

Original Research Article

Chemotherapy-induced adverse drug reaction of antineoplastic drugs among oncology patients in a tertiary care teaching hospital

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ABSTRACT

Background: The main objectives of the study were to assess the pattern of adverse drug reactions (ADRs) associated with the use of antineoplastic drugs along with their causality and severity. The study also aims to analyse the different stages of cancer, cycles of chemotherapy and the quality of life of the patients.

Methods: This prospective, cross-sectional and descriptive study was conducted among 100 patients of either sex for 6 months from April 2023 to October 2023. This study included patients above the age of 18 years who were clinically diagnosed with cancer and prescribed at least one antineoplastic drug.

Results: Most of the cancer patients belonged to stage 2 and were undergoing the third cycle of chemotherapy. Most common ADRs were alopecia, anemia and anorexia. The study revealed that 79% of ADRs were possible and nearly 21% were probable in nature. After the severity assessment, it was found that all of the ADRs were mild (level 1). It was also identified that quality of life (QoL) decreases with advancing stages of cancer.

Conclusions: Cancer, along with therapeutic agents, can impair a patient's quality of life, prompting the development of effective management strategies. Assessing the severity and causation of ADRs can help determine the right supportive care agent to improve patients' general well-being.

Keywords: Stages of cancer, Chemotherapy cycle, Adverse drug reactions, Quality of life

INTRODUCTION

Staging of cancer aids in therapeutic decision-making and provides information on prognosis. The staging work-up is typically repeated after the treatment initiation to evaluate its efficacy. A staging work-up may include X-rays, CT scans, MRI, ultrasounds, bone-marrow biopsies, bone scans, lumbar puncture, and a variety of laboratory tests, including appropriate tumor markers. The most popular staging method for solid tumors is the TNM classification, where T = tumor, N = node, and M indicates metastases. Each letter is assigned a numerical value to represent the size or extent of disease.¹ To make the staging process simpler, the majority of malignancies are categorized

using a numerical system that includes stage I to IV according to the severity of the disease. Stage I usually indicates the presence of a localized tumour, stage II and stage III suggest cancer has spread locally and regionally, and stage IV indicates the presence of distant metastases.² A course of treatment usually includes 4 to 8 chemotherapy cycles. The interval between one round of therapy and the beginning of the following is known as a cycle. There will be a gap to allow the body to recover after each round of treatment.³ Chemotherapy regimens are highly complex and associated with intolerable adverse effects which are ubiquitous and can injure some normal cells during this process, like those in the blood, mouth, digestive system, hair follicles and so on.⁴ According to

the World Health Organisation (WHO), ADR can be defined as ‘A response to a drug, which is noxious and unintended, and which occurs at doses normally used in a man for prophylaxis, diagnosis, or therapy of disease or for modification of physiological function’.⁵ Therefore, ADRs associated with cancer chemotherapy should be documented to assess their severity and preventability in order to prevent their recurrence in further chemotherapeutic cycles, thereby enhancing the social, physical and emotional well-being of the patients. The study aimed to assess the pattern of adverse drug reactions associated with the use of antineoplastic drugs along with the assessment of their causality and severity in different stages and cycles of chemotherapy.

Quality of life is defined by the WHO as “an individual’s perception of their position in life in the context of the culture and value systems in which they live and concerning their goals, expectations, standards and concerns”.⁶ Despite its therapeutic benefits, chemotherapy is associated with the development of unfavourable adverse effects that negatively impact the QoL of the patients.⁷ It is one of the major concerns among cancer patients. The majority of them either have an average or below-average quality of life which are attributable to the symptoms associated with cancer and ADRs that occur with the use of anti-cancer drugs.⁷ Therefore it is necessary to prevent and manage these ADRs as much as possible. In the present therapeutic setting, many medications are available that can be used to prevent and treat the ADRs associated with the use of anti-cancer drugs. So proper utilization of these agents is necessary to improve the quality of life of the patients.

METHODS

A prospective cross sectional was conducted in SS Institute of Medical Science and Research Centre, Davangere including 100 cancer patients over 6 months from April 2023 to October 2023. The study was conducted after obtaining ethical approval from the Institutional Ethics Committee (BPC/IEC No.90/2022-23).

Inclusion criteria

The study included both male and female patients who were clinically diagnosed with cancer and were above 18 years of age, at least on one anticancer drug and those who have experienced adverse drug reactions.

Exclusion criteria

Pregnant and lactating women, patients who were not willing to participate in the study, and those with concurrent psychiatric illness and prescriptions that were not liable and had insufficient patient data.

The materials used

Naranjo causality assessment scale.^{8,9}

Modified Hart wig and Siegel scale.^{8,9}

Karnofsky Performance status scale.¹⁰

Detailed information was collected regarding the stages of cancer, chemotherapy cycles, and adverse drug reaction, and their severity and causality were assessed by using the Naranjo causality assessment scale and the Hart wig and Siegel scale. The quality of life of the patients was assessed using the Karnofsky performance scale.

Data collection

Data was collected from both in-patients and out-patients using a specially designed data collection form after receiving consent from them or their relatives. Patient’s demographic details, stage of cancer as well as chemotherapy cycle, anticancer treatment given, and ADRs identified were recorded. ADRs were analysed in terms of causality and severity together with the assessment of the quality of life of the patients.

Statistical analysis

Categorical data is represented in the form of frequency and percentage. Association between variables is assessed with Chi-Square Test and Fisher’s exact test if the cell values are small. Quantitative data was represented as Mean & Sd. Comparison will be done with independent t-test. A P value <0.05 is considered statistically significant. Data is analysed with IBM SPSS Version 28 for Windows.

RESULTS

A total of 100 cancer patients were included in the study, among which 32 were male and 68 were female. Majority of the patients belonged to the age group of 31-75 years. Within the study population, 14 different types of cancer were found, breast cancer 40%, followed by carcinoma of ovary 20% and carcinoma of colon 11%. Other types of cancer found among the patients were carcinoma of oesophagus, lungs, anus, cervix and so on. Patients diagnosed with cancer were examined to identify the stage of cancer and results showed that 27% patients belonged to stage 1, 48% had stage 2, stage 3 patients were about 16% and 9% patients belonged to stage 4. Majority of the patients were undergoing third cycle of chemotherapy followed by first and second cycle.

The antineoplastic agents prescribed among the study participants were cyclophosphamide, doxorubicin, 5 fluorouracil (5-FU), Paclitaxel, carboplatin, cisplatin, oxaliplatin, etoposide, pemetrexed, bleomycin and gemcitabine. ADRs were found in 76 patients out of the 100 participants and a total of 163 ADRs were recorded and analysed. Among the ADRs encountered, the most

common were alopecia 57%, anemia 42%, and anorexia 25%. Other ADRs observed were nail discoloration 10%, nausea 9%, vomiting 5%, and skin pigmentation 1% (Table 1).

Table 1: Adverse drug reactions in cancer patients.

Adverse drug reactions	No. of cases (n=100)	Percentage (%)
Alopecia	57	57
Anemia	42	42
Anorexia	25	25
Nail discoloration	10	10
Nausea	9	9
Vomiting	5	5
Diarrhea	5	5
Constipation	4	4
Menstrual irregularities	3	3
Skin rashes	1	1
Fatigue	1	1
Skin pigmentation	1	1

ADRs were found in 76 patients out of the 100 participants and a total of 163 ADRs were recorded and analyzed. Among the ADRs encountered, the most common were alopecia, anemia, and anorexia. Other ADRs observed were nail discoloration, nausea, vomiting, and skin pigmentation.

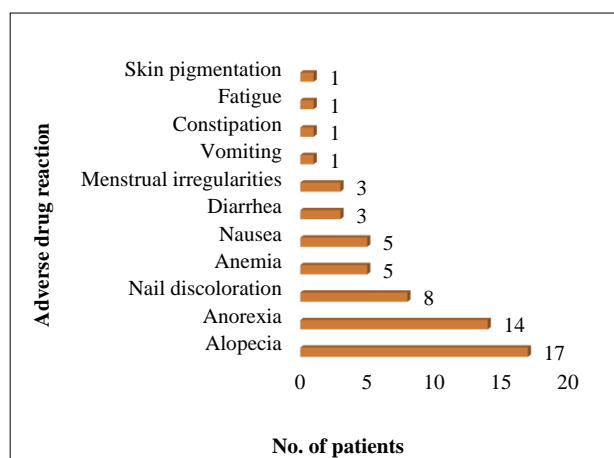


Figure 1: ADR associated with cyclophosphamide.

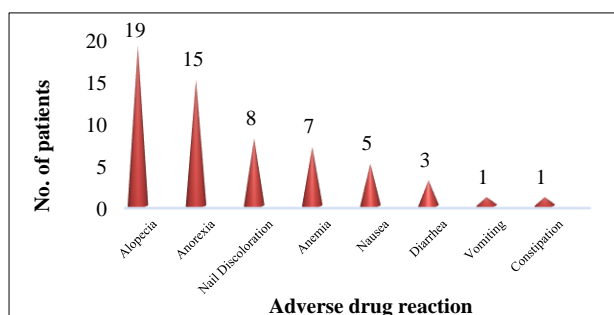


Figure 2: ADR associated with doxorubicin.

Doxorubicin lead to development of alopecia in 19 patients, followed by anorexia (15) and nail discoloration (8).

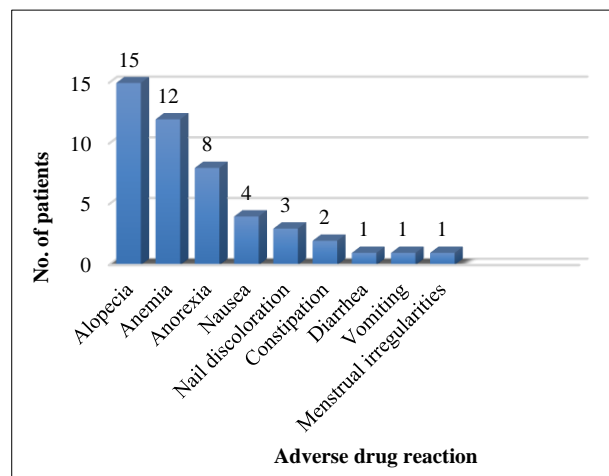


Figure 3: ADR associated with 5-FU.

5- Fluorouracil lead to development of alopecia in 15 patients, followed by anemia (12) and anorexia (8).

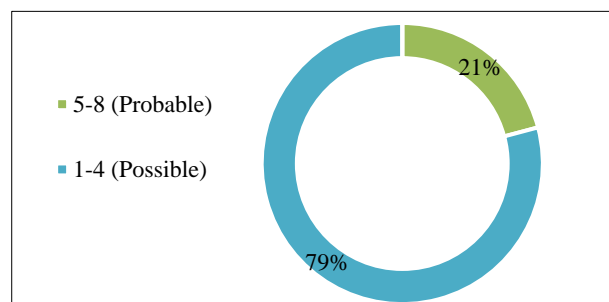


Figure 4: Naranjo's causality assessment.

The ADRs were analysed using Naranjo's Causality assessment scale and it was found that 79% of ADRs were possible in nature and nearly 21% of the ADRs were probable in nature.

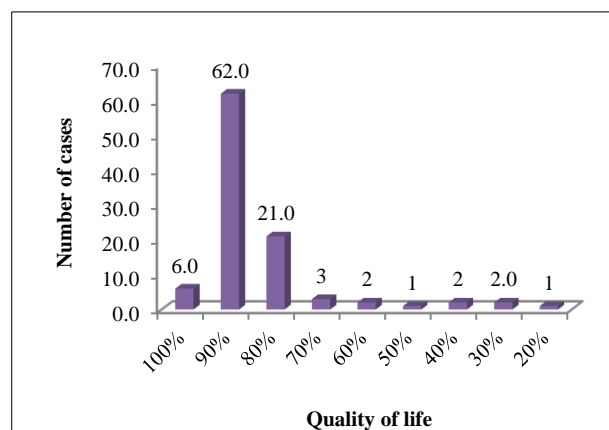


Figure 5: Patient distribution based on QoL.

A total of 100 cancer patients were included in the study. After the assessment of QoL with karnofsky performance status scale, 100% quality of life was found in 6 patients followed by 90% in 62 and 80% in 21 patients who are included in the study. Other participants had a QoL 70%

or below, that is 70% in 3 patients, 60% in 2 patients, 50% in 1 patient, 40% in 2 patients, 30% in 2 and 20% in 1 patient respectively due to different advance stages of cancer.

Table 2: Association between antineoplastic drugs and the resulting ADRs.

Anticancer drugs	ADRS	No. of patients	χ^2 value	P value
Cyclophosphamide	Anemia	5	25.34	p<0.001
	Alopecia	17	7.438	p<0.006
	Nail discolouration	8	6.986	p<0.008
Doxorubicin	Anemia	7	16.427	p<0.001
	Anorexia	15	5.556	p<0.018
	Nail discolouration	8	-	p<0.009
Carboplatin	Anemia	20	13.826	p<0.001
	Alopecia	21	4.853	p<0.028
	Anorexia	2	-	p<0.007
Paclitaxel	Vomiting	4	-	p<0.027
	Alopecia	24	8.861	p<0.002
Cisplatin	Vomiting	3	-	p<0.027
	Alopecia	13	4.379	p<0.027
Oxaliplatin	Anemia	10	5.787	p<0.016

A p value <0.05 is considered statistically significant

Cyclophosphamide lead to development of anemia in 17 patients, followed by anorexia in 4 and nail discoloration in 8 patients.

The drugs associated with the greatest number of ADRs were Cyclophosphamide (Figure 1), Doxorubicin (Figure 2) and 5-FU (Figure 3). Chi-square and Fisher's exact tests were used to analyse the association between antineoplastic drugs and the resulting adverse drug reactions (Table 2).

Causality assessment (Naranjo's scale) highlighted that 79% were possible and 21% of the ADRs were probable (Figure 4). After severity assessment, it was observed that all of the ADRs were mild (level 1) in nature. An assessment of QoL was done among cancer patients included in the study using the Karnofsky Performance status scale and it was found that 6% of the patients had a QoL of 100% and 62% of patients had 90% QoL (Figure 5).

DISCUSSION

The present study emphasizes the importance of active monitoring to promptly identify and manage adverse drug reactions occurring in patients. In our study a total of 163 ADRs were recorded among which alopecia, anaemia, and anorexia were the most common type. The drugs associated with the greatest number of ADRs were Cyclophosphamide, 5-FU, Doxorubicin and Paclitaxel. In contrast, in a similar study conducted by Wahlang JB et al of 119 patients, 70 patients developed a total of 106 ADRs of which they experienced alopecia, vomiting,

constipation, anorexia, and the drugs associated were Cyclophosphamide, Doxorubicin, Paclitaxel and Cisplatin.¹¹

While considering the relationship between the anticancer drug and ADRs, it was identified that in our study cyclophosphamide, doxorubicin and carboplatin had high level of association with the development of anaemia, alopecia, nail discolouration, anorexia and vomiting while in a similar study by Singh S et al the patient's temporal relation of ADRs with the chemotherapy is assessed and its shown a higher chance of developing common ADR like nausea and vomiting, alopecia, tingling and numbness blurring of vision, pain and heaviness in chest were reported. An assessment of causality and severity was done using Naranjo Causality assessment scale and Hartwig's severity assessment scale respectively. After causality assessment it was found that majority of the ADRs were possible 79% and 21% of the ADRs were probable. Following severity assessment, it was discovered that all of the ADRs were minor (level 1) and did not necessitate any changes in treatment while considering the study conducted by Wahlang JB et al the majority of ADRs were kept in possible of 86.7% followed by probable with 13.2% on considering causality, while in-case of severity it was found that 77.4% mild (Level 1), 18.9% moderate (Level 3-4), and 3.8% were severe (Level 5).¹¹

Most of the ADRs were successfully managed with the adjuvant drugs. The use of pre-medications were able to prevent ADRs like nausea, vomiting, to a greater extent although it occurred in few patients. Common ADRs like nausea, and vomiting were managed with the aid of

supportive care agents like proton pump inhibitors, anti-emetics, and so on.

In this study majority of the patients achieved 90% of QoL. But in general, the patients had a moderate to poor QoL which is attributable to the cancer symptoms and also to the ADRs associated with the use of anti-cancer drugs. It can be related by the study of quality of life of Head and Neck cancer patients by Prima Jenevive Jyothi D' Souza et.al, study assessed 89 patients with HNC, 54% aged 45-64, 40% from oral cavity and 84% with addiction including smoking, chewing tobacco and alcoholism which greatly affect quality of life of patient. An assessment of QoL indicates that QoL decreases with the advancing stages of cancer.¹⁰

Despite the higher potential for drug toxicity, there is a lack of data regarding anticancer drugs, so proper monitoring and analysis of the ADR profile of the drug is needed. Causality assessment of ADRs is crucial for identifying drug's frequency and developing better alternatives, guiding optimal patient combinations. Effective management of cancer and therapeutic agents is crucial for patients quality of life, and assessing adverse drug reaction severity identify the appropriate supportive care agent for improving the QoL of the patients.

The study conducted in a single centre, may not provide a comprehensive understanding of the subject context and it was not conducted in a cancer-based hospital, causing issues during the data collection. Time constraints may have hindered proper patient follow up leading to lack of comprehensive information's which limits the study objectives.

CONCLUSION

This study emphasizes the importance of active monitoring of drug therapy to manage adverse drug reactions occurring in the patients for increasing the patient compliance and their quality of life. Causality assessment of adverse drug reactions was crucial in generating treatment plans and developing various other treatment alternatives. Assessing severity of adverse drug reactions along with causality contributes in identifying and choosing appropriate supportive care for the patients.

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