 1), 8.9% were moderate (level 3–4) and 3.8% were severe (level 5). Preventability was assessed by using the Modified Schumock and Thornton scale which showed that 85.3 % of reactions seen in our study were mostly preventable, while 14.7% were not preventable. High-risk emetogenic drugs used in our hospital were cisplatin and cyclophosphamide.

DISCUSSION

After the ADRs were collected and analyzed, we observed that the population belonging to the mean age group of 52.71±10.14 years were more prone to the development of ADRs during Anticancer treatment which can be compared with one study that was conducted in Bangladesh by Poddar et al.[6] The incidence of ADRs was greater in male patients in comparison with female patients in our study. However, studies from other parts of India and Bangladesh showed a higher preponderance of ADRs in cases affecting female patients as done by Sharma et al.[7] Nausea and vomiting in particular are the most common ADR's encountered in our study which can be explained from the premedication drugs most commonly prescribed along with these regimens were granisetron 3 mg, ranitidine 50 mg and dexamethasone 8 mg. Patients receiving moderate emetogenic drugs such as paclitaxel, carboplatin, doxorubicin and oxaliplatin were given premedications with ondansetron 16 mg, dexamethasone 4 mg and pantoprazole 40 mg. Higher incidence of lung cancer (n=65) seen in our setting as also reported from western and eastern parts of India as in study done by Goyale et al[8] and prasad et al.[9] Cisplatin, cyclophosphamide, paclitaxel and 5-FU containing regimens were commonly used and were found to be associated with most of the ADRs in our setting which is comparable with other study reports.[10]

The system that was most frequently affected by ADRs was the gastrointestinal tract (GIT), a feature which is similar to another study reported by Guo et al[11] and another study done by chopra et al.[12] Almost 96 percent of cases had nausea and vomiting, including breakthrough vomiting (within 24 h) and delayed onset vomiting cases, is reported in our setting which is significantly higher as compared with 31.5% and 48.1% that was reported in two other studies.[10,13] The incidence of this adverse reaction in our patients can be lowered or prevented by prompt premedication with antiemetic drugs such as ondansetron as well as to the judicious administration of ranitidine, pantoprazole. The most common mechanism of chemotherapy- induced nausea and vomiting is the activation of the chemoreceptor trigger zone (CTZ). The management plan in our setting for most of these reactions was the administration of a higher dose of ondansetron which is consistent with the findings of other studies where patients received higher doses of antiemetic drugs to treat chemo- therapy-induced nausea and vomiting.[6]

Drugs used in cancer chemotherapy can alter an individual's metabolism through changes in taste and this itself will lead to weight loss. Therefore, symptoms of anorexia and weakness seen in some of our patients were noteworthy in cancer therapy, as response to treatment diminishes with subsequent decrease in weight.[14]

We have seen from the present study that the drug regimen comprising paclitaxel and cyclophosphamide, administered especially for the treatment of lymphomas, was associated with hematological disorders particularly thrombocytopenia in our study. Another prospective study among the patients with non-Hodgkin's lymphoma treated with the same regimen had reported life-threatening neutropenia.[14] In contrast to our evaluation, two other reports suggested hematological disorders as the most common ADR.[7,15]

On analyzing the causality assessment of the ADRs by the Naranjo score, we found that 1.7% cases showed possible and 98.3 % showed probable association similar to study done by Khandelwal[16] who reported 100% of probable association while another study[8] reported 61% of probable scores using the same scale. The reason for this can be attributed to the observed occurrence of ADRs which were mostly vomiting and other gastrointestinal disturbances. Analyses of the severity of these adverse reactions using Hartwig's severity scale revealed that majority of the ADRs (83.4%) were mild followed by moderate (8.1%) and severe (3.8%), a finding which was comparable with the above two studies conducted in western and southern India. Assessment of the preventability by the Modified Schumock and Thornton scale showed that only 85.3% of the ADRs could have probably been prevented in patients who had symptoms of vomiting, general weakness where appropriate premedication was given and proper diet advice was ensured before the start of chemotherapy. All 474 reported ADR cases in our study were managed symptomatically and 467 cases among these patients had recovered fully with no further untoward reactions while rest of patients were recovering.

CONCLUSION

The exploration of ADRs related with the cancer chemotherapy in a tertiary care hospital setup gives an understanding about the causality, severity and preventability of the identified ADRs. It also create awareness among the treating physicians that can prevent further occurrence of similar ADRs in the same patient. Pharmacovigilance is of paramount importance to ensure safe and effective medications, more so in palliative health care services. Proper evaluation of ADRs helps in preventing their recurrence in subsequent chemotherapeutic cycles. Our study emphasized the common ADRs of anticancer drugs as well as their causality, severity and preventability. Hence a thorough surveillance will help in identifying and preventing preventable ADRs in future.

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