

Relations Between Occurrence of the Risk of Food-Drug Interactions and Patients' Socio-Demographic Characteristics and Selected Nutrition Habits

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The objective of the study was to investigate the patients' exposure to food-drug interactions, and to analyse the main factors leading to a risk of interactions in the examined patients. A high (62.4%) risk of food-drug interactions incidence, which may cause various complications in therapy, was found in the study. The majority of patients (52.8%) were not aware that the timing of drug intake in relation to meals may affect treatment.

High exposure to food-drug interactions in patients results generally from their lack of awareness of such interactions and of their effects. The results of the study show that educating patients, physicians, dietitians and nurses on the impact of food on the effects of drugs is necessary to mitigate pharmacotherapy complications.

INTRODUCTION

In recent years, more attention has been paid to the importance of food and dietary habits for the pharmacotherapy process. The constituents of our diet (such as: proteins, fats, fiber, flavonoids, furanocoumarins, mineral salts, vitamins, caffeine and others) may modify the drug pharmacokinetic phases, *i.e.* its absorption, metabolism and excretion [Arayne *et al.*, 2005; Bailey *et al.*, 2000; Bressler, 2006; Dresser *et al.*, 2000; Fraga *et al.*, 1997; Ho *et al.*, 2001; Johnson *et al.*, 1987; Latinen *et al.*, 2000; Lilja *et al.*, 2004; Zhi, 1995; Jung, 1997]. The majority of currently known food-drug interactions are connected with drug absorption and with its biochemical metabolism in organism, mostly in the liver and the intestines, as well as with its excretion. Sometimes a synergy is observed between the effects of drug and food constituents, with a possible multifold increase in the effect of a drug. Some of such interactions pose a serious threat and may even lead to irregularity in heart rhythm, as well as to rapid growth of blood pressure or to orthostatic hypotonia. It was found that food-drugs interactions may significantly decrease the effectiveness of treatment and prolong hospitalization, thus increasing its costs [McCabe, 2004; Genser, 2008].

For the above-mentioned reasons, if the treatment is to be effective and safe, the physician and dietician should be aware of threats related to food-drug interactions. Possible impact of food constituents on the absorption of drugs or on their metabolism is often neglected when advising patients how to take

a given drug, usually due to the unawareness of the problem or to insufficient understanding of its scope. Knowledge about drug-nutrient interactions was examined in a national sample of 834 family medicine residents in the USA. Most of them reported they had little or no formal training in drug-nutrient interactions in medical school (83%) or residency (80%). Residents correctly answered only $61 \pm 19\%$ of fourteen drug-nutrient interaction knowledge items [Lasswel, 1995]. Healthcare practitioners ($n=160$) from 10 hospitals were surveyed using a questionnaire on the most common and/or important food interactions with warfarin, drug interactions with warfarin and general drug-nutrient interactions involving vitamin K. The mean scores on the overall test were 72.5 ± 9.0 for pharmacists, 62.5 ± 10.6 for physicians, 56.9 ± 8.8 for dietitians and 50.2 ± 9.3 for nurses, with 100 being a perfect score. Dietitians scored higher in the area of food interactions (73.0 ± 10.3) [Couris *et al.*, 2000]. Consequently, many patients taking drugs on chronic basis, as well as people taking various no-prescription drugs, know very little about interactions between food and drugs.

There is very little data in the world on the patients' exposure to food-drug interactions [Lewis *et al.*, 1995; Magnus, 1994]. Even though numerous food-drug interactions have been proved beyond any doubt, the scale of this negative phenomenon in the population of patients in Poland has not been assessed so far. While it is difficult, or sometimes even impossible, to prove pharmacotherapeutic complications related to food-drug interactions, it is possible to determine if such a risk exists for a given patient – through dietary recall and analysis of nutritional habits.

The objective of the study was to find the scale of the risk of food-drug interaction incidence, which in turn may re-

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sult in various clinical complications, as well as to analyse the main factors leading to the risk of food-drug interactions in the examined patients.

SUBJECTS AND METHODS

The study was based on a random sample (each 10th patient) of 481 patients at three levels of health care in Warsaw, and covered patients of the Family Physician Outpatient Clinic – 158 persons, Specialist Outpatient Clinics of the Bródnowski Hospital (outpatient clinics: Cardiologic – 56, Allergologic – 48, Neurologic – 48 and Endocrinologic – 48), and patients referred to hospital for treatment (Internal Medicine and Gastroenterological Department of the Bródnowski Hospital – 123).

A sociological data questionnaire as well as a questionnaire of data on the way of taking drugs by patients contained close-ended questions, with some questions allowing for a different answer (e.g. the kind of juice drunk most often to wash drugs down). The questionnaire of data on drug intake contained questions on the type of taken drugs, their dose, intake frequency, regularity, timing, drug intake with respect to meals, and the kind of beverage drunk most often with drugs. In the studies performed, 24-h dietary recalls preceding them, with some questions on the timing of drug intake, were used to evaluate the exposure to interactions between drugs taken at specific times of day and in different ways and the ingredients of individual meals of patients. Collected data on timing of drug intake with respect to meals, e.g. within 1.5 h before the meal or within 2 h after it, or during the meal, were compared with data from database as well as from literature concerning the proper intake of individual drugs and the possible food-drug interactions.

The database on proper timing of taking drugs with respect to meals and on food-drug interactions, which was used to evaluate the food-drug risk, was developed by the National Food and Nutrition Institute and it covered more than 2000 drugs. It was developed on the basis of data, literature, available monographs and compendia of drugs [Boullata & Armenti, 2004; Jarosz & Dzieniszewski, 2004; Podlewski & Chwalibogowska-Podlowska, 1999]. Statistical analysis of data was performed using the χ^2 test. This study was formally approved by the Bioethics Committee.

Characteristics of the studied population

The majority of patients covered by the study were between 41 and 65 years old (55.1%) and over 65 (33.7%). Women constituted 61.7% of the total studied population. Furthermore, 25.6% of research subjects completed elementary education, 44.9% – secondary education, 18.5% – vocational education, and 11% – higher education. The largest group consisted of the retired and pensioners (63.8%). In the studied population, 27% were economically active, and the retired with extra earnings constituted 2.3% of the group.

RESULTS

Occurrence of risk of food-drug interactions

An analysis of dietary recalls, accompanied by information on drugs taken by patients, proved that 62.4% of them took drugs improperly with respect to meals, which resulted in their expo-

sure to various food-drug interactions. The results of own studies, performed in a group of 481 patients, showed that 300 patients were exposed to food-drug interactions due to improper intake of at least one drug with respect to meals, including 164 persons exposed to one interaction, 85 – to two interactions, 37 – to three, 10 – to four, 3 – to five, and 1 – to six interactions. The risk of interaction was observed for 506 (23.4%) out of the total of 2163 drugs taken in the examined group of patients.

The risk most frequently observed in the examined group consisted in a decrease in the extent of the absorption of drugs, leading to a decrease in, or a lack of, drug effect. It was found that individual food constituents, such as fiber, calcium and tannins, as well as the presence of gastric contents, in 299 cases could have led to a decrease or delay in the absorption of drugs (among others, digitalis, tricyclic antidepressants, tetracyclines, fluoroquinolones and iron preparations). Taking certain drugs (among others theophylline preparations and tricyclic antidepressants) together with high-fat food might have exposed the patients to their increased absorption in 146 cases. The studies performed showed that a relatively large group of patients was exposed to drug metabolism disorders due to washing drugs down with grapefruit juice or multi-fruit juice containing grapefruit, or to grapefruit consumption. The flavonoids and furanocoumarins, contained in particular in grapefruits and in grapefruit juice, inhibit the activity of enzymatic system – P-450 cytochrome (CYP3A4), especially of the small intestine, which may cause a considerable increase (even by 300–900%) of drug concentration in blood of some patients. In 28 patients, washing down the following drugs – benzodiazepines, hipolipemic drugs – lovastatin and simvastatin, calcium channel blockers – with grapefruit juice or eating grapefruits within 4 h from drug intake exposed them to an increase in concentration of these drugs in serum. In 9 patients, the antagonistic action of vitamin K towards anticoagulants might have taken place in result of co-ingestion of vitamin K-rich products and such drugs. In addition, in 24 cases a risk of synergic drug-caffeine interaction was observed in the examined group of patients (Table 1).

TABLE 1. Diet factors impact on the risk of food-drug interactions in the examined patients.

Diet factors	Number of drugs prone to the risk of food-drug interaction N(%*)
Fiber	25(1.2)
Calcium	13(0.6)
Tannins	2(0.1)
Factors connected with consumed food such as: digestion time in stomach, pH of gastric content	259(12.0)
Fats	146(6.7)
Flavonoids and furanocoumarins of grapefruit juice	28(1.3)
Vitamin K	9(0.4)
Caffeine	24(1.1)
Total	506(23.4%)

*in proportion to all (2163) taken drugs

TABLE 2. The number of taken drugs and the risk of interactions depending on sex and age of the examined patients.

	≤3	4–6	7–9	≥10	p-value
	N(%)	N(%)	N(%)	N(%)	
Total	203(42.2)	165(34.3)	89(18.5)	24(5)	
Sex					p= .4
Women	117(39.4)	104(35)	60(20.2)	16(5.4)	
Men	86(46.7)	61(33.1)	29(15.7)	8(4.3)	
Age (years)					p< .001
18–40	46(85.2)	7(13.0)	0(0)	1(1.9)	
41–65	120(45.3)	93(35.1)	44(16.6)	8(3.0)	
>65	37(22.8)	65(40.1)	45(27.8)	15(9.3)	
Risk of interactions					p< .001
Yes	84(28.0)	117(39)	75(25)	24(8)	
No	119(65.7)	48(26.5)	14(7.7)	0(0)	

Data on the number of drugs taken by the examined patients

Polypragmasy was observed in some of the patients participating in the study. The number of drugs taken by one person in the group of patients over 65 was between 4 and 6 (40.1% of patients), 27.8% of patients took between 7 and 9 drugs, whereas 9.3% took more than 10 drugs. Older people were the largest group of patients taking more than 10 drugs. The statistical significance of differences between the oldest group and the remaining ones was p<.001, which meant that this group was most exposed to various pharmacotherapeutic complications. However, it would be worth noting that in the group of patients between 41 and 65 years old 51.7% of patients were taking 4–9 drugs in this age group. This group is also exposed to undesirable pharmacotherapeutic complications. No difference was observed in the number of drugs taken by men and women.

In the group of 481 examined patients it was observed that the risk of food-drug interactions increased with the number of drugs taken (Table 2).

The manner of washing drugs down in the examined group of patients

The patients taking drugs were asked what beverages they usually take to wash drugs down. The patients most frequently mentioned 1 or 2 beverages. Only 29.5% of patients declared washing drugs down exclusively with water, without mentioning any other beverages. Most often the respondents washed drugs down with tea. A large group of patients declared that they washed drugs down also with water (65.9%). Different kinds of juice were co-ingested with drugs by 22.4% of patients, and milk beverages – by 14.6%. Patients also mentioned coffee, carbonated beverages, herbal brews and compotes (Figure 1).

A data analysis was performed to check if drugs were taken with water, as they ought to be, or with some other beverages. No statistical differences were observed between the age of examined patients and the manner of washing drugs down. Women washed drugs down only with water (properly) more

TABLE 3. The manner of washing drugs down by the examined patients depending on selected factors.

	Patients washing drugs down		p-value
	only with water N(%)	with other beverages N(%)	
Total	142(29.5)	339(70.5)	
Sex			p= .02
Women	99(69.7)	198(58.4)	
Men	43(30.3)	141(41.6)	
Age (years)			p= .8
18–40	17(12)	37(10.9)	
41–65	75(52.8)	190(56)	
>65	50(35.2)	112(33)	
Education			p= .04
Elementary	26(18.3)	97(28.6)	
Vocational	18.3(24)	65(19.2)	
Secondary	71(50)	145(42.8)	
Higher	21(14.8)	32(9.4)	

often than men. It was found that the higher education level of the examined patients, the more often they washed drugs down only with water (Table 3). Persons aware that the timing of taking drugs with respect to meals (before, after or during a meal) has a important impact on effectiveness of drug activity most frequently exhibited a tendency to take drugs only with water (the proper method) but only at a level of p=0.1 (Table 4).

Opinions expressed by the examined patients on the importance of proper timing of taking drugs with respect to meals and of following the appropriate recommendations

The issue of interactions between food constituents and drugs is underestimated both, by physicians and patients, which results from the latter having little knowledge on the subject. Among the 481 examined patients – 31% believed that the timing of taking drugs with respect to meals was definitely important for their treatment while 16.2% thought that it might sometimes be important. However, almost a half of the respondents (47.6%) stated that they had no opinion on the issue. Patients with higher education were definitely more aware of the issue (Table 4). The older persons were more like-

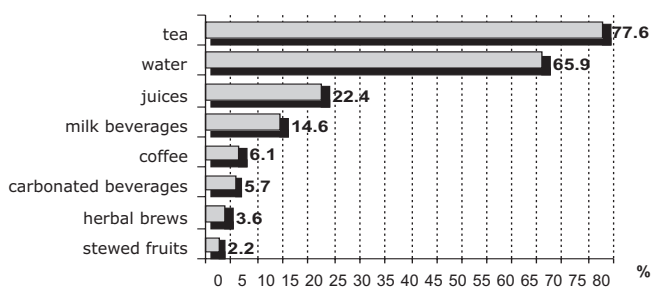


FIGURE. 1. Beverages with which the examined patients usually wash drugs down.

ly to be ignorant of possible interactions resulting from a bad timing of taking drugs with respect to meals – a total of 71% answered ‘I do not know’ and ‘not important’, compared to 35.2% in the youngest age group. Women more frequently than men declared that the timing of taking drugs with respect to meals was ‘important’ or ‘sometimes important’ for treatment. No significant impact was observed of the answers to the question whether the timing of taking drugs with respect to meals was important for treatment on the occurrence of food-drug interactions risk.

The patients were asked if they followed the recommendations for the timing of taking drugs with respect to meals (on empty stomach, during the meal, *etc.*), given by the physician or in a leaflet. In response 31% patients answered that they never, rarely or only sometimes followed such recommendations. Patients with lower education level were less likely to follow recommendations on the manner of taking drugs (Table 5). The patients over 65 answered more often, as compared to those in 18–40 and 41–65 age groups, that they did not follow the recommendations, did it rarely or from time to time. Women declared more frequently than men that they adhered to recommendations on how to take drugs always or very often.

The risk of interactions between food and drugs was observed less frequently but only at the statistical trend level

TABLE 4. Patients’ opinion on the importance of proper timing of taking drugs with respect to meals and risk of food-drug interactions depending on selected factors.

	Do you think that the timing of taking drugs with respect to meals may be important for the treatment?		p-value
	It is definitely important, it may be sometimes important N(%)	It is rarely important, it is not important, I do not know N(%)	
Total	227(47.2)	254(52.8)	
Sex			p= .016
Women	153(51.5)	144(48.5)	
Men	74(40.2)	110(59.8)	
Age (years)			p< .001
18–40	35(64.8)	19(35.2)	
41–65	145(54.7)	120(45.3)	
>65	47(29.0)	115(71.0)	
Education			p< .001
Elementary	33(26.8)	90(73.2)	
Vocational	41(46.1)	48(53.8)	
Secondary	116(53.7)	100(46.3)	
Higher	37(69.8)	16(30.2)	
Risk of interactions			p= .7
Yes	140(46.7)	160(53.3)	
No	87(48.1)	94(51.9)	
Washing drugs down			p= .1
Only with water	75(52.8)	67(47.2)	
With other beverages	152(44.8)	187(55.2)	

in patients following the recommendations on how to take drugs, as in those who did not.

Sources of information on proper timing of taking drugs with respect to meals

The examined patients were asked if their physician informed them how to take drugs with respect to meals. 20.8% answered that they did not receive such information, whereas 7.1% did not remember whether they received information on how they should take drugs in respect to meals (Table 6).

This question was analysed in terms of age groups, education level and sex of the subjects. Neither the age nor the level of education had a significant impact on the answer to the question if the physician informed a given patient how drugs should be taken. Men, however, more often than women failed to remember whether their physician gave them such information. No statistically significant differences were found between the answers to this question and washing drugs down with water (proper manner), and the occurrence of the risk of interactions. These results proved that the information, even if it was given by the physician, was not sufficient to affect the respondents’ attitudes.

Furthermore, 74% of the total number of respondents answered always or very often to the question ‘Do you read leaflets accompanying drugs?’ (Table 7). Women read such leaflets more often than men. Age had an impact on answers to this question. Leaflets accompanying drugs were read more often by patients in the 41–65 age group than by those in the group of over 65 .

TABLE 5. Following the recommendations on the timing of taking drugs with respect to meals and risk of food-drug interactions depending on selected factors.

	Do you follow the recommendations on the timing of taking drugs with respect to meals?		p-value
	Yes – always, very often N(%)	Never, rarely, sometimes N(%)	
Total	332(69)	149(31)	
Sex			p= .008
Women	218(73.4)	79(26.6)	
Men	114(62.0)	70(38)	
Age (years)			p= .07
18–40	42(77.8)	12(22.2)	
41–65	188(70.9)	77(29.1)	
>65	102(63.0)	60(37.0)	
Education			p= .001
Elementary	69(56.1)	54(43.9)	
Vocational	59(66.3)	30(33.7)	
Secondary	161(74.5)	55(25.5)	
Higher	43(81.1)	10(18.9)	
Risk of interactions			p= .1
Yes	199(66.3)	101(33.7)	
No	133(73.5)	48(26.5)	

TABLE 6. Information given by the physician on the manner of taking drugs and risk of food-drug interactions depending on selected factors.

	Did your physician advised you how the drug should be taken?			p-value
	Yes N(%)	No N(%)	I don't remember N(%)	
Total	347(72.1)	100(20.8)	34(7.1)	
Sex				p= .02
Women	216(72.7)	67(22.6)	14(4.7)	
Men	131(71.2)	33(17.9)	20(10.9)	
Age (years)				p= .3
18-40	38(70.4)	9(16.7)	7(13.0)	
41-65	193(72.8)	58(21.9)	14(5.3)	
>65	116(71.6)	33(20.4)	13(8.0)	
Education				p= .7
Elementary	82(66.7)	29(23.6)	12(9.8)	
Vocational	66(74.2)	17(19.1)	6(6.7)	
Secondary	159(73.6)	45(20.8)	9(17)	
Higher	40(75.5)	9(17)	4(7.5)	
Risk of interactions				p= .6
Yes	216(72.0)	65(21.7)	19(6.3)	
No	131(72.4)	35(19.3)	15(8.3)	
Washing drugs down				p= .8
Only with water	102(71.8)	31(21.8)	9(6.3)	
With other beverages	245(72.3)	69(20.4)	25(7.4)	

The higher educational level of patients, the more frequently the leaflets were read (Table 7). The educational level influenced the answer at a statistically significance level. No statistical differences, on the other hand, were observed between the answer to this question and washing drugs down with water or other beverages, and the occurrence of interactions risk in the examined patients.

DISCUSSION

In recent years, greater focus has been placed on the possibility of occurrence of food-drug interactions. Such interactions are probably a large part of all pharmacotherapeutic complications suffered by patients. However, the resulting clinical complications are often difficult to prove. Nevertheless, several thousand of cases of such complications in humans have been well documented. Also several experimental tests on animals have been carried out, proving the effect of numerous food constituents on the absorption and metabolism of several drugs [Boullata & Armenti, 2004; Conner, 2005; Jarosz & Dzieniszewski, 2004; Schmidt & Dalhoff, 2002].

This study attempted to address the question of what is the risk of interactions between the constituents of food and drugs, and to which related clinical complications might the examined patients be exposed. Identification of these clinical complications would be very difficult, because all patients were taking several drugs for various diseases of respiratory,

TABLE 7. Reading the leaflets accompanying drugs depending on selected factors.

	Do you read leaflets accompanying drugs?		p-value
	Yes – always, very often N(%)	Never, rarely, sometimes N(%)	
Total	358(74.4)	123(25.6)	
Sex			p= .001
Women	237(79.8)	60(20.2)	
Men	121(65.8)	63(34.2)	
Age (years)			p= .02
18-40	39(72.2)	15(27.8)	
41-65	210(79.2)	55(20.8)	
>65	109(67.3)	53(32.7)	
Education			p= .001
Elementary	72(58.5)	51(41.5)	
Vocational	65(73)	24(27)	
Secondary	171(79.2)	45(20.8)	
Higher	50(79.2)	3(20.8)	
Risk of interactions			p= .9
Yes	224(74.7)	76(25.3)	
No	134(74)	47(26.0)	
Washing drugs down			p= .5
Only with water	109(76.8)	33(23.2)	
With other beverages	249(73.5)	90(26.5)	

circulatory and alimentary systems. It would be impossible to determine whether a given symptom, *e.g.* increase or decrease of blood pressure, was related to an exacerbation of disease, an interaction between drugs, or an adverse drug effect caused by food-drug interactions. However, on the basis of a detailed medical history, an interview with the patient on the amount and types of taken drugs, and a dietary recall, it was possible to determine with high probability a potential risk of food-drug interactions in each patient.

It was found that in the case of 300 patients (62.4%) the type of drugs, the manner of taking them and the timing of their intake in respect to meals, as well as dietary habits and the type of beverages used to wash drugs down, exposed the patients to various pharmacotherapeutic complications, resulting from a possible impact of food constituents on different phases of pharmacokinetics of taken drugs. It should be emphasized that not every interaction causes significant clinical results. However, even if only a half of them results in a lack of drug activity or leads to some undesirable effects requiring treatment or hospitalization, we may state that this phenomenon is a significant issue of concern for public health, in particular in the view of growing sale of drugs in Poland and globally.

A study, covering 158 patients from three long-term health care facilities in the USA, used the data collected from medical documentation and concerning all the drugs and dietary supplements administered, their doses and timing of their administration, as well as the timing of meals and snacks,

and the dietary recommendations given. Patients consumed a mean of 4.86, 4.04, and 5.27 drugs. A risk of food-drug interactions was observed in, respectively, 22.1%, 55.6% and 36.5% of patients of the health care facilities under examination in relation to drugs which were to be administered on empty stomach, some time before or after meals, because food had an impact on their bioavailability, but were taken during the meal or directly after it. The most commonly observed interactions were gastrointestinal interactions affecting drug bioavailability [Lewis *et al.*, 1995].

Other work assessed the interactions between hypotensive drugs and dietary constituents and supplements in hypertensive patients in Poland. It has been found that the risk of interactions between food constituents, dietary supplements and hypotensive drugs in hypertensive patients is high [Suliburska, 2010].

The study also revealed a worrying phenomenon of polypragmasy in most of the examined patients, *i.e.* 57.8% of them took more than 4 drugs a day, and 5% took more than 10. Polypragmasy is one of the reasons behind pharmacotherapeutic complications; it is an adverse phenomenon, important for the entire treatment process, since patients taking several drugs at the same time are exposed to various pharmacotherapeutic complications related to undesirable effects of drugs, as well as to various food-drug interactions [Rajska-Neumann & Wieczorowska-Tobis, 2006].

It is assumed from the research undertaken globally that the biggest consumers of drugs are the elderly – they use more than 50% of all the sold drugs [Magnus, 1994; McCabe, 2004]. The analysed and discussed study revealed that in the group of patients over 66, usually 4–6 drugs were taken (40.1%) at the same time. The elderly were also the largest group among patients taking more than 10 drugs, so this group was most exposed to various pharmacotherapeutic complications. The studies among inhabitants of Poznań show that more than a half of respondents over 65 years old used 4–6 different medicines, and 7.5% of the whole group were treated with 10 and more [Rajska-Neumann & Wieczorowska-Tobis, 2004].

It was observed in the examined group of 481 patients that the risk of food-drug interactions incidence increased with the number of drugs taken. In the study performed in the USA with 290 patients, the risk of food-drug interaction was significantly higher for older patients, women, and – likewise in study discussed – for persons who were taking a greater number of drugs [Magnus, 1994].

Authors of study covering 158 patients from three long-term health care facilities in the USA also concluded that patients, who are primarily elderly and chronically ill and who consume multiple medications, are at a notable risk for certain food-drug interactions [Lewis *et al.*, 1995].

The issue of food-drug interaction is underestimated by physicians and by patients alike, which results from the latter having little knowledge on the subject [Couris *et al.*, 2000]. An analysis of results of own studies revealed that patients had highly insufficient knowledge on interactions between food constituents and drugs. Over a half of patients were not aware that the timing of taking drugs with respect to meals may influence their treatment. Persons with a lower educational level and the elderly showed lesser awareness of this dependency.

Women more often than men declared that the timing of taking drugs with respect to meal was ‘important’ or ‘sometimes important’ in their treatment. Answers to the question whether the timing of taking drugs with respect to meals is important in the treatment process appeared to have no influence on the risk of food-drug interactions. In theory, the awareness that proper timing of taking drugs with respect to meals is important for treatment, should influence the number of interactions. The results obtained showed that the information given on the subject – both by the physician and in leaflets accompanying drugs – must have been insufficient. Patients, despite being aware of the impact that meals have on taken drugs, either did not adhere to those recommendations, or lacked precise recommendations when to take drugs with respect to meals, or misinterpreted such recommendations.

In work assessing the interactions between hypotensive drugs and dietary constituents and supplements in hypertensive patients in Poland it was found that only 39% of the patients were aware that the timing of taking drugs with respect to meals may influence their treatment. It was also observed that subjects awareness of drug-food interactions depended on their educational status [Suliburska, 2010].

Beverages used to wash drugs down are also an important factor in food-drug interactions. To prevent disturbance of therapeutic process by an undesirable interaction, drugs should be taken only with water, unless the physician recommends otherwise.

Only 29.5% of patients declared washing drugs down only with water, without mentioning of any other beverages. However, it was found that persons who responded that the timing of taking drugs with respect to meals (before, after or during a meal) had an important impact on the effects of drugs were more likely to take drugs only with water (the proper manner) but the results were not significant.

The collected data showed that not more than 69% of the respondents always or often followed the recommendations on how to take drugs, *i.e.* read the leaflet accompanying the drugs or the relevant recommendations of the physician, *etc.* The lower education level of the patients, the less frequent they followed the recommendations how to take drugs. Women and persons in the younger age groups more often than men and people over 65 declared that they always or often followed the recommendations how to take drugs.

According to Kardas & Ratajczyk-Pakalska [2000], there are several consequences of not adhering to the medical recommendations in relation to pharmacotherapy, and the occurrence of that fact is quite common. In a specified research, the medical recommendations were not followed by 30–40% of older patients using digoxin. As the authors continue, older people with hypertension during 365-day observation period used medicines in the right way only for 179 days, *i.e.* less than half a year. Further interesting data is given by Kosińska [2004] who claims that as much as 60% of patients over 75 years take medicines in non-compliance with doctor's prescription. It is believed – the author writes – that only 1/3 of elderly patients take medicines in the right way [Kardas & Ratajczyk-Pakalska, 2000; Kosińska, 2004].

Patients who follow the recommendations concerning drug intake were less exposed to the risk of food-drug interac-

tions, as compared to those who failed to follow such recommendations. This proves that a potential risk of interactions is lower in patients paying attention to the proper timing of taking drugs with respect to meals and follow physician's recommendations.

No statistical difference was found between the answer given to the question, whether the physician informed a patient how to take drugs and washing drugs down with water (proper manner), and the risk of interactions. The findings proved that the information given by the physician was insufficient to influence the respondents' attitudes, the patients did not understand or did not follow those recommendations.

Results show that 74% of the total number of the respondents answered 'always' or 'often' to the question if they read leaflets accompanying the drugs; women and persons with higher education read such leaflets more often than men and people whose level of education was lower. No statistical differences were found in the examined patients in terms of answers to this question and taking drugs with water or other beverages, and the risk of interactions. These results also indicated that the leaflets accompanying drugs were usually not a source of information for the patient how to take drugs with respect to meals or what to drink with them, or that such leaflets did not contain information on food-drug interactions, or were misinterpreted by patients.

A growing phenomenon of polypragmasy and pharmacotherapeutic complications, as well as a rapidly growing consumption of drugs, force all the medical staff preparing and distributing drugs as well as dieticians and persons taking drugs on their own to pay attention to food-drug interactions [Rajska-Neuman & Wieczorowska-Tobis, 2004, 2006; Fulton & Allen, 2005].

The importance of the issue of food-drug interactions has been demonstrated by the attempts made in some countries to develop internal hospital methods and procedures with the aim to lower the frequency of pharmacotherapeutic complications related to the unfavourable effect of food on drugs absorption, metabolism and excretion [Gauthier *et al.*, 1997; Lewis *et al.*, 1995; McCabe, 2004; Yonkowski *et al.*, 1996].

CONCLUSIONS

The research carried out showed that the risk of food-drug interactions incidence was high in patients treated in primary health care, and thus probably negatively affected the treatment by making it, or the hospitalization period, longer, and increasing the costs of pharmacotherapy in case of many patients.

Patients, who are primarily elderly and who consume multiple medications, are at a notable risk for certain food-drug interactions.

It was found that awareness of patients of the importance of this issue for the effectiveness of treatment was low and depended on their education and age.

Therefore, it would be important to disseminate the knowledge, to both physicians and patients, on possible food-drug interactions. Educating physicians, nurses, dieticians and patients may lower the risk of pharmacotherapeutic complications.

REFERENCES

1. Arayne M.S., Sultana N., Bibi Z., Grapefruit juice-drug interactions. *Pak. J. Pharm. Sci.*, 2005, 18, 4, 45–57.
2. Bailey D.G., Dresser G.K., Grapefruit juice-lovastatin interaction. *Clin. Pharmacol. Ther.*, 2000, 67, 690.
3. Boullata J.I., Armenti V.T. eds. *Handbook of Drug-Nutrient Interactions*. 2004, Humana Press, New Jersey, pp. 3–515.
4. Bressler R., Grapefruit juice and prescription drug interactions. Exploring mechanisms of this interaction and potential toxicity for certain drugs. *Geriatrics*, 2006, 61, 12–18.
5. Conner K.G., Drug-nutrient interactions. 2005, *in: Encyclopedia of Human Nutrition*. vol 2. (eds. B. Coballero, L. Allen, A. Prentice). Elsevier Press, Oxford, pp. 1904–1912.
6. Couris R.R., Tataronis G.R., Dallal G.E., Blumberg J.B., Dwyer J.T., Assessment of healthcare professionals' knowledge about warfarin-vitamin K drug-nutrient interactions. *J. Am. Coll. Nutr.*, 2000, 19, 439–445.
7. Dresser G.K., Spence J.D., Bailey D.G., Pharmacokinetic-pharmacodynamic consequences and clinical relevance of cytochrome P450 3A4 inhibition. *Clin. Pharmacokinet.*, 2000, 38, 41–57.
8. Fraga Fuentes M.D., Garcia Diaz B., de Juana Velasco P., Bermejo Vicedo M.T., Influence of foods on the absorption of antimicrobial agents. *Nutr. Hosp.* 1997, 12, 277–288 (in Spanish; English abstract).
9. Fulton M.M., Allen E.R., Polypharmacy in the elderly: a literature review. *J. Am. Acad. Nurse Pract.*, 2005, 17, 123–132.
10. Gauthier I., Malone M., Lesar T.S., Aronovitch S., Comparison of programs for preventing drug-nutrient interactions in hospitalized patients. *Am. J. Health. Syst. Pharm.*, 1997, 54, 405–411.
11. Genser D., Food and drug interaction: consequences for the nutrition/health status. *Ann. Nutr. Metab.*, 2008, 52, Suppl. 1, 29–32.
12. Ho P.C., Saville D.J., Wanwimolruk S., Inhibition of human CYP3A4 activity by grapefruit flavonoids, furanocoumarins and related compounds. *J. Pharm. Pharmaceut. Sci.*, 2001, 4, 217–227.
13. Jarosz M., Dzieniszewski J. eds., *Interakcje leków z żywnością i alkoholem*. 2004, Borgis, Warsaw, pp. 3–215 (in Polish).
14. Johnson B.F., Rodin S.M., Hoch K., Shekar V., The effect of dietary fiber on the bioavailability of digoxin in capsules. *J. Clin. Pharmacol.*, 1987, 27, 487–490.
15. Jung H., Peregrina A.A., Rodriguez J.M., Moreno-Esparza R., The influence of coffee with milk and tea with milk on the bioavailability of tetracycline. *Biopharm. Drug Dispos.*, 1997, 18, 459–463.
16. Kardas P., Ratajczyk-Pakalska E., Not adhering to the medical recommendations – medical and social problem. *Gerontologia Polska*, 2000, 8, 11–17 (in Polish; English abstract).
17. Kosińska K., Drug problems in the elderly. *Gerontologia Polska*, 2004, 12, 155–159 (in Polish; English abstract).
18. Laitinen K., Patronen A., Harju P., Löytyniemi E., Pylkkänen L., Kleimola T., Perttunen K., Timing and food intake has a marked effect on the bioavailability of clodronate. *Bone*, 2000, 27, 293–296.
19. Lasswell A.B., DeForge B.R., Sobal J., Muncie Jr H.L., Michocki R., Family medicine residents' knowledge and attitudes about drug-nutrient interactions. *J. Am. Coll. Nutr.*, 1995, 14, 137–143.
20. Lewis C.W., Frongillo E.A., Roe D.A., Drug-nutrient interactions in three long-term care facilities. *J Am Diet Assoc.*, 1995, 95, 309–315.

21. Lilja J.J., Neuvonen M., Neuvonen P.J., Effects of regular consumption of grapefruit juice on the pharmacokinetics of simvastatin. *Br. J. Clin. Pharmacol.*, 2004, 58, 56–60.
 22. Magnus M.H., Difficulties in assessing drug/food interactions from chart audit in an elderly Barbadian sample group. *J. Nutr. Elder.*, 1994, 14, 33–43.
 23. McCabe B.J., Prevention of food-drug interactions with special emphasis on older adults. *Curr. Opin. Clin. Nutr. Metab. Care*, 2004, 7, 21–26.
 24. Podlewski J.K., Chwalibogowska-Podlowska A. eds., *Leki współczesnej terapii*. 1999, Split Trading, Warsaw, pp. 3–776 (in Polish).
 25. Rajska-Neumann A., Wieczorowska-Tobis K., Polypragmasy in the group of elderly in Poznań. *Gerontologia Polska*, 2004, 12, 201–204 (in Polish; English abstract).
 26. Rajska-Neumann A., Wieczorowska-Tobis K., Polypragmasy in the elder patient as a potential risk of drugs interactions-case study. *Geriatrics Polska*, 2006, 2, 80–82 (in Polish; English abstract).
 27. Schmidt L.E., Dalhoff K., Food – drug interactions. *Drugs*, 2002, 62, 1481–1502.
 28. Suliburska J., The assessment of the interaction between hypertension drugs and nutritional constituents and supplements in hypertension patients. *Bromat. Chem. Toksykol.*, 2010, 1, 35–40 (in Polish; English abstract).
 29. Yonkowski D., Flanders J., Kerestes-Smith J., Ginsberg S., Meeting Joint Commission Standards for Drug/Food Interactions Utilizing Computers and Existing Personnel. *J. Am. Diet. Assoc.*, 1996, 96, 9, Suppl. A81.
 30. Zhi J., Rakhit A., Patel I.H., Effects of dietary fats on drug absorption. *Clin. Pharmacol. Ther.*, 1995, 58, 487–491.
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