Research Paper

Frequency of Chemotherapy Medication Errors: A Systematic Review

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Abstract

Objective: To synthesize peer-reviewed knowledge on the frequency of different types of chemotherapy medication errors. **Methods:** The data were collected from studies published between January 1, 2000, and March 3, 2018, and are identified through online resources such as Medline/PubMed, PubMed Central, Agency for Healthcare Research, and Quality and the Cochrane Library. The manuscripts published in peer-reviewed scientific journals in English language were included in the study. Initially, 19,723 articles were retrieved and finally 11 were found to be eligible to include in the review and were assessed for quality. Error percentages were calculated from the ratio of error type (numerator) to sample size (denominator: medication orders or prescriptions). **Results:** Overall, the chemotherapy medication errors ranged from 0.004% to 41.6% among various studies. Chemotherapy medication errors ranged from 0.1% to 24.6% in prescribing, 0.40% to 0.50% in preparation, 0.03% in dispensing, and 0.02% to 0.10% in administering phases. **Conclusion:** Prescribing phase had the highest number of chemotherapy medication errors reported, and least was reported during dispensing phase. We also noticed a need for harmonization for reporting of medication errors.

Keywords: Administration errors, chemotherapy errors, dispencing errors, medication errors, preparation errors, prescription errors

Background

The report from the Institute of Medicine, "To Err is Human," estimated that about 44,000 and 98,000 patients die each year in the United States of America because of medication errors.[1] Chemotherapeutic drugs were the second-most common cause of fatal medication errors.[2] Due to the complexity of chemotherapy regimens, medication errors can occur at any point from prescribing to administration.[3] In particular, errors in multiple-dose administration can result in catastrophic reaction or death.[4]

The reported frequency of medication errors among cancer patients varies between studies, within studies by setting (e.g., outpatient vs. inpatient),[5-7] and route of administration (e.g., oral, intravenous, or intrathecal).[8] Nevertheless, it is unclear whether these suggested within-study factors explain the observed variation in medication errors between studies. To the best of our knowledge, the frequency of chemotherapy medication errors in prescribing, preparation, dispensing, and drug administration phases has not been compared at the time of drafting this manuscript. The present study is aimed to perform systematic review of published literature regarding the frequency of chemotherapy errors among cancer patients during various phases of therapy, i.e., prescribing, preparation, dispensing, and administration.

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Methods

Search strategy

A systematic search of the literature was conducted in Medline/PubMed, Agency for Healthcare Research and

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Quality (AHRQ), and the Cochrane Library [Figure 1]. The studies published between January 1, 2000, and March 3, 2018, were identified. Articles were searched using the Medical Subject Headings terms "chemotherapy error," "medication error," "prescribing error," "prescription error," "dispensing error," "administration error," "Cancer," "Oncology," and "Chemotherapy." The search strategy included English language, all age groups, and research articles. References of studies were also hand searched to identify other potential studies matching the search criteria.

Definitions of medication errors

Standard definitions by the Committee of Experts on Management of Safety and Quality in Health Care were followed to define prescribing, preparation, dispensing, and administration errors.[9]

Review procedure

Two review authors, SS and RA, independently screened titles and abstracts of studies that were potentially relevant to the systematic review. Two review authors independently assessed the abstracts or full texts for inclusion criteria. There was an initial disagreement on few articles for inclusion, which was resolved by discussion with the other authors. Final verification of inclusion and exclusion criteria was reviewed by all authors for consensus. We sought further information from the authors of the articles that had insufficient information to make a decision about eligibility as depicted in Figure 1. Quality assessment of all the studies included in the review was performed using 13 different criteria. These criteria except for ethical committee approval were proposed earlier[10] and are as follows: (1) Aims/objectives of the study clearly stated; (2) Definition of what constitutes a medication error; (3) Error categories specified; (4) Error categories defined; (5) Presence of a clearly defined denominator; (6) Data collection method described clearly; (7) Setting in which study conducted described; (8) Sampling and calculation of sample size described; (9) Reliability measures; (10) Measures in place to ensure that results are valid; (11) Limitations of study listed; and (12) Mention of any assumptions made, and (13) Ethical Committee approval.[11,12] A score of "1" was given if the study met the criteria and "0" if not met.

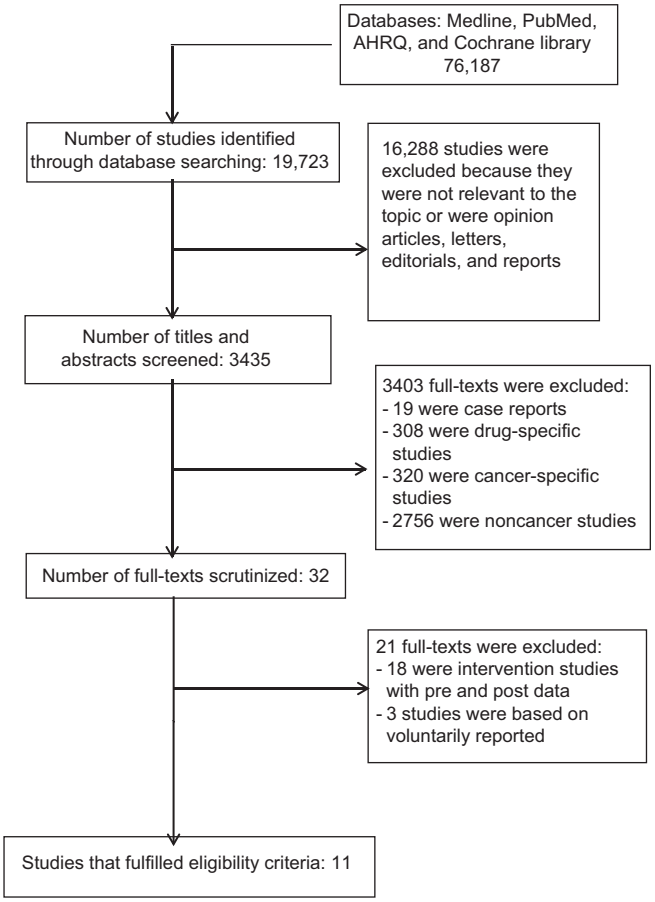

Figure 1: Flow diagram of the literature search conducted for the present systematic review (for details please refer to methods section)

Inclusion criteria

We included studies reporting chemotherapy medication error incidences during any or all of the four phases of drug treatment, i.e., prescribing, preparation, dispensing, and administration. The original research studies reported in English language published during January 1, 2000–March 3, 2018 were included.

Exclusion criteria

Studies reporting medication errors from any medications other than chemotherapy were excluded. The clinical trials were not included in the analyses. The studies evaluating strategies in preventing medication errors were also excluded. The surveys based on voluntary reporting of medication errors were also excluded. The studies of chemotherapy medication errors restricted to only one specific cancer were also excluded.

Analyses

Event rates were noted from reports, and 95% confidence intervals (95% CI) were calculated using SMR tools.[13] Further, event rates and 95% CI were presented as percentages. Cumulative scores were used for qualitative analysis of studies.

Results

Our search criteria identified 11 eligible studies; four studies focused on inpatient setting, two focused on outpatient setting, and five studies were based on both inpatient and outpatient settings [Table 1]. Quality assessment showed that five studies (45.5%) had a cumulative quality score of ≤7 and the remaining six studies (54.5%) scored >7, suggesting acceptable quality level of the studies included [Figure 2]. Event rates with 95% CI, study setting, geographical location, and type of each eligible study along with route of drug administration are outlined in Table 1. The denominators used to report medication error rates by each study are described in Table 1.

Incidence of chemotherapy medication errors

The results were grouped according to phases during the chemotherapy treatment process: prescribing, preparation, dispensing, and administration [Table 1]. Overall chemotherapy

Table 1: Chemotherapy medication error rates segregated by phases

Study ID	Events	Total	Event rate (%)	95% CI	Denominator	Setting	Route	Type	Country
Prescribing errors (*n*=10)									
Slama *et al*., 2005[14]	310	1262	24.60	22.30-27.00	Prescribed products	Inpatient	Oral and parenteral	P	France
Garzás-Martín de Almagro *et al*., 2008[15]	92	6741	1.36	1.35-1.36	Prescriptions	Inpatient and outpatient	IV	P	Spain
Nerich *et al*., 2010[16]	218	14,854	1.46	1.44-1.47	Orders	Inpatient and outpatient	Oral, IV and Intrathecal	P	France
Serrano-Fabiá *et al*., 2010[17]	209	13,158	1.58	1.56-1.59	Patient-days	Inpatient and outpatient	Oral and parenteral	P	US
Ranchon *et al*., 2011[18]	408	6607	6.20	5.60-6.80	Prescriptions	Inpatient	IV and intrathecal	P	France
Ranchon *et al*., 2012[19]	540	17,150	3.10	2.90-3.40	Prescriptions	Inpatient	IV and intrathecal	P	France
Watts and Parsons, 2013[20]	37	34,111	0.10	0.10-0.10	Medications	Inpatient and outpatient	Oral, IV, and intrathecal	P	USA
Aita *et al*., 2013[21]	165	835	19.80	17.20-22.60	Prescriptions	Outpatient	Oral and IV	R	Italy
Dhamija *et al*., 2014[22]	8	205	3.9	3.83-3.96	Observations (patients)	Inpatients	Parenteral	P	India
Mathaiyan *et al*., 2016[23]	121	500	24.2	24.0-24.2	Observations patients	Outpatients	Parenteral	P	India
Preparation errors									
Limat *et al*., 2001[24]	140	30,819	0.50	0.40-0.50	Preparations	Inpatient and outpatient	IV	R	France
Serrano-Fabiá *et al*., 2010[17]	58	13,158	0.44	0.41-0.46	Patient-days	Inpatient and outpatient	Oral and parenteral	P	US
Ranchon *et al*., 2011[18]	26	6607	0.40	0.3-0.60	Prescriptions	Inpatient	IV and Intrathecal	P	France
Dispensing errors									
Serrano-Fabiá *et al*., 2010[17]	4.9	13,158	0.03	0.02-0.03	Patient days	Inpatient and outpatient	Oral and parenteral	P	US
Administration errors									
Serrano-Fabiá *et al*., 2010[17]	3	13,158	0.02	0.01-0.02	Patient days	Inpatient and outpatient	Oral, IV, and intrathecal	P	US
Ranchon *et al*., 2011[18]	5	6607	0.10	0.0-0.20	Prescriptions	Inpatient	IV and Intrathecal	P	France

P=Prospective; R=Retrospective, CI=Confidence interval

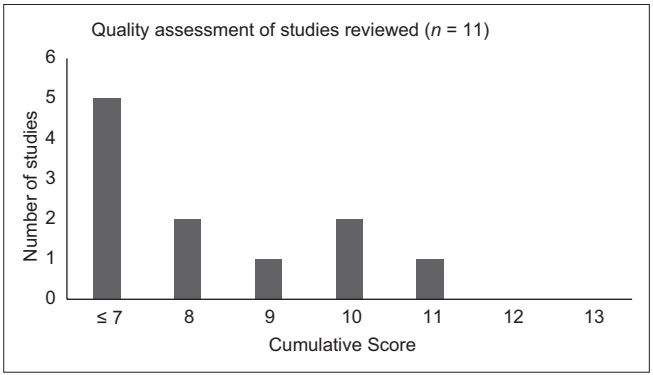

Figure 2: Summary of cumulative quality scores of the eligible studies

medication errors among these studies ranged from 0.004% to 41.6%. Of the 11 studies reviewed,[14-24] one study exclusively examined preparation errors. Ten studies focused on prescribing errors, three studies measured preparation errors, one reported dispensing errors, and two reported administration errors. Nine studies were prospective studies and two were retrospective studies. Overall rates of chemotherapy medication errors ranged from 0.1% to 24.6% in prescribing, 0.40% to 0.50% in preparation, 0.03% in dispensing, and 0.02% to 0.10% in administering categories. Majority of studies investigated medication errors for oral and intravenous routes of chemotherapy [Table 1] and were conducted mostly in adult populations [14,17-19,21] and few in pediatric populations.[20] The studies included in this review were mainly from the United States of America, Europe, and South Asia (few), indicating scarcity of data from other parts of the world.

Discussion

Medical error is one of the leading causes of death in the United States of America; it accounted for 9.7% of all deaths in the year 2013.[25] Medication error accounts for

440,000 deaths and it was attributed to 7000 deaths in the year 1993.[1,26] These reports indicate that medication errors including prescription, preparation, dispensing, and administering errors constitute major causes of adverse events leading to increased mortality. In this analysis, we observed that prescription error rate is the highest (among all the four phases investigated) and deserves attention to implement measures to minimize prescription errors. "Bad readability" is considered as a crucial cause for more than 50% of prescription errors.[27] Prescription errors were reported to be more common in ambulatory day-care units (54.8%) followed by other errors such as administration errors (20.7%).[23] As prescription phase is an initial step of medical care, preventive measures at this stage may aid in alleviating consequences, for example, prevention of irreversible damage due to an error of dose/drug during intravenous chemotherapeutic drug treatment. It is warranted to minimize prescribing errors by e-prescription systems.[28] E-prescription systems help physician or oncologist to send accurate, error-free, and understandable prescription and it can slash medication error rate in a hospital by two-thirds.[29] Implementation of e-prescription systems also reduced the percentage of primary nonadherence to treatment.[30] Electronic prescriptions may also provide cumulative dose alerts and decrease errors because of the confusion with drug names.[31] Implementation of computerized physician order entry (CPOE), a process of electronic entry medication by medical practitioner, will reduce/prevent the medication errors due to wrong identification of drugs, dose, cumulative dose, and dispensing errors. Approximately 20% of reported events after 2 years of CPOE implementation also reduced the risk of prescribing errors.[31,32]

Preparation errors were found to be the second highest errors (0.4%–0.5%) and were reported by three out of 11 studies [Table 1]. Automated preparation using robotic units may improve the quality of preparation, maintenance standards, and may improve safety of the pharmacy staff along with accurate preparation.[33] However, serious medication errors were not avoided with the use of robots, indicating other sources of preparation errors.[34] Pharmacies with better infrastructure and skilled personnel usually implement quality control systems to rectify the preparation errors. Quantifying the chemotherapeutic agent from the preparation before dispensing would allow rapid rectification of preparation errors in both settings of manual and robotic preparations.[35]

Dispensing errors were the least (0.1%), indicating that this error is preventable effectively, and had preventive measures in place already compared to prescribing errors. Predominant causes for dispensing errors are handwritten prescriptions, similarities in packing, interruptions, and lack of effective control on prescription label and medicine.[36] The most common dispensing errors reported were dispensing of wrong medication, wrong dose/strength, and wrong dosage form. The factors such as workload, inadequate knowledge on drugs, dosage forms, and communication gap between drug dispensing team increase the chances of dispensing errors.[37]

About 67 administration errors have been reported by four studies from Europe and one study from India. Administration errors have major impact especially with chemotherapy preparations.[38] Jeon *et al*. highlighted the importance of CPOE to reduce chemotherapy ordering, preparation, and administration errors.[39] CPOE is one of the best tools to minimize the medication error at any following stage. For example, Potts *et al*. observed 2.2% of potential adverse events, 30.1% of medication-prescribing errors, and 6.8% of rule violations before implementation of CPOE and were reduced to 1.3%, 0.2%, and 0.1%, respectively, after implementation of CPOE.[40] Similarly, reduction in chemotherapy order errors from 30.6% to 12.6% occurred after changing ordering system from handwritten orders to CPOE.[41] In limited resource settings, chemotherapy medication errors can be minimized by improving prescription practices, pharmacy and nursing services by a system that recognizes mistakes rapidly.[42]

This analysis has its own limitations. The first limitation of this review is that the results have to be seen considering reporting bias due to underreporting of medication errors. Many surveys in large American hospitals have suggested that on an average, less than half of the medication errors get reported.[43-45] The second limitation is the difficulty in comparing medication error rates in oncology across facilities of different size, using different methodologies and processes. Studies have used a different denominator while reporting medication error rates such as reported prescriptions, medications, patient years, and patients (observations).

Hence, we suggest peers in this arena to follow specific guidelines and best practices to report chemotherapy medication errors.[46,47] The American Society of Hospital Pharmacists guidelines emphasize the need for harmonization of reporting of medication errors in accordance with our observations in this analyses.[46] Standard way of reporting of medication errors will facilitate comparison among the reports or databases and thus can offer early solutions.

Conclusion

Prescription errors constitute the most common type of chemotherapy medication errors followed by preparation phase. This study also highlighted the need for harmonization of medication error reporting using common denominators.

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Conflicts of interest

There are no conflicts of interest.

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