ROLE OF THE PHARMACIST IN DETECTING CHEMOTHERAPY MEDICATION ERRORS IN MEDICAL CITY DEPARTMENT


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ABSTRACT

Medication errors in hematology could cause clinical problems because of low therapeutic indexes and high toxicity of hazardous drugs. In each situation all doses should be calculated accurately by the physician and the pharmacist. The most common errors are involved in prescribing and ordering, so we need new strategies to eliminate the chemotherapy medication error by using a computerized prescribing system, specialized chemotherapy equipment to protect the personals by using closed system technique in reconstitution of chemotherapy drugs, chemical quality testing and proper assessment are needed for technician, education to be undertaken as often as possible, continue efforts to promote standards, guidelines, technological innovation and a national prescription form for hospitals, to be applied uniformly and used as training tool.

So the aim of this study is to reduce the possibility of errors that occurs during chemotherapy preparation, and the importance role of the clinical pharmacist in hematology department in detecting errors in prescription of hazardous drugs. A retrospective study in hematology center (adult department) was designed to compare between two periods, (24) months at the beginning of working and the last (24) months which reviewed errors detected by the pharmacists in the chemotherapy request, we got a reduction of documented paper errors (18.6834%). We conclude that the important components to avoid errors are computerized system, standard guidelines, technological innovation and chemical quality testing.
KEYWORDS: Medication error, Chemotherapy, Chemotherapy preparation, Hazardous drugs.

INTRODUCTION
An error is "something incorrectly done due to ignorance or inadvertence; a mistake, for example in calculation, judgment, speech, writing, action, etc."[7], in other words it is "a failure to complete a planned action as intended, or the use of incorrect plan of action to achieve a given aim."[15] The national coordinating council on medication error reporting and prevention (NCCMERP) defined the medication error is any preventable event that may lead to inappropriate medication used, or harm to the patient while the medication is under the control of the health care provider to the patient[6]. There are nine types of medication errors all of them are important and needs to avoid them as possible, the more dangerous are either wrong in rout of injection which may cause death to the patient or because of the rate of administration of Anthrayclines infusion or interfere with the disease that the patient complained as well as, we have to identified the error whatever its level's effect on the patient, so in this study searching of the error that occurs in each type of the nine and managing it, is our concentration to minimize the errors and that is the roll of the pharmacist in mixing unit, thus in this paper we will compare between two period of time to improve the minimizing of the medication errors in hazardous drugs.

Types of medication error
A. The events that have the capacity to cause no error.
B. An error happened but did not reach the patient, while an error of inattention dose reach the patient.
C. An error happened that reached the patient without any harm.
D. An error happened that reached to the patient and needed monitoring to ensure that no harm reached the patient and/or needed intervention to avoid harm.
E. An error happened and resulted in temporary harm to the patient so the intervention is required.
F. An error happened that resulted in temporary harm to the patient and required prolonged hospitalization.
G. An error happened that resulted in permanent harm to the patient.
H. An error happened that needed intervention to sustain life.
I. An error happened may ended in the patient’s death.
The incorrect use of hazardous drugs produces serious adverted effects so extra precaution is needed to avoid toxicity at FDA-approved administration schedules\textsuperscript{[4]}, for examples of chemotherapy errors:\textsuperscript{[10]}

1. **Vincristine and Vinblastine**
   - Accidental intra-ethical administration cause Patient death.
   - Accidental vincristine dosing based on vinblastine dosing also cause patient death (max dose: 2mg adults & pediatrics).

2. **Carboplatin, Cisplatin**
   - Overdose for carboplatin may cause deafness.
   - Confusion of dosing of Cisplatin according to carboplatin dosing has a fatal outcome.

3. **Docetaxel and paclitaxel**
   Case report of 260mg of Docetaxel instead of Paclitaxel found the patient died five days later while error may have not cause death.

4. **Lomustin**
   Taken daily instead of every 6 weeks, it also Increases hospital stay and death.

5. **Methotrexate**
   Oral Methotrexate daily instead of weekly lead to serious patient harm.

6. **Doxorubicin**
   Liposomal doxorubicin instead of doxorubicin hydrochloride caused a lot of morbidities and possible patient death.

**The risk reduction strategies depend on**
1. Preventing the errors.
2. Making the errors visible.
3. Mitigating the harm

**We have three levels of risk mitigation\textsuperscript{[25]}**
   a) High leverage: It is impossible to make an error by (using IV bags to prepare and administer vincristine because it is known that cannot give a medication from a bag intra-ethically but can from a syringe).
b) Medium leverage are protocols and checklists, which rely on humans follows the set of policies and procedures.

c) Low leverage is education and training.

**Professional practice Health care products systems procedures**

1) **Communication and access to data**[^18]

Patient's medical record should be insure whether medication history, prior admission, allergy to drugs, and surgeries must be well arranged and accessible by who prescribe, dispense and administer the chemotherapy drugs.

2) **Prescribing**[^4]

It should never give verbal order for hazardous drugs to the patient but using special order forms whatever computerized or handwrite orders in printed tall man letters also write full information about the patient and his chemotherapy protocol with details which are date, time of chemotherapy is to be administered by writing (AM), (PM) or (12 noon), generic name of drugs, dose route and for continuous infusion. Also using the word (units) and (mg) for all doses with caution that do not use trailing zero for any dose more than (1) mg. (e.g. 2 mg) and for doses less than (1) mg use leading zero (e.g. 0.6 mg.) keep in mind double-check dose calculations done before preparation.

To avoid look- alike sound- alike should have to use TALL- man lettering, for example, vinblastine ➔ vinBLAStine, vincristine ➔ vinCRiSTiNe).[^1] See table (1).[^14]

**Table 1: Look- alike, Sound- alike Agents**

<table>
<thead>
<tr>
<th>Drug</th>
<th>Can look and/or sound like</th>
</tr>
</thead>
<tbody>
<tr>
<td>Adriamycin</td>
<td>Aredia, Idarmycin</td>
</tr>
<tr>
<td>Alkeran</td>
<td>Leukeran</td>
</tr>
<tr>
<td>Carboplatin</td>
<td>Cisplatin</td>
</tr>
<tr>
<td>Caytoxin</td>
<td>Cytarabine</td>
</tr>
<tr>
<td>Cyclophosphamide</td>
<td>Cyclosporine</td>
</tr>
<tr>
<td>Mitomycin</td>
<td>Mitoxantrone</td>
</tr>
<tr>
<td>Vinicristine</td>
<td>Vinorelabine, vinblastine</td>
</tr>
</tbody>
</table>

* It is important to check that chemotherapy order including anti- emetics, hydration, and protective agents. And using only metric system (e.g., mg/kg) for weight documentation error.[^13]
* Finally the signature of hematologist should be documented to verify the chemotherapy regimens.[^6],[^11]
The order request form provides S. Q. E.C.

1. Safety: Reduce medication errors (alerts and reminders).
2. Quality: Reduce variation through standardization and improve compliance with evidence-based best practices.
3. Efficiency: Improve communication and team approach Enhance time-saving workflow.
4. First step through CPOE (computerized order entry system) to improve documentation.

In addition it includes at the top patient's body surface area for calculation of proper dose, defined regimen protocol acronym and number, also cycle number, individual single daily doses in mg/m², and hydration.

3) Preparation\textsuperscript{[10], [18]}

Before mixing it is necessary to check the label with the chemotherapy request include patient and drug name, date of preparation, expiration time route of administration diluent and the final volume calculation on the back side of the label, specify the vials number of chemotherapy according to the dose, double checking is done by technician. The preparation is according to guidelines, another technicians to check the preparation and then check done by the pharmacist.

4) Packaging and transporting\textsuperscript{[8], [12]}

Labels that be used for, storage conditions, vesicant and intra-ethical drugs must be unique packaging and distinguishing colors. what we do know is that wrong route vincristine errors continue to occur, although they may happen rarely. So that "WHO" and "JCI" did not endorse syringe to prepare vincristin but they endorsed to prepare it for IV administration in a small volume IV bag. IV and intra-ethical drugs deliver separately and the intra-ethical dispense just prior to use and should be exist at least two practitioners document all intra-ethical doses before administration.

5) Administration

When the does deliver to the patient and before administration review the chemotherapy request and be sure all required medications are present including pre medications anti emetic anti-allergy and compare between the labels on the prepared chemotherapy drugs and the orders form. For patient identity using number of the case inanition to the patient's room number and bed then administer the drug as prescribe.
The medication order verification system to be ensured the drug accurately to the patients for whom it was intended as in the following diagram (1).

6) Education
Patients must be known about the names of their drugs, color of infusion, route of administration, and encouraged him to remind care team for patients to verify their identity and ask question about their chemotherapy.\cite{18}

Role of the nurse is fill an incident report in case an error happened and commitment by the policies and procedures of the hospital, that is represented by the reporting and safety culture. For ensure safety and prevention error, avoid "naming, blaming, and shaming"\cite{9} to the persons involved in Chemotherapy errors and instead of that asking, "How did this happen?"\cite{9}

The focusing on punitive persons involved in a medication error is dangerous because of:\cite{9}
- Preventing open discussion about errors.
- Causes a defensive and excuses environment.
- Delaying the care and unbiased consideration of the system-based root causes the error.

The role of clinical pharmacists is to educate the patients, their families and the accompanying person about medication doses, routes of administration, adverse event. Although we consider everyone is good in his job, well trained and motivated still everyone should look out for others. The physician, pharmacist and nurse should all double check chemotherapy, also everyone in the team should be encouraged to ask questions.\cite{6}

7) Monitoring
The patients are monitored for adverse events from medication errors by the clinical staff.
Diagram (1): Medication order verification system.

METHOD
This paper is limited on the prescription in the mixing unit of the hematology center at adult department in Medical city for the first (24) months from 2014 which is the beginning of the preparation of the full protocols for patients, compared with the last (24) months until Jun/2018, and the pharmaceutical work was mixing the chemotherapy doses with average of (6) hours daily, and focus on all the information required as shown in diagram (2) and (3).
Diagram (2): The chemotherapy reconstitution request form.

<table>
<thead>
<tr>
<th>No</th>
<th>Drug</th>
<th>Dose</th>
<th>Suitable Solution and Volume</th>
<th>Route of Administration</th>
<th>Time to Start Administration</th>
<th>Duration of Administration</th>
<th>Notes</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

*This should be signed first by the hematologist, then the pharmacist, then the reconstituter and fit by the nurse.
*The nurse should compare this paper to what it has been written in the case sheet which should be 100% compatible.
*The premedications are not included, so the nurse should check the case sheet.

Hematologist's sign  Pharmacist's sign  Reconstitutes sign  Nurse's sign

Diagram (3): Label document In the hematology center.

RESULTS AND CALCULATION

Manual transcription of prescription includes writing of the physician's order to the reconstitution request and this is error prone.\cite{17} The patient may receive uncorrected drug or uncorrected dose. Although the request had checks, manual error checking processes leads to fail unsafely.\cite{2,19}

New error may produce like wrong sized syringes are used or the technician Misinterpretation of the mixing volume, two sites staged materials for same patient in one
bin, creating the possibility of uncorrected drugs, syringes, final containers, as well as stickers to be loaded into the BSC, leading to mixing errors.\textsuperscript{[14]}

Some chemotherapy drugs is powder in dosage form and it needs accurate type and volume of diluent for reconstitute before being reconstituting. Some manufacturers package the drug with the exact diluent while others not and need the manual selection and measurement of diluent from the pharmacy's inventory.

The technician will need to learn how to deal with hazardous drugs correctly. The pharmacist checks reconstitution after the completed admixture only.

A technician should need to learn and scan entire document to search for specific instructions for the drug and then interpret them correctly. The pharmacist shall Check the reconstitution only after the completed admixture had left the mixing room and using proxy method, such as examination of the diluents bag to estimate correctness.

One of the challenges with mixing is the dealing with vials of chemotherapy drugs during the day is keeping the vials in the BSC until they are empty or keeping the residue vials in refrigerator Once the mix is complete, then may use it back to the BSC the next time they needed. Using BSC to keep the vials for achieving less exposure and less chance of spilling it, however, the possibility of the risk error is exist. If there was partially used vial of the target drug available in the BSC, it should be used first then followed by a new vial. The technician might mistakenly choose the new vial.

Another challenge with mixing to reduce the environmental waste is the management of syringes, which is reuse of the same syringe to achieve total dose, as in case of achieving a total volume of (15) ml, a 10 ml syringe may be used to withdraw (5) ml, inject it into the bag, and repeat it twice more. The risk is the possibility of injecting too little or too much drug into the final container.

In this study-group the number of errors were calculated as an example the error in patient's name per month multiply by 12 months and divided on the number of chemotherapy request then multiply it by 100 we got the percentage of error in name per year, and so on the calculation of other errors which observed during the study-group.
RESULT'S ANALYSIS

In this paragraph, we will analyze the results of the tables represented by the data for prescription & doses in (48) months as shown in table (2), the number of errors calculated in months shown in table (3), the percentage of error calculated in month as in table (4) and the comparison between the first and the last (24) months by numbers for prescription, doses mixed and medication error shown in figure (1).

Table (2): The Data of (48) Months for prescriptions & doses.

<table>
<thead>
<tr>
<th>Month</th>
<th>2014</th>
<th>2015</th>
<th>2016</th>
<th>2017</th>
<th>2018</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Pr.</td>
<td>Dose</td>
<td>Pr.</td>
<td>Dose</td>
<td>Pr.</td>
</tr>
<tr>
<td>1</td>
<td>380</td>
<td>940</td>
<td>846</td>
<td>1266</td>
<td>-</td>
</tr>
<tr>
<td>2</td>
<td>295</td>
<td>699</td>
<td>845</td>
<td>1141</td>
<td>-</td>
</tr>
<tr>
<td>3</td>
<td>371</td>
<td>684</td>
<td>903</td>
<td>1303</td>
<td>-</td>
</tr>
<tr>
<td>4</td>
<td>378</td>
<td>758</td>
<td>996</td>
<td>1390</td>
<td>-</td>
</tr>
<tr>
<td>5</td>
<td>421</td>
<td>834</td>
<td>754</td>
<td>1098</td>
<td>-</td>
</tr>
<tr>
<td>6</td>
<td>522</td>
<td>965</td>
<td>855</td>
<td>1152</td>
<td>-</td>
</tr>
<tr>
<td>7</td>
<td>377</td>
<td>701</td>
<td>805</td>
<td>1769</td>
<td>-</td>
</tr>
<tr>
<td>8</td>
<td>585</td>
<td>1059</td>
<td>1107</td>
<td>992</td>
<td>1259</td>
</tr>
<tr>
<td>9</td>
<td>487</td>
<td>925</td>
<td>1065</td>
<td>1721</td>
<td>814</td>
</tr>
<tr>
<td>10</td>
<td>665</td>
<td>893</td>
<td>1132</td>
<td>1598</td>
<td>1094</td>
</tr>
<tr>
<td>11</td>
<td>881</td>
<td>965</td>
<td>1146</td>
<td>1568</td>
<td>1653</td>
</tr>
<tr>
<td>12</td>
<td>875</td>
<td>1013</td>
<td>1045</td>
<td>1568</td>
<td>1129</td>
</tr>
<tr>
<td>Total</td>
<td>6237</td>
<td>10436</td>
<td>11499</td>
<td>16605</td>
<td>5949</td>
</tr>
<tr>
<td>Total Pr.</td>
<td>17736</td>
<td>28092</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total doses</td>
<td>29676</td>
<td>50495</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

It is shown from this table, the total prescriptions number for the first (24) months is (17736) and the total doses number that received by the patients is (29676) while for the last (24) month are (28092) and (50495) respectively.

Table (3): Number of errors calculated in months.

<table>
<thead>
<tr>
<th>No. of errors % Months</th>
<th>Name</th>
<th>Dose/Drug</th>
<th>Administration</th>
<th>Mixing</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>12 months/2014</td>
<td>336</td>
<td>288</td>
<td>240</td>
<td>192</td>
<td>1056</td>
</tr>
<tr>
<td>12 months/2015</td>
<td>288</td>
<td>240</td>
<td>192</td>
<td>144</td>
<td>864</td>
</tr>
<tr>
<td>Total</td>
<td>624</td>
<td>528</td>
<td>432</td>
<td>336</td>
<td>1920</td>
</tr>
<tr>
<td>5 months/2016</td>
<td>100</td>
<td>80</td>
<td>60</td>
<td>40</td>
<td>280</td>
</tr>
<tr>
<td>12 months/2017</td>
<td>72</td>
<td>60</td>
<td>48</td>
<td>36</td>
<td>216</td>
</tr>
<tr>
<td>7 months/2018</td>
<td>35</td>
<td>28</td>
<td>21</td>
<td>14</td>
<td>98</td>
</tr>
<tr>
<td>Total</td>
<td>207</td>
<td>168</td>
<td>129</td>
<td>90</td>
<td>594</td>
</tr>
</tbody>
</table>
It is shown from table (3) the total medication error numbers for the first (24) months is (1920) and for the last (24) months is (594), so the medication errors number is minimized.

Table (4): The percentage of error calculated in months.

<table>
<thead>
<tr>
<th>Percentages Months</th>
<th>Name%</th>
<th>Dose/Drug%</th>
<th>Administration%</th>
<th>Mixing%</th>
<th>Total%</th>
</tr>
</thead>
<tbody>
<tr>
<td>12 months/2014</td>
<td>5.8682</td>
<td>4.6176</td>
<td>3.8480</td>
<td>3.0784</td>
<td>17.4122</td>
</tr>
<tr>
<td>12 months/2015</td>
<td>2.5045</td>
<td>2.871</td>
<td>1.6697</td>
<td>1.2522</td>
<td>8.2974</td>
</tr>
<tr>
<td>Total</td>
<td>8.3727</td>
<td>7.4886</td>
<td>5.5177</td>
<td>4.3306</td>
<td>25.7096</td>
</tr>
<tr>
<td>5 months/2016</td>
<td>1.6809</td>
<td>1.3447</td>
<td>1.0085</td>
<td>0.6723</td>
<td>4.7064</td>
</tr>
<tr>
<td>12 months/2017</td>
<td>0.5497</td>
<td>0.0458</td>
<td>0.3665</td>
<td>0.2748</td>
<td>1.2368</td>
</tr>
<tr>
<td>7 months/2018</td>
<td>0.3868</td>
<td>0.3094</td>
<td>0.2321</td>
<td>0.1547</td>
<td>1.083</td>
</tr>
<tr>
<td>Total%</td>
<td>2.6174</td>
<td>1.6999</td>
<td>1.6071</td>
<td>1.1018</td>
<td>7.0262</td>
</tr>
</tbody>
</table>

We see from this table, the total percentage in the last (24) months is (7.0262%) which is less than the first (24) months, so it is minimized in a good percentage.

![Fig. 1: Comparison between the first and the last (24) months by numbers for prescription, doses mixed and medication error.](image)

**DISCUSSION**

In this study the total chemotherapy medication errors percentage in the first (24) months is (25.7096%) because of:

1) The handwriting transcription of prescriptions into the mixing unit
2) No instruction specified for drug reconstitution with mix
3) Waste of partially used vials in BSC
4) Two or more doses mix at the same time in BSC
5) Using the same syringe to achieve the total dose.
6) There is no reference to avoid these practices that prepared by the National Association of Pharmacy Regulatory Authorities.[1],[2],[11]
7) Both American standards of USP 797[16] and USP800[15] focusing on the safety and sterilization of the product and on protecting the environment and staff from hazardous exposure rather than guideline for reconstitution and mixing.
8) Also the Safety standards from ASCO[19], Guidelines for the prevention of error from the American Society of Hospital Pharmacists[5], and standards of practice of the Canadian Association of Oncology Pharmacists[7], do not have any declaration that directly address the issues.
9) There is no unified guideline addresses issue of all errors to the pharmacist. While the last (24) months percentage is (7.0262%), the reason for the percentage drop is the increase in precision in.

Based on the results analysis, it has been reached to follows

The pharmacists identified (1920) name related problem (8.3727%) of the prescription, dosing-drug problem (7.4886%) inappropriate administration (5.5177%), and the technician related problem (4.3306%) while the last (24) months identified (592) name related problem (2.6174%) of the prescription, dosing-drug problem (1.6999%), inappropriate administration (1.6071%) and technician related problem (1.1018), Thus the total percentage in the first (24) months is (25.7096%) which minimized to (7.0262%) in the last (24) months.

CONCLUSIONS AND RECOMMENDATIONS

As a result, of the conclusions of the analysis of this paper, the recommendations are:
1) Used simple strategies to prevent chemotherapy errors.
2) Computerized prescriber order entry, and reliable method to verify identity, metric measurement.
3) There is a need for continued efforts to advance standard, guidelines, technological innovation and chemical quality testing.
4) Determination the adequate protective measures and establish multi-stepcontrol mechanisms.

ACKNOWLEDGEMENT

To the hematology center medical city department and my family for their help and support.
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