

Chemotherapy Administration Safety Standards for Preventing Medication Error in Patients with Hodgkin and Non-Hodgkin Lymphoma

Maryam Mousavi*, Sepideh Elyasi**, Maryam Esmaeili**,
Mohammad Mahdi Kooshyar***, Azar Fani Pakdel****

*Research Center for Rational use of Drugs, Tehran University of Medical Sciences, Tehran, Iran

**Department of Clinical Pharmacy, School of Pharmacy, Mashhad University of Medical Sciences, Mashhad, Iran

***Department of Hematology and Oncology, Faculty of Medicine, Mashhad University of Medical Sciences, Mashhad, Iran

****Cancer Research Center, Mashhad University of Medical Sciences, Mashhad, Iran

Abstract

Background: Antineoplastic drugs are among medications that have narrow therapeutic index and high toxicity. For this reason, medication errors in patients with cancer are important and there have been myriads of efforts to decrease them. In this study, we attempted to assess the medication errors by designing chemotherapy standard forms for patients with Hodgkin's and non-Hodgkin's lymphomas.

Method: This cross-sectional study was performed in Omid and Imam Reza Hospitals, Mashhad, Iran from January 2016 to October 2016. The forms have been designed by clinical pharmacist based on available international guidelines and validated by clinical oncologists working in these two centers. Therapeutic regimens were selected by clinical oncologists and adherence of the oncologists and nurses to this form and probable medication errors were identified by the pharmacy students.

Result: In 206 visits of 62 Hodgkin's and non-Hodgkin's lymphoma patients, overall 790 antineoplastic drugs were administered to patients in whom 160 drugs were associated with medication error. The most common errors included improper dose (65%) and wrong infusion time (35%). One of the most important reasons for dosing errors was miscalculation of the BSA (40%).

Conclusion: This study shows that about two third of errors were improper dose. It seems that chemotherapy standard forms, if properly followed by nurses and physicians, could be useful and effective to reduce medication errors.

Keywords: Medication error, Hodgkin's disease, Non-Hodgkin's lymphomas, Chemotherapy standard form

*Corresponding Author:

Azar Fani Pakdel, MD
Omid Hospital, Koohsangi St.,
Mashhad, Iran
Tel: +98 51 38426082 051
Fax: +98 51 38428622 051
Email: fanipa@mums.ac.ir

Introduction

Medication errors are very serious in healthcare system. Antineoplastic drugs have narrow therapeutic index, which can cause serious toxicities even at FDA-approved indications and dosing plans.¹ Extra precautions are consequently necessary to prevent antineoplastic-related medication errors.²

The National Coordinating Council for Medication Error Reporting and Prevention (NCCMERP)'s definition of a medication error is "any preventable event that may cause or lead to inappropriate medication use or patient harm while the medication is in the control of the health care provider, patient, or consumer. Such events may be related to professional practice, health care products, procedures, and systems, including prescribing, order communication product labeling, packaging and nomenclature, compounding, dispensing, distribution, administration, education, monitoring, and use."³

The important concern for all oncologists and hematologists is administering these agents with the best possible safety and efficacy. This is necessary, since chemotherapy protocols are very complex involving several comedications and may also be given to elderly patients with several comorbidities. Although all precautions are taken, there is still the potential of serious medical errors during chemotherapy.⁴⁻⁷

If errors are not found during each treatment course, they may be repeated during the following chemotherapy courses. Chemotherapeutic agents must be viewed as "high-alert" medications in order to prevent medication error.⁸ To enhance the safety of chemotherapy administration, it is necessary to practically standardize chemotherapy protocols.⁷ Using validated preprinted form⁹ has been recommended as a method to decrease medication errors. Data from the literature have revealed that standardized chemotherapy forms reduce the incidence of medication errors and improve oncology patient care.⁹⁻¹³

The aim of this study was to evaluate the effects of chemotherapy standard form and identify the rate and types of medication errors in outpatient setting in patients with Hodgkin's and

non-Hodgkin's lymphomas.

Method

This was a cross-sectional interventional study conducted during January 2016 to October 2016 at oncology wards of two teaching hospitals, Imam Reza and Omid, affiliated to Mashhad University of Medical Sciences, Mashhad, Iran in outpatient setting. The patients with Hodgkin's (HL) and non-Hodgkin's lymphoma (NHL) aged between 17 and 70 years old signed the written consent form. Patients using herbal medications and those with renal (estimated glomerular filtration rate <50 mL/min), heart (ejection fraction <50, if echocardiography was available), or liver impairment were excluded from the study.

The study protocol was approved by the local Ethics Committee of Mashhad University of Medical Sciences (Ethics code: 930637).

A standard chemotherapy form was prepared by the clinical pharmacist based on the international available guidelines¹⁴ and reviewed and approved by all clinical oncologists working in these centers. Patients' demographic and clinical information consisted of age, weight, height, body surface area (BSA), past medical drug history, diagnosis, and stage of disease were collected in this form. Besides, all of the approved chemotherapy regimens for HL and NHL regimen (including type of regimen, dose of medications, route of administration and duration of the treatment course, type of diluent solution and its volume) were specified. Then, the oncologists selected the appropriate chemotherapy regimen for each patient in these preprinted forms. Then nurses prepared and administered the medications based on the form. These forms were collected by a pharmacy student in chemotherapy wards. All medication errors (e.g. selection of regimen, dose of medication, route of administration, duration of therapy, selection of suitable diluent, and rate of infusion) and possible adverse effect were evaluated and recorded by pharmacy student. Also the patient's height and weight were measured and BSA was recalculated based on the Du Bois formula to detect any error in calculation of BSA. If the difference was more

than 5%, we considered it as an error. The Du Bois formula, which is the western standard formula, was validated to a greater extent and its accuracy was confirmed more than others.¹⁵ Doses were recalculated according to the right BSA to detect any medication error.

Any medication order that was >10% over or under the calculated dose or defined duration was considered dosing or duration error.¹⁶⁻¹⁷ In addition, acute adverse drug reactions occurred in patients during drug administration, were also recorded based on Common Terminology Criteria for Adverse Events (CTCAE) version 4. Results were tabulated and analyzed using MATLAB software and shown as mean \pm standard deviation (SD) or number (percentages) for nominal variables.

Result

During the 7-month prospective study on 62 adult patients, 206 chemotherapy course and 790 medications were assessed. The mean patient age in HL was 31.57 ± 12.31 and NHL was 53.72 ± 14.07 years. All patients with HL and NHL received ABVD and CHOP or CHOP-R regimens, respectively. In total, 160 medication errors were recorded, 65% of which were improper dose (104

Table 1. Data of this study

Parameter	Number
Patients	62
Visits	206
Medications	790
Medication errors	160
Improper dose	104
Incorrect duration of infusion	56
Wrong route of administration	0
Wrong medication	0
Incorrect selection of solution	0

courses out of 206 courses of chemotherapy) and 35% were nurse administration errors. Dosing error in these 104 courses included under dosing (75.96% of improper dose), overdosing (13.46% of improper dose), and mixed of under and over dosing for different medications of regimen (10.58%). Moreover, in 84 out of these 104 courses (40%), miscalculation of BSA occurred via Du Bois formula. BSA was considered lower than actual value in most of these cases (93%).

Incorrect duration of infusion was reported in 56 courses out of 206 evaluated courses which was longer than recommended duration in 75% of cases. Rituximab was the most common medication involved in this type of error, because nurses were too much cautious about the infusion-

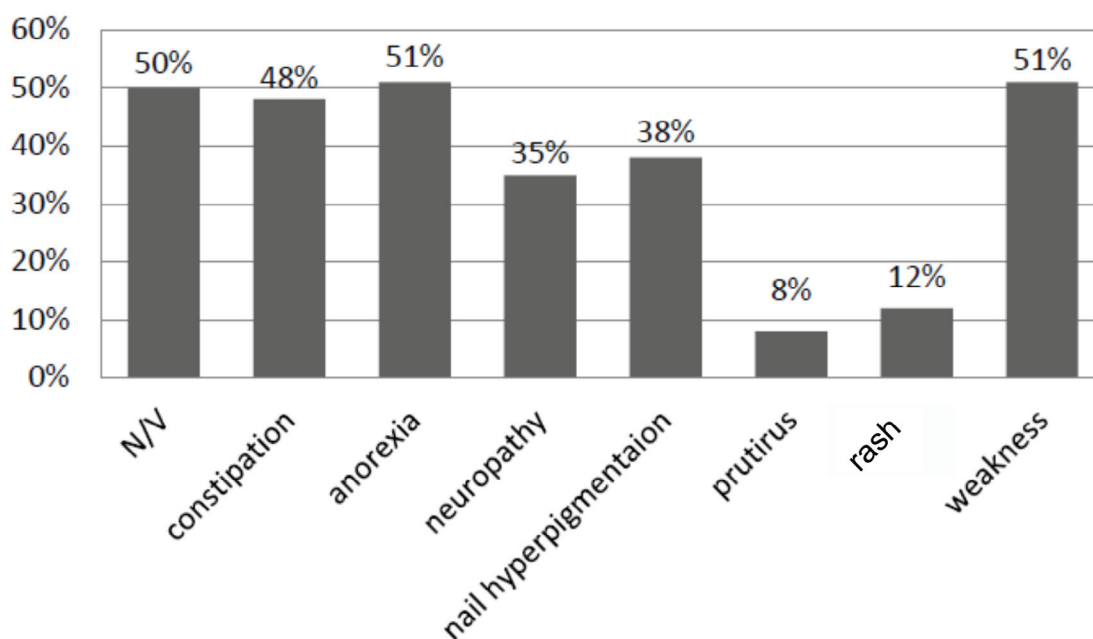


Figure 1. The frequency of reported adverse reactions during the study in Hodgkin's disease patients. (N/V: Nausea / Vomiting).

related reactions of rituximab. The diluent solution selection and its volume and also route of administration were correct in all courses. No patient received wrong medication (Table 1).

The most common adverse drug reaction observed in this study in HL was weakness and anorexia (51%), followed by nausea and vomiting (50%) (Figure 1). In NHL patients neuropathy (66%), weakness (45%), and nail hyperpigmentation were the most common adverse reactions, respectively (Figure 2). It is important to mention that in 8 out of 102 courses, in which patients received rituximab infusion (7.84%), the infusion related reactions occurred and all of these cases were managed properly by using hydrocortisone and chlorpheniramine injections and also supplement oxygen. Two cases of extravasation also occurred with vincristine and doxorubicin managed appropriately by the oncologist.

Discussion

There are few number of studies evaluating medication errors in chemotherapy in inpatient or outpatient setting. In the present study, the error rate was 77 %. Rinke et al. reported merely 1% chemotherapy error rate in adult and pediatric patients;¹⁷ whereas, Walsh et al. reported an 8.1%

error rate in the outpatient setting.¹⁸ The error rate in Dhemaji's study was 11%.¹⁶ By assessing the standard forms, it was concluded that the physicians selected all the regimens according to the standard guideline. It means that using this preprinted standard form made this part of prescribing process flawless. By reviewing patients' files, it was observed that the most common error was dose calculation. In administration phase, nurses did not use standard forms properly and even this part of the forms was incomplete in some cases; thus, evaluation of the standard forms effect in this phase was not possible. However, in some parts such as selecting the type and volume of diluents, there were no medication errors. Fyhr noted that prescribing errors (42%) occurred more than administering errors (16%).¹⁹ However, some studies reported the opposite (Table 2).¹⁶⁻¹⁸

While analyzing the epidemiology of errors in the present study, it was observed that 63% of errors occurred in prescribing phase and 37% occurred during the administering phase of chemotherapy. The dosing error rate in the present study was more than the mean dosing error rate of similar studies.

While analyzing the epidemiology of errors

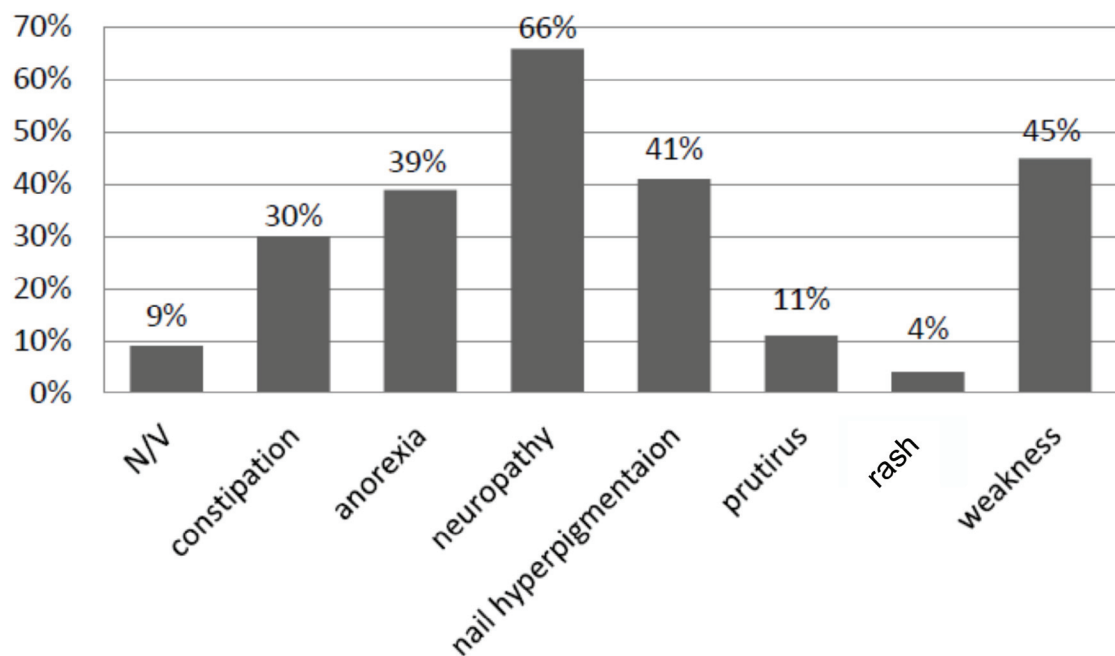


Figure 2. The frequency of reported adverse reactions during the study in non-Hodgkin's disease patients. (N/V: Nausea / Vomiting).

Table 2. Epidemiology of ME in chemotherapy and comparison with published literature

References	Fyhr et al.	Rinke et al.	Dhamij et al.	Walsh et al.	Current study
Year	1996-2008	1999-2004	2012	2008	2015
Length of the study	12 years	5 years	8 months	9 month	6 months
Design	Retrospective	Retrospective	Retrospective	Retrospective	Prospective
Patients age (y)	All ages	<18	<18	All ages	18-70
ME rate (%)	NS	1	11	8.1	77.6
Dosing error rate (%)	45	22.9	9	NS	65
Rate of error in duration of infusion	NS	NS	26	NS	35
Wrong route	NS	12.2	NS	NS	0
Wrong patients	0.08	NS	NS	NS	0
Wrong drug	30	NS	NS	NS	0

ME: Medication errors; NS: Not significant

in the present study, we observed that 63% of errors occurred in prescribing phase and 37% occurred during the administering phase of chemotherapy. In the present study, the dosing error rate was more than the mean dosing error rate of similar studies. Incorrect calculation of drug doses included both over and under dosing. However, under dosing errors did not lead to serious side-effects because if the dose is too low, it will just make the treatment ineffective; whereas, at excessive doses, the toxicity can occur in patients.²⁰

It is quite essential to reduce the potential for errors in the prescribing and administering stage, which could be done via electronic chemotherapy order form. In the electronic forms, the ordering program calculated the BSA after inserting the height and weight, eliminating the potential for a manual miscalculation. The computer program electronically calculated the total dose to be administered based on the calculated BSA.²¹

A study conducted in order to compare the traditional unstandardized blank order sheets, the standard written forms, and electronic chemotherapy form. Results showed that the completeness of chemotherapy order improves significantly through the standardization of chemotherapy order forms. The electronic forms also demonstrate an additional improvement over hand-written standard forms in terms of completeness and electronic calculation of BSA and chemotherapy doses.²¹ Patients are the last line of defense against an error; thus, they should be well-educated about their chemotherapy

regimens.²² To be informed of their treatment, they would be able to involve in the detection and prevention of errors.²³

However, it should be mentioned that the high rate of prescription errors in this center might be due to limited access to medications and their high prices, which forced oncologists in most cases to round the doses to the available dosage form and reduce the cost. In practice, there are many limitations to prescribe the exact amount of medicine (e.g. high price and limited dose packages). Often, the prescribing dose of a cytotoxic drug is not solely based on a protocol. Dose modification is based on other medical factors - performance status, nutritional status, existence of comorbidities, bone marrow reserve, current blood counts, and previous adverse effects of the chemotherapy regimen. In numerous cases, the standard regimens were modified because of the lack of facilities to admit patients, which forced them to use outpatient chemotherapy and resulted in shorter infusion time or duration of treatment course. Prescribing a specific dose of a cytotoxic agent is mainly a medical judgment based on patient status and not solely on the protocol of a regimen.

This study suffered some limitations. First, time of the study was short and thus limited number of patients was included. Second, as we did not perform a preimplementation phase study, we could not compare pre- and post-implementation error rate. Third, some types of possible medication errors particularly in the preparation phase by nurses was not evaluated

in this study, neither was the chronic drug adverse reactions.

Conclusion

In conclusion, for this study, we examined 217 chemotherapy visits and 89 medication errors were recorded in two outpatient centers. The result showed that chemotherapy standard forms were efficient if it was used accurately. Fortunately, no life-threatening morbidity was observed during study.

References

- Muller T. Typical medication errors in oncology: analysis and prevention strategies. *Onkologie*. 2003; 26(6): 539-44.
- Gilbar PJ. Preventing medication errors in cancer chemotherapy referred to rural and remote hospitals. *Aust J Rural Health*. 2001; 9(1):47-51.
- National Coordinating Council for Medication Error Reporting and Prevention. NCC MERP Index for Categorizing Medication Errors. [cited on: February 20, 2001]. Available from: <http://www.nccmerp.org/sites/default/files/indexColor2001-06-12.pdf>.
- Bates DW, Spell N, Cullen DJ, Burdick E, Laird N, Petersen LA, et al. The costs of adverse drug events in hospitalized patients. Adverse Drug Events Prevention Study Group. *JAMA*. 1997; 277(4):307-11.
- Gandhi TK, Bartel SB, Shulman LN, Verrier D, Burdick E, Cleary A, et al. Medication safety in the ambulatory chemotherapy setting. *Cancer*. 2005; 104(11):2477-83.
- Kohn LT. The Institute of Medicine report on medical error: overview and implications for pharmacy. *Am J Health Syst Pharm*. 2001; 58(1):63-6.
- Markert A, Thierry V, Kleber M, Behrens M, Engelhardt M. Chemotherapy safety and severe adverse events in cancer patients: strategies to efficiently avoid chemotherapy errors in in- and outpatient treatment. *Int J Cancer*. 2009; 124(3): 722-8.
- Schulmeister L. Preventing chemotherapy errors. *Oncologist*. 2006; 11(5):463-8.
- Cohen MR, Davis NM. Developing safe and effective preprinted physician's order forms. *Hosp Pharm*. 1992; 27(6):508-28.
- Goldspiel BR, DeChristoforo R, Daniels CE. A continuous-improvement approach for reducing the number of chemotherapy-related. *Am J Health-Syst Pharm*. 2000; 57(4): S4-9.
- Olsen M. Order sheets help prevent chemotherapy administration errors. *Oncol Nurs Forum*. 1997; 24(5):802-3.
- Opfer KB1, Wirtz DM, Farley K. A chemotherapy standard order form: preventing errors. *Oncol Nurs Forum*. 1999;26(1):123-8.
- Thorn DB, Sexton MG, Lemay AP, Sarigianis JS, Melita DD, Gustafson NJ. Effect of a cancer chemotherapy prescription form on prescription completeness. *Am J Hosp Pharm*. 1989; 46(9):1802-6.
- Herdrich K, Weinberger H. Selected schedules in the therapy of malignant tumors. 17th ed. Frankfurt: Baxter Oncology. 2014.p.119 -147.
- Kouno T, Katsumata N, Mukai H, Ando M, Watanabe T. Standardization of the body surface area (BSA) formula to calculate the dose of anticancer agents in Japan. *Jpn J Clin Oncol*. 2003; 33(6):309-13.
- Dhamija M, Kapoor G, Juneja A. Infusional chemotherapy and medication errors in a tertiary care pediatric cancer unit in a resource-limited setting. *J Pediatr Hematol Oncol*. 2014;36(7):e412-5.
- Dickens DS, Sinsabaugh D, Fahner JB. Characteristics of pediatric chemotherapy medication errors in a national error reporting database. *Cancer*. 2007; 110(1):186-95.
- Walsh KE, Dodd KS, Seetharaman K, Roblin DW, Herrinton LJ, Von Worley A, et al. Medication errors among adults and children with cancer in the outpatient setting. *J Clin Oncol*. 2009; 27(6):891-6.
- Fyhr A, Akselsson R. Characteristics of medication errors with parenteral cytotoxic drugs. *Eur J Cancer Care*. 2012; 21(5):606-13.
- Corrie PG. Cytotoxic chemotherapy: clinical aspects. *Medicine*. 2008; 36(1):24-8.
- Dumasia L, Harris E, Drelichman A. Quality performance improvement with the implementation of standard chemotherapy order forms. *J Oncol Pract*. 2006;2(3):104-7.
- Kloth D. Guide to the prevention of chemotherapy medication errors. *Clin Oncol News*. 2009; 1:1-7.
- Schwappach DL, Wernli M. Medication errors in chemotherapy: incidence, types and involvement of patients in prevention. A review of the literature. *Eur J Cancer Care*. 2010. 19(3): 285-92.