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Research Article

ADVERSE EFFECTS ASSOCIATED WITH CISPLATIN CHEMOTHERAPY IN CANCER PATIENTS IN A TERTIARY CARE TEACHING HOSPITAL JAMNAGAR

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ABSTRACT

Introduction: The majority of therapies for malignant tumours are based on chemotherapeutic drugs with cytotoxic effects, which cause death of tumour cells by direct damage to DNA or by inhibition of cell division. The most frequent adverse effects of cisplatin are ototoxicity, nausea/emesis, neurotoxicity, myelosuppression and nephrotoxicity. **Methods:** This is retrospective study conducted in tertiary care teaching hospital in chemotherapy ward. Total 35 adverse effects recorded in adverse drug reaction reporting form version 1.4 from record of chemotherapy ward. The ADRs were assessed for causality and preventability. Causality assessed by WHO causality assessment scale and Naranjo's Algorithm. Preventability of ADRs were assessed by modified Schumock and Thornton scale. **Result:** Most common adverse effect was Bone marrow depression which occurred in 16 patients (45.71%) out of these 4 patients developed Thrombocytopenia, 7 patients developed leukopenia, 4 patients developed mild degree anaemia and 1 patient developed severe degree anaemia. Chemotherapy induced nausea and vomiting developed in 9 patients (25.71%). Sensory neural hearing loss developed in 4 patients (11.42%). On basis of Naranjo's algorithm 33 reactions were probable and 2 were possible. On basis of WHO causality assessment scale all reactions were possible. On basis of modified Schumock and Thornton scale all reactions were not preventable. **Conclusion:** Most of the adverse drug reactions in present this study was mild, and not preventable; therefore, they not affect the therapy.

INTRODUCTION

Cisplatin, or cis-diamminedichloroplatinum (II) (CDDP) is the first platinum based anticancer drug developed for clinical uses[1]. Antineoplastic action of cisplatin consisted in binding with nuclear DNA. The formation of DNA adducts activates several signalling mechanisms including DNA repair, cell cycle arrest and apoptosis[2].

The majority of therapies for malignant tumours are based on chemotherapeutic drugs with cytotoxic effects[1], which cause death of tumour cells by direct damage to DNA or by inhibition of cell division[1]. Unfortunately, these drugs are mostly unspecific, therefore, their administration often causes extended tissue toxicity[1,3].

The most frequent adverse effects of cisplatin are ototoxicity, nausea/emesis, neurotoxicity, myelosuppression and nephrotoxicity[4]. Pharmacovigilance deals with detection, assessment and prevention of adverse drug reactions (ADRs)[5].The National Pharmacovigilance Program in India was started with the objectives of monitoring the safety of drugs and reaction of an adverse drug reaction database for the Indian population[6]. The major aims of pharmacovigilance are early detection of unknown adverse reactions, detection of increase in frequency of known adverse reactions, identification of risk factors and dissemination of information[7].

MATERIAL AND METHODS

This is retrospective study conducted in tertiary care teaching hospital in chemotherapy ward. Ethical approval was taken from Institutional ethical committee of our institute. The study was conducted during April 2021 to June 2022 and sample size calculated with 90% confidence interval and 15% margin of error using online calculator.

A total 35 adverse effects were recorded in adverse drug reaction reporting form (version 1.4) from record of chemotherapy ward. The ADRs were assessed for causality and preventability. Causality was assessed by both WHO causality assessment scale[8] and Naranjo's Algorithm[9]. Preventability of ADRs were assessed by modified Schumock and Thornton scale.The WHO causality assessment scale is recommended by

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the WHO Uppsala Monitoring Centre, a WHO collaborating Centre for International Drug Monitoring[8], for category, evaluation of the causal relationship of drugs to adverse effects.

The Naranjo's Algorithm, a questionnaire developed by Naranjo et al. compromises of objective questions with three types of answers - yes, no or do not know[9]. Scores are given accordingly and the drug reaction can be classified as definite (>9 score), probable (5-8 score), possible (1-4 score) or doubtful ADR (0 score). The modified Schumock and Thornton scale classifies ADRs as definitely preventable and not preventable based on a set of 7 questions for each level[10]. If answer of the any question is YES, then adverse drug reaction is falls under preventable.

RESULT

The study was conducted taking 35 ADRs and analysed on basis of age distribution, gender distribution, name of ADR, WHO causality assessment scale, Naranjo's Algorithm, The modified Schumock and Thornton scale, type of ADR and seriousness of ADR. Most of the patients were from the age group of 41-50 years followed by 61-70 years (Table 1). Most of the patients were male patients. The most common adverse effect was bone marrow depression which occurred in 16 patients (45.71%) and out of these, 4 patients developed thrombocytopenia, 7 patients developed leukopenia, 4 patients developed mild degree anaemia and 1 patient developed severe degree anaemia. Chemotherapy induced nausea and vomiting developed in 9 patients (25.71%) out of these 7 patients had vomiting and rest 2 only had nausea.Sensory neural hearing loss developed in 4 patients (11.42%). Grade I Mucositis developed in 2 patients (5.71%). Two patients (5.71%) developed oral ulcer, 1 patient (2.85%) developed hypernatremia and 1 patient (2.85%) developed alopecia (Fig. 1).

Table 1 Age distributionof patients included in cisplatin induced adverse drug reactions

Age group (years)	Number of patients
21-30	1
31-40	6
41-50	14
51-60	4
61-70	10
Total	35

Figure 1 Frequency of Cisplatin induced adverse drug reaction

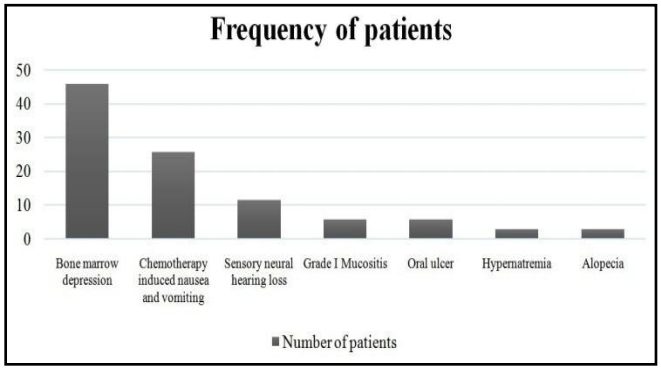


Figure 2 Seriousness of adverse drug reactions due to cisplatin chemotherapy

Twenty one reactions were not serious and 14 reactions were serious which requires prolonged hospitalization or caused disability (Fig. 2). On the basis of Naranjo's algorithm 33 reactions were probable and 2 were possible (Fig. 3). On the basis of WHO causality assessment scale all reactions were possible because reintroduction of suspected drug was not done. On the basis of modified Schumock and Thornton scale all reactions were not preventable, and all the reactions were type A reactions.

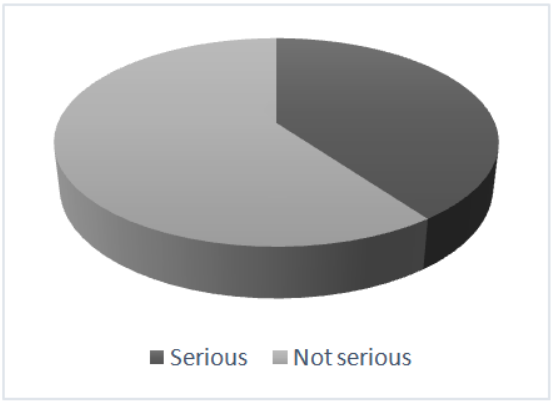
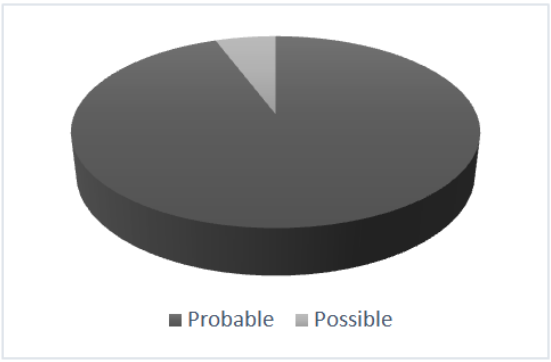


Figure 3 Naranjo's algorithm for adverse drug reactions due to cisplatin chemotherapy



DISCUSSION

All platinum-based drugs, have a range of severe side effects because of their poor selectivity for cancerous tissue over normal tissue. They have poor selectivity for cancerous tissue is because of the high nutrient requirements of cancer cells. So, cisplatin is taken up by fast growing cancer cells, and taken up into other tissues that are fast growing.

The present study describes the frequency of side effects in 35 patients treated with cisplatin at tertiary hospital of Jamnagar, Gujarat during 2021 and 2022. Total 35 cases were included out of which 16 patients developed haematological abnormalities, 9 patients developed chemotherapy induced nausea and vomiting, 4 patients developed sensorineural hearing loss, 2 patients developed grade I mucositis, 2 patients developed oral ulcers, 1 patient developed hypernatremia and 1 patient developed alopecia.

A study by Bahl et al[11], 40 patients who have locally advanced non-small cell lung cancer, receivesd cisplatin and etoposide, described the ADR pattern to cisplatin. However, our study included all patients who received cisplatin chemotherapy irrespective of their diagnosis. The frequency of alopecia was 88% in their study while was 2.85% in our study. Occurrence of nausea and vomiting almost similar in both studies. Though both of these studies reported haematological abnormalities (81%) like leukopenia, anaemia and thrombocytopenia, while in our study 45.71% patients had haematological abnormalities.

A study by Surendiran et al[5], among 51 patients, 48 developed ADRs to cisplatin chemotherapy while we only included all patients with adverse reactions with cisplatin. In their study WHO causality assessment scale indicated that 69% of the reactions was possible, and 31% probable while in our study all reactions were possible because we never applied re challenge of the suspected drug. As per Naranjo's Algorithm 62% of the ADRs were probable and 38% of the ADRs were possible while in our study 94% reactions were probable and 6 % were possible. Assessment of preventability of the adverse drug reactions were done on the basis of modified Schumock and Thornton scale. Most of the adverse drug reactions were from the category of not preventable. However, the more common reactions like nausea and vomiting belonged to the category of definitely preventable while in our study all reactions were not preventable.

CONCLUSION

Cisplatin therapy has a high potential to cause adverse effects in patients on chemotherapy. Most of the adverse drug reactions in present study were mild, and not preventable; therefore, they didn't affect the therapy. Present study also emphasizes the need for active reporting of adverse drug reactions and pharmacovigilance awareness among physicians to strengthen the pharmacovigilance programme in India.

Limitation of Study

Present study is retrospective study and only cases with adverse reactions were included, so we could decide the incidence of adverse reactions with cisplatin chemotherapy. We could only calculate percentage of various adverse reactions occurs with cisplatin chemotherapy. Sample size in present study was small so result may not be representation of total population.

Conflict of Interest

No conflict of interest.

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