Journal of Pharmaceutical Care
jpc.tums.ac.ir

Medication Reconciliation and Drug–Drug Interactions: An Old Process with a New Approach

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Received: 2020-12-11, Revised: 2021-02-23, Accepted: 2021-02-27, Published: 2021-03-30

ARTICLE INFO

Article type:
Original article

Keywords:
Drug Interactions;
Medication reconciliation;
Drug Therapy;
Patient Safety

ABSTRACT

Background: The occurrence of drug–drug interactions (DDIs) and insufficient attention to medication reconciliation is one of the important challenges of pharmacotherapy in hospitalized patients. The aim of this study was to determine the extent of drug–drug interactions in patients based on medication reconciliation strategy.

Methods: This descriptive cross-sectional study was performed for six months in patients admitted to Imam Reza Hospital in Amol, North of Iran. The data were obtained by using a medication reconciliation tool through a random sampling of patients admitted in Hospital wards from May 2014 until October 2014. A total of 200 patients were enrolled in the study. All patients had a history of medication use before admission. The drug interactions have been checked according to Drug Interaction Facts between newly prescribed drug and medication patient using before admission. The number and frequency of data were summarized by SPSS21 statistical software.

Results: Major and Moderate DDIs were found in 7.5% and 64% of prescriptions. The most frequent DDIs were seen in those who were taking psychiatric drugs (33%) and cardiovascular drugs (30%). Most DDIs occurred among women over 60 years of age. The most frequently occurring DDIs was pharmacokinetics interaction between clopidogrel and atorvastatin (n=9). Other frequent interactions were between ceftriaxone and heparin (n=8) and metoprolol and insulin (n=3).

Conclusion: This study showed a high rate of drug interactions and especially confirms the importance of medication reconciliation in providing a comprehensive drug history and exploring drug interactions.

J Pharm Care 2021; 9(1): 39-44.

► **Please cite this paper as:**
Ala Sh, Tonkaboni S, Bazi A, Salehifar E. Medication Reconciliation and Drug–Drug Interactions: An Old Process with a New Approach. J Pharm Care 2021; 9(1): 39-44.

Introduction

The occurrence of drug-drug interactions (DDIs) and insufficient attention to medication reconciliation (MR) is one of the important challenges of pharmacotherapy in hospitalized patients (1, 2). Recent studies have shown that preventable adverse drug events (ADEs) occurs in 45.11% of hospitalized patients (3). These ADEs has poor consequences, including readmission, prolonged admission, occupational disability, the imposition of additional therapeutic costs and reduced patient satisfaction with medical care (4). DDIs occurs when the drug effects are altered by another drug that is simultaneously consumed (5). The interaction can reduce, increase or neutralize the effects of the other drug. Evidence from epidemiological studies suggest that 6-30% of DDIs may lead to death or hospitalization (6).

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MR is a process by which a complete list of drugs is obtained according to a complete drug history including name, dose, frequency, route of administration. The updated list of previous drugs is compared with the list of current drugs ordered by physician after admission, transfer to a different ward or discharge from the hospital. MR is a method of increasing therapeutic safety that has been accepted by many organizations, including the World Health Organization (7). Although MR is almost often performed by nurses in developing countries, optimally it should be conducted by pharmacist especially hospital and clinical pharmacists due to their thorough knowledge regarding the safety and efficacy of drugs (8). Previous studies have demonstrated that a lack of medication reconciliation is responsible for 46% of all medication errors and >20% of AEDs including drug interactions in the hospital setting (9, 10).

Considering lack of data about the MR and DDIs in North of Iran, the aim of this study was to determine the extent of DDIs in patients by using of MR strategy.

Methods

This observational cross-sectional study was carried out in Imam Reza hospital with 250 beds that is affiliated to Mazandaran University of Medical Sciences (MAZUMS), located in North of Iran. Patients who admittedto the hospital wards from May 2014 until October 2014 were eligible to enter the study. The list of patients was extracted from Health Information Service (HIS) system of the hospital based on simple random selection by random number table. Data was gathered by a Pharm-D student of the MAZUMS who was trained and supervised by a clinical pharmacy specialist. The sample size was chosen according to the similar previous studies (11). This hospital consists of eight different units: Cardiology, Internal Medicine, Surgery, Neurology, Infectious diseases, Emergency, Intensive care unit (ICU) and Coronary Care Unit (CCU). The study was approved by the ethics committee of Mazandaran University of Medical Sciences (IR.Mazums.Rec.93.902). Written informed consent was obtained from all patients before enrollment.

Patients were included if they had at least two prescribed medications before admission, aged 18 years or older, and admitted to the hospital in the past 24 h. Patients were excluded if they were confused or in a coma and did not have an alert caregiver.

The trained pharmacy student performed patient interviews and achieved complete medication histories. MR was executed by reviewing the pre-hospitalization medication list obtained by interviewing the patient and/or reliable caregiver and checking the pre-hospitalization documents to obtain the most correct pre-hospitalization medication list. The primary outcome was to determine the rate of DDI in different drug classes using medication reconciliation tool. Secondary outcome was detecting the most frequent drug-drug interactions.

To collect the data, a data gathering form which included demographic information, previous medications, current medical diagnosis and details of dosing of drugs (including the dose, dosage form, frequency and route of administration) were prepared. The origin of data was the patients, their caregivers, previous medical records and the Health Information system (HIS) of the hospital. Prescriptions were analyzed in terms of the number of drugs per prescription, the number of DDIs, and the number of morbid/comorbid conditions per patient. The list of prescribed drugs during hospitalization of patients and the list of drugs used by patient before admission were assessed by using a software developed by Food and Drug Deputy of MAZUMS based on the Facts Drug Interaction Textbook (12). The characteristics of interactions defined by Facts Drug Interactions including the onset and severity of interactions were summarized in Table 1. The results were reported descriptively.

Table1. Classification of drug interactions according to onset and severity.

Onset	**Rapid:** The effects of interaction happen within 24 hours of administration of the drug pair.
	Delayed: The effects of interaction happen after more than 24 hours (i.e, days to weeks) when administered together.
Severity	**Major:** Potentially life-threatening or capable of causing permanent damage
	Moderate: Deterioration in patient's clinical status. Additional treatment, hospitalization or an extended hospital stay may be necessary.
	Minor: Usually mild, may be bothersome or unnoticeable, but not significantly affect the therapeutic outcome. Additional treatment is not required.

Results

A total of 200 patients were enrolled in the study. Demographic and basic characteristics of the patients were summarized in Table 2. Most of the medications used by patients before admission were cardiovascular drugs (49%), psychiatric drugs (22%) and antidiabetic agents (22%). Stroke (28.5%) was the most common reason of admission in hospital.

Table 2: Demographic and basic characteristics of the patients.

Demographics	Frequency
Sex	
Male, N (%)	84 (42%)
Female, N (%)	116 (58%)
Age in years, Mean ± SD[a]	68± 15.8
The most common reason for hospitalization	
Psychiatric diseases	57(28.5%)
Gastrointestinal diseases	30(15%)
Respiratory diseases	26(13%)
Infectious diseases	21(10.5%)
Cardiovascular diseases	17(8.5%)
Diabetic foot	11(5.5%)
Kidney diseases	8(4%)
others	12(6%)
Prescribed medications before admission	
Cardiovascular drugs	98 (49%)
Psychiatric drugs	44 (22%)
Anti -diabetes drugs	44 (22%)
Gastrointestinal drugs	6 (3%)
Respiratory system drugs	4 (2%)
Others	4 (2%)

[a]SD:standard deviation ,[b]International classification of diseases, 10th revision(21),

DDIs between prescribed drugs in the hospital with previous drugs and between prescribed drugs before and after hospitalization were considered. Most DDIs were detected with psychiatric drugs (33%) and cardiovascular drugs (30%) before hospitalization. Most DDIs occurred in prescriptions written for women over 60 years of age (55%). The most prevalent interactions were found in prescriptions of neurologists. There were 30 cases of major and moderate interactions following adding a new medicine to the previous medications which were prescribed for chronic diseases (asthma, diabetes, hypertension, etc.). On average, the number of drugs used at the time of admission for each patient was 12 (7-18) drugs. Some of the most important DDIs were presented in Table 3. The three most frequent occurring DDIs were clopidogrel and atorvastatin (n=9), ceftriaxone and heparin (n=8) and metoprolol and insulin (n=3).

Table 3. List of some of major and moderate severity drug-drug interactions, their clinical significance and frequency.

Drug combination	Severity/onset	Type of DDIs	Significance of interaction	Number of prescription whit DDI[a]	Number of medicine in prescription
atorvastatin / clopidogrel	Moderate/Delayed	PK	reduce the metabolic activation of the prodrug clopidogrel and its antiplatelet effects	9	8
sodium valproate/ carbamazepine	Moderate/Delayed	PK	sodium valproate, carbamazepine. plasma protein binding competition. Valproic acid may increase or decrease carbamazepine levels.. carbamazepine decreases levels of divalproex sodium by increasing metabolism.	3	11
citalopram / metoprolol	Moderate/Delayed	PK	citalopram increases levels of metoprolol by decreasing metabolism. Increased metoprolol plasma levels have been associated with decreased cardioselectivity.	3	7
sertraline / metoprolol	Moderate/Delayed	PK	sertraline will increase the level or effect of metoprolol by affecting hepatic enzyme CYP2D6 metabolism.	2	6
warfarin / azithromycin	Major/ Delayed	PK[b]	azithromycin increases effects of warfarin by decreasing metabolism.	1	16
warfarin /metronidazole	Major/ Delayed	PK	metronidazole increases levels of warfarin by decreasing metabolism.	1	5
methotrexate /omeprazole	Major/ Rapid	PK	omeprazole increases levels of methotrexate by decreasing renal clearance.	1	13
methotrexate /omeprazole	Major/ Rapid	PK	omeprazole increases levels of methotrexate by decreasing renal clearance.	1	13
methotrexate /sulfasalazine	Major/ Delayed	PK	sulfadiazine increases toxicity of methotrexate by plasma protein binding competition.	1	7
warfarin /indomethacin	Major/ Delayed	PD[c]	warfarin and indomethacin both increase anticoagulation	1	8
Levothyroxine/ warfarin	Major/ Delayed	PD	levothyroxine increases effects of warfarin by pharmacodynamics synergism	1	16
Captopril/triamterene	Major/ Delayed	PD	captopril, triamterene. Either increases toxicity of the other. Both drugs lower blood pressure. Increased risk of hyperkalemia.	1	7
Captopril/spironolactone	Major/ Delayed	PD	captopril, spironolactone. Either increases toxicity of the other. Both drugs lower blood pressure. Risk of hyperkalemia	1	9
Captopril/ allopurinol	Major/ Delayed	unknown	increases risk of anaphylaxis, Stevens Johnson syndrome.	1	14
indomethacin /metoprolol	Moderate/Delayed	PD	indomethacin decreases effects of metoprolol by pharmacodynamics antagonism. Long term (>1 wk) NSAID use. NSAIDs decrease prostaglandin synthesis and NSAIDs increase blood pressure	1	13
propranolol / warfarin	Moderate/Delayed	PK	propranolol increases levels of warfarin by decreasing metabolism. The anticoagulant effect of warfarin may be increased.	1	14
omeprazole /warfarin	Moderate/Delayed	PK	omeprazole will increase the level or effect of warfarin by affecting hepatic enzyme CYP2C19and CYP2C9/10 metabolism	1	7
Carbamazepine/ lithium	Moderate/Delayed	unknown	Risk of neurotoxicity	1	10
allopurinol / theophylline	Moderate/Delayed	PK	allopurinol increases levels of theophylline by decreasing metabolism.	1	9
furosemide + hydrochlorothiazide	Moderate/Delayed	PD	furosemide and hydrochlorothiazide both decrease serum potassium	1	8
Diltiazem/atenolol	Major	PD	atenolol and diltiazem both increase anti-hypertensive channel blocking. Either increases toxicity of the other by unspecified interaction mechanism	1	11

Discussion

Our results show that ignoring the drugs used by the patient before hospitalization and the drugs prescribed by other physicians during admission was an important origin of drug interactions. Also, old age, female gender, and polypharmacy were associated with a higher rate of drug interactions.

Our results are in concordance with the result of Busa et al. found that wards such as neurology may be associated with a higher risk of drug interactions due to the hospitalization of patients with chronic diseases and advanced age (14).

Previous studies on MR in Iran mostly focused on the medication errors due to medication discrepancies (8, 15, 16), Few studies have pointed the importance of MR in identifying DDIs in hospitalized patients (10).

Aging is associated with a higher incidence of chronic diseases and subsequently a higher number of medications used by older individuals. Polypharmacy predisposes the aged patient to more and most severe form of DDIs (17, 18).In this study, the incidence of DDIs was more common in women compared to men. The biological differences between men and women including differences in anatomy and physiology, weight, gastrointestinal tract characteristics, liver metabolism and renal function may somewhat explain the higher rate of drug interactions in women. Women have fewer weight and size of organs compared to men. While women's body fat is more, the gastrointestinal motility and glomerular filtration rates of women are lower compared to men. These differences can influence the interaction of the body with drugs, including absorption, distribution, metabolism, and removal of drugs (19, 20). As mentioned in previous studies, our results also emphasize the role of pharmacists in detecting the DDIs and taking measures to reduce the DDIs in hospitalized patients.

Tools such as Screening Tool of Older Persons' Prescriptions (STOPP) and Screening Tool to Alert to Right Treatment (START) are used to reduce ADE (21), but experience with these tools is not as good as working with MR. For this reason, MR is a simpler and more accessible tool for reducing drug errors such as drug interactions

In conclusion, according to the results of this study, the use of medication reconciliation can be an effective way to find timely drug interactions between patients' previous medications for their chronic illness and new medications prescribed and these results supports that medication reconciliation effectively help prevent the occurrence of drug interactions.

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