Investigation of drug -drug interactions status, in University-Based Pharmacies, in Lorestan, IRAN

Investigación del estado de las interacciones entre medicamentos y drogas, en farmacias universitarias, en Lorestan, IRAN

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Abstract

Drug drug interaction, is an important cause for disturbing of medical management of a disease that usually is preventive, must be continuously investigated for detection of causes. Due to little data about it in recently years in this area, study was done, to investigate of quantity of interactions, and some related factors. In this cross sectional study, all prescriptions data from April to October 2016 were collected. Variable data included: type and name of drugs- the number of drugs in each prescription and characteristics of interactions. We used software of drug interaction fact and lexicomp on desk top DI and textbook 'Drug Interaction Facts' .Statistical analysis done by t test and use of SPSS 19. Finally, 41096 prescriptions were collected. From these data 56% were male. 3043 of subjects had DDI (7.4%). most interaction was in 5th degree and majority of interactions were mild. DDI between ammonium chloride and pseudoephedrine –antihypertensive drugs and others-omeprazole and chlordiazepoxide had the most frequency, respectively. About interaction show, 53% was delay and 43% was rapid. The mean quantity of drugs was less than four type drugs in each prescription. We conclude that, general and even OTC drug had great DDI that must be notice to these drugs in prescriptions. There was no correlation between gender or specialty of physician and frequency of DDI (p=0.08). Quantity of drugs in each prescription, correlate with rate of DDI (p=.003). Attendance a pharmacist in treatment team of patients could be helpful, for decrease the rate of DDI. In all centers, continuous and more research for detecting DDI is necessary.

Keywords: drug interaction, DDI, physician.

Resumen

La interacción farmacológica, es una causa importante para alterar el manejo médico de una enfermedad que generalmente es preventiva, debe investigarse continuamente para detectar causas. Debido a la poca información al respecto en los últimos años en esta área, se realizó un estudio para investigar la cantidad de interacciones y algunos factores relacionados. En este estudio transversal, se recopilaron todos los datos de las prescripciones de abril a octubre de 2016. Los datos variables incluyeron: tipo y nombre de los medicamentos: la cantidad de medicamentos en cada receta y las características de las interacciones. Usamos software de hechos de interacción de drogas y lexicomp en el escritorio y en el libro de texto "Datos de interacción de drogas". Análisis estadístico realizado mediante la prueba t y uso de SPSS 19. Finalmente, se recogieron 41096 recetas. De estos datos el 56% eran hombres. 3043 de los sujetos tenían DDI (7,4%). la mayor parte de la interacción fue de 5 t h grado y la mayoría de las interacciones fueron leves. La DDI entre el cloruro de amonio y la pseudoefedrina (medicamentos antihipertensivos y otros), omeprazol y clordiazepóxido tuvieron la mayor frecuencia, respectivamente. Sobre el programa de interacción, el 53% fue retraso y el 43% fue rápido. La cantidad media de medicamentos fue menos de cuatro medicamentos de tipo en cada receta. Llegamos a la conclusión de que, en general, e incluso el medicamento de venta libre tuvo un gran DDI que debe notificarse a estos medicamentos en las recetas. No hubo correlación entre el sexo o la especialidad del médico y la frecuencia de DDI (p=0.08). La cantidad de medicamentos en cada receta, se correlaciona con la tasa de DDI (p=.003). La asistencia de un farmacéutico en el equipo de tratamiento de pacientes podría ser útil para disminuir la tasa de DDI. En todos los centros, es necesaria una investigación continua y más para detectar DDI.

Palabras clave: interacción farmacológica, DDI, médico.

Introduction

Medical errors are life threatening events in management of diseases. for increasing safety of patients; physician must be noticed to their causes. DDI (drug drug interactions), is an important cause for disturbing of medical management of a disease.

Patients frequently use more than one medication at a time. Unanticipated, unrecognized, or mismanaged DDIs are important causes of morbidity and mortality associated with prescription drug uses that usually are preventive[1,2].

Patients, often come to physician with a legacy of drugs, during previous medical experience that if physician not notice to it, risk of DDI may be increased. Some groups of patients, especially old age with multiple long standings disease are predisposed to DDI[3].

Drug interaction is defined as the pharmacologic or clinical responses to administration of a drug combination, differing from the anticipated known effect of two agents.

Combining drugs may cause pharmacokinetic and/or pharmacodynamics interactions. Pharmacokinetic mechanisms of interaction include alterations of absorption, distribution, biotransformation, or elimination. Pharmacokinetic interactions in general result in an altered concentration of active drug or metabolite in the body, modifying the expected therapeutic response. Interaction must be considered in differential diagnosis of any unusual responses occurring during drug treatment[4,5,6].

Beside above, DDI may be occurring between prescription drugs but also between food& drug and chemical and drug.it is a dynamic problem , belong to all time and location.it must be continuously investigated for detection of causes and preventive schedule of it. Due to little data about it in recently years in this area, the aim of this study is to investigate of quantity of interactions, and to assay what physicians' prescriptions cause more interactions and to identify common interactions.

Materials and methods

In this cross sectional study, all prescriptions data from April to October 2016 were collected. These data were belonging to 2 general hospital pharmacies affiliated to Lorestan University of medical sciences (in capital of province).

All outpatients and inpatients prescriptions were enrolled in study. Variable data included: type and name of drugs - the number of drugs in each prescription - physician specialty and gender, and characteristics of interactions. For detection of DDI, we used software of drug interaction fact and lexicomp on desk top DI. Also, we used reference textbook 'Drug Interaction Facts' published in 2010 for completion of study[7].

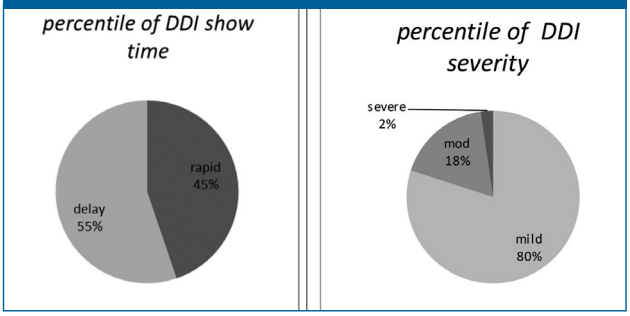
Mean +/- SD and percentage parameters were used.Statistical analysis done by t test and use of SPSS version 19. P value less than 0.05 was considered significant.

Results

Finally, 41096 prescriptions were collected. From these data 56% were male and others female subjects. Minimum age of patients was 2 and maximum age was 89 years old. Average subject age was 35.5 years old.

Out of all them, 3043 subjects had DDI (7.4%).based on importance, most interaction was in 5th degree and respectively, 3th and 2th degrees were common. Between all DDIs, majority of interactions were mild. About interaction show, 53% was delay and 43% was rapid summarized data was showed in fig 1.

Fig 1. Percentile of DDI characteristics



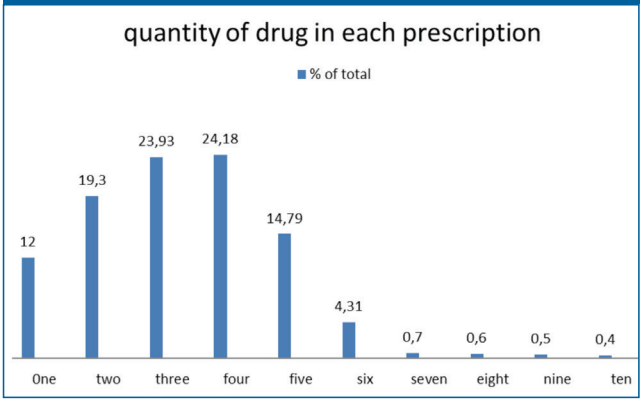
In this study, most of DDIs belong to combination of pseudo ephedrine and ammonium chloride (in diphenhydramine compound), then respectively: antihypertensive drugs (especially beta blockers and other drugs), omeprazole and chlordiazepoxide.

In between all prescriptions, NSAIDs – corticosteroids – azithromycin –metoclopramide were the most frequent type of prescribed drugs.

The most quantity of drugs was four type drugs in each prescription. Between one and ten drugs type prescribed in total of papers. Distribution of drugs numbers in each prescription was summarized in figure 2.

Between all paper contained DDI, 59% was prescribed by general practitioners and 41% by specialist.

Fig 2. Quantity of drug in each prescription



Discussion

In term of the DDI severity, interactions can be classified by: Mild interaction denotes that they are not of clinical importance or the effect on the interaction has not been established. Moderate interaction means, that possible changes in therapeutic effect or may cause adverse effects, but can be avoided adjusting the drug doses. Major interaction means, result in potential adverse effects and necessitates individual dose adjustment in the cases.

About time of onset of action: rapid means that the effect will be evident within 24 hr, after administration of drugs and delay reaction means that the effect will not be evident until days or weeks.

About importance of interaction: they divided in five groups. 1. Established: proven to occur in well controlled studies, 2. probable: very likely but not proven clinically, 3. suspected: may occur; need more study, 4. possible: could occur but data are limited, 5. Unlikely: doubtful; no good evidence of an altered clinical effect.

At first, in review of literature, we conclude that, there is wide variability between frequencies of DDI in the all centers. In ahmadizadeh study in Iran 77% and in namazi study at least 1 DDI in 43%of all patients reported[8,9].

In other study (in birjand .Iran), 42% of prescription had DDI. Also, similar study out of Iran showed wide variability in DDI frequency. 18.5% in Greece and9.8% in Finland and 41% in Nepal[10-13].

In comparison, we could not detect any rational relation between or result and other study about frequency of DDI. We noticed to methodological effect of studies-different distribution of people age and sex and diversity of type of disease and specialty of physician – time and location of studies for this variation of results. For example some studies, only evaluate patients in critical ward that increase the rate of DDI due to longer admission of patients[14]. Previous study in 2013 showed that drug interactions are somewhat inevitable and like other provinces[15].

Finally, we suggested that each group of patients must be compare with same groups in other time and other position but no other population.

In our study, the most frequent DDI occurred between ammonium chloride (in diphenhydramine compound) and pseudoephedrine, although these reactions are mild. After it, the most important reaction (related to moderate- severe reactions), was seen between antihypertensive drugs with others. Especially, angiotensin receptor blockers or angiotensin converting enzyme inhibitors and diuretics had more reaction versus other antihypertensive drug. We noticed to multiple prescriptions of these types of drugs, because of high frequency of uncontrolled hypertension in this area. Another frequent DDI was seen between beta blockers (especially, propranolol) and acetaminophen. Notwithstanding, NSAIDs, corticosteroids, azithromycin had the most quantity of prescribed drug in all subjects.

In nabovati study, beta blockers and diuretics and in Farzaneh study, Aspirin had most frequent drug interaction in prescriptions[16,17], previous study in east of Iran showed that, dexamethasone & ranitidine and then corticosteroids & NSAIDs had majority of DDI[18]. Interaction between beta adrenergic blockers and glimepiride (oral hypoglycemic agents) was the most commonly observed interaction in Jaskumar Nk study[19].

We conclude that, general and even OTC drug (not specialized drugs), had great DDI and physicians must be notice to these general drugs in prescriptions.in majority of studies, only limited drugs included in DDI that necessities awareness of prescribers[20].

Similar to other study, there was no significant relation between gender of patients and rate of DDI In our study (Esmaeil Farzaneh, & Khouri et al study)[17,21].

Our result showed that, no correlation between gender or specialty of physician and frequency of DDI was documented (p=0.08), but in other study, male gender was factor for drug interaction in mousavi study, specialist had more DDI in their prescription than general practitioners, in Ardabil study, 84.8% of drug interactions have ben occurred by male and 15.2% by female physicians and there was significant relation between sex of physician

and number of interferences in mousavi study, Medical specialist's prescriptions in comparison with general practitioners had significantly more moderate severity interactions. Similar results reported in podasani study[22,23].

In our study, DDI severity, classified as: 2.3% in severe category and 17.7% in moderate and 80% in mild category. There is some difference between characteristic of DDI in our study and others.in previous study in Kurdistan 15.6% ,42.6% and 41.8% of interaction were severe, moderate and mild respectively, in gorgan study result was: 35.5%,63.1% and 1.4% respectively[24,25]

We suppose that some factor, including: type of disease may be influence on the type of drugs resulting in variation of DDI in different centers. We supposed that, duration time of disease management, variation of patients' age, and other comorbidity, especially: renal or hepatic disease and hemodynamic instability may be influence on the interaction between drugs in different studies[38-40].

Previous studies showed that 1.3 -2.1 mean drug in each paper is suitable for reducing risk of DDI[26-28]. In this study, mean number of drugs in each prescription was 3.8 that was near to other studies (by Soleymani and mousavi)[29,30]. Previous study by nabovati and et al (in Iran), showed that mean number of drugs in each prescription is high[16]. In our study, quantity of five drugs type in each prescription had more rate of DDI than fewer quantities. Analyses show that quantity of drugs in each prescription, correlate with rate of DDI (p=.003). We conclude, the multidrug prescription may be a risk factor for DDI, this result documented in previous studies[31-33]. Patients with 2 or more disorders may be use different type of drugs result in more DDI[34].

Increased knowledge of practitioners, for Better diagnosis of disease may decrease the quantity of drugs in prescription, although some chronic and end stage patients need more and more drugs[35,36].

Physician in subspecialty, due to visit of more complicated patients and especially, physician in ICU must be notice to more risk of prescription with DDI.

Finally, for reduction rate of DDI below approaches is recommended:

1. Documentation of all drugs, including over-the- counters.
2. Reduce the number of prescriptions drugs in each prescription.
3. be especially vigilant in high risk situations: elderly, patients in an intensive care unit, or with co-morbid illnesses such as renal or hepatic failure.
4. more knowledge about the pharmacology of the drugs , route of excretion, the type of liver or renal metabolism if it exists, the half- life of the drug, and its bioavailability.

If there is an unexpected deterioration or change in the patient condition, consider drug- drug interactions, which usually present in a subtle manner. We (and others), conclude that use of software for detects of DDI or attendance a pharmacist in treatment team of patients could be helpful, for decrease the rate of DDI[37].

Drug interactions are tricky and are easy to miss if not quite. More and more research for detecting type and frequency of DDI in much prescription may turn on a light for solving the problem.

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