A PHARMACEUTICAL CARE PLAN TO MINIMIZE THE INCIDENCE OF POTENTIAL DRUG-DRUG INTERACTIONS IN ONCOLOGY PATIENTS

A Thesis

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List of abbreviations

5-FU	5-fluorouracil
ACE	Angiotensin converting enzyme
ADE	Adverse drug event
ADR	Adverse drug reactions
AUC	Area under the curve
DDI	Drug-drug interaction
DI	Drug interactions
INR	International normalized ratio
MTX	Methotrexate
NSAIDs	Non steroidal anti inflammatory drugs
PDDI	Potential drug-drug interactions
PDI	Potential drug interactions
TDM	Therapeutic drug monitoring
WHO	World Health Organization
SPSS	Statistical Package for Social Science
NCI	National Cancer Institute
MIMS	Master Index of Medical Specialties
ECG	Electrocardiograph

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Abstract

Background and objectives:

The pharmacological treatment of patients with cancer is associated with multiple side-effects. Although the cause of side-effects usually lies in the toxicity and narrow therapeutic index of the cytotoxic drugs themselves, drug-drug interactions (DDIs) can reinforce or intensify adverse events and even seem to be the cause of hospital admission and death in cancer patients. Polypharmacy is the main cause of DDIs. Cancer patients commonly receive multiple medications, including cytotoxic chemotherapy, hormonal agents and supportive care drugs. Most of cancer patients are elderly, and so require medications for co-morbid conditions such as cardiovascular, gastrointestinal, and hematologic diseases. The age-related decline in hepatic and renal function reduces their ability to metabolize and clear drugs and so increases the potential for toxicity. Most of the available literature about the incidence of DDIs and their prevention in cancer patients was performed in developed countries. There is no published information regarding the incidence and prevention of DDIs in Egypt or any other country in Middle East. This study aimed to explore the incidence of potential DDIs as well as their severity and degree of scientific evidence, and perform a care plan to minimize their incidence in oncology patients.

Methods:

The current study was a pre-post study of the potential drug-drug interactions in the oncology department of Ain Shams University Hospital in Cairo, Egypt. The study involved a total of 1000 prescription in the oncology department (500 in the pre-intervention phase, 500 in the post-intervention phase). Potential DDIs were detected using the following drug information resources: Text books (Stockley's

Drug Interactions and Drug Interactions in the Therapy of Malignant Diseases), Published studies on Pubmed, and Internet drug interactions checking systems ("Drug" drug interaction checker, "Medscape" drug interaction checker and "MIMS" -master index of medical specialties- drug interaction checker). G-standard was used to classify the detected interactions according to their degree of severity and level of scientific evidence. The incidence, degree of severity and level of scientific evidence of the detected potential DDIs were determined in pre-intervention phase of the study. This was followed by implementing DDIs reducing measures to deliver the detected results to physicians in the form of group meetings, wall charts, and brochures containing the detected potential DDIs. Post-intervention, incidence, degree of severity and level of scientific evidence were determined using the same methods for DDIs detection and classification in the pre-intervention phase of the study.

Results:

Pre-intervention phase: 500 prescription analyses resulted in 1440 potential drug-drug interaction, that the average interaction per prescription was 2.88 interactions per prescription. Interactions between two cytotoxic drugs (into anticancer/anticancer) were 313(21.8%), Interactions between a cytotoxic drug and a non-cytotoxic one (anticancer/non-anticancer) were 642(44.5%) and interactions between two non-cytotoxic drugs (non-anticancer/non-anticancer**)** were 485(33.7%). These interactions were classified by taking G-standard as a guide. According to degree of severity interactions were: grade A (4.5%), grade B (12.6%), grade C (9.5%), grade D (15.2%), grade E (55%) and grade F (3.2%).

Post-intervention phase: 500 prescriptions were analyzed after intervention phase and results were compared to those of pre-intervention phase. The total number of interactions was 1116 interaction (DDIs decreased by 22.5%). Interactions between two cytotoxic drugs (into anticancer/anticancer) were 204(18.3%),

Interactions between a cytotoxic drug and a non-cytotoxic one (anticancer/non-anticancer) were 556(49.8%) and interactions between two non-cytotoxic drugs (non-anticancer/non-anticancer**)** were 356(31.9%). According to degree of severity interactions were: grade A (6.1%), grade B (10.75%), grade C (5.74%), grade D (18.91%), grade E (53.4%) and grade F (5.1%). Using unpaired t-test, showed that there is no statistical difference between mean number of potential DDIs in pre-intervention and post-intervention phases (P =0.447). Using of Wilcoxon signed ranks test, showed that there is no statistical difference in percent of potential DDIs in the different degrees of severity between pre-intervention and post-intervention phase (Z=0 , P= 1).

Conclusion:

High incidence of potential DDIs was found in the current study. Clinical pharmacist's activities focusing on improving drug knowledge and awareness of DDIs were shown effective in reducing their incidence. These activities didn't remove all the risks and cancer patients at the hospital are still subjected to significant potential DDIs. This calls for more pharmacists' involvement in medication use process to improve patients' safety.

Introduction

Chapter 1
Introduction

1.1 components and scope of clinical pharmacy practice

There are eight basic components of clinical pharmacy practice; Prescribing drugs, Administering drugs, Documenting professional services, Reviewing drug use, Communication, Counseling, Consulting and Preventing Medication Errors **(Betty, 2010)**. While the scope of clinical pharmacy comprised of: Drug Information, Drug Utilization, Drug Evaluation and Selection, Medication Therapy Management, Formal Education and Training Program, Disease State Management and Application of Electronic Data Processing. The major segments of this discipline are pharamcovigilance, pharmacoeconomics, therapeutic drug monitoring (TDM), biosafety, drug information, and aseptic dispensary.

The probability of wrong medication can be reduced if the prescription are reviewed properly, the clinical plan evaluates the situation correctly and pharmaceutical services are provided **(Teichman and Caffee, 2002)**. World Health Organization (WHO) highlighted the importance of pharmacovigilance as a useful constraint to minimize the therapeutic complications by detection, assessment, understanding and prevention of adverse effects of medicine **(WHO,2002).**

1.2 Role of clinical pharmacist in oncology unit (Hoare and Beer, 1995):

a) Multidisciplinary approach

- Treatment of cancer patients is multidisciplinary. The oncology pharmacist should be aware of the role of doctors, nurses and other therapists in their unit and liaise closely with them on all drug-related aspects of patient care, to ensure continuity, consistency and safety in the use of drugs.

b) Communication

- Formal lines of communication should be set up between the pharmacists at the cancer unit to ensure effective and efficient flow of information in both directions.

c) Therapeutic policies

- The oncology pharmacist should ensure the approved therapeutic policies for areas of cancer care specific to oncology medicine are in operation. Written policies must be available in all oncology and pharmacy clinical areas and cancer units linking in to the cancer center.

d) Dispensing

- It is recommended that at least one pharmacist, experienced in oncology pharmacy must be available for prescription checking and/or advice. Written procedures for the dispensing of oral cytotoxic drugs, including inpatient supply, must individually dispensed and labeled with full dosing instructions and the length of course.

e) Patient counseling

- Patient counseling by pharmacist about the nature of their treatment is particularly important for the oncology patient, because they receive multiple drug therapy and have frequently changing dosage regimens and short courses of drugs superimposed on chronic treatments.

f) Cytotoxic reconstitution

- Cytotoxic preparation must be managed by a pharmacist with permanent responsibility for the service and be staffed by technicians. Cytotoxic reconstitution should be in a pharmacy or pharmacy satellite. If –unavoidably- preparation occurs outside the pharmacy, pharmacists must be involved in the

preparation and maintenance of procedures and training of medical and/or nursing staff. Procedures must be available for handling techniques, dose preparation, dealing with spillage and disposal of cytotoxic drugs.

g) Drug information

- Much of oncology practice is research based and therefore not in textbooks. The oncology pharmacist should provide their drug information service or have access to a drug information service.

h) Clinical trials

- There should be a designated, named pharmacist responsible for liaising with the clinical research team and the sponsor on all pharmaceutical aspects of clinical trials. The pharmacist should be involved at all stages of the clinical trial to ensure the safety of patients and the provision of robust data to Food and Drug Administration or good clinical practice standards.

i) Oncology training

The basic standard of training pharmacists and pharmacy technicians working in oncology should include clinical and technical training.

1.3 Review of the role of oncology clinical pharmacist in literature

Drug –drug interactions (DDIs) are a cause of adverse drug reactions (ADRs), resulting in adverse outcomes associated with drug therapy **(Cruciol-Souza and Thomson, 2006)**. In 2004, some researchers have authored a paper titled "*Death by Medicine*" that presents compelling evidence that today's system frequently causes more harm than good **(Gary et al., 2004)**. This paper has