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Narrative Review

Chemotherapy medication errors in patients with cancer: A narrative review

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Abstract

Background and aims: Chemotherapy medications have narrow therapeutic index and high toxicity and hence, chemotherapy medications errors (CMEs) are very common and are associated with serious consequences. The aim of the present study was to evaluate the types, severity, contributing factors, and preventive strategies of CMEs in patients with cancer.

Methods: This narrative review was conducted in 2021. Data were collected through searching the Google Scholar, Elsevier, PubMed, ProQuest, Scientific Information Database (SID), Magiran, IranDoc, and IranMedex databases. Search key terms were "adverse events", "medication error", "cancer", "patient safety", "safety management", "chemotherapy", "antineoplastic agents", "neoplasm", and "cancer".

Results: In total, 125 articles were retrieved and finally, eighteen articles were reviewed. Findings came into four main categories, namely types of CMEs, causes of CMEs, severity of CMEs, and strategies to prevent CMEs. The four main types of CMEs are prescription, dispensing, preparation, and administration errors. Prescription and preparation errors are the most common CMEs.

Conclusion: Strategies such as computerized physician order entry software, educational programs for nurses, improvement of nurses' work conditions, and employment of well-trained nurses are recommended to reduce CMEs and improve patient safety.

Keywords: Cancer, Medication error, Chemotherapy, Patient safety, Neoplasm, Antineoplastic medications

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Introduction

Cancer is a leading cause of death worldwide. The prevalence of cancer is gradually increasing throughout the world and in our country (1) and hence, the number of patients who receive cancer treatments, including chemotherapy, is also progressively increasing (2). The increasing prevalence of chemotherapy is associated with the increasing risk of chemotherapy medication errors (CMEs) (1).

Medication error is an endless problem in healthcare settings and one of the most important errors which endanger patient safety (1,3). The prevalence of medication error among hospitalized patients is 0.6%–28% (1). Such wide prevalence rate of medication error is due to the lack of a clear definition for medication error (1). Broadly, medication error is defined as failure in the process of treatment which leads to potential or actual harm to the patient (4). Medication error is a major cause of complications and death. A study reported that 180 000 patients annually die in the United States due to medication errors (2). Two other studies reported that the annual number of deaths due to medication errors in the United States is 44 000–98 000 (5,6). In Canada, more than 185 000 cases of hospitalization occur each year due to medication errors which 70 000 of them are preventable (7).

Chemotherapy regimens are highly complex and hence, CMEs are very likely in all steps of chemotherapy, from prescription to administration (4,5). Chemotherapy medications have narrow therapeutic index and high toxicity and are among the most dangerous medications (1,2,8). Consequently, inappropriate use of them may result in serious intoxication, reduced responsiveness of cancer cells to treatment, and low treatment success (3,8). On the other hand, patients with cancer are highly vulnerable to the side effects of chemotherapy medications (9) and CMEs can cause them serious consequences (5,8,9). Currently, CMEs are the second leading cause of the deaths induced by medication errors (4,5,9).

The high prevalence and the serious complications of CMEs necessitate improvement of healthcare providers' and patients' awareness of CMEs in order to improve patient safety, reduce healthcare providers' workload, shorten hospital stay, and reduce treatment-related costs for patients, their families, healthcare systems, and insurance organizations (2,5,7-9). However, the prevalence of new treatment regimens and protocols and the wide variety of medication administration techniques have made accurate medication management very difficult (2). The most basic step to the management of CMEs is the identification of them, their complications (1), and their contributing factors (5,7). On the other hand, CMEs are not adequately reported and hence, there are limited data about CMEs and the severity of their consequences (5). Accurate reporting and analysis of CMEs and adequate

support for CME reporters are essential for effective CME prevention (8).

Our literature search revealed that most previous studies focused on medication error prevention in hospitals and there are still limited data about the different types of CMEs in patients with cancer and their contributing factors. Therefore, the present study sought to narrow this gap. The aim of the study was to evaluate the types, severity, contributing factors, and preventive strategies of CMEs in patients with cancer.

Methods

Design

This narrative review was conducted in 2021.

Data collection

Data were collected through searching different English and Persian databases namely Google Scholar, Elsevier, PubMed, ProQuest, Scientific Information Database (SID), Magiran, IranDoc, and IranMedex. Search key terms were "adverse events", "medication error", "cancer", "patient safety", "safety management", "chemotherapy", "antineoplastic agents", "neoplasm", and "cancer". The reference lists of the retrieved articles were also hand searched. Inclusion criteria were publication in 2003–2021, relevance to CMEs in chemotherapy wards, and accessible full-text. Commentaries, theoretical analyses, letters to the editor, conference articles, studies into adverse drug reactions, and studies into one particular type of cancer were not included. The bibliographic data and the abstracts of the retrieved studies were assessed for eligibility, duplicated records were omitted and the remaining articles were manually reviewed by the two authors.

Results

The primary database search yielded 125 articles, while eighteen studies were finally included in the study (Figure 1). The reviewed studies had used various methodologies, including qualitative, quantitative, review, case analysis, and prospective cohort designs. During data analysis, four main categories were developed which were types of CMEs, causes of CMEs, severity of CMEs, and strategies to prevent CMEs. These four categories are explained in what follows.

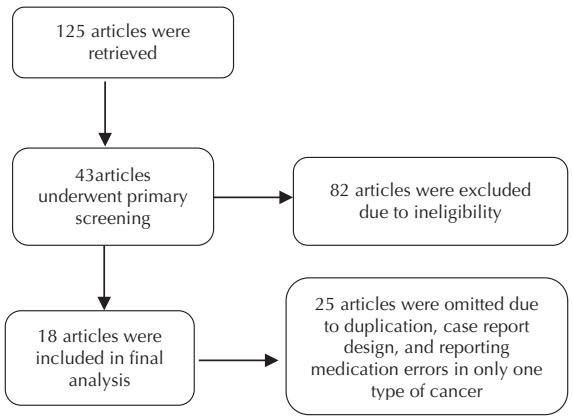

Figure 1. The Flow Diagram of the Study.

Types of CMEs

CMEs can occur at different stages of treatment, namely prescription, dispensing, preparation, and administration (Table 1). Moreover, CMEs may happen during treatment with both oral and intravenous medications and among both child and adult patients (5), though CMEs are more prevalent among child patients (10). Moreover, CMEs may occur in hospitals, outpatient settings, and even at patient homes (9-11). CMEs in hospitals mostly occur during prescription, while CMEs in outpatient centers and at patient homes mostly occur during medication administration (10).

Prescription errors: By definition, prescription errors are errors due to incorrect medication selection which lead to its improper use or harms to patients (2). Prescription errors are among the major causes of death in healthcare settings in the United States (2). The incidence of CMEs in prescription is 1%–24.6% (4). Illegible prescription is a leading cause of prescription errors in more than 50% of cases (4). Prescription errors may happen when physicians write their medication orders or when nurses transcribe medical orders in the medication Kardex (8). Different studies reported that the most prevalent CMEs happen when writing medication orders (1,4,12). Incomplete prescription is a leading cause of prescription errors and can lead to the use of medications with wrong doses, selection of an inappropriate treatment regimen, use of a wrong medication, or administration of a medication to a wrong patient (5,13). Incomplete prescription, such as not writing medication dose, administration route, or dilution method, as well as errors in writing dosage units (i.e., gram, milligram, microgram, etc.) are also among prescription errors (14). Other types of prescription errors are the use of trade names of medications instead of their generic names or the use of the abbreviated names of medications in prescriptions (9). As more than 50% of CMEs in prescription are preventable, preventive strategies can reduce the risk and the prevalence of irreversible complications of CMEs among patients with cancer (4,15).

Dispensing errors: Dispensing errors are the least common CMEs and are largely preventable. The most prevalent dispensing errors are delivery of wrong medication, delivery of medication with wrong dose, delivery of medication with wrong potency, and delivery of wrong medication form (4,8). Wrong entry of medication name in software, storage of wrong medication, delivery of wrong medication to chemotherapy ward, no label on medication, and delay in medication preparation are other examples of dispensing error (5). The most prevalent causes of CMEs in dispensing are related to hand-written prescriptions, similar packaging, and ineffective supervision and control of medication labels (4,16). Two

Table 1. Types and contributing factors of errors

Types of CMEs	Contributing factors of CMEs
Wrong dose	Hurry in writing prescriptions
Missing a dose	Heavy workload
Wrong medication	Low nurse-patient ratio
Wrong medication indication	Job burnout
Inadequate knowledge about medication	Delay in medication preparation and dispensing in pharmacy
Wrong time	Employment of inexperienced staff
Failure to dilute with a right volume of solution	Lack of rechecking by another staff
Dilution using a wrong solution	Errors in transcribing medications from medical orders
No fluid therapy before medication administration	Staff's confrontational behaviors
Wrong administration	Teaching hospitals
Wrong documentation	Poor professional communication
No hand wash	Limited supervision and non-continuous assessments
Incomplete order	Lack of quality policies
Use of trade or abbreviated name instead of generic or full name of medication	Parents' limited knowledge about accurate medication administration to their children
No use of gloves	Missing a medication for children by parents
Inattention to drug interactions	Inattention to changes in patients' conditions
Wrong patient	Prescription of all medications of a patient altogether at the beginning of treatment
Wrong infusion rate	No use of medication labels
Selection of a wrong treatment regimen	Staff's fatigue and inadequate sleep
Adding a wrong medication to the chemotherapy solution	Systemic errors
Wrong date	Staff's limited knowledge
Using an expired medication	Medications with similar names or pronunciations
Wrong dosage units	Errors in medication storage
Incomplete prescription of pre-chemotherapy medications	
Inattention to medication sequencing in multi-medication regimens	

studies reported that most CMEs in dispensing are due to the preparation of medications in pharmacies (5,17).

Preparation errors: Medication preparation errors usually occur after prescription errors (4) and mostly by nurses who do not observe medication preparation standards (2). Examples of these errors are no hand wash before and after medication preparation, no use of gloves for medication injection, lack of adequate disinfected places for medication preparation, non-observance of standard protocols for preparing medications which are photosensitive, non-performance of allergy test, improper dilution, improper medication infusion rate, wrong calculation of medication dose, using a wrong solution for administration, adding wrong medications to chemotherapy medications, and wrong medication label (1,2,18).

Administration errors: These errors occur when nurses administer medications to patients (2). Examples of administration errors are forgetting medication administration, no fluid therapy before medication administration, using defective infusion pumps which deliver wrong dose of medication to patients, medication administration to a wrong patient, medication administration through a wrong route, medication administration at a wrong time (1,3,5), non-observance of accurate medication sequencing, and inattention to infusion time period particularly when administering multiple medications (1).

Contributing factors of CMEs

Many different factors can contribute to CMEs in different stages of treatment, from prescription to administration. For example, heavy workload, low nurse-patient ratio, and job burnout are CME contributing factors in the medication preparation and administration stages (1,2). The Institute of Medicine also reported that medication errors are still a major problem in healthcare environments with heavy workload (8). Moreover, nurses' delay in receiving medications from pharmacy is a reason for administration error and delay in medication administration (3,8). Independent checking of medications by a single staff and lack of rechecking by a colleague is also a major factor contributing to prescription errors in pharmacy and administration errors by nurses (8). In addition, problems in medication administration and medication transcription, inadequate staff supervision, communication barriers such as poor professional communication or confrontational behaviors, poor professional performance of staff, illegible prescriptions, staff's limited up-to-date knowledge, employment of

inexperienced staff, improper policies and procedures, incomplete prescriptions (5), and non-continuous assessments during medication management (9) can contribute to CMEs. In children, some chemotherapy medications are dissolved in water and orally prescribed. However, children may refrain from taking medications or vomit them, leading to inadequate delivery of medications to them (10). Some errors also may happen due to limited attention to changes in patients' clinical conditions and laboratory tests such as complete blood count (10). Prescription of all chemotherapy medications of a patient altogether at the beginning of treatment for the whole treatment course or hurry in writing prescriptions are also among the contributing factors of prescription errors by physicians (10,14). In teaching hospitals, rotation of medical residents in different wards can also lead to CMEs. Moreover, CMEs in pharmacies can be caused by underreporting of errors due to fear over blame, lengthiness of the reporting process, and institutional policies for error management (5). Inappropriate environmental conditions such as crowdedness, noises, staff fatigue, stress among patients' companions (1), inadequate knowledge about medications, and poor communication among medication dispensing team members are other factors contributing to CMEs.

Severity of CMEs

According to their severity, CMEs can be categorized into four main categories, namely significant, serious, life-threatening, and fatal (5,9,10). CMEs can lead to serious complications such as hematologic toxicity, neurologic toxicity, renal problems, hepatic cytolysis, and dermatologic toxicity and problems (5). Chemotherapy medications with the highest toxicity are methotrexate, fluorouracil, cyclophosphamide, and vincristine (2). Moreover, vinblastine is a chemotherapy medication with a high risk of dose-related medication error (5).

Strategies to prevent CMEs

Many CMEs in children occur at home and by parents. These CMEs can be prevented using syringes with color numbers for administering liquid medications. Strengthening the relationships of cancer patients' family members with healthcare providers and facilitating their access to healthcare providers can also reduce the risk of CMEs at home (10). In outpatient and inpatient healthcare settings, the use of computerized control system can be useful, though such systems may not be available in all settings (5). A study reported that using electronic medication prescription and standardized medication orders significantly reduced medication errors (19). The computerized physician order entry software also analyzes the different aspects of medication orders (9) and hence, can reduce the risk of medication errors by two third (4,9,20,21). Modification of medication prescription forms and using colored forms with specific coding for multiple medication regimens can also prevent prescription errors (20). Double signature of chemotherapy medication prescriptions by physicians, particularly in teaching hospitals, involvement of pharmacists and nurses in reassessing chemotherapy medications and their accurate doses, standardization of medication dilution procedures by pharmacies (20,21), and provision of a copy of the prescribed chemotherapy medications to patients (19) are also useful strategies to prevent CMEs. Patients' characteristics, such as height, weight, body surface area, and allergy history should be documented in medication prescription and administration forms. Other strategies to prevent CMEs are assessment of the accuracy of the medication order using standard therapeutic protocols, use of the generic names of medications, careful attention to the zeros and decimal numbers in prescriptions, avoidance from using nonstandard terms, employment of nurses and medicinal technicians trained in chemotherapy, and double signature of medication prescriptions by senior technicians before medication dispensing (20,22-24).

Discussion

This study aimed at evaluating the types, severity, contributing factors, and preventive strategies of CMEs in patients with cancer. Findings showed that the four main types of CMEs are prescription, preparation, dispensing, and administration errors (25). Prescription errors are the most prevalent CMEs and prescription illegibility is the most common contributing factor of CMEs (4). Prescription stage is the first stage of chemotherapy and hence, preventive strategies in this stage can help significantly reduce CME consequences (4,26). Electronic prescription systems and software can reduce medication errors caused by dose calculation, prescription illegibility, wrong medication identification, cumulative doses, and dispensing errors (9) by two-thirds (15). Therefore, healthcare systems need to pay more attention to identify and prevent prescription errors (4,27).

Preparation errors are the second most prevalent CMEs in cancer patients. These errors are often occurred by nurses and a study reported that two-thirds of nurses commit at least one medication error during their practice (21). Therefore, employment of knowledgeable and experienced nurses, using quality control systems (28), and using robot-based automated preparation systems (29) may improve the quality of medication preparation. However, a study reported that robot-based systems may be ineffective in preventing serious preparation errors, denoting that preparation errors may have different sources (30). Determination of the accurate dose, the amount of the solution for dilution, and infusion rate either manually or through robot-based systems can reduce the risk of preparation errors (31).

Medication dispensing errors were the least common CMEs, denoting their high preventability. The most common contributing factors of dispensing errors are illegible prescriptions, use of similar labels and packages for different medications, and limited control over

What does this paper contribute to the wider global clinical community?

- The findings of the present study can help physicians, nurses, and other healthcare providers prevent CMEs.
- Identification and prevention of CMEs at any stage of cancer treatment can improve patient safety.
- The managers of inpatient and outpatient healthcare settings are recommended to use advanced technologies to prevent CMEs.

medication therapy. Moreover, factors such as staff's limited knowledge about medications, medication doses, and medication forms, their heavy workload, and their ineffective communication can increase the risk of dispensing errors (32).

Our findings also revealed administration errors among the most important CMEs. Improvement of staff's work conditions and employment of competent staff can improve patient safety and reduce medication errors. Strategies to reduce administration errors may include use of a pharmacist-led medication therapy program in hospitals and improvement of nurses' knowledge about the principles of chemotherapy medication administrations (33,34).

The computerized physician order entry software is a potentially effective strategy to reduce medication errors throughout the process of treatment, from prescription to administration. Several previous studies reported that using this software was effective in preventing medication errors in patients receiving chemotherapy (9,27,28). Moreover, chemotherapy medications should be considered as high-alert medications and strict guidelines, protocols, and procedures should be employed to buy, transport, store, order, dispense, administer, and monitor them (35).

Limitations

This study had some limitations. The first limitation was the difficulty of comparing healthcare settings with different sizes and different chemotherapy procedures respecting their CMEs. The second limitation was the possibility of some reporting biases due to the underreporting of CMEs. Therefore, further studies are recommended to improve error reporting and error management.

Conclusion

CMEs are very common and the most common types of them are prescription and preparation errors. Further studies are needed to assess CME-associated consequences and the most effective strategies for CME prevention. Integration of safety sciences into clinical researches may produce better outcomes in clinical oncology.

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