Revista de Ciências Farmacêuticas Básica e Aplicada
Journal of Basic and Applied Pharmaceutical Sciences

Rev Ciênc Farm Básica Apl, 2018;39:e625
ISSN 1808-4532

Prescription errors and associated factors in patients with oncologic and hematologic diseases in a tertiary hospital

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ABSTRACT

Medication errors extend inpatient stay, increase costs and double the risk of death. Identify patients more likely to present prescription errors would be one manner that could be used to decrease the impact of such events. Thus, the present study identified the prevalence of prescription errors with patients with oncohematologic diseases and the factors associated with these events. A cross-sectional study was performed in a Brazilian tertiary hospital. Data regarding service, patients and their clinical condition, drug therapy and prescription errors were retrieved and analyzed. Of 344 drug prescriptions identified, 26.2% showed at least one prescription error, mainly involving a wrong drug (48.3%). According to the logistic regression, the factors associated with errors include: presence of neutropenia OR 1.92 (95% CI 1.10-3.35), physicians on holiday or weekend shifts OR 0.40 (95% CI 0.18-0.86) and prescriptions with higher proportion of parenteral administration route OR 1.05 (95% CI 1.03-1.08). In conclusion, identify the factors associated with errors can be useful in developing clinical tools for predicting patients at higher risk for the occurrence of prescribing errors, as well as to contribute to the optimization of health professionals' clinical performance.

Keywords: Patient Safety. Inappropriate Prescribing. Risk Management. Neoplasms. Oncology Service, Hospital.

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INTRODUCTION

Adverse drug events (ADE) include all of the errors made in the medication process that can cause the inappropriate use of drug and the patient's harm (National Coordinating Council for Medication Error Reporting and Prevention, 2001). ADE extend inpatient stay (McCarthy et al., 2017), increase risk of death (Classen et al., 1997; Ferrah et al., 2017), decrease health-related quality of life (Mhatre & Sansgiry, 2016) and increase costs (McCarthy et al., 2017; Walsh et al., 2017). A Korean study has identified in a large volume chemotherapy preparation unit that for every dollar spent with clinical pharmacist a net benefit of 3.64 dollar is expected (Han et al., 2016).

Regarding antineoplastic agents, León Villar et al. (2008) identified that prescription errors are the most frequent (45%) medication errors. In a Brazilian outpatient oncology and chemotherapy clinic, 6% prescriptions contained errors (Duarte et al., 2019).

As it may be impossible to intercept all prescription errors depending on the context, some authors proposed the monitoring of risk factors in order to optimize the practice of clinical pharmacists. Sakuma et al. (2012), in critical condition and with patients undergoing surgical procedures, described risk factors associated with adverse drug events, such as the patient's clinical condition, type of admission and drugs used before admission and during hospitalization. However, there is no evidence about potential risk factors in the Brazilian context of oncohematologic diseases.

To identify patients more likely to present prescription errors would be one manner that could be used to decrease the impact of such events and contribute to making clinical pharmacist practice more accessible and efficient. Thus, the objective of this study was to identify the prevalence of prescription errors of drug prescriptions of patients diagnosed with oncologic and hematologic diseases and the factors associated with these errors.

METHOD

Study design and Ethical

This is an observational, analytical, cross-sectional study reported considering Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) statement (Von Elm et al., 2007).

Setting and Participants

The study was carried out in a tertiary teaching hospital located in the state of Parana, south of Brazil. The hospital has 550 active beds, in which 10 beds correspond to the assessed unit. There, the drugs prescription was reviewed by the clinical pharmacy team. The inclusion criteria were prescriptions for patients with the main diagnosis of oncologic and hematologic disease. Exclusion criteria were prescriptions not being assessed by clinical pharmacy team.

The clinical pharmacy team in the High Risk Chemotherapy Unit is comprised by one pharmacist residents under preceptorship of one pharmacist. This service consists of a daily medication review of drug prescription, including antineoplastic agents, support drugs, and treatment of chronic diseases, as well as participation in clinic visits and contact with prescribing physician and nursing team. Electronic drug prescriptions are generated every 24 hours and drugs are administered only after clinical pharmacist review.

Variables, data sources and measurement

Data collection was accomplished by considering the drug prescription from the given day, through information obtained from the patients' charts, as well as from the laboratory test results obtained via the hospital's electronic database. The extracted data were related to service characteristics, patient characteristics, clinical parameters, prescribed drugs and type of prescription error (Table 1).

Prescription errors were classified according to the National Coordinating Council for Medication Error Reporting and Prevention (5) taxonomy (NCCMERP). The prescription errors were further classified into two kinds: errors related to the choice of therapy and errors related to writing errors. In order to obtain a more comprehensive assessment of the prescriptions, two additional types of errors not considered by NCCMERP were included: the need for additional therapy and the availability of a more cost-effective drug.

Quantitative variables

For the descriptive analysis of the most frequent drugs, there were two kinds of frequencies: the first consists of the ratio between the absolute number of events related to a given drug and the total number of errors and the second is the ratio between the absolute number of events related to a given drug and the total number of times this drug was prescribed. Thus, the first frequency allowed for the identification of the drugs most involved with errors without the adjustment for its number of prescriptions. The second frequency allowed for the identification of the drugs most likely to be related to errors, with an adjustment for its number of prescriptions.

Statistical methods

Data were analyzed using the Statistical Package for Social Sciences, version 20. Since the variables have non-parametric distributions (Kolmogorov-Smirnov), the bivariate analysis consisted of relative frequencies, the median and the Spearman test. From this analysis, eligible variables for the predisposing factors with correlation ($p<0.05$) with prescription errors were identified. Collinearity diagnosis was made by the variance inflation factor, and collinear variables were excluded from the model. The selected variables were included in the logistic regression associated with the Hosmer-Lemeshow grip, by the method enter. The Wald test was used to determine the coefficient for a given predictor model differed significantly from 0. The results were expressed as an odds ratio confidence interval, and values were considered significant at $p < 0.05$ (95% confidence interval, 95% CI).

Standard protocol approvals

The present study was approved by the Research Ethics Committee of the Clinics Hospital, Federal University of Parana (nº 14122113.3.0000.0096).

RESULTS

During the study, were identified 977 drug prescriptions, in which 633 were excluded due to not being assessed by clinical pharmacy team. Therefore, data from 344 drug prescriptions from 31 patients were collected (Figure 1 and Table 2).

Table 1. Variables and sources.

Variable	Source
Service characteristics	
Admission data	Medical prescription
Admission type (scheduled or emergency)	Medical prescription
Admission unit	Medical prescription
Patient characteristics	
Age	Medical prescription
Sex	Medical prescription
Body surface area	Medical prescription or patients' charts
Clinical parameters	
Diagnosis	Patients' charts
Stage of disease	Patients' charts
Renal failure	Patients' charts
Hepatic dysfunction	Patients' charts
Infection	Patients' charts
Prescribed drugs (name and administration route)	Medical prescription
Prescription error (NCC-MERP)	Medication review
Type of prescription error (choice or writing)	Medication review

The 344 drug prescriptions represented 3,658 drugs, or 10 drugs per prescription (interquartile range 8 to 12); parenteral administration was the most common route of the drugs (54,5%); 10,8% drug prescriptions were made on holiday or weekend shifts. The five most frequently prescribed drugs were support drugs for antineoplastic agents and antimicrobial therapy: metamizole (8.1%), ondansetron (8.0%), sulfamethoxazole/trimethoprim (7.2%), omeprazole (6.3%), fluconazole (6.3%).

Regarding prevalence and errors characteristics, out of 344 assessed prescriptions, 90 (26.2%) showed at least one error, totaling 116 prescription errors (1.3 errors/prescription). The most frequent error, according to the NCCMERP taxonomy, was the prescribing of the wrong drug (48.3%) (Table 3). Regarding the wrong drug, 26 (46.4%) prescriptions were for unnecessary therapy, 18 (32.1%) involved wrong drug choice and 12 (21.4%) involved therapy duplication. Errors evolving a need for additional therapy and the prescription of a less cost-effective drug were found in 14.6% of the total of the prescription errors identified. Strictly considering the NCCMERP classification, the frequency of prescriptions with at least one error was 23.5%.

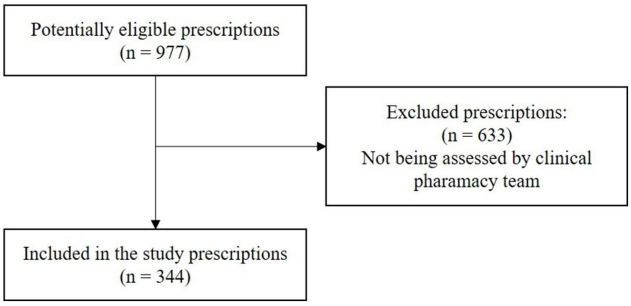

Figure 1. Flow chart of selection of medical prescriptions.

Table 2. Characteristics of drug prescriptions and patients.

Characteristics	
Total number of patients, n	31
Age, median (IQR)	39 (22-57)
Female, n (%)	19 (61.3)
Patients with comorbidity, n (%)	9 (29.0)
Type of cancer	
Hematologic, n (%)	23 (74.2)
Solid Tumors, n (%)	8 (25.8)

IQR: Interquartile range 25%-75%.

Table 3. Types of prescription errors and frequency of occurrence (n = 116).

Type of prescription error	N (%)
Wrong drug	56 (48.3)
Non-mentioned by NCCMERP	17 (14.7)
Improper dose resulting in extra dose	16 (13.8)
Improper dose resulting in under dosage	14 (12.1)
Wrong route of administration	4 (3.4)
Wrong duration	4 (3.4)
Monitoring error – clinical	3 (2.6)
Improper dose resulting in overdosage	1 (0.9)
Wrong rate – too slow	1 (0.9)
Total	116 (100.0)

A total of 127 different drugs were identified in the prescriptions analyzed and five drugs were involved in 41.1% of the prescription errors. These drugs were dexamethasone/polymyxin B (10.7%), vancomycin (10.7%), morphine (8.9%), ranitidine (5.4%) and allopurinol (5.4%). The drugs most likely to be related to errors, in decreasing order of frequency, are daptomycin (100.0%), dexamethasone/polymyxin B (100.0%), ranitidine (100.0%), anidulafungin (100.0%), glibenclamide (100.0%). Thus, dexamethasone/polymyxin B, vancomycin and ranitidine are drugs related to high frequency, both in terms of total errors and their total prescriptions.

In bivariate analysis, a correlation was found ($p < 0.05$) between prescription errors and physicians on the holiday or weekend shift, comorbidity, presence of neutropenia, administrations number and higher proportion of parenteral route of administration. No correlation was found with length of stay, age, sex, diagnosis, stage of disease, renal or hepatic dysfunction, body surface area, infection, drugs and other drug delivery routes.

The prevalence of prescription errors related to the therapy or drug regimen selection (51.7%) and to the prescription writing were similar (48.3%). However, among the errors related to therapy choice, a predominance of improper dosage resulting in an under-dosage, as well as errors not considered in NCCMERP, were also observed. On the other hand, among the errors related to writing, there was a predominance of improper dosages resulting in an extra dose ($p < 0.05$).

In the multivariate analysis, only variables with a statistically significant bivariate correlation with the absence or presence of a prescription error adjusted for age and sex were included. Only comorbidity ($p = 0.550$), sex ($p = 0.820$) and age ($p = 0.690$) were not correlated. Presence of neutropenia OR 1.92 (95% CI 1.10-3.35; $p = 0.022$), physicians on holiday or weekend shifts OR 0.40 (95% CI 0.18-0.86; $p = 0.019$) and prescriptions with higher proportion of parenteral administration route OR 1.05 (95% CI 1.03-1.08; $p < 0.001$), were factors associated with the presence of a prescription error ($R^2 = 0.22$).

DISCUSSION

A high prevalence of errors involving mainly drug choice and improper dose was identified. Prescription errors are common in units that focus on the care of patients with oncologic and hematologic diseases. In this population, specific and dynamic clinical performance of the pharmacist is required, with a goal of optimizing the time and the convergence of information among different healthcare teams, patient and caregivers (Leveque et al., 2014; Delpeuch et al., 2015).

Our study shows a high prevalence of prescription errors (26.2%), even excluding the ones not mentioned by NCCMERP (23.5%), of which 6.9% are errors contemplating only the antineoplastic agents. Other studies involving patients diagnosed with neoplasms and comprising only antineoplastic agents identified a prevalence of 1.5% to 20.0%

(Ranchon et al., 2011, 2012; Aita et al., 2013; Meisenberg et al., 2014; Ferracini et al., 2018; Duarte et al., 2019). Thus, although antineoplastic drugs are considered potential harmful, the drugs most related to errors were antimicrobial agents and support therapy in our study, resulting in a high prevalence of prescription errors which show the importance of clinical pharmacy in oncology and hematology consider all type of drugs in medication review.

It was observed that resident physician coverings holiday or weekend shift had protective effect on the occurrence of prescription errors, which may occur due to higher available time for each patient. On the other hand, presence of neutropenia and prescriptions with higher proportion of parenteral administration route had risk of effect, indicating that patients may be associated with a higher critical state of the patient, corresponds to a marker of risk. Ranchon et al. (2012), in a French study that assess different variables, identified protocols involving carboplatin (OR: 4.47, 95% CI 3.45-5.79, p< 0.001), protocols with more than three drugs (OR: 2.4, 95% CI 1.92-3.00, p< 0.001) and protocols requiring at least one modification (OR: 1.33, 95% CI 1.04-1.69, p= 0.02) as independent factors for prescribing drug. As the variables assessed were different is not possible to infer probable reasons for the difference.

This study presents limitations related to its design and sample size, which may have impaired the statistical power of the analysis. Although the external validity of the study results is low, current results suggest the importance of considering all types of drug in medication review, as well as in defining the risk factor for prescribing errors.

Physicians on holiday or weekend shifts (protective effect), presence of neutropenia (risk effect), and prescriptions with higher proportion of parenteral administration route (risk effect) were the main factors associated with prescription errors. Recognizing them can be valuable in developing clinical prediction tools, alerts to clinical pharmacists or designing preventive services focused on identifying patients who are more susceptible to prescription errors.

RESUMO

Erros de prescrição e fatores associados em pacientes com doenças oncológicas e hematológicas em um hospital terciário

Os erros de prescrição prolongam a internação, aumentam os custos e duplicam o risco de morte. Identificar os pacientes mais propensos a apresentar erros de prescrição seria uma maneira que poderia ser usada para diminuir o impacto de tais eventos. Assim, o presente estudo identificou a prevalência de erros de prescrição com pacientes com doenças oncohematológicas e os fatores associados a esses eventos. Um estudo transversal foi conduzido em um hospital terciário brasileiro. Os dados referentes ao serviço, aos pacientes, às condições clínicas, à terapia medicamentosa e aos erros de prescrição foram coletados e analisados. De 344 prescrições de medicamentos, 26,2% apresentaram pelo menos um erro de prescrição, envolvendo principalmente medicamento inadequado (48,3%). De acordo com a regressão logística, os fatores associados aos erros incluem: presença de neutropenia OR 1,92 (IC 95%: 1,10-3,35), médicos em turnos de férias ou em fim de semana OR 0,40 (IC 95%: 0,18-0,86) e prescrições com maior proporção de via parenteral de administração OR 1,05 (IC 95%: 1,03-1,08). Em conclusão, identificar os fatores associados aos erros pode ser útil no desenvolvimento de ferramentas clínicas para prever pacientes com maior risco de ocorrência de erros de prescrição, além de contribuir para a otimização do desempenho clínico dos profissionais de saúde.

Palavras-chave: Segurança do Paciente. Prescrição Inadequada. Gestão de Riscos. Neoplasias. Serviço Hospitalar de Oncologia.

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Received on November 16th 2018
Accepted on December 21st 2018