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Studying the Prevalence of Medical Interventions in the Recipes

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Abstract

BACKGROUND: Drug interaction is a term used to refer to unfavourable side effects caused by mixing or taking two or more drugs simultaneously. Although it is not possible to identify all drug interactions, awareness of therapeutic team of potential drug interactions, risk factors that enhance the possibility of these interactions and familiarity with mechanisms of drug interactions can help reduce real drug interactions.

AIM: The present research seeks to study the frequency and intensity of possible interactions among various age groups and their correlation with doctor's speciality, time of drug prescription, patient's gender, etc.

MATERIAL AND METHOD: This is observational, cross-sectional research conducted in spring and winter to study the prevalence of drug interactions among 6000 recipes belonging to 2 private and 2 public drug stores. The information associated with recipes was recorded, and drug interactions were studied based upon quick index of interactions using Up to Date software. Quick index of medical interactions is a response to data dealing with how drugs interact with one another. The risk factor is divided into groups A, B, C, D, and X according to this index with each one having its own definition. The data analysis was studied in terms of prevalence type of drug interactions and the possible correlation with other parameters. SPSS v.16 was used for statistical analysis.

RESULTS: The average age of the patients was 42.07 ± 21.56 years. The frequency of male patients was 41.7%. An average number of 4.82 ± 1.91 drugs were prescribed for each patient and an average number of 1.95 ± 2.40 drugs had interaction with one another with levels C, D, and X having the following drug interaction levels: 1.60 ± 2.05, 0.275 ± 0.69, and 0.072 ± 0.31. No such interactions were observed in 31.1% (1846 cases) of recipes. The presence of drug interaction was statistically significant in terms of age, season, drug store and speciality of doctor (P-value < 0.05). The average number of interactions in the recipes issued by psychologists, cardiologists, rheumatologist, neurologists, and general practitioners was more, and this result was statistically significant (P-value < 0.05).

CONCLUSION: Considering the results achieved in this research, we may conclude that the drug interactions in recipes exhibit a noticeable frequency with the highest frequency observed in level C influenced by factors such as age, season, class of drugs, and expertise of the doctor.

Introduction

Drug interaction is a term used to refer to unwanted side effects caused by mixing or taking two or more drugs simultaneously. No such side effects are observed when the drugs are taken individually. Drug interaction may take place between various drugs, drugs prescribed by the doctor and those without a recipe, drugs and herbal medicines, supplementary drugs or vitamin supplements, drugs and some foods [1]. These interactions usually present themselves in a pharmacokinetic or pharmacodynamic fashion. In pharmacokinetic interactions, one drug may change metabolism, disposal or distribution of another medicine. In pharmacodynamic interventions, the exclusive function of drug changes as a result of other drugs'

influence [2]. Drug interactions are classified based upon the degree of importance, and this degree comprises intensity and evidence. The quick index of drug interactions is a response to data describing how drugs interact with one another. This index divides risk factor indexes to groups A, B, C, D, and X with each one having an exclusive definition. As we move from level A to level X, the urgency of response to drug interaction increases. Generally speaking, classes A and B are important only in scientific discussion, and no importance is attached to them in clinical discussions. However, the remaining three interactions always require clinical considerations [3].

According to the report issued by American Association of Doctors, as many as 44 to 98 thousand deaths occur every year as a result of drug interaction with more than 7 thousand cases being the result of negative side effects of medicines. As many as 6.7%

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of the patients in a hospital experience unfavourable drug side effects and this causes 0.34% of the death toll among them. In 2012, the death caused by the unfavourable side effects of interactions had the 4th place following cardiovascular diseases, diabetes, and AIDS in the U.S. [4]. The danger of occurrence and intensity of drug interventions are influenced by factors such as number of drugs taken, length of treatment, patient's age, number of doctors prescribing the medicine and stage of disease [1], [4].

Drug interaction is an important issue in drug safety, and it is a potential reason for the drug's side effects among those patients hospitalised in the hospital. Their effect is well known as an important factor in drug therapy, and it may result in the total failure of the treatment process [5]. Drug interactions may potentially increase the death toll of patients as they cause unwanted side effects, reduce the effectiveness and increase the toxicity of medicine and impair patient's cooperation with the treatment diet prescribed [6]. Drug interactions are estimated to be responsible for 20 to 30% of all unwanted medical reactions. These interactions require clinical action and consideration in 70% of the cases and may result in life-threatening incidents or death in 1 to 2% of the cases [7]. Although it is not possible to identify all drug interactions, awareness of therapeutic team of potential drug interactions, risk factors that enhance the possibility of these interactions and familiarity with mechanisms of drug interactions can help reduce real drug interactions [8].

As there is no detailed and exact information concerning the prevalence of such interactions in Iran, and no research has been conducted on drug interactions in recipes of private and public drug stores in any Iranian cities, the present research seeks to study the frequency and intensity of possible interactions in various age groups, different classes of medicines and their correlation with doctor's specialty, level of interactions and the correlation between the level of interactions with when the recipes were taken to these drug stores.

Material and Methods

This is observational, cross-sectional research conducted in spring and winter to study the prevalence of drug interactions in 2 private and 2 public drug stores. According to calculations, as many as 3000 recipes were found for each season. Then, the information associated with these private and public drug stores including the name and number of drugs prescribed, doctor's speciality, age and gender of patients, date of drug prescription and patient's insurance coverage was recorded. Drug interaction was studied based on the quick index of interventions (Table 1) using Up to Date software. As levels A and

B interventions are not clinically important; they are not reported here [9].

Table 1: Different types of interventions and their classification

Classification	Interaction	Definition
A	No intervention specified	The data indicate no pharmacodynamic or pharmacokinetic interactions between factors
B	No action needed	Data indicate drug interactions during simultaneous usage without any evidence indicating clinical concerns
C	Monitor Therapy	Data indicate drug interactions with clinical symptoms. The good points of simultaneous use of these drugs are more than their harms. Appropriate monitoring is required for the potential negative effects. It is probably necessary to adjust the dose of one or both drugs during treatment.
D	Consider Therapy Modification	The data show that drugs may have a clinical interaction with one another. It is necessary to exclusively examine each patient to see if the positive results outnumber the negative ones or not. It is also necessary to take the actions required to minimise the toxicity caused by simultaneous use. These actions may range from invasive monitoring, changing the empirical dose, and taking alternative measures
X	Preventing the interaction	Data indicate interactions with clinical side effects. The dangers usually outweigh the benefits. The

The data were analysed in terms of prevalence and type of medical interactions and possible correlation with other parameters. SPSS v.16 was used for statistical analysis.

Results

The patients and recipes studied in this research numbered 6000 with 3000 recipes for winter and a similar number for the spring of 2015. The average age of the patients was 42.07 ± 21.56 years old. The frequency of male patients was 2500 (41.7%) people. To study drug interaction, only those recipes with at least two drugs were included. The average number of drugs in each recipe, the number of interacting medicines and the number of interacting medicines in terms of their interaction is presented in Table 2.

Table 2: Frequency of variables

Variable	Average	SD	Minimum	Maximum
Number of drugs per recipe	4.820	1.91	2	16
Number of interactions per recipe	1.95	2.40	0	21
C interactions	1.60	2.05	0	20
D interactions	0.275	0.69	0	13
X interactions	0.072	0.31	0	5

As many as 4 drug stores were selected as targets. As the approximate number of monthly recipes within that period was 8000 in Isar drug store and 6000 in three drug stores in Karaj, Sharyar, and Taleghan, a 30% share was defined for Isar drugstore (900 for each season) and the share of each of the three remaining drugstores was 23.3% (700 for each season). The frequency of insurance coverage was also studied in the recipes of patients. For this purpose, the insurances were divided into 4 categories: Social Security, Medical Services, Armed Forces, and others. The frequencies of insurance among these patients were 76.8%, 15.5%, 6.9%, and

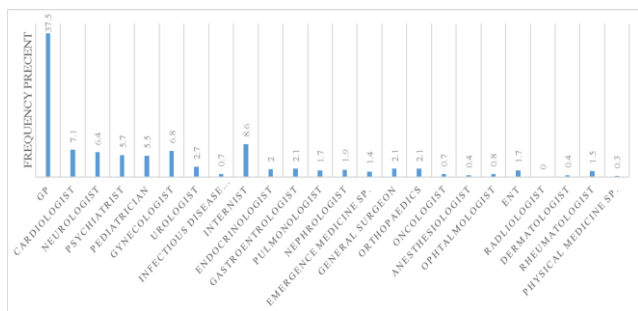0.7% respectively. The expertise of those doctors prescribing the medicines was also studied (Figure 1).

Figure 1: The frequency of doctors' shares in the number of recipes

The prevalence of drug interactions was studied based on different variables. The average number of interacting items with various levels of drug interactions was studied for each variable. The average number of interacting items in each interaction level is presented in Table 3. The result shows there is a significant relationship between all frequency of interaction and the average number of interacting items with various levels of interaction for each variable (p-value < 0.05), except the frequency of interaction between male and female and items C, X and total (p-value > 0.05).

Table 3: The frequency of interaction and the average number of interacting items with various levels of interaction for each variable

Variable		Frequency of interaction (%)	The average number of interacting items			
			Total	C	D	X
gender	Male	69.1	2.34 ± 1.937	2.00 ± 1.596	0.71 ± .0261	0.32 ± 0.079
	Female	68.9	2.44 ± 1.948	2.09 ± 1.596	0.68 ± 0.284	0.30 ± 0.068
P-value		*0.865	**0.785	**0.387	**0.021	**0.097
Age	< 18	59.4	1.74 ± 1.231	1.61 ± 1.125	0.31 ± 0.074	0.17 ± 0.029
	18-64	69.6	2.43 ± 1.994	2.05 ± 1.607	0.74 ± 0.308	0.32 ± 0.079
	≥ 64	74.6	2.61 ± 2.354	2.31 ± 1.962	0.70 ± 0.308	0.34 ± 0.083
P-value		***0.000	***0.000	***0.000	***0.000	***0.000
Season	Winter	6.71	2.25 ± 1.834	1.95 ± 1.517	0.69 ± 0.255	0.27 ± 0.060
	Spring	70.8	2.53 ± 2.053	2.14 ± 1.675	0.70 ± 0.294	0.34 ± 0.084
P-value		*0.003	**0.001	**0.005	**0.003	**0.007
Drug store	Isar	70.1	2.32 ± 1.891	1.20 ± 1.551	0.69 ± 0.278	0.27 ± 0.064
	Shahryar	71.5	2.76 ± 2.180	2.30 ± 1.801	0.73 ± 0.286	0.39 ± 0.90
	Taleghani	66.2	2.16 ± 1.776	1.90 ± 1.447	0.60 ± 0.263	0.26 ± 0.063
	Karaj	67.7	2.31 ± 1.941	1.99 ± 1.598	0.75 ± 0.270	0.29 ± 0.075
P-value		***0.011	****0.000	****0.000	****0.000	****0.000
Doctor	General	76.5	2.46 ± 2.235	2.11 ± 1.904	0.76 ± 0.255	0.38 ± 0.105
	Specialist	64.4	2.34 ± 1.768	1.99 ± 1.411	0.71 ± 0.304	0.25 ± 0.053
P-value		*0.000	**0.000	**0.000	**0.000	**0.000

* Fisher's Exact Test; ** Mann-Whitney U test; *** Pearson Chi-Square; **** Kruskal Wallis test.

The prevalence of drug interactions was also studied based on the speciality of the doctor. According to the results, the prevalence of drug interactions among patients undergoing treatment under doctors with different specialities is significantly different (Table 4).

Table 4: Prevalence of drug interactions in terms of the speciality of doctors

	Drug interaction				Total	
	No		Yes			
	Number	%	Number	%	Number	%
General	530	23.5	1722	76.5	2252	100
Cardiologist	98	22.9	330	77.1	428	100
Neurologists	60	15.7	321	84.3	381	100
Psychologists	32	9.4	307	90.6	339	100
Pediatrician	183	55.5	147	44.5	330	100
Gynecologist	241	59.5	164	40.5	405	100
Urinary tract	71	43.6	92	56.4	163	100
Infection	18	43.9	23	56.1	41	100
Internist	183	35.3	335	64.7	518	100
Glands	38	31.7	82	68.3	120	100
Digestion	69	55.6	55	44.4	124	100
Lungs	26	26.3	73	73.7	99	100
Nephrology	31	27.0	84	73.0	115	100
Emergency service	30	35.3	55	64.7	85	100
General surgery	63	50.0	63	50.0	126	100
Orthopedist	36	28.3	91	71.7	127	100
Cancer	22	53.7	19	46.3	41	100
Anesthesia	9	40.9	13	59.1	22	100
Eye	31	63.3	18	36.7	49	100
Ear, pharynx, nose	54	53.5	47	46.5	101	100
Radiology	1	50.0	1	50.0	2	100
Skin	16	64.0	9	36.0	25	100
Rheumatology	16	17.6	75	82.4	91	100
Physical medicine	5	31.3	4137	69.0	6000	100
Total	1863	31.1	4137	69.0	6000	100

The average number of interacting items in various levels of drug interventions was investigated about the type of doctors, including general practitioners and specialists, to determine the correlation between each class of interactions with doctor's speciality.

The average number of interacting items in each class of interaction can be observed in Figure 2. The difference across all variables was statistically significant (P-value = 0.000).
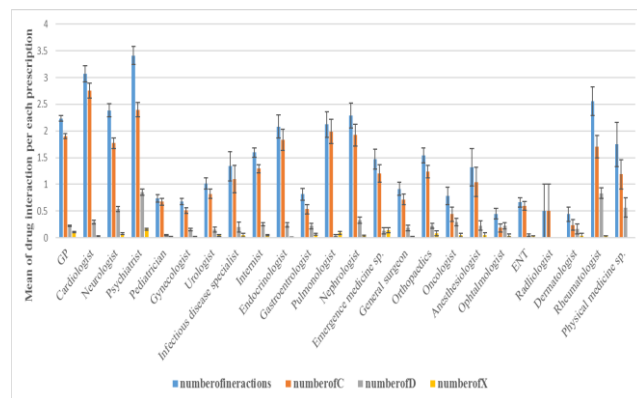

Figure 2: The average number of interacting items in terms of the level of interaction in the recipe of each doctor

The frequency of interaction was also calculated for various drug classes and reported in table 5. According to results, the drugs associated with the nervous system had a frequency of 38%.

The drugs prescribed for the musculoskeletal system, alimentary tract and metabolism, and cardiovascular system had frequency levels of 19%, 15% and 10%.

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Table 5: Frequency of interaction in various classes of drugs

Frequency (%)	Number of interactions	Drug category
38	1574	Nervous system
19	785	Musculoskeletal system
15	616	Alimentary tract and metabolism
10	399	Cardiovascular system
6	228	Blood and blood-forming organs
4	150	Antiinfectives for systemic use
3	140	Systemic hormonal preparations, excl. Sex hormones and insulins
3	108	Respiratory system
1	35	Genitourinary system and sex hormones
0.608569	25	Antiparasitic products, insecticides and repellents
0.608569	25	Sensory organs
0.438169	18	Antineoplastic and immunomodulating agents
0.121714	5	Dermatologicals

Discussion

Drug interaction is a general term used to talk about cases where the expected therapeutic effect of one medicine is modified by another. When two or more drugs are prescribed simultaneously, they may intervene with one another. As new drugs are introduced to the market every year, the importance of having medical information including awareness of contraindications, interventions and interactions of drugs with one another, the cautions and warnings associated with them, important side effects, etc. increases [3].

According to the results of this research, an average number of 4.82 ± 1.91 items were prescribed for each patient of whom 1.95 ± 2.40 had drug interaction in each recipe with levels C, D, and X interactions having a share of 1.60 ± 2.05, 0.275 ± 0.69, and 0.0 ± 072.31 respectively. No interactions were observed in 31.1% (1846 cases) of recipes.

Crucial-Souza and Jaos Carlos Thomson (2006) conducted research and studied the frequency of drug interaction in an educational hospital in Brazil [10]. In this research, 300 recipes belonging to those patients hospitalised in the hospital were studied. This group utilised DrugReax system to analyse drug interaction. According to their results, drug interactions were observed in 49.7% of all recipes, while 3.4% of the recipes exhibited acute interactions. Compared to the results achieved in this research, the total frequency of interaction and acute interaction in the population studied in Iran was much less. According to their results, digoxin-hydrochlorothiazide interaction was the most common one. These two drugs played a minor role in the recipes studied in this research, and it might be due to the greater generality of the population studied in this research. The frequency of interaction and the average number of interacting items with various levels of interaction for the age variable shows there is a significant relationship between them. Also, according to the results of this research, the frequency of interaction among females older than 55 years suffering from cardiovascular diseases was significantly higher than other patients. In line with the results of the research conducted in Brazil, older age can influence drug interaction.

Furthermore, gender has no significant influence on the occurrence of interactions except level D. As shown in Table 3; only level D has a significant difference in interaction. Although the frequency of intervention was so great among the recipes issued by cardiologists in our research, the greatest level of frequency was observed in the recipes issued by psychologists. This difference might be due to the large statistical population of our research.

In 2003, Sabin S. Egger et al., [11] researched to study the frequency of drug interaction in the recipes of those patients who were being discharged from hospitals. As many as 500 patients were studied in this research and 60% of the recipes reported at least one drug interaction. According to this group, the level of frequency of low, average, and high interactions was 17.9%, 69.9%, and 12.2% respectively. This frequency is different from what we found in our research, and this difference can be attributed to the difference in the size of the population.

Juan Merlo et al. (2001) published the results of the research they had conducted on all the recipes of January 1999 in Sweden [12]. As many as 962013 recipes with at least 2 items fetched from the database of Swedish Health Organization were studied. Data were stratified by age and sex, and odds ratios were calculated using multilevel logistic regression. According to the results of their research, 13.6% of all the recipes had at least one drug interaction. They claimed that factors such as older age and a higher number of drugs per recipe increase the possibility of a drug interaction. This fact is in line with the results of the current research. They also showed that level C drug interactions exhibited the greatest frequency in the Swedish population, and this result was also observed in the Iranian population, too. According to their research, level D drug interactions exhibited the second highest frequency in both the Iranian and Swedish population.

Rachel P. Riechelmann et al., (2007) [13] studied drug interaction in the recipes of those patients who have cancer. They utilised Drug Interaction Facts software version 4.0 for their research. As many as 405 patients were studied in this research. Considering the items prescribed in each recipe, as many as 276 potential cases of drug intervention were predicted, but only 109 patients experienced such interactions. Nine of these interactions were acute, and 77% were mild. As it turned out in this research, the highest level of frequency was observed in drugs not associated with cancer such as warfarin, antihypertensive, corticosteroids and anticonvulsants. The authors

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concluded that the prevalence of drug interaction in the population studied was influenced by the number of medical items in the recipe, the therapeutic method utilised and the tumour.

In 2011, Fariba Ahmadizar et al., [14] studied the frequency of drug interactions in the recipes of general and specialised practitioners in Iranian population. As many as 28956638 recipes in 2007 and 15510912 recipes in 2008 were collected from Iran Medical Sciences University and analysed using _Pardazesh Nosakh_, a prescription processing software program, provided by the National Committee of Rational Drug Use. This program was developed for the DOS operating system and Novell Network in 1998. Drug interactions were observed in the recipes issued by internists, cardiologists, neurologists, psychiatrists, neurosurgeons, general surgeons, infectious diseases specialists, urologists, dermatologists, ear, throat and nose specialists, optometrists, orthopedists, and paediatricians. According to the results, the highest degree of frequency was observed in the recipes issued by cardiologists, internists, urologists, and neurologists. Similar to the results achieved in our research, cardiologists and neurologists have the greatest share in drug interactions.

In conclusion, considering the results achieved in this research, a noticeable frequency was found for drug interaction in recipes. The highest frequency of drug interaction was observed in level C interactions. On the other hand, it has been proved that factors such as age increase the possibility of interactions, and as people grow older, the number of interacting items and level of interaction goes up. As some diseases are dependent upon season, the time and season when the drug is prescribed can also increase the possibility of drug interactions. Furthermore, gender has no significant influence on the occurrence of interactions except level D. As shown; only level D has a significant difference in interaction. Type of drug store and patients' insurance coverage were the other factors that had a noticeable influence on the occurrence of interactions. The frequency of these interactions in the class of the nervous system and the musculoskeletal system was so great. Doctor's speciality also plays a major role in the occurrence of interactions with greater degrees of frequency observed in the recipes of general practitioners. As of specialists, the highest rate of interaction was observed in the items issued by psychiatrists.

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