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Short communication

Medication errors in prescription of chemotherapy regimens: A prospective observational study among cancer patients at Iranian referral hospital

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Abstract

Background: Medication errors are a significant cause of adverse events in cancer patients. The study aimed to investigate unintentional medication errors during chemotherapy regimen prescription.

Methods: During the six months' follow-ups, 201 adult patients admitted to outpatients' chemotherapy ward of Omid Hospital, Isfahan, Iran were examined. An information checklist by the aim of data gathering including patients' demographic information, laboratory data, medications history, chemotherapy drug doses and protocol of administration, pre-medications drugs, and supportive treatment was prepared. The data was compared by standard guidelines and data were presented in percent and frequency.

Results: Among the enrolled patients, 327 errors were identified. Sixty-five percent of patients were females and the mean age of patients was 49.2±2.8 years old. Gastrointestinal and breast cancers were among the most frequently reported cancers. The highest frequency of errors (67.27%) was attributed to the prescription of pre-medication drug administration primarily in the management of chemotherapy-induced nausea and vomiting. Medication errors in selection and volume of infused serums (20.18%) and in adjusting the dosage of chemotherapy regimens (10.39%) were the most observed errors.

Conclusion: This study highlighted the important areas to improve cancer management at the medical center. By addressing these challenges and implementing necessary changes, the center can enhance the quality of care provided to cancer patients, ensure adherence to international standards, and improve patient outcomes.

Keywords: Chemotherapy, Medication errors, Chemotherapy regimen, Pre-medication, Adverse effects

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Medication errors pose one of the biggest challenges in the field of healthcare. Apart from impacting the quality of a patient's life, these errors can cause harm to their health (1). Medication errors encompass preventable events that may result from inappropriate drug use or damage to the patient, ultimately leading to increased healthcare costs (2). Such errors can interfere with the optimal outcome of medication therapy, occurring during prescription by physicians, drug distribution, or drug administration by nurses. These issues can have significant implications, ranging from mortality or substantial morbidity to increased healthcare expenses, affecting both patients and society (3). Medication errors in oncology can have severe consequences for patients and can compromise the effectiveness of their treatment. Oncology medications are often complex, with specific dosing requirements and potential for significant side effects (4, 5). Examples of medication errors in oncology include incorrect dosing, chemotherapy drug mix-ups, wrong route of administration, drug interactions, and mislabeling/packaging errors.

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To prevent medication errors in oncology, various strategies can be implemented. These include computerized physician order entry (CPOE) systems to reduce handwriting errors and provide decision support tools, barcode medication administration (BCMA) systems to verify the "five rights" of medication administration, standardized order sets and protocols for consistent prescribing practices, independent double checks for high-risk medications, comprehensive education and training programs for healthcare professionals, medication reconciliation at care transitions, and establishing a reporting and learning culture to identify system weaknesses and implement preventive measures (4, 5). Several studies have addressed the medication errors in oncology ward (6, 7). For example, *Ford et al.* (6) conducted a study to review the nurse reporting of observed medication administration errors, classifying them and formulating the preventive strategies among 200 chemotherapy orders in a referral hospital in Salt Lake City, Utah.

They concluded that most of the medication errors happened during order writing and transcribing errors, nurse or pharmacy medication dispending, and nurse administration. Omid Hospital, Isfahan, Iran is a university-affiliated hospital specialized for the treatment of patients suffering from hematology malignancies or solid tumor. By working as a clinical pharmacist in this hospital, we found that medication errors frequently happened in different aspect of patients' management while there is no documented data for addressing or minimizing them. Furthermore, we decided to conduct a prospective cross-sectional study to evaluate the performance of healthcare professionals within the institution concerning the prescription of chemotherapy medications and management of associated side effects for their patients. The study investigated the alignment of treatment plans with patient conditions, the prudent administration of pre-medications, and the accuracy of dosage prescribed by healthcare providers. Furthermore, potential errors in the cancer treatment process are also scrutinized within the study framework.

Methods

The present study is a prospective cross-sectional study conducted over 6 months (October 2021 to March 2022) on 201 adult patients in the outpatient chemotherapy department of Omid Hospital in Isfahan. The protocol of the study has been approved by the Research Ethics Committee of the Isfahan University of Medical Sciences, Isfahan, Iran (IR.MUI.RESEARCH.REC.1401.047).

In Omid Hospital, each patient autonomously prepares their medication in accordance with the physician's' instructions outlined in their medical records and subsequently admitted into the outpatient chemotherapy unit of Omid Hospital for prescription refills. Medications dispensed via the outpatient chemotherapy department are meticulously crafted in a designated clean room facility following stringent protocols to minimize microbial contamination and preparation errors. To collect the data, the researcher collected the data by being present in the outpatient chemotherapy ward (in the file reception section), interviewing patients, examining the prescription, calculating the dosage, and ensuring compliance with the underlying disease and chemotherapy regimen preparation instructions. To implement this plan, initially the patient's file and the patient themselves were matched. In this stage, based on the patient's file and the physician's prescription, the patient's treatment regimen was determined through reliable guidelines such as online up-to-date website and British Columbia (BC) protocols (6-11). The information collection form was included from several parts including the following:

- The patient's identification data
- The patients' medical and drug allergy history
- Date of visit
- The patients' demographic information
- The patients' body surface area
- Treatment regimen information including doses, the way of drug administration, selected infusion serum and volume as well as injection time and instruction and serum administration sequences.
- The patients' laboratories' tests
- The pre-treatment regimens including drugs used as anti-emetic, anti-hypersensitive
- Education process for taking oral chemotherapy medications or management of risk factor in neutropenic period and, etc.

If the recorded information in the patient's file was incomplete, if the patient or physician did not cooperate or if the patient did not return for follow-up, or whether we had duplicate information from a patient under the supervision of a unit oncologist in different chemotherapy courses were excluded from our study.

On the other hand, after data collection, prescription compatibility among all above checked criteria in our institute and the mentioned (8, 9) protocol was determined for each cancer patient. In this study, we defined adherence

failure in treatment chemotherapy and pre-treatment regimen as follows;

1) If the recommended regimens were not correctly prescribed.

2) If the dose, duration and, sequence of chemotherapy medications or selected infusion serum were not correctly matched.

3) If non-recommended medications were prescribed.

In case of any discrepancy in the prescribed chemotherapy regimens and standard protocols, the researcher double-checked the regimens with relevant oncologist and if any errors confirmed, the necessary corrections were made before chemotherapy regimen prescription or preparation.

Statistical analysis: The sample size was determined to estimate the prevalence of various types errors when prescribing and injecting anticancer medications in the mentioned department. Using a formula with a 5% error level, a 95% confidence level and a p-value of 0.05 based on similar studies (10) carried out with the aim of investigating the general prevalence of errors related to the prescription and injection of anticancer medications and obtaining the d value of 0.02, the number of 456 samples was obtained, which is estimated to be 501 samples by taking into account the dropout rate of the statistical population:

$$N = P \times (1-P) \times (Z_{\alpha/2})^2 / d^2 = \frac{0.05 \times 0.95 \times 1.96^2}{0.02^2} = 456+5=501$$

Due to the large sample size and the limited timeframe for data collection, a convenient sampling method was employed, resulting in a total of 201 samples. Convenient sampling was chosen as it allowed for the efficient collection of data within the given time constraints. Descriptive statistics (measures of central tendency and dispersion) was used in this study to determine the frequency and percentage of qualitative variables. Categorical variables were expressed as a percentage. Continuous variables were reported as mean± standard deviation (SD).

Results

In this study, a total of 201 patients who were admitted to the outpatient chemotherapy department of Omid Hospital in Isfahan, Iran, were included. Table 1 demonstrates that out of all the enrolled patients, 131 (65.2%) individuals were women. The average age of the patients was 49.2±4.8 years old, ranging from 18 to 90 years old. Among the patients, the highest frequency of underlying malignancies was gastrointestinal cancer with 72 cases and the lowest frequency were reported by lung cancer with 4 cases.

Table1. Demographic characteristics of enrolled patients

Variables (N= 201)	
Gender **Female (n (%))**	131 (65.2%)
Age (mean±SD)	49.2±8.4
Body surface area (m2)	1.8±0.2
Type of malignancies (n (%)) **Breast** **Gastrointestinal** **Lymphoma** **Sarcoma** **Lung** **Brain** **Miscellaneous** **(Other unspecified hematologic and non-hematologic malignancies)**	 67 (33.3%) 72 (35.8%) 18 (9%) 7 (3.5%) 4 (2%) 7 (3.5%) 26 (12.9%)

SD: standard deviation.

Table 2 indicates that there were no identified errors in terms of patient identification or the selection of chemotherapy regimens based on the diagnosis of malignancies. However, a small number of patients (3 patients, 0.91%) were referred at inappropriate times according to the chemotherapy schedule. The highest frequency of errors was found in the administration of pre-medication, with 327 cumulative errors. This category of error included errors in the pre-medication dose, selection of pre-medication type, and mismanagement of hypersensitivity. Regarding the dose category, as shown in table 1, different dose of dexamethasone (4 mg) and

granisetron (3 mg) were prescribed. Our study revealed that many errors occurred due to missing doses of olanzapine (20.79%), aprepitant (14.98%), or inappropriate use of metoclopramide (6.11%) for the management of chemotherapy-induced nausea and vomiting.

One of the most commonly reported errors was the lack of adherence by healthcare providers to the docetaxel hypersensitivity reaction (15.59%). Our results showed three errors in the pre-administration of atropine for irinotecan and 1 case of missing serum therapy before cisplatin administration. However, several cases of overdose were identified during the prescription of oxaliplatin, doxorubicin, and cyclophosphamide, and 25 cases of underdose of fluorouracil were noted during the 48-hour continuous infusion in the FOLFOX regimen. Nevertheless, dose corrections were made after consulting the responsible physicians through phone calls.

The selection of the dose and volume of infusion were the sections that reported errors most frequently. In 2 cases, the type of serum selected was found to be mismatched according to the standard protocol during carboplatin administration, and in 19.57% of prepared infusion serums, the prescribed volumes did not match the standard protocol. For example, in numerous cases (31 patients), cyclophosphamide was prescribed in 1-liter normal saline instead of 500 milliliters, and in 26 patients receiving fluorouracil, the volume of serum administered was higher than recommended. No error found in term of sequences in infused volume during chemotherapy regimens administration.

Table 2. Frequency of error based on total detected errors (n=327)

Type of errors based on total detected errors	Number (n=327)	Frequency (%)
Patient identification	0	0
Patient appointments for administration	3	0.91
Matching chemotherapy regimen based on diagnosis	0	0
Pre-medication administration		
• **Error in the dose of premedication**	220	67.27
Lower dose of dexamethasone	32	9.78
The higher dose of granisetron	25	7.64
	7	2.14
• **Error in type of premedication**	137	41.89
Missing dose of olanzapine	68	20.79
Missing dose of aprepitant	49	14.98
Inappropriate prescription of metoclopramide	20	6.11
	51	15.59
• **Error in hypersensitivity management**		
Glucocorticoid prescription duration		
Supportive treatment during chemotherapy administration*	4	1.22
• **Error in anticholinergic drug administration**		
Missing atropine injection	3	0.91
• **Error in fluid administration**	1	0.3
Missing of fluid pretreatment before cisplatin administration		
Dose of chemotherapy regimen	34	10.39
Infused fluid administration	66	20.18
• **Error in type of infused fluid based on the chemotherapy regimen**	2	0.61
• **Error in volume of infused fluid**	64	19.57
• **Error in infused fluid sequences and time of administration**	0	0

• We considered blood pressure measurement before anti-angiogenesis medications, administration of 1 liter of normal saline before cisplatin administration and 0.5 mg of atropine before irinotecan-containing regimens, as well as performance of serial echocardiography during trastuzumab chemotherapy courses as a routine supportive treatment in our center.

Discussion

The findings of this study shed light on the performance of the specialized treatment team at the medical center and highlight areas where improvements are needed. The results indicate that there are discrepancies between the practices at the center and international standards in certain aspects of cancer treatment. The most significant identified error in the treatment process is the pre-medications administration, selection and volume of infused serums and adjusting the dosage of chemotherapy regimens. As our hospital plays a prominent role in the middle of our country, any shortcomings or problems regarding cancer treatment will have far-reaching effects, not only in cancer treatment but also in educational and economic aspects. In the present study, adherence to international standard guidelines (8, 9) was found to be inadequate due to reasons such as irrational prescription of pre-medications and insufficient support before chemotherapy regimen administration regarding chemotherapy-related side effects. Ensuring adherence to established guidelines for prescribing preventive medications is crucial in mitigating these side effects and providing optimal care for cancer patients. Supportive care measures and appropriate chemotherapy dosing were found to be challenging areas at the cancer treatment center. Supportive care plays a crucial role in managing treatment-related symptoms, addressing psychological needs, and improving overall patient well-being, but implementation of these interventions required enhancement. Accurately dosing chemotherapy medications is essential to achieve therapeutic effects while minimizing toxicity, but the study identified issues in this area, indicating a need for improved practices, such as developing dosing guidelines, providing training, implementing close supervision and regular reviews, and promoting error reporting and disclosure.

In the examination of prescribed serums for patients conducted in this study, there were a 19.57% errors in the prescription volume of serums used for dissolving chemotherapeutic medications, and 0.61% errors in the type of prescribed serum. Errors resulting from incorrect selection of serum volume can often lead to inappropriate drug concentration in the serum, causing drug-related complications and reducing the effectiveness of medications. For example, the effective drug concentration of docetaxel is maintained within the range of 0.3-0.74 milligrams per milliliter, and the selection of serum volume is essential for maintaining this concentration.

The study conducted by *Ulas et al*. (7) aimed to evaluate unintentional medication errors in 18 adult chemotherapy units. They found that one or more errors occurred during chemotherapy preparation and administration. The findings of this study were not aligned with the results of our study. *Ulas* et al. reported that the most common errors were prescribing or ordering the wrong doses by physicians (65.7%) and noncompliance with administration sequences during chemotherapy (50.5%). In contrast, our study found that the selection and administration of premedication drugs were the most frequently reported medication errors in your setting. A descriptive cross-sectional study was conducted in the chemotherapy department of Imam Reza Hospital in Kermanshah to identify and evaluate errors made by physicians and nurses during the chemotherapy process and establish principles of risk and safety. During 3 months, a total of 459 errors were identified from 122 treatment procedures using a standardized questionnaire. Most errors occurred in the proper use of oral medications and timing of medication administration. These mistakes were attributed to a shortage of physicians and nurses due to a high number of patients, the absence of comprehensive guidelines, lack of physician cooperation, and inadequate training (12).

In addition to the chemotherapy department, medication errors occur in various departments of healthcare centers. For instance, according to a study conducted in Norwegian hospitals between 2016 and 2017, out of 3,557 randomly selected cases of medication prescribing, the highest percentage of errors occurred during administration (68%) and prescribing (24%) of medications. The most common types of errors were dosage errors (38%), omission of drugs from the treatment regimen (23%), and prescribing the wrong medication (15%). In this study, it was observed that more than half of all errors (62%) had an adverse impact on the patients' quality of life. Specifically, 2.5% of these errors led to severe harm, and 0.8% were fatal. The significant number of severe and fatal errors resulting in preventable harm and patient death necessitates immediate action to determine error prevention strategies (13).

In our study, the number of dose determination errors accounted for only 10.39% of all errors, which is much lower compared to the study conducted in Norwegian hospitals. This could be attributed to a higher compliance and concern of physicians at oncology hospital with existing guidelines. In the current study, the highest errors were related to the prescribing of pre-medications specially for the management of chemotherapy-induced nausea/vomiting accounted for approximately 67.27% of all errors in the study. In a study conducted at this center in 2019 by *Ebrahimi et al.* results demonstrated that the compliance rate with guidelines for antiemetic prophylaxis was very low. In fact, 83.6% of patients receiving chemotherapy regimens did not adhere to the guidelines. This lack of compliance was particularly high for medications with high

emetogenic potential, with a reported rate of 0% for this category. Other medication categories also had poor compliance rates, with less than 40% adherence for medications with moderate, low, and very low emetogenic potential (14). Although in our study which was a follow-up study after 3 years, non-compliance rate of antiemetic premedication reported to be decreased since then but still persisted. The European Society for Medical Oncology (ESMO) (11) guideline recommends an intravenous dexamethasone dose between 8-12 mg daily for 4 days, whereas the routine physician order in our chemotherapy ward was 4 mg before chemotherapy regimen administration. As for granisetron, the routine prescribed dose was 3 mg, corresponding to the dosage form of injection in our country, while the ESMO (11) guideline recommends a daily intravenous injection of 1 mg. Moreover, according to the Multinational Association of Supportive Care in Cancer (MASCC) (11) classification, a prophylactic combination of 4 medications, including NK-1 antagonists, 5-HT3 antagonists, corticosteroids, and dopamine antagonists (especially olanzapine), is suggested for the management of highly emetogenic chemotherapy medication. According to the latest recommendations from the MASCC/ESMO guidelines (11), the use of metoclopramide is no longer recommended. In the previous study (14), it was shown that 63.3% of patients had received metoclopramide as an unrecommended and unnecessary medication while in our study, metoclopramide was prescribed in 20 out of 201 (9.95%) patients, which is significantly lower.

According to the BC Cancer guidelines (8), for the control of hypersensitivity reactions-induced by docetaxel, 3-day dose of dexamethasone (one day before chemotherapy administration, the day of administration, and one day after) should be prescribed for patients while it was administered as a single high dose only in the day of administration. Based on information provided, the reasons for the improper prescription of dexamethasone to patients at the center can include: 1) Lack of awareness among physicians about new guidelines: It is possible that the physicians at this center are not aware of the new guidelines for prescribing pre-medications to control allergic reactions, 2) concerns about potential side effects: corticosteroids can have significant side effects, especially when used long-term or in high doses. Physicians may have concerns about these side effects and may be hesitant to prescribe corticosteroids unless absolutely necessary. 3) Short duration of hospitalization in outpatient center and lack of access to patients for three days. To address the identified challenges and improve the overall quality of care, it is recommended that the medical center take several steps. These include providing regular training and refresher courses for the specialized treatment team to ensure they are updated with the latest guidelines and best practices. Implementing robust monitoring systems to track changes in patient's conditions during the treatment period can also help identify the need for adjustments in medication regimens and supportive care interventions.

In conclusion, this study highlights important areas for improvement in cancer management at the medical center. By addressing these challenges and implementing necessary changes, the center can enhance the quality of care provided to cancer patients, ensure adherence to international standards and improve patient outcomes. The results of this study have shown that the performance of the specialized treatment team at this medical center differed from international standards in some areas. Both direct treatment with chemotherapy medications and prevention of treatment-related complications in cancer patients were still facing challenges. Compliance with prescribing pre-medication drugs for chemotherapy-induced nausea and vomiting, determining appropriate chemotherapy drug doses, selection and volume of infused serum and supportive care measures for patients in this center were found to be non-optimal.

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