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Medication reconciliation and drug–drug interactions: An old process with a new approach

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Abstract:	Background: 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. Objective: The aim of this study was to determine the extent of DDIs in patients by using of MR strategy. Methods: This descriptive cross-sectional study was performed for six months in patients admitted to Imam Reza Hospital in Amol, north of Iran. who had a history of medication use before admission. medication history obtained from patients and their medical records and comparing that list of the physician's orders to identify drug interactions . After MR, DDIs were screened using Software developed by Mazandaran University of Medical Sciences base on the reference of drug interaction facts 2013. The collected data were statistically analyzed using SPSS21 statistical software. Results: Between physicians' prescriptions and medications is taking by patients before admission, were observed 7.5% major DDIs and 64% moderate DDIs. The DDIs were seen in those who were taking psychiatric drugs (33%), cardiovascular drugs (30%) before hospitalization. most DDIs occurred among women over 60 years of age. The three most frequently occurring DDIs were clopidogrel and atorvastatin (n=9), ceftriaxone and heparin (n=8) and metoprolol and insulin (n=3). Conclusion : Failure to pay attention to the medications that patients take for their chronic diseases increases the risk of potential drug interactions, especially in the elderly, MR can be effective in better identifying drug–drug interactions.

Dear Editor-in-Chief,

I am pleased to submit an original research article entitled “Medication reconciliation and drug-drug interactions: An old process with a new approach” by Ala et al. in the “International Journal of Clinical Pharmacy”. I hope you would consider our manuscript for publication in your journal. To the best of our knowledge, the role of Medication reconciliation as a strategy in the detection of drug-drug interactions in hospitalized patients has been evaluated in limited studies that were associated. Our results suggest that Medication reconciliation is an effective and non-expensive strategy for the detection of drug-drug interactions in hospitalized patients. I believe that the findings of this study are relevant to the scope of your journal and will be of interest to its readership.

We declare that this manuscript, or closely related research, has not been published before, in whole or in part, and is not currently being considered for publication elsewhere. All authors approved the final version of the manuscript and agree with its submission to the “International Journal of Clinical Pharmacy”. The authors have no conflicts of interest to declare. The journal is allowed to reproduce any previously published material. This study was the Pharm.D thesis of my student SufiaTonkaboni and was supported by a grant from the research council of Mazandaran University of Medical Sciences.

Thank you for your consideration of this manuscript. We look forward to hearing from you at your earliest convenience.

With my best regards,

Ebrahim Salehifar

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Medication reconciliation and drug–drug interactions: An old process with a new approach

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Abstract

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Objective: The aim of this study was to determine the extent of DDIs in patients by using of MR strategy.

Methods: This descriptive cross-sectional study was performed for six months in patients admitted to Imam Reza Hospital in Amol, north of Iran. who had a history of medication use before admission. medication history obtained from patients and their medical records and comparing that list of the physician's orders to identify drug interactions. After MR, DDIs were screened using Software developed by Mazandaran University of Medical Sciences base on the reference of drug interaction facts 2013. The collected data were statistically analyzed using SPSS21 statistical software.

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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 45.11% of hospitalizations are associated with preventable adverse drug events (ADEs)[3]. These ADEs has unpleasant consequences, including readmission, prolonged admission, occupational disability, the imposition of additional therapeutic costs and reduced patient satisfaction with medical care[4]. DDIs are a special type of ADE, which occurs when the drug effects are altered by another drug that is simultaneously consumed. This interaction can reduce, increase or neutralize the effects of the drug[5]. Evidence from epidemiological study suggests that 6-30% of DDIs leading to death or hospitalization[6]. MR is a process by which a complete list of drugs is recorded that a person normally consumes at home, including name, dose, frequency, route of administration, and is compared with the list of drugs that the physician orders for admission, transfer or discharge. MR is a method of increasing therapeutic safety that has been accepted by many organizations, including the World Health Organization[7] Although for many years in Iranian hospitals MR is almost often performed by nurses and medical students (who have no proper pharmacological information.) [8],today, with the increase in the number of clinical pharmacy graduates, MR is done in a more specialized way.

Aim of the study

The aim of this study was to determine the extent of DDIs in patients by using of MR strategy.

Ethics approval

this study was approved by the university ethics committee (IR.Mazums.Rec.93.902). written informed consent was obtained from all the patients before the enrollment.

METHODS

Study design

This observational cross-sectional study was carried out in all ward except the emergency department of a 250-bed Imam Reza hospital affiliated to Mazandaran University of Medical Sciences (MAZUMS), Amol, north of Iran. In this prospective single-center observational study, 200 patients who were admitted to hospital from May 2014 until October 2014 were assessed by Pharm. D., student of the MAZUMS with the supervision of a clinical pharmacy specialist. This hospital consists of eight different units: Cardiology, internal medicine, surgery, neurology, Infection, Emergency, Intensive care unit(ICU), coronary care unit (CCU). 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.

Data collection and screening for DDIs

Pharmacy student was trained by her preceptor, a clinical pharmacy faculty member, to performed patient interviews and achieve complete medication histories. MR, for this study, was defined as reviewing the pre-hospitalization medication list (s) obtained by interviewing the patient and/or reliable caregiver and checking the pre-hospitalization documents (if available) to obtain the most correct pre-hospitalization medication list. All patients, even those who not meet inclusion criteria in this study, had MR performed by the hospital pharmacist. To collect the data, a questionnaire containing demographic information, consumed medications, and information of medications prescribed by the physician, including the dose, dosage form, frequency, route of administration, were prepared. The questionnaire

was completed according to the patient's statements or their caregivers and nursing Kardex. Patients' demographic details were noted. Prescriptions were analyzed for the number of drugs prescribed per prescription, the number of DDIs, and the number of morbid/comorbid conditions per patient. After MR, DDIs were screened using Software developed by MAZUMS base on the reference of drug interaction facts 2013[9]. Characteristics of interaction onset time and severity is summarized in Table 1. The collected data were statistically analyzed using SPSS21 statistical software.

---- Table 1----

Results: A total of 200 patients were enrolled in the study according to inclusion criteria, and their Demographic and basic characteristics of the patients is summarized in Table 2. Most of the medication used by patients before admission were cardiovascular drugs (49%), psychiatric drugs (22%), antidiabetic drugs (22%).stroke(28.5%) were most reason of admission in hospital in this study.

---- Table 2----

The DDIs were seen in those who were taking psychiatric drugs (33%), cardiovascular drugs (30%) before hospitalization. most DDIs occurred among women over 60 years of age. the largest interaction was related to the prescriptions ordered by neurologists. In the present study, there were 30 cases (major and moderate interactions) that occurred as a result of adding a new medicine to the medications that patients received for their 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) items. The three most frequently occurring DDIs were

clopidogrel and atorvastatin (n=9), ceftriaxone and heparin (n=8) and metoprolol and insulin (n=3). In Table3 lists some of the most important DDIs.

---- Table 3----

DISCUSSION

Studies on MR in Iran have often focused on medication errors due to medication discrepancies[8, 10, 11], Few studies have been conducted on MR and its role in better identifying DDIs in hospitalized patients[12].

Our results show that ignoring the drugs used by the patient before hospitalization and the drugs prescribed by other physicians during admission was one of the factors causing DDIs. Also, according to other findings of this study, old age, female gender, and polypharmacy are important causes of DDIs in hospitalized patients. Aging causes chronic diseases and increases the number of medications used by individuals and is on the ground for the occurrence of DDIs in this population is favorable[13-16]. In this study, the incidence of DDIs in women more than in men, this difference may also be based on biological differences between men and women[16, 17].A Similar study shows that pharmacist, as one who has more pharmacological awareness than other medical staff, plays the key role in reducing DDIs in hospitalized patients especially in elderly patients who have more DDIs than others[2] There are some limitations in this study, including the lack of full access to medical records of the patients after discharge, uncertain timing of patient discharge to determine whether medication reconciliation is done correctly during discharge or not.

CONCLUSION

Failure to pay attention to the medications that patients take for their chronic diseases increases the risk of potential drug interactions, especially in the elderly, medication reconciliation can be effective in better identifying drug–drug interactions.

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Conflicts of interest The authors declare that they have no conflicts of interest.

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Table1. Characteristics of interaction onset time and severity

Parameter Drug checker interaction	
Onset time	**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 (ie, 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.

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197 **Table 2.** Demographic and basic characteristics of the patients.

Demographics	**Frequency**
Sex Male, N (%) Female, N (%)	 84 (42%) 116 (58%)
Age in years, Mean ± SD	68 ± 15.8
The most common reason for hospitalization*	
Cardiovascular diseases	8.5%
Infectious diseases	10.5%
Gastrointestinal diseases	15%
Kidney diseases	4%
Weakness and lethargy	5.5%
Diabetic foot	5.5%
Psychiatric diseases	28.5%
respiratory diseases	13%
others	0.5%
prescribed medications before admission	
Cardiovascular drugs	49%
respiratory system drugs	2%
Psychiatric drugs	22%
Gastrointestinal drugs	3%
Anti -diabetes drugs	22%
others	2%
* International classification of diseases, 10th revision[18], SD: standard deviation	

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Table3.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	Number of medicine in prescription
warfarin / azithromycin	Major/ Delayed	PK[1]	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[2]	warfarin and indomethacin both increase anticoagulation	1	8
Levothyroxine/ warfarin	Major/ Delayed	PD	levothyroxine increases effects of warfarin by pharmacodynamic 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
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
indomethacin /metoprolol	Moderate/Delayed	PD	indomethacin decreases effects of metoprolol by pharmacodynamic 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

DDIs: drug-drug interactions, PK
:Pharmacokinetics, PD:Pharmacodynamics

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