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Factors Associated with Potential Food-Drug Interaction in Hospitalized Patients: A Cross-Sectional Study in Northeast Iran

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Abstract

Background: The minimization of adverse food-drug interactions will improve patient care by optimizing the therapeutic effects and maintaining proper nutritional status.

Aim: The aim of the present study was to find the main factors that may place the hospitalized patients at risk of potential food-drug interactions.

Method: This cross-sectional, descriptive study was conducted on 400 inpatients admitted to the Department of Internal Medicine of a teaching hospital in Mashhad, Northeast Iran, within 20 March 2013 to 20 April 2013. The potential food-drug interactions were evaluated for 19 commonly prescribed medications. The main factors (e.g., age, gender, education level, number of medications, and duration of the disease) that may place the patients at risk of potential food-drug interactions were analyzed for each patient.

Results: Out of the 19 commonly prescribed medications, 17 drugs (89%) were not properly used with respect to meal. Furthermore, 14 commonly prescribed drugs were found to have a high frequency (≥50%) of potential food-drug interactions. Most of the patients (n=359, 89.8%) consumed their medicines at inappropriate time with respect to meals. The results of a multiple logistic regression after adjustment for confounders revealed that the age [β=0.005, CI: 0.0-0.01; P=033], number of medications [β=0.1, CI: 0.083-0.117; P<0.001], and duration of disease [β=-0.037, CI: -0.05 to -0.023; P<0.001] were significantly associated with higher risk for potential food-drug interactions.

Implications for Practice: As the findings of the present study indicated, the number of medications was associated with the higher risk of potential food-drug interactions. Regarding this, it seems necessary to decrease the number of the prescribed medicines to lower the frequency of potential interactions among the inpatients.

Keywords: Inpatients, Northeast Iran, Potential food-drug interactions, Prescriptions

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Introduction

The aim of pharmacotherapy is the achievement of definite therapeutic outcomes that recover the patient's quality of life while minimizing patient risk (1). Drugs show their efficacy only if administered in appropriate quantity with proper combination of drugs and foods and at suitable times (2). A drug interaction is a situation in which a substance affects the activity of a drug in a way that the effects are increased or decreased, or produces a new effect. When discussing drug interaction, what first occurs to mind is typically drug-drug interaction. However, interactions may also exist between drugs and foods, as well as between drugs and herbs/supplements (2).

Foods may alter the effects of drugs by interfering with pharmacodynamic mechanisms through exerting synergistic, additive, or antagonistic impacts or with pharmacokinetics process, such as absorption, metabolism, and excretion, resulting in decreased drug efficacy or increased drug toxicity (3). They may also produce a new effect that might not produce on its own (4). A medication can also change the body's ability to utilize particular foods or nutrients, which are important in supporting human health (2).

The interaction of food and drug is a common hidden problem encountered in clinical practice that can cause pharmacotherapeutic complications through prolonged hospitalization or readmission to hospital, prescription cascades, and deterioration of the patient's health condition (5). Therefore, the determination of the factors associated with the occurrence of food-drug interactions are important for both clinical and economic reasons. Although it is difficult to identify the pharmacotherapeutic complications caused by food-drug interactions (6), it is possible to determine the factors exposing the patients to such complications (5).

To the best of our knowledge, there is no study investigating this issue in Iran. Even though numerous food-drug interactions have been reported, the scale of this negative phenomenon has not been assessed in the population of patients in Iran. With this background in mind, this study aimed to investigate the main factors that can expose the patients to the risk of potential food-drug interactions among inpatients in Northeast Iran. This study was conducted in the Department of Internal Medicine of a teaching hospital in Mashhad, Iran, to determine the frequency and also the factors associated with the risk of food-drug interactions.

Methods

This cross-sectional, descriptive study was conducted on 400 patients admitted to the Department of Internal Medicine of a teaching hospital (a 1000-bed tertiary general grade A hospital), affiliated to the Mashhad University of Medical Sciences, Mashhad, Iran, from 20 March 2013 to 20 April 2013. This center is a medical education research unit and a training center for students at professional and super professional levels.

The study protocol was approved by the Institutional Review Board and the Local Ethics Committee (IR.MUMS.REC.1391.754). Informed consent was obtained from all patients prior to their inclusion. The investigator was trained to achieve adequate qualification prior to performing the study assessments. The patients who received at least one of the above mentioned drugs were screened for eligibility to enter the study. The subjects with more than 48 h hospital stay and those taking oral medication were included in the study. On the other hands, the patients who were not able to communicate verbally or those who could not take a drug orally were excluded from the study. Nutritional supplements and vitamins were not in the scope of this study.

To evaluate the potential food-drug interactions, 19 commonly prescribed medications with tough guidelines regarding the time of consumption in regard to meals were selected. The undesirable potential food-drug interactions (i.e., the improper use of drugs in relation to meals) for each drug were checked with the United States pharmacopeia dispensing information (also called drug information for the health care provider) or/and patient information leaflets and expressed in percentage as the ratio of the number of cases with potential interaction to all cases.

All demographic information (e.g., age, gender, education level) and other relevant data, including duration of disease, drug name/dosage form/dosage, and timing of the administration, were recorded for each patient. In addition, the presence of a companion during hospitalization, as well as the physician, nurse, and patient's knowledge for the proper use of drugs were considered. All the above required data were collected from the patients' medical records, treatment charts, and/or patient

interview by the investigator. The sample size was determined as 384 case rounded up to 400 patients with a margin of error of 5% and a confidence level of 95%.

A descriptive analysis was established for summarizing the study variables (i.e., potential food-drug interactions, gender, level of education, number of patients accompanied by someone, and number of patients educated to consume their medicines at an appropriate time with respect to meals). The non-normally distributed quantitative data were presented as median and interquartile range (IQR). Furthermore, the qualitative data were expressed in terms of frequency and percentage. There were no missing data.

Multiple logistic regression (forward selection) was used in order to identify the factors associated with food-drug interaction, including those factors previously defined as statistically significant according to the univariate regression analysis. Additionally, 95% confidence intervals were calculated for the most interesting variables (i.e., gender, age, duration of disease, number of medications, education level, companionship).

The Brier Score as the quadratic scoring rule was also determined calculating the mean squared differences between the predicted and actual outcomes. The Brier Score ranges from 0 for a perfect model to 0.25 for a model with 50% incidence of the outcome. The area under the receiver operating characteristic curve (AUC) is reported as a measure of accuracy (an area of 1 indicates an accurate model). All statistical analyses were performed using SPSS (version 16.0; SPSS Inc., Chicago, IL, USA). P-value equal to or less than 0.05 was considered statistically significant.

Results

Out of the 400 patients, 44.5% of them were male. The median age of the patients was 47 years (IQR=11). Most of the hospitalized patients were suffering from cardiovascular and gastrointestinal diseases. Furthermore, 89.8% of the patients (n=359) often consumed their medicines at an inappropriate time with respect to meals. The prevalence rates of potential food-drug interactions regarding the 19 investigated drugs in the study participants are briefly summarized in Table 1. According to the results, nitroglycerin (100%) and metronidazole (100%) had the highest potential interactions among the investigated drugs, followed by captopril (86.7%), and ferrous sulfate (83.8%). However, no potential interaction was detected for aspirin and magnesium hydroxide (Table 1).

Table 1. Potential interactions between foods/nutrients and drugs prescribed for inpatients

Drugs		Food/nutrients	Mechanism/effect	Recommendation	Number of cases with potential interaction/all cases (%)
1	Carvedilol	Foods in general	Administered with foods, decreases orthostatic hypertension	To be administered with foods	21/42 (50%)
2	Diclofenac	Foods in general	Decrease risk of lesion in the gastrointestinal tract	To be taken with foods to decrease the risk of gastric mucosa lesion	13/19 (68.4%)
3	Isosorbide dinitrate	Foods in general	Decrease absorption rate of drug	Better to be administered with empty stomach	125/178 (70.2%)
4	Magnesium Hydroxide	Protein	Decreases the neutralizing capacity of the antacid	To be avoided with foods rich in protein	0/298 (0%)
5	Spironolactone	Milk and meat (potassium)	Retains potassium (K)	To avoid administration with foods rich in K	35/56 (62.5%)

Continuous of Table 1.

6	Ranitidin	Milk and meat (vitamin B12)	Depletes the absorption of vitamin B12	Not to eat foods rich in vitamin B12 close to or during the administration of the drug	58/96 (60.4%)
7	Nitroglycerin	Foods in general	Decreases the absorption rate of drug	Better to be administered with empty stomach	77/77 (100%)
8	Triamterene-H	Cheese, fried egg, and meat	Increases the absorption of the drug and depletes sodium	To be administered with fatty foods To avoid administration with foods rich in Na	14/35 (40%)
9	Metronidazole	Foods in general	Administered with foods, it decreases stomach upset	To be taken with food	26/26 (100%)
10	Ferrous sulfate	Food in general Foods high in Vitamin C	Decrease absorption of the drug Increase absorption of the drug	To avoid administration with foods To administrate with Vitamin C-rich food	62/74 (83.8%)
11	Metoprolol	Food in general	Increase absorption of the drug	To administer with foods	140/196 (71.4%)
12	Co-trimoxazole	Food in general	Administered with foods, increases stomach upset	To avoid administration with foods	22/30 (72.3%)
13	Captopril	Foods in general	Decreases the absorption of the drug	To be consumed one hour before or two hours after meals	137/158 (86.7%)
14	Aspirin	Food/ beverage rich in vitamin C and vitamin K	Depletes the absorption of the vitamins	Not to eat foods rich in vitamins C and K, folic acid, thiamine, and amino acids, close to or during the administration of the medicines	0/298 (0%)
15	Omeprazole	Chicken and milk (vitamin B12)	Depletes the absorption of vitamin B12	No to eat foods rich in vitamin B12 close to or During the administration of the drug	34/122 (27.9%)
16	Amiodarone	Food in general Grapefruit juice (not available on hospital menu)	Increases the rate and extent of absorption Drinking grapefruit juice with this medication may increase the risk of dangerous side effects	To be administered in a consistent manner relative to food intake To avoid administration with grapefruit juice	14/21 (66.7%)

Continuous of Table 1.

17	Clidinium – c	Foods in general	Reduces digestive secretions	To be administered 30-60 min before food	33/76 (43.4%)
18	Lovastatin	Evening meal Grapefruit juice (not available on hospital menu)	Increases the efficacy of drug Drinking grapefruit juice with this medication may increase the risk of liver damage	To be administered with evening meals To avoid administration with grapefruit juice	49/63 (77.8%)
19	Propranolol	Milk (proteins)	Increases the bioavailability of the drug	To be administered with foods high in protein	28/42 (66.7%)

Table 2 presents the demographic variables and nature of potential food-drug interactions. The results revealed that the patients would be less exposed to potential food-drug interactions as their age increased (Table 2). As shown in Table 2, the food-drug interactions were more frequent among the women. In terms of the patient education level, 49.2% of the participants had less than high school educational level, and 21% of them were highly educated. The food-drug interactions were most commonly observed in the poorly educated patients (45.1%). As indicted in Table 2, 84 (21%) patients had a high education level, and food-drug interactions observed in all these patients.

Only 33.2% of the patients were educated (only by nurses) on how to use their medications with respect to meal. However, the patients educated by nurses were also at a high risk of food-drug interactions. Despite the recommendations, all these patients consumed their medications at the inappropriate time with respect to meal. Due to the lack of dispersion, patient education was excluded from the further analysis.

Table 2. Prevalence of food-drug interactions based on patients' characteristics

Patient factor	Frequency	At least one potential food-drug interactions (n=359)	No potential food-drug interactions (n=41)
Age*(year)	47 (11)	46 (10)	56 (6)
Duration of disease* (years)	2 (3)	1 (2)	5 (2)
Number of medications*	4 (2)	4 (3)	2 (3)
Gender†			
Male	178 (44.5%)	157 (43.7%)	21 (51.2%)
Female	222 (55.5%)	202 (56.3%)	20 (48.8%)
Patient education†			
− Below high school diploma	197 (49.2%)	162 (45.1%)	35 (85.3%)
− Above high school diploma	203 (50.8%)	197 (54.9%)	6 (14.6%)
Patients instruction †	133 (33.2%)	133 (37%)	0
Having a companion	181 (45.2%)	159 (44.3%)	22 (53.7%)

* Variables are described in median (interquartile range)

† Variables are described in number (%)

The median number of drugs given on a regular basis per patient was 4 cases (IQR=2) per day. The large number of the concurrently used drugs placed the patients at higher risk for food-drug interactions (Table 2). The majority of the patients (54.8%) had no companion. Out of the 359 patients who had at least one potential food-drug interaction, 159 accompanied patients (44.3%) took their medicine at inappropriate time with respect to meal.

As the findings indicated, longer duration of the disease resulted in higher possibility of food-drug interaction (Table 2). It was also revealed that the number of potential food-drug interactions increased in parallel with the number of drugs used by the patients (Table 2). The results of the univariate and multiple logistic regression analyses are tabulated in Table 3.

According to the univariate analysis, the patient's age, disease duration, number of medications, and education level were significantly associated with higher risk of food-drug interactions ($P<0.001$).

Table 3. Univariate and multivariate analysis of food-drug interaction in hospitalized patients admitted to the internal medicine ward (n=400)

Characteristic	Univariate analysis			Multiple logistic regression [c]	
	FDI	No-FDI	P value	β [95% CI]	P-value
Gender					
Male	157 (43.7%)	21 (51.2%)	0.536 [a]		
Female	202 (56.3%)	20 (48.8%)			
Age	47±6.4	56±2.7	<0.001 [b]	0.005 [0.0 to 0.01]	0.033
Duration of disease	2±1.8	4±0.7	<0.001 [b]	-0.037 [-0.05 to -0.023]	<0.001
Number of medications	4±1.6	0.1±0.3	<0.001 [b]	0.1 [0.083 to 0.117]	<0.001
Education level					
Below high school diploma	162 (45.1%)	35 (85.3%)	<0.001 [a]		
Above high school diploma	197 (54.9%)	6 (14.6%)			
Having a companion					
Yes	159 (44.3%)	22 (53.7%)	0.249 [a]		

[a] Analysis by Fisher's exact test.
[b] Analysis by independent-samples t-test.
[c] To adjust for multiple comparison, P<0.05 is considered as statistically significant. The R^2 for the final model is 0.68.

However, food-drug interaction showed no statistically significant association with gender (P=0.36) and having a companion (P=0.25). After adjustment for confounders, age [β=0.005, CI: 0.0 to 0.01, P=0.033, OR=0.88, (CI 0.78-0.99), P=0.048], number of medications [β=0.1, CI: 0.083 to 0.117, P<0.001, OR=1.52, (CI 1.19–1.93), P<0.001], and duration of disease [β=-0.037, CI: -0.05 to -0.023; P<0.001] remained statistically significant. The R^2 for the final model was 0.68, and the AUC revealed a good level of accuracy (AUC=0.83).

Discussion

According to the findings of the present study, the age, number of medications, and duration of disease were the most important factors significantly associated with higher risk for potential food-drug interactions in hospitalized patients admitted to the Department of Internal Medicine. In this regard, the older patients or those with longer duration of disease were at lower risk for exposure to potential food-drug interactions, and the patients were more likely to be exposed to potential food-drug interactions as the number of their medication increased.

The lower frequency of possible interactions in older individuals is inconsistent with the reports in the literature (7-9). This finding can be due to the fact that the older patients are more concerned about the control of their health; therefore, they often share their personal health information and decision-making with caregivers when needed. Moreover, they may be also more willing to ask questions about how and when to take their medications in relation to food and drugs. In addition, older patients with chronic health problems receive more attention from caregivers, especially nurses. Therefore, they were at lower risk of exposure to potential food-drug interactions.

In the present study, it was concluded that the patients with a long history of disease faced with lower possibility of food-drug interactions. Paying more attention to the details of pharmacotherapy over a long period of time may explain this. In the current study, it was observed that the frequency of potential food-drug interactions increased in parallel with the number of drugs used by the patients. This is in line with the findings obtained by Mayur et al. (10) and Rasheed et. al. (11) showing a significant relationship between the number of medications a patient consumed and the number of drug-nutrient interactions for which a patient was at risk.

In this respect, the easiest way to reduce the frequency of potential food-drug interactions is to decrease the number of medicines prescribed, which is not rational for patients with multiple chronic conditions; therefore, a careful selection of therapeutic alternatives is recommended (1, 12).

In this study, no association was obtained between lower knowledge about the proper use of medications with regard to meal and a higher possibility of food-drug interactions. Similar to a study conducted by Jarosz and Wolnicka (2, 5), in our study, the majority of the patients (66.8%) were not educated about the factors (like meals) that might affect the medicinal impact. The patients are needed to be aware of the protective measures to avoid potential food-drug interactions (3, 13).

Accordingly, in the previous studies, the implementation of educational programs in this regard was reported to decrease the rate of drug-food interactions in hospital (3, 4, 13, 14). Many of potential food-drug interactions can be avoided by advising the patient to take their medicines at the appropriate time with respect to meals. It is emphasized that the nurses as the final link in the treatment chain are able to play a key role in food-drug interaction education to patients (5, 6, 15, 16). Knowledge and assessment skills are required to improve the patient safety (2, 5, 7, 8, 17, 18). Moreover, the clinical pharmacists can play an important role in nurse training as an effective method to reduce food-drug interactions in hospitals (4, 14).

However, we found that the patients who were educated by the nurses were also at high risk of potential food-drug interactions. It means that sometimes the patients do not pay enough attention to nurses' recommendations. Nonetheless, they should be informed that communicating with caregivers (i.e., nurses, physicians, and pharmaceutical consultants) is an effective way to prevent food-drug interactions (18). Moreover, nurses need to have adequate knowledge of food-drug interactions to be able to educate the patients in this regard. Therefore, the health professionals and pharmacists are recommended to inform the nurses and patients for the signs and risk of possible side effects (12) .

One of the limitations of this study was the different social and psychological conditions of the patients, which might have affected the results. In addition, we did not evaluate the actual pharmacotherapeutic complications due to the potential food-drug interactions. This study was conducted in only one inpatient teaching hospital, and the results may differ from the results of the studies carried out in other centres. Furthermore, this study was conducted in the Internal Subdivision; as a result, the findings may not be much comparable with those of other divisions due to the use of different medications in different divisions (especially specialized departments and ICUs where patients receive more drugs).

Implications for Practice

As findings of the present study revealed, the number of medication was associated with higher risk of potential food-drug interactions. Therefore, to lower the frequency of potential interactions among the inpatients, it could be necessary to decrease the number of medicines prescribed or make a careful selection of therapeutic alternatives. It is also suggested to consider patient's knowledge of food-drug interaction to avoid impairment in the treatment process.

Future studies are warranted to further evaluate the real outcomes of food-drug interactions. Moreover, future research is recommended to determine the knowledge of physicians, pharmacists, nutritionists, and nurses about the food-drug interactions. The establishment of nurse-patient communication seems to be an effective way to prevent food-drug interactions. To improve the performance of medication administration, the pharmacists are suggested to implement training courses on food-drug interactions for the physicians, nutritionists, and nurses.

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Conflicts of Interest

The authors declare that they have no conflicts of interest.

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