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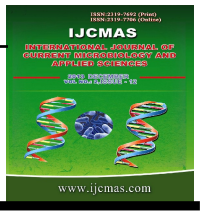


Original Research Article

Rates and Types of Prescribing Errors and Related Interventions in Oncology

Nouran Ameen Hamza[1], Sunny Abdou Sallam[2] and Nessrin Ahmed El-Nimr[3*]

[1]Oncology trained pharmacist, Alexandria Main University Hospital, Egypt
[2]Professor of Epidemiology, Epidemiology Department, High Institute of Public Health, Alexandria University, Egypt
[3]Lecturer of Epidemiology, Epidemiology Department, High Institute of Public Health, Alexandria University, Egypt
Corresponding author

Keywords

Chemotherapy drug; pharmacist interventions; Carboplatin; Cisplatin.

A B S T R A C T

Chemotherapy drug errors can be devastating because these agents have one of the lowest therapeutic indices and safety margins of any drug class. Clinical interventions made by pharmacists have a significant impact on patient care. The aims of the current study were to determine the daily average number of medication orders reviewed by the pharmacist, to quantify the types of prescribing errors, to indicate the drugs most commonly involved in medication errors and the proportion of pharmacist interventions, and finally to calculate physician/pharmacist percent concordance/discordance. In a cross sectional study at an Adult Oncology Clinic in a main hospital, medication orders were consecutively reviewed on daily basis. Data were collected from the patients' profile and medication orders. On the average, pharmacists reviewed 17 medication orders per day. The proportion of errors in chemotherapy medication orders and hence the intervention rate was 66%. Missed information, wrong dose and the protocol breach were the most frequent errors in chemotherapy medication orders. Common cytotoxic drugs involved in the errors were Carboplatin, Cisplatin and Taxol. Almost all pharmacists' interventions were accepted by the physicians. Errors in chemotherapy orders are common, which gives the validation process performed by the clinical pharmacists a key role in improving patients' safety.

Introduction

Pharmacoepidemiology is the study of interactions between drugs and populations (Be'gaud, 2000). It is an applied field bridging between clinical pharmacology and epidemiology (Storm, 2006). An increase in the number of patients, pharmaceuticals, and an increased awareness of drug-related morbidity and mortality have coincided to stimulate more "clinical" practice of pharmacists (Doecke, 2004). Clinical pharmacy is relatively a new field

(Ankinson Jr *et al*., 2012). It is a branch of pharmacy where pharmacists provide patient care that optimizes the use of medication and promotes health, wellness and disease prevention (American College of Clinical Pharmacy, 2008). The field of clinical pharmacy practice focuses on patient-oriented rather than drug product-oriented service. Clinical pharmacists are a primary source of scientifically valid information and advice regarding the rational use of medications (Bond and Franke, 2002; Bero *et al*., 2000; Abu-Gharbieh *et al*., 2010), including prescribing, transcribing, dispensing, administering and monitoring (Abood, 2014; Hess, 2007).

Preceding 1997, the responsibilities of pharmacists working in Egyptian hospitals were mainly dispensing drugs to patients as prescribed by their physicians. Actual work for clinical pharmacy started in September 1997 at the National Cancer Institute (NCI) then at Nasser Institute in Cairo. In February 2001, clinical pharmacy was established in Assuit at South Egypt Cancer Institute, followed by Alexandria in 2002 at the Oncology Department, Alexandria University Hospital (Al-Anowr, 2011), and two private hospitals (personal communication).

Medication errors (MEs) occur frequently in medical settings (Khalili *et al*., 2011), despite being the single most preventable cause of patient harm (Williams, 2007). The National Coordinating Council for Medication Error Reporting and Prevention (NCCMERP) defines a ME as "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 professional, 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" (The National Coordinating Council for Medication Error Reporting and Prevention, 2013).

The World Health Organization (WHO) estimates that more than half of all medicines are prescribed, dispensed or sold inappropriately, and that half of all patients fail to take them correctly. This incorrect use may take the form of overuse, underuse and misuse of prescription or non-prescription medicines (WHO, 2010). In the USA, the incidence of MEs varies between 2% and 14% for patients admitted to hospitals, with 1–2% of patients being harmed as a result, and the majority is due to poor prescribing. The incidence is likely to be similar in the UK (Williams, 2007).

Oncologists have no greater or lesser chance of erring than most other physicians (Dinning *et al*., 2005), but the consequences of chemotherapy drug errors can be devastating because these agents have one of the lowest therapeutic indices and safety margins of any drug class (Kloth, 2010). They are carcinogenic, cardiotoxic and nephrotoxic even at therapeutic doses (Hemat, 2004).

Chemotherapy errors have been attributed to many causes, including mis-communicated verbal orders, lack of pertinent patient health care information, use of incorrect patient information or laboratory data, poor packaging and labeling by manufacturers, illegible

prescription order, "look-alike, sound-alike" chemotherapy drug names, use of acronyms and abbreviations of drug names, transcription errors and dose miscalculation (Kloth, 2010). In a study in Spain, MEs were identified among 17.2% of the patients receiving chemotherapy. The detected errors distribution according to pharmacotherapeutic stage was: prescription 75.7%, preparation 21.0%, dispensing 1.8%, administration 1.1%, and follow-up 0.4% (Serrano-Fabiá *et al*., 2010).

Clinical interventions made by pharmacists had a significant impact on patient care. The integration of pharmacists' technical and clinical roles into dispensing of chemotherapy doses is required for providing high-quality cancer services (Knez *et al*, 2010). A study conducted at the National Cancer Institute (NCI) in Cairo, Egypt reported that clinical pharmacy interventions reduced the number of medication errors from 1548 to 444, 45% of clinical pharmacy interventions led to increase in the efficacy of chemotherapy regimen and 54.7% of the interventions led to decrease in the chemotherapy toxicity (El-Hamamsy, 2012).

The aims of the current study were to determine the daily average number of medication orders reviewed by the pharmacist at an Adult Oncology Clinic, to quantify the types of prescribing errors, to indicate the drugs most commonly involved and the proportion of pharmacists' interventions and finally to calculate physician/pharmacist percent concordance/discordance.

Materials and Methods

A cross sectional study was conducted at the Adult Oncology Clinic in a main Hospital in Alexandria, Egypt. The study was approved by the ethics committee at the High Institute of Public Health, Alexandria University. Using Epi info 2008 and based on an expected prevalence of 12.9% for prescription errors in chemotherapy (Serrano-Fabiá *et al*., 2010) and a 2.5% level of precision**,** the minimum required sample size at 95% confidence level was 690 which was rounded to 700 medication orders. The medication orders were consecutively reviewed on daily basis until completing the determined sample size.

Data about the patient were collected using the patient's profile and included the patient's age and sex, type of cancer, laboratory results and the chosen treatment protocol. Data about the medication order included the number of drugs in the protocol, the cycle number, pharmacist's intervention, the drugs involved in the prescribing error and the type of prescribing errors. Detecting medication errors was done guided by the American Society of Hospital Pharmacists (ASHP) Guidelines for Preventing Medication Errors with Antineoplastic Agents and Guidelines for Preventing Medication Errors in Hospitals (American Society of Hospital Pharmacists, 2011). The detected errors were then corrected and the recommendations were then sent to the medical staff. The concordance\discordance degree between the physicians and pharmacists regarding the interventions was then recorded.

Data management

The collected data were coded, cleaned and entered using SPSS for Windows version 16.0 (SPSS Inc., Chicago, IL, USA). The following was calculated:

The mean number of medication orders reviewed by the pharmacist per day.

Types and quantities of prescribing errors.
The top 10 drugs involved in the chemotherapy medication orders errors.

The proportion of interventions by the pharmacist.

Physician / pharmacist percent concordance / discordance after interventions. It was calculated by dividing the number of accepted/refused interventions by the whole interventions multiplied by one hundred.

Result and Discussion

After reviewing 700 chemotherapy medication orders in 42 days, it was found that on the average, pharmacists reviewed 17 medication orders/day. Among the reviewed medication orders, a total of 462 prescribing errors were detected and therefore the proportion of errors in chemotherapy medication orders was 66%. Hence, the pharmacists' intervention rate was 66%, figure 1.

Table.1 shows that among the chemotherapy medication orders, missed information, errors in the calculation of the chemotherapy dose and protocol breach were the most frequent types of prescribing errors (19.86%, 19.14% and 13.71%, respectively), followed by hydration error and omission error (6.86% and 4.14%, respectively). The least frequent prescribing errors were the wrong information error and wrong administration route error (1.57% and 0.71%, respectively).

Among the prescribing errors, missed information comprised about one third (30.08%) of the interventions, followed by errors in the chemotherapy dose (29%) and protocol breach errors (20.78%). Wrong information error and wrong administration route error comprised the least proportion of interventions (2.39% and 1.08%, respectively).

Missed dose was the most frequent type of missed information (10.57%), while calculations that were based on wrong patient parameters (weight and height) and error in dose adjustment due to renal causes were the most frequent errors in the calculation of the chemotherapy dose (6.29% each). Wrong infusion rate was the commonest form of protocol breach (3.14%), while wrong amounts of diluents was the most frequent type of hydration errors (4.89%).

The table also shows that chemotherapy doses were given when they should have been omitted in 1.86% of cases due to unacceptable laboratory results. Forms of wrong information encountered in the medication orders included wrong drug, wrong cycle number, referral to diagnostic clinic instead of writing the date of next cycle and writing more cycles instead of referring the patient to the diagnostic clinic. In five medication orders, the administration route was incorrect.

The top 10 drugs involved in the chemotherapy medication orders errors and in the interventions are shown in figure 2. One fourth of the errors, and accordingly of the interventions, involved Carboplatin (25.6%), followed by Cisplatin, Taxol, Cyclophosphamid and Flourouracil which were involved in 9.2 % to 12.1% of the errors and interventions. From 3% to 4.6% of the errors and interventions were attributed to the following drugs: Vincristine, Leucovorin,

Table.1 Distribution of the types of prescribing errors in chemotherapy medication orders (Adult Oncology Clinic, Main Hospital, Alexandria)

Types of prescribing errors	**No. (%) (n=700)**	**% among errors = Intervention rate (n=462)**
Missed information	139 (19.86)	30.08
Wrong dose error	134 (19.14)	29.00
Protocol breach error	96 (13.71)	20.78
Hydration error	48 (6.86)	10.39
Omission error	29 (4.14)	6.28
Wrong information error	11 (1.57)	2.39
Wrong administration route error	5 (0.71)	1.08
1- Missed information:		
Missed dose	74 (10.57)	16.00
Missed date of the next cycle	17 (2.43)	3.68
Missed documentation in blue and white sheet	12 (1.71)	2.60
Missed drug and missed note for referring the patient to diagnostic clinic after the last cycle	12 (1.71)	2.60
Missed intra-venous saline administration after an irritant parentral cytotoxic drug	9 (1.29)	1.95
Missed antihistaminic (Pheniramin) administration	9 (1.29)	1.95
Missed required hydration and missed patient parameter	6 (0.86)	1.30
2- Wrong dose error:		
Calculation based on wrong patient parameter	44 (6.29)	9.50
Error in dose adjustment due to renal impairment	44 (6.29)	9.50
Errors in using the calculator	28 (4.00)	6.10
Error in dose adjustment due to hepatic impairment	16 (2.29)	3.46
Error in dose adjustment due to abnormal Neutrophil count	2 (0.29)	0.44
3- Protocol breach error:		
Wrong infusion rate	22 (3.14)	4.76
Fixed by physician order	15 (2.14)	3.25
Incorrect days	15 (2.14)	3.25
Wrong dose/m^2	14 (2.00)	3.03
Error in drugs sequence	13 (1.86)	2.81
Error in protocol interval	8 (1.14)	1.73
Others (error in drug interval, exceeded the maximum dose, error in drug frequency)	9 (1.29)	1.95
4- Hydration error:		
Wrong amount of diluents for stability	34 (4.89)	7.36
Wrong diluents and missed post-hydration	14 (2.00)	3.03
5- Omission error:		
Laboratory results were not acceptable	13 (1.86)	2.81
Laboratory results were absent	6 (0.86)	1.3
Others (ejection fraction were not acceptable or not	10 (1.43)	2.16

satisfactory, liver enzymes and serum calcium were not available or absent)		
6- Wrong information error:		
Wrong drug	4 (0.57)	0.86
Wrong cycle number	3 (0.43)	0.65
Others (referral to diagnostic clinic instead of writing the date of next cycle, more cycles were written instead of referring the patient to the diagnostic clinic)	4 (0.57)	0.86
7- Wrong administration route error:		
Intramuscular, intravenous and oral	3 (0.43)	0.65
Not through the Y canula	2 (0.29)	0.22

Figure.1 Intervention rate by the pharmacists
(Adult Oncology Clinic, Main Hospital, Alexandria)

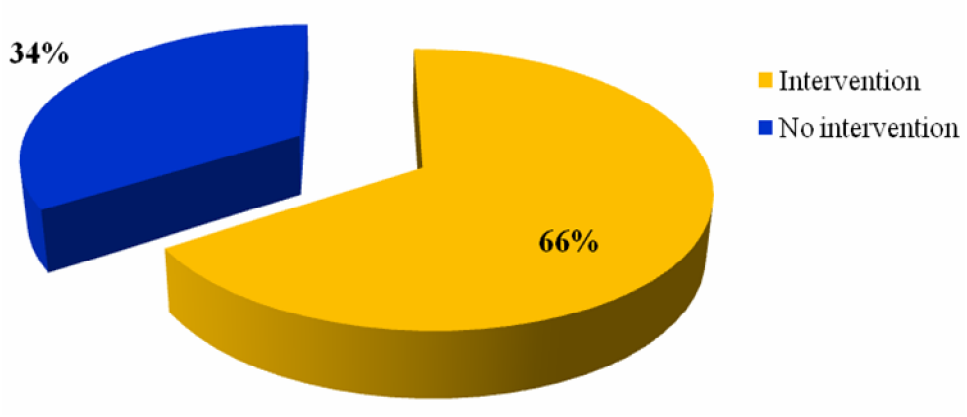


Figure.2 The top 10 drugs involved in chemotherapy medication orders errors and in interventions (Adult Oncology Clinic, Main Hospital, Alexandria)

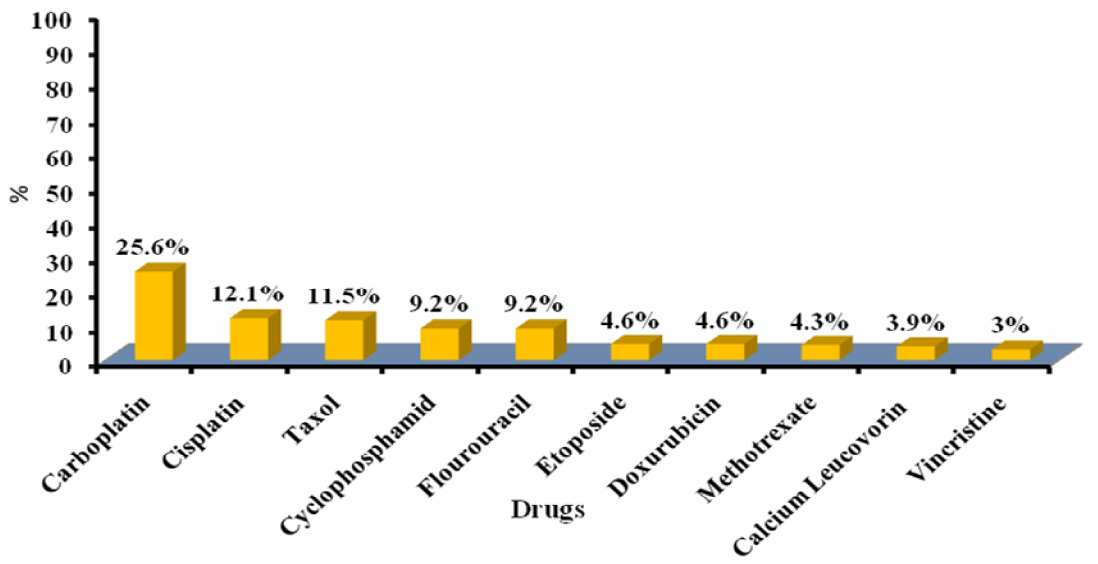
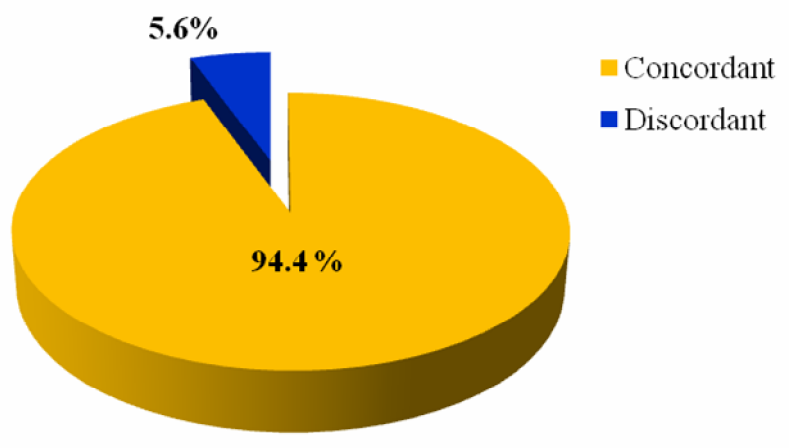


Figure.3 Distribution of physician/pharmacist concordance/discordance after interventions (Adult Oncology Clinic, Main Hospital, Alexandria)



Calcium, Methotrexate, Doxurubicin and Etoposide. Figure 3 illustrates that after interventions, the physician/pharmacist percent concordance was 94.4%.

Much effort and research have been presented over the past years regarding the future of the practice of oncology. It is estimated that a significant shortage of qualified oncology and hematology health care professionals will be seen by 2020 (Erikson *et al*., 2007). The information published regarding workforce implications has focused on physicians, nurse practitioners and physician assistants and overlooked the growing number of oncology clinical pharmacists who can assist with direct patient care and patient education activities (Sessions *et al*., 2010). Clinical pharmacists review all drug orders for the cancer patient and ensure that the orders are accurate and complete, and in keeping with the patient's laboratory results (Ministry of Health Singapore, 2011).

In the present study, the average number of medication orders reviewed was 17 medication orders/day. Lower averages were reported in Spain (10 medication orders/day) (Arredondo *et al*., 2003)) and Cairo, Egypt (9 interventions/day) (El-Hamamsy, 2012). On the other hand, a higher number was reported for ambulatory cancer patients at a London Cancer Centre (48 medication orders/day) (Verbic *et al*., 2013). The proportion of medication errors in chemotherapy prescription orders in the present work was 66%, with an equal proportion of interventions. Several studies reported lower rates of medication errors in chemotherapy prescription orders that ranged from 0.31% to 36% (Verbic *et al*., 2013; Markert *et al*., 2009; Slama *et al*., 2005; Díaz-Carrasco *et al*., 2007; Mertens *et al*., 2006).

In the current work, missed information was the most frequent type of prescribing errors in the chemotherapy medication orders, comprising about one third of the total errors and interventions. This rate was consistent with that reported in 2013 by Verbic *et al* (34%) for ambulatory cancer patients ((Verbic *et al*., 2013).

Missed dose was the most frequent prescribing error involved in the two outpatient chemotherapy infusion units at the Dana-Farber Cancer Institute, Boston (23%) (Gandhi *et al*., 2005). Wrong dose involving oral chemotherapy was the most frequent type reported by Weingart *et al* in 2010 (38.8%) (Weingart *et al*., 2010), while wrong drug and failure to order the needed drug (40.33% and 18.77%, respectively) were the most frequent errors in prescribing reported in 2013 in the USA (Kuo *et al*., 2013).

Missed dose was the most frequent type of missed information in the present study. Other forms included missed date of the next cycle, missed documentation in the blue and white sheet, missed drug and missed note of referral, missed intravenous saline administration, missed antihistaminic administration, missed required hydration and missed patient parameter. Types of missed information reported in 2005 in primary care in Bahrain included absence of physician's stamp (34.4%), date (9.8%), and information about patients' address (3.8%), age (3.5%) and sex (0.5%). These data represented 52% of missed information (Al Khaja *et al*., 2005). Treatment errors in a Teaching Hospital in Iran revealed that missed drugs amounted to 52% of the missed information (Fahimi *et al*., 2009), which was much higher than the present results.

Wrong dose error represented 29% of the total errors in the current study. This finding is comparable with that reported in Israel in 2002 (27.5%) (Lustig, 2000) and Texas in 2006 (Shah *et al*., 2006). Higher rates were reported by the pharmacists in Spain from the Hospital Universitario Virgen de la Arrixaca, 2007 (38.5%) (Díaz-Carrasco *et al*., 2007) and Saul N *et al*., in 2010 from 14 comprehensive American cancer centers (38.8%) (Weingart *et al*, 2010). Calculations based on wrong patient parameters and doses that needed renal adjustment were the most frequent forms of wrong dose error in the present work. In the Department of Nephrology in a Hospital in Paris, renal impairment was common in patients with cancer and 53.4% of anticancer drug prescriptions required dose adjustments for renal impairment (Launay-Vacher *et al*., 2007). A study in the USA reported that errors in dose calculation were detected in 2% of chemotherapy medication orders (Mertens *et al*., 2006), which was much lower than the current results.

In the present work, protocol breach error represented one fifth of the detected errors, omission error accounted for 6.28%, while wrong administration route accounted for 1.08% of the detected errors. In Díaz-Carrasco *et al* retrospective study, errors were distributed as follows: incorrect dose (38.5%), drug omission (21.5%), frequency error and incorrect treatment duration (9.6% each), incorrect patient (7.4%) and incorrect administration route (0.7%) (Díaz-Carrasco *et al*., 2007). Interventions regarding laboratory results that may lead to omission of drug or delay of chemotherapy cycle amounted to 2.81 % of the total interventions in acute care government funded hospitals in Australia in 2004 (Dooley *et al*., 2004).

The drug most frequently involved in errors in the medication orders in the present study was Carboplatin (25.6%). Ranchon *et al* in 2011reported that Carboplatin was involved in 21% of dose errors (Ranchon *et al*., 2011). Methotrexate, Etoposide, Doxorubicin, Cyclophosphamide and Vincristine were

among the top 10 drugs in the United States Pharmacopeia MEDMARX database; a national, voluntary, Internet-accessible error reporting system, for all error reports from 1999 through 2004 that involved chemotherapy medications (Rinke, 2007). Those five drugs were also among the top 10 chemotherapy drugs involved in the errors in the medication orders detected in the current study.

The present work showed a high physician/pharmacist degree concordance after the interventions. This rate was higher than that reported by United States clinical pharmacists, where approximately 89% of clinical pharmacist recommendations were accepted by the prescribers: 5% with drug therapy modifications, 28% due to clinical pharmacist prescriptive authority, and 56% without drug therapy modifications (Kuo *et al*., 2013).

It conclusion, errors in chemotherapy orders are common, which gives the validation process performed by the clinical pharmacists a key role in improving patients' safety. The predominant errors were missed information, wrong dose and protocol breach. Common chemotherapy drugs that contributed to the errors were Carboplatin, Cisplatin and Taxol. Almost all of the pharmacists' interventions were accepted by the physicians.

Ensuring chemotherapy safety requires improvements in the way these drugs are ordered, dispensed, administered and monitored. Therefore, since a substantial proportion of chemotherapy medication orders related errors was detected, a medication order errors surveillance system is recommended. It could act as an important safety check thereby ensuring that chemotherapies are delivered error-free to cancer patients. In addition, the implementation of electronic systems for prescribing and dispensing chemotherapy drugs would assist in preventing medication orders errors.

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