Medication errors in hematology-oncology ward by consultation: The role of the clinical pharmacologist

Abstract

Background: The aim was to describe, evaluate and document the prevention of medication errors by clinical pharmacologist consultations in patients with cancer.

Methods: We assessed the effect of clinical pharmacologist consultation by the acceptance of interventions recommended due to dosage, frequency, duration of therapy errors and drug-drug interactions (DDIs). All medication errors detected by clinical pharmacologist were reported in the format of medical consultation. A documentation template was designed to collect the patient’s data (sex, age, and diagnosis), prescriptions written, and drug-specific recommendations. For the descriptive analysis of medication errors, the unit of analysis was the number and percentage of errors.

Results: A total of 296 patients included in this study with a median age of 48.67±19.76 years of which 47.30% were females. 936 prescribing errors were detected and recommended for their correction. The specialist physicians accepted 897 of prescribed errors. DDIs that were detected in 66.22% of patients, were the most errors in this group of errors (47%). Improper dose (17.41%) wrong frequency (16.67%) and drug-food interaction (10.26%) were after that.

Conclusion: Pharmacological consultation in the hematology-oncology ward revealed many medication errors. The trust of physicians in the views of the clinical pharmacologist led to a large part of these errors being accepted and resolved.

Keywords: Clinical pharmacologist, Medication error, Patient safety

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Medication errors can occur every time and at any stage of the treatment process from prescribing to delivery of the drug to the patient. Moreover, the medication process involves the whole medical team, including physicians pharmacists and nurses (1). Medication errors with antineoplastic drugs can be very harmful and difficult, because this group of drugs are very toxic and have small therapeutical index (2). Antineoplastic agents are the second most common cause of fatal medication errors. (3). From the patient's safety perspective, the prevention of anticancer drug errors in hospitals has a significant priority and several recommendations have been published in various ways to reduce the likelihood of these errors (4). Currently, there are no positions for clinical pharmacologists specialized for onward activities in Iran. The number of hospital pharmacists are not enough, (on average, 0.86 hospital pharmacists are available per 100 hospital beds), in comparison with 1.42 in the United Kingdom and 14.1 in the USA. Also back-office activities (such as drug delivery to wards, medication logistics) take- up most of the hospital pharmacist’s time. On the other hand, the majority of them are not specialized pharmacists (5). Few clinical pharmacologists are doing consultation as well.

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For this reason, the implementation of interventions by clinical pharmacologists in other countries such as Denmark, Russia, etc. (6, 7) in our hospital setting was not possible in this study. To run such programs, we need to have a full-time clinical pharmacologist. But given the fact that the information of doctors, nurses and health providers about the drug safety problems is rising, constructive interventions of Iranian clinical pharmacologists seem to be desirable.

We therefore designed a pharmacologic consultation program for a clinical pharmacologist that was tailored to our specific setting, and conducted an intervention study to explore whether consultation could improve medication safety in an Iranian hospital ward (hematology and oncology) or not. Our main research questions were: a- Is the designed program associated with a reduction in prescribing errors and increasing patient safety? b- Can the study results be generalized to other wards of a hospital?

Methods

Design and setting: Following approval from the Ethics Committee of Urmia University of Medical Sciences, the study was performed in the hematology-oncology ward of an academic tertiary care 300-bed hospital in Urmia-Iran. The medical staff of the closed-format, 25-bed hematology-oncology ward consisted of board-certified intensivists attends, residents, interns and nurses.

The aim of the study was to describe, evaluate and document the prevention of medication errors by clinical pharmacologist interventions in patients with cancer. We assessed the effect of clinical pharmacologist consultation by the number and acceptance of interventions recommended by the clinical pharmacologist due to dosage, frequency, duration of therapy errors and DDIs based on the interventions identified by Leape et al. (8). The intervention was the assignment of an experienced senior clinical pharmacologist to evaluate drug chart of 296 patients admitted in the hematology-oncology ward between March to September 2017. All medication errors detected by clinical pharmacologist were reported in the format of medical consultation, reviewed and analyzed accordingly. A documentation template was designed to collect the following information: patient data (sex, age, and diagnosis), prescriptions written and drug-specific recommendations and outcome measures. The clinical pharmacologist tells his comments and recommendations to the residents, and attending staff to reform them. All possible paired combinations drug-drug were recorded and analyzed using the book Drug Interaction Facts 2015 by David S. Tatro- a book chosen because of its high accuracy when compared to other references (9). In this study, nutritional supplements, serums, electrolytes and vitamins have not been investigated. Patients readmitted during the study period and received the same drugs were excluded from the present study. Consecutive patients who fulfilled the inclusion criteria were recruited.

Statistical Analysis: Quantitative data were analyzed using SPSS for Windows Version 17.0. For the descriptive analysis of medication errors, the unit of analysis was the number and percentage of errors, with a prescribing medication order containing one or more drugs was considered to correspond to one or more medication errors. We used proportional-odds ordinal logistic-regression models to compare multiple outcome categories to assess the independent effect of age, gender and number of drugs on the frequency of the patient’s errors.

Results

A total of 296 patients included in this study with a median age of 48.67±19.76 of which 47.30% were females. The median number of drugs used per person was 5.65. Demographic characteristics are listed in table 1. During the 6-month study period, 1672 prescriptions (including chemotherapy and support) of 296 adult cancer patients were prospectively analyzed. The clinical pharmacologist identified 936 drug-related problems (55.98% of the prescriptions). One or more medication errors were identified for 262 (88.50%) of the 296 patients. The specialist physicians accepted 897 of prescribed errors (95.83%). DDIs that were detected in 66.22% of patients, were the most errors in this group of errors (47%). Improper dose error (17.41%), wrong frequency (16.67%) and food-drug interaction (10.26%) were after that. Wrong route of administration and wrong drug for indication included the minimum number of errors (5.13% and 3.53%, respectively). The most drugs involved in medication errors were cardiovascular system drugs followed by gastrointestinal related drugs, nervous system agents, anticancer and anti-infective drugs, respectively. Examples of the most significant DDIs (grade 1) that need attention by physicians were shown in table-2. Examples of the most drugs that have been prescribed improperly from the point of dose have been shown in table-3.
Table 1. Demographic profile of 296 in-patients hospitalized during the period under study

| Average number of drugs per encounter | Type of Cancer and Number of Patients | Sex | Age/Year Mean±SD |
|---------------------------------------|--------------------------------------|-----|------------------|
| 5.65 Others:38 Multiple Leukemia Lymphoma | Genitourinary Lung Gastrointestinal Breast Female Male | 48.67±19.7 |
| Myeloma:47 a:126 :35 | :19 :5 :18 :8 | :140 :156 | 6 |

Table 2- The most prevalent potential drug interactions

| The Five most prevalent potential drugs with Grade=1 Significance interactions | Examples |
|---------------------------------|----------|
| ASA                             | ASA+Heparin |
| Heparin                         | ASA+Warfarin |
| Antifungal Azoles               | Azoles+Vincristine |
| Warfarin                        | Azoles+Opioid |
| Opioides                        | Warfarin+NSAID |

Table 3- Examples of improper dose

| Drug        | Cause of improper dose                          |
|-------------|-------------------------------------------------|
| Vancomycin  | No dose adjustment due to GFR reduction         |
| Gentamicin  | No dose adjustment due to GFR reduction         |
| Pantoprazole| Due to a prescription abroad from the relevant Guideline |
| IVIG        | Due to a prescription abroad from the relevant Guideline |
| Warfarin    | Due to drug-drug interaction                     |
| Methotrexate| Due to drug-drug interaction                     |

Table 4. Prescription Errors

| Prescription Errors (936) | Type of errors(No.) | Type of recommendations(No.) | Outcome |
|--------------------------|---------------------|------------------------------|---------|
| Improper dose(163)       | Change in drug dosing | Consensus (158)              | No Consensus(5) |
| Wrong frequency(156)    | Change in dosing frequency | Consensus(151)              | No Consensus(5) |
| Wrong route of administration(48) | Change in route of administration | Consensus(45)              | No Consensus(3) |
| Wrong drug for indication(33) | Discontinue drug | Consensus(29)              | No Consensus(4) |
| Drug-food interaction(96) | Change in delivery time | Consensus(92)              | No Consensus(4) |
| Drug-drug interaction(440) | Discontinue drug(57) | Consensus(53)              | No Consensus(4) |
| Drug-drug interaction(440) | Change in drug dosing (126) | Consensus(117)              | No Consensus(9) |
| Drug-drug interaction(440) | Monitor the Lab values frequently(43) | Consensus(38)              | No Consensus(5) |
| Drug-drug interaction(440) | Monitor patients closely(214) | Consensus(214)              | No Consensus(0) |
The accepted recommendations (897/936) involved different interventions like changing in prescribed drug doses (275/289) or dosing frequency (151/156), Change in delivery time (92/96), drug discontinuation (82/90), changing the route of administration (45/48), and laboratory values monitoring (38/43). Examples of interventions are shown in table 4.

After adjustment for confounder effect of drugs, gender and the frequency of errors in the proportional-odds model, female gender increases the odds of error 2.66 in wrong indication, 1.79 in wrong route while it decreases the odds of making errors in DDI with the odds ratio of 0.56. Number of drugs as an independent variable increases the odds of errors with odds ratio of 2.21 for wrong dose, 1.21 for wrong frequency and 1.42 for drug-food interactions while in DDI, it decreases the odds by 0.64. Age was an important factor only in DDI (table 5).

| Type of Error          | Predictor          | Odds Ratio       | P>|z|   |
|------------------------|--------------------|------------------|------|
| DDI                    | Drugs              | 0.64 (0.56 – 0.74) | <.0001 |
|                        | Female sex         | 0.56 (0.37 – 0.86) | 0.007 |
|                        | Age (per year)     | 0.98 (0.97 – 0.99) | 0.026 |
| Drug-food interaction  | Drugs              | 1.42 (1.20 – 1.67) | <.0001 |
|                        | Age (per year)     | 1.01 (0.99 – 1.02) | 0.086 |
|                        | Female sex         | 0.90 (0.53 – 1.52) | 0.70  |
| Wrong indication       | Drugs              | 0.90 (0.71 – 1.16) | 0.43  |
|                        | Age (per year)     | 0.99 (0.97 – 1.01) | 0.90  |
|                        | Female sex         | 2.66 (1.20 – 5.92) | 0.018 |
| Wrong route            | Drugs              | 0.90 (0.73 – 1.11) | 0.35  |
|                        | Age (per year)     | 0.99 (0.98 – 1.01) | 0.81  |
|                        | Female sex         | 1.79 (0.93 – 3.43) | 0.067 |
| Wrong frequency        | Age (per year)     | 1.00 (0.99 – 1.02) | 0.088 |
|                        | Drugs              | 1.21 (1.04 – 1.40) | 0.009 |
|                        | Female sex         | 0.90 (0.57 – 1.42) | 0.65  |
| Wrong dose             | Drugs              | 2.21 (1.82 – 2.67) | <0.0001 |
|                        | Age (per year)     | 1.00 (0.99 – 1.02) | 0.27  |
|                        | Female sex         | 0.68 (0.41 – 1.14) | 0.152 |

**Discussion**

The role of clinical pharmacologists in reducing medication errors have been proven in many studies (10-15). Our study has shown that the clinical pharmacist intervention could reveal medical errors in patients hospitalized in hematology-oncology ward and given the physician’s welcome to this intervention, is effective at reducing the prevalence per patient of error, preventing potentially DDIs and improving the efficiency of medication use. We found the incidence of error and its reduction nearly in line with other studies. Percentage of accepted recommendations in our study was 95.83%. This percentage in the case of Leape L. et al’s study was 99% (8). The reason for not accepting some recommendations was that counseling was initiated after the start of the treatment, for example, fluconazole was administered in combination with vincristine without dose adjustment before the consultation. However, the rate of agreement of physicians in this study was higher than the Klopotowska’s study, in which the pharmacist stayed in ward (ICU) (95.83 vs 71%) (5). The most errors in this study were the DDIs. In patients with cancer, DDIs are common. Patients treated systemically for cancer are particularly at risk for DDIs (16, 17). In total, 440 DDIs were identified in 188 patients (2.34DDI/patient). Of all DDIs, 15.45% were classified as major. In the point of clinical significance, 14.55% of DDIs were grade1. This interaction is associated with significant outcomes and drug discontinuation or close monitoring was recommended. These findings in the point of severity of interactions and significance rating scale were approximately similar with the results of other studies that investigated DDIs in patients with cancer (16, 18).
Although DDIs was the most error in our study (47%) but there are several studies that reported DDIs frequency more than the present study (19-22). Physicians agreed with clinical pharmacologist to verify orders associated with DDIs in the 95.9% of cases. Verification included: drug discontinuation, dose changing, monitoring of plasma levels or close observation of patients. The second most commonly reported medical error in this study was the improper dose (17.41%) that was less than the other studies (10, 14, 23, 24) but more than Ho’s study (25). Given the fact that the number of patients in these studies was not equal, we think that this difference in results is probably related to the sample size and the pharmacological information of physicians.

Wrong frequency that means the incorrect interval between doses was the third error revealed by clinical pharmacologist in the present study (16.67%). Wrong frequency differs from omission dose that leads to a patient receiving the drug in wrong time. In other studies, wrong frequency was lower than our study (1, 11) often these errors were corrected before the start of the second dose and the patients were not harmed by this error. Our findings suggest that despite the part time attendance of clinical pharmacist and of the fact that specialist physicians were not accustomed to pharmacologic consultations, the high number of recommendations acceptance by these physicians shows that pharmacologic recommendations were clinically appropriate. As a first step, one can hope that, given the results obtained, this method might be generalized to other wards of a hospital. Because of insufficient qualified staff, our work did not study adverse drug reactions (results from medication errors) and savings due to the correction of irrational prescriptions. Another limitation of our study was the lack of constant presence of the clinical pharmacologist in the ward, and some of the errors occurred before the intervention of clinical pharmacologist. To our knowledge, this is the first study that investigated the effect of pharmacologic consultation in an Iranian hospital for patients with cancer with the aim of reducing medication errors. Despite these limitations, our priority was to conduct a practical study to explore the potential effect of this approach to a patient safety.

In conclusion, the results of our study showed that pharmacological consultation in the hematology-oncology ward revealed many medication errors, including DDIs. The trust of physicians in the views of the clinical pharmacologist led to a large part of these errors being accepted and resolved.

Clinical pharmacologist full-time presence in wards seems to prevent more errors.

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**Conflict of Interests:** The authors declare that there is no conflict of interest among them.

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