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Knowledge, Principles, and Clinical Consequences of Drug Interaction: A Cross-Sectional Study in Subratha Teaching Hospital, Libya

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Abstract

Background: Drug interactions are considered one of the adverse drug events, which are known as drug interaction injuries (DDIS), which can lead to severe side effects in addition to their impact on therapeutic effectiveness.

Objective: The study aimed to identify the concept of drug interactions, how they occur, and their types, evaluate the prevalence among patients, and determine the medications most susceptible to drug interactions. It also aimed to determine the levels of potential drug interactions from prescriptions collected randomly from the Internal Medicine Department at Sabratha Teaching Hospital

Methods: A cross-sectional study was conducted at Sabratha Teaching Hospital, Libya. Prescriptions were randomly collected from the Internal Medicine Department, and potential drug interactions were analyzed. The study evaluated the prevalence and types of drug interactions, focusing on identifying the most susceptible medications and the age groups most affected.

Results: The study found that there was a high percentage of drug interactions among patients who were admitted as shelter cases, and the age group most exposed to drug interactions was between 61 and 80 years, at a rate of 31.5%.

Conclusion: Among the medications that had the most drug interactions with a large number of medications was aspirin.

Keywords: Aspirin, Cross-Sectional Studies, Drug- interaction, Prevalence

INTRODUCTION

Drug interaction is an interaction between a drug and some other substances. In other words, it could be an interaction between a drug and a certain type of food. This may lead to an interaction that manifests as an increase or decrease in the effectiveness of an adverse reaction or a totally new side effect that is not seen [1].

There are several pharmacologic, pharmacokinetic, and pharmacodynamic mechanisms through which drugs might interact [2]. These interactions could be brought on by concurrently prescribed therapy modalities, external factors, or the patient's particular behaviors, including eating, drinking, or smoking [2].

By being aware of the possible reactions of drugs' mechanisms to food, herbs, vitamins, and other medications, we can confidently navigate the potentially dangerous effects of mixing drugs with food, herbs, vitamins, and other medications [3]. Some of these interactions have positive synergistic effects, while others have a range of clinically significant outcomes [3].

Even though clinical chemists are aware of the shared underlying mechanisms, interest in the contribution of pharmacogenetics to the clinical importance of interactions has grown in recent years [3]. For example, in its 2012 medication interaction guidelines for industry, the FDA first discussed interactions involving organic anion-transporting polypeptides. Since then, more known output substrates and inhibitors have been found [3].

Drug interactions are categorized using several mechanisms, such as when a medication changes a patient's behavior to affect their compliance with another medication; this is known as a behavioral drug-drug interaction. For instance, when their symptoms improve, a depressed patient on an antidepressant may start to comply with adjustment more readily [4].

Moreover, Pharmaceutical medication interactions happen when one drug is formulated differently than another before it is administered—for instance, the precipitation of Vecuronium and sodium Thiopentone in an intravenous giving set [4].

Drug interactions, known as pharmacodynamics interactions, happen when medications interact and have opposing or additive effects. This can decrease the overall effect or even cancel it out [4].

However, to identify pharmacodynamics (altered effect) and pharmacokinetic (altered concentration) interactions, clinicians must be knowledgeable about the pharmacology of the medication, including metabolic pathways [5]. When several medications combine to potentially enhance an everyday activity, like QT prolongation, serotonin elevation, or seizure threshold reduction, it can be challenging to determine the clinical relevance of these interactions [6]. Patient characteristics that could affect the risk or intensity of the interaction include organ failure, age, coexisting medical disorders, electrolyte imbalances, and genetics [5].

Drug-drug interactions can cause toxicity not just when starting or stopping a

treatment but also when the treatment is stopped [5]. For instance, it takes at least two weeks for carbamazepine's substantial induction effect on cytochrome enzymes to reverse. Some medications require time [5]. Amiodarone is one medication that takes a long time to disappear from the body [7) entirely.

To create practical therapeutic combinations, pharmacological, reparative, and clinically beneficial interactions are investigated [8]. An enormous variety of in vitro and in vivo techniques for identifying and forecasting medication interactions have been developed due to intensive study [8]. Drug interactions and their repercussions can be avoided by having appropriate awareness of and understanding of potential interactions between drugs [8].

According to previous research, drugs that affect closely regulated bodily functions, such as antihypertensive, antidiabetic, and anticoagulant medications, as well as those with saturated kinetics, high first-pass metabolism, or a single inhibition route of elimination, may also be clinically relevant to drug interactions [8].

A few extra pharmacokinetic variables are essential in explaining how medication interactions arise. Drug interactions are often more common in medications with high plasma protein binding, pharmaceuticals metabolized mainly by the CYP3A4 isoform, and drugs that activate or inhibit the cytochrome P450 (CYP450) enzyme system [8].

The objectives of this study is to identify the concept of drug interactions, how they occur, and their types. Evaluate the prevalence of drug interactions for patients, know the kinds of medications most susceptible to drug interactions, and determine the levels of potential drug interactions from prescriptions collected randomly from the Internal Medicine Department at Sabratha Teaching Hospital.

MATERIALS AND METHODS

This study was conducted within the Department of Internal Medicine at Sabratha Teaching Hospital, where the inpatients' prescriptions and the department's movement system were reviewed, and the severity of the interferences within the department was counted. Medicines for each patient separately. This study continued for four consecutive months regularly from 1/5/2023 to 4/9/2023, with regular timing and commitment to attendance and follow-up of cases with the presence of the morning traffic of the medical staff and monitoring all updates that may occur in the list of medicines treatment received by each patient.

86 internal prescriptions, including several drug interactions, were collected. The patient's age and gender were determined, and a list of medications prescribed for each patient was created. Then, all potential DDIs among the co-prescribed drugs were screened and collected using Medscape (a website and information resource for medical specialties].

Study population:

The study population included patients

admitted to the internal medicine department of Sabratha Teaching Hospital. After permission from the hospital administration, medical prescriptions (Therapy Sheets) were collected from the medical records of all these patients.

Study sample:

The study sample included 86 internal prescriptions, including 73 prescriptions containing drug interactions.

Statistical method:

The statistical program Microsoft Excel 2010 was used.

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RESULTS

Distribution of the sample according to gender:

Table (1) clearly shows that the percentage of males is higher than the percentage of females, as the percentage of males was 53.4%, while the percentage of females was 46.5% of the total sample

istribution of sample members according to age groups:

Table (2) shows that the highest percentage was for the age group (61-80) years, representing 31.50%. The next age group was the age group (41-60) years, and the lowest age group was (>20). Year and the rate was 2.73%.

Table (1) Shows the distribution of sample members by gender.

Sex	Frequency	%
Males	39	53.49%
females	34	46.51%
Total	73	100%

Table (2) The distribution of respondents according to age groups

Age	Frequency	%
20>	2	2.73%
21-40	14	19.17%
41-60	22	30.13%
61-80	23	31.54%
81-100	12	16.43%
Total	**73**	**100 %**

Distribution of the sample according to the number of medicines for each prescription:

According to Table (3), the number of drugs for each prescription, the highest percentage of drug interactions was for 8 or more drugs, with a rate of 58.9%, while the lowest percentage was when the number of medications prescribed was less than three drugs, with a rate of 1.36%.

Distribution of the sample according to the number of drug interactions for each prescription:

According to Table (4), drug interactions were found 1-3 in prescriptions by (52%), 4-7 DDIs by (28.7%) of prescriptions, and more than 8 (19.3%) DDIs for prescriptions.

Table (3) Shows the number of medicines for each prescription.

Drugs	Frequency	%
>3	1	1.36%
7-4	29	39.75%
>8	43	58.9%
Total	**73**	**100%**

Table (4) Number of drug interactions for each prescription

Number of drug interactions in prescription	Frequency	%
1-3	38	52 %
4-71	21	%28.7
8 ≥	14	19.3%
Total	**73**	**100%**

Distribution of the sample by months:

By looking at the three tables (5, 6, 7), it is clear that August was one of the months that included the most drug interactions, 47, with a rate of (38.5%].

Table (5) The intensity of drug interaction by month of July

intensity of interference	Frequency	%
Contraindicated	1	2.7%
Serious	8	22.2%
Monitor	14	%38.8
Minor	13	36.3%
Total	36	**100 %**

Table (6) Intensity of drug interaction by month of August

intensity of interference	Frequency	%
Contraindicated	1	%2.1
Serious	8	%17.1
Monitor	21	%44.6
Minor	17	36.2%
Total	**47**	**%100**

Table (7) Intensity of drug interaction by month of September

Intensity of interference	Frequency	%
Contraindicated	3	%7.7
Serious	4	%10.2
Monitor	21	%53.8
Minor	11	%28.3
Total	**39**	**%100**

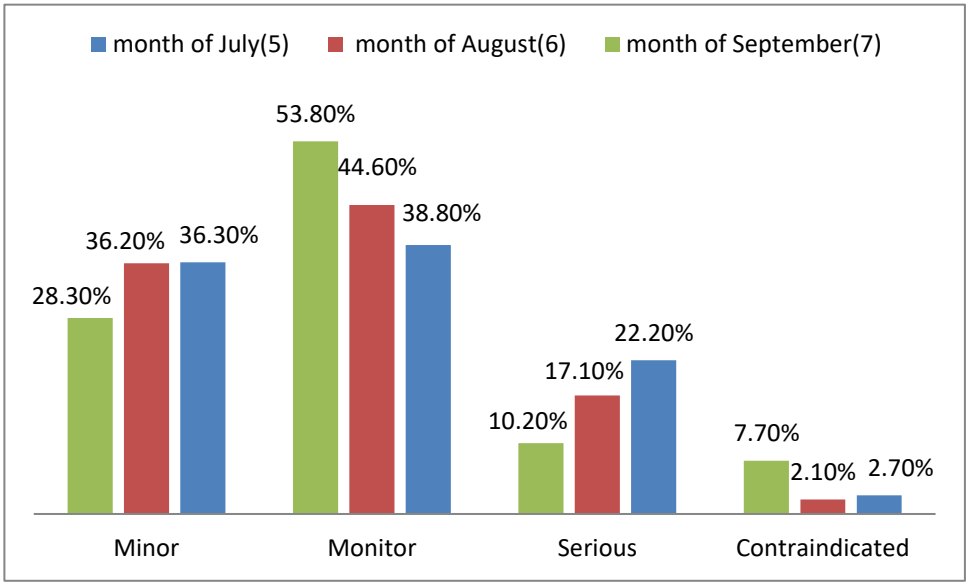

Fig (1) the distribution of drug interaction rates over three months

Distribution of the sample according to the severity of drug interaction for the three months:

According to Table (8), which shows the intensity of drug interaction according to the three months, it is clear that the highest rate of interaction was for August, with a rate of (38.5%), and the lowest percentage was for July, which amounted to (29.5%).

Distribution of the sample according to the drugs most exposed to drug interaction:

The analysis of drug interactions within the sample reveals significant findings regarding their prevalence and severity see table 9. Among the various drug interactions identified, the most frequent were:

Pantoprazole + Plavix: This interaction was the most common, appearing in 11 cases. The severity of this interaction is categorized as needing monitoring, highlighting its impact on the effectiveness of Plavix.

Aspirin + Plavix: This combination was noted in 9 cases and is classified as a minor interaction. Despite its lower severity, it still necessitates attention due to the potential for adverse effects.

Ceftriaxone + Fraxiparin: This drug pair was involved in 8 serious interactions, indicating a high risk of increased bleeding. This interaction requires vigilant monitoring due to its severe consequences see table 9

Table (8) the intensity of drug interaction in three months

Months	Frequency	%
July	36	29.5%
August	47	38.5%

September	39	32%

Table (9) the most common drug interactions

Item	Repetition	Severity	Side effects
Meropenem+Depakin	1	contraindications	Increases the risk of seizure
Nevirapine +Tegretol	1	contraindications	Cause treatment failure
Dexamethasone+ tegretol	1	contraindications	Decreases the effectiveness of Dexamethasone
Ceftriaxone + R-Lactate	2	contraindications	Ceftriaxone is deposited in the kidneys
Aspirin + heparin	3	needs monitoring	It increases the risk of bleeding
Aspirin +Plavix	9	needs monitoring	It increases the risk of bleeding
Ciprofloxacin + Insulin	4	needs monitoring	It reduces the effectiveness of insulin, which causes a drop in blood sugar
Pantoprazole + Plavix	11	Minor	Decrease the effectiveness of Plavix.
Adalat + simvastatin	1	Serious	It may cause liver failure, kidney failure, and may lead to death
Flagyl+ Atorvastatin	4	needs monitoring	It leads to an increased risk of neurological damage
Ceftriaxone + fraxiparin	8	Serious	Increase the risk of bleeding.
Total	**45**		

***** The percentage of total DDIs was (84.9%), and the most susceptible drug-to-drug interaction was Pantoprazole with Plavix found in 11 cases, and its type was monitored.

* Aspirine and Plavix were found in 9 cases, and their type was minor.

* Ceftriaxone with fraxiparin was found in 8 serious cases.

DISCUSSION

A high rate of drug interactions was found among patients who were admitted to shelters, where (84.9%) of the patients suffered from drug interactions, whose severity ranged from slight to very serious, and the use had to be discontinued. According to a different study conducted in Pakistan, 91.6% of potential drug-drug interactions (PDDIs) occur.9. Related results were also noted in research from Mexico, India, and Iran. The findings of our investigation are consistent with the findings of several other studies, which revealed that a higher number of drugs is a predictor of PDDI in patients despite differences in study design and study population characteristics [9].

Drug interactions are the main reason for patient deaths and morbidities among patients admitted to various hospital levels. When two or more medications are given to a hospitalized patient, this commonly results in DDI, which worsens the patient's overall health [10].

The age group most exposed to drug interaction is between 61-80 years, with a rate of (31.5%]. This may be because the most significant number of patients admitted to the hospital during that period were within that age period. The study found that patients between the ages of 70 and 74 had a higher frequency of DDIs than patients between the ages of 80 and 89. This difference in prevalence may have resulted from medical professionals' cautious prescription procedures for the later age group [11]. Due to a multitude of issues, such as patient overcrowding, a shortage of medical experts, rapid patient turnover, and poor communication amongst multidisciplinary teams, the emergency service is especially vulnerable to DDIs. As a result, the emergency service is an essential location for issues to arise [11].

One of the most common drugs that had drug interactions with the most number of drugs is aspirin. This may be because taking aspirin with other drugs increases the risk of bleeding. Heparin and aspirin were the most prevalent medications linked to DDIs, and bleeding was the most common clinical result, according to an observational study done in the cardiology ward of an Indian hospital [12]. Many medications, such as the antidiabetic medications tolbutamide and chlorpropamide, warfarin, methotrexate, phenytoin, probenecid, valproic acid (as well as interfering with beta-oxidation, an essential part of valproate metabolism), and other NSAIDs, are known to be replaced by aspirin from protein-binding sites in the blood [13].

It became clear through the study that the greater the number of prescribed drugs, the greater the percentage of drug interactions, and this is consistent with previous studies [14].

CONCLUSIONS

It is clear from our research that PDDIs are prevalent in the internal medicine ward. Most of the PDDIs that were found fell into the risk category and had moderate severity. Additionally, a sizable number of significant PDDIs were noted.

Physicians, while recommending new drugs in conjunction with existing ones, should know drug interactions. When it comes to helping patients, pharmacists can be very helpful with the safe and efficient use of any drug. To optimize the

effectiveness of a medication, it is essential to consider drug-disease interactions and the timing of administration about diet. Carefully before administering several medicines at once. Doctors and pharmacists should inform patients about the risks of toxicity and unfavorable drug interactions when using over-the-counter (OTC) analgesics improperly and for an extended period.

RECOMMENDATION

Through the presented results and conclusions, the researchers recommend the following **:**

✓ Holding seminars and conferences to educate doctors and pharmacists about medication errors.

✓ Reviewing the medical prescription by a clinical pharmacist before dispensing the medication.

✓ Distribution of awareness leaflets about the danger of drug interactions.

✓ Providing modern references in which DDIs are mentioned periodically.

✓ Using technology in health facilities to identify potential drug interactions.

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Ethical Approval

This research was conducted under ethical registration and approval from University of Zawia, Libya

Conflict Of Interest

None

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