

ESTIMATION OF DIETARY SUPPLEMENTS INTAKE IN A SELECTED GROUP OF WOMEN OVER 50 AND THE RISK ASSESSMENT OF INTERACTIONS BETWEEN THE INGREDIENTS OF DIETARY SUPPLEMENTS AND DRUGS

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ABSTRACT

Background. Concurrent use of dietary supplements and drugs may result in complications of pharmacotherapy due to possible interactions between their ingredients.

Objectives. The aim of the survey was to estimate the intake of dietary supplements in a group of women over 50 and to analyse the risk of interactions between the ingredients of dietary supplements and drugs taken by the women.

Material and Methods. The study was carried out among 146 women over 50 years of age. Questionnaire included detailed questions on the type of prescription drugs, OTC (over-the-counter) drugs, and dietary supplements taken. The risk of interactions was determined on the basis of chemical composition of the drugs and supplements specified by the manufacturer, by comparing the obtained data with literature reports on known interactions.

Results. The analysis has shown that 88.4% of respondents constantly took prescription drugs, 44.5% of them took OTC drugs, and 66.4% of respondents took dietary supplements throughout the survey period. It has been found that 71.3% of surveyed women taking prescription drugs, took dietary supplements as well. Among women taking supplements and drugs, 36.9% of respondents were taking them concurrently, 60.9% kept such an interval, but only 21.8% of them waited for at least two hours. It has been found that the drug-supplement interactions might occur in 35.8% women under the survey.

Conclusions. The analysis of the obtained results has revealed that taking dietary supplements by the group under survey was frequent, and the risk of interactions between dietary supplements and drugs was significant. It is recommended that doctors ask their patients about taken supplements during regular check-ups, and inform them about possible interactions between dietary supplements and drugs. Moreover, appropriate would be to change the labelling of dietary supplements, so that the packaging provides information on possible interactions between their ingredients and drugs.

Key words: *dietary supplements, drugs, interaction, women over 50*

STRESZCZENIE

Wprowadzenie. Jednoczesne spożywanie suplementów diety i leków może być przyczyną powikłań farmakoterapii, ze względu na możliwość wystąpienia interakcji pomiędzy ich składnikami.

Cel. Celem przeprowadzonych badań była ocena spożycia suplementów diety w wybranej grupie kobiet po 50 roku życia oraz analiza ryzyka wystąpienia interakcji pomiędzy składnikami suplementów diety a przyjmowanymi przez te kobiety lekami.

Material i metody. Badania przeprowadzono wśród 146 kobiet po 50 roku życia. W ankietach zawarto szczegółowe pytania dotyczące rodzaju zażywanych leków przepisanych przez lekarza, przyjmowanych leków bez recepty oraz spożywanych suplementów diety. Ryzyko wystąpienia interakcji określono na podstawie składu stosowanych przez badane leków oraz suplementów, odnosząc uzyskane dane do informacji o interakcjach podanych w literaturze.

Wyniki. Analizując uzyskane wyniki stwierdzono, że 88,4% badanych przyjmowało na stałe leki przepisane przez lekarza 44,5% stosowało leki bez recepty, a 66,4% badanych w okresie badania zażywało suplementy diety. Stwierdzono, że 71,3% badanych kobiet, przyjmujących leki przepisane przez lekarza, stosowało także suplementy diety. Spośród kobiet stosujących suplementy i leki 36,9% przyjmowało je w jednym czasie, przerwę stosowało 60,9% badanych, jednak tylko u 21,8% badanych była ona co najmniej 2 godzinna. Stwierdzono, że interakcja lek - suplement mogła zachodzić u 35,8% badanych kobiet.

Wnioski. Analizując uzyskane wyniki stwierdzono, że przyjmowanie suplementów diety w badanej grupie osób było częste, a ryzyko wystąpienia interakcji pomiędzy przyjmowanymi suplementami diety a lekami było znaczne. Wskazane byłoby wprowadzenie rutynowych pytań podczas wizyty lekarskiej o stosowaniu suplementacji i informowanie pacjenta

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o możliwości interakcji pomiędzy składnikami suplementów diety a lekami. Celowa wydaje się także zmiana oznakowania na opakowaniach suplementów diety, uwzględniająca informacje o możliwości zajścia interakcji pomiędzy składnikami suplementów i przyjmowanymi lekami.

Słowa kluczowe: *suplementy diety, leki, interakcja, kobiety powyżej 50 roku życia*

INTRODUCTION

Reduced level of sex hormones observed in women undergoing menopause results in deteriorated physiological functions in a number of internal organs, and leads to unfavourable changes in skin appearance [22]. This is often followed by mood deterioration, and contributes to the search for ways of effective health maintaining. One of commonly observed behaviours is taking dietary supplements [11], particularly in older age groups [16].

Menopause and géripause are the time when many factors accumulate that increase the risk of disease. This risk is still enhanced by the modern lifestyle change connected with inadequate nutrition and the lack of physical activity, which leads to more frequent and earlier onset of chronic diseases, previously typical to older age. Therefore, the age of chronic sufferers is decreasing, while increasing is the number of people taking drugs for chronic diseases, such as arterial hypertension or type 2 diabetes [27].

Concurrent use of dietary supplements and drugs may result in complications of pharmacotherapy due to possible interactions between their ingredients. It has been proved that many ingredients of dietary supplements may alter various stages of drug pharmacokinetics and hamper the healing process, as well as cause adverse effects leading to serious complications [1]. Despite this knowledge, both doctors and patients do not pay attention to the necessity of the time interval between taking drugs and dietary supplements. The available literature lacks detailed test results regarding the behavior of the related in a group of elderly people who often use pharmacotherapy.

The aim of the survey was to estimate the intake of dietary supplements in a group of women over 50 and to analyse the risk of interactions between the ingredients of dietary supplements and drugs taken by the women.

MATERIAL AND METHODS

The study was carried out in spring 2015, as a survey among 146 women over 50 years of age, attending the University of the Third Age in a city with over a hundred thousand inhabitants. Some 250 questionnaires were handed out, that included detailed questions on the type of prescription drugs, OTC

(over-the-counter) drugs, and dietary supplements taken. The women were asked about taking dietary supplements in the past 6 months, and currently (in the term of interview). They were also asked to write down the names of all taking dietary supplements. The questions also concerned the reasons for taking dietary supplements, and expected results. Some 152 questionnaires were returned, 146 of which were filled in correctly and completely. 96% of respondents lived in the city (above 100 thousand inhabitants), in which the survey was carried out, 4% of respondents commute from nearby towns. In the self-assessment 76% of respondents identified their health as good (but describing it also as “typical for the age”), the other person declared a general malaise. The occurrence of chronic diseases was declared by 86% of respondents.

The risk of interactions was determined on the basis of chemical composition of the drugs and supplements specified by the manufacturer, by comparing the obtained data with literature reports on known interactions [9, 24, 25].

RESULTS

The analysis has shown that 88.4% of respondents constantly took prescription drugs (mainly those for arterial hypertension and hypothyreosis), 44.5% of them took OTC drugs (mainly painkillers and cardiovascular drugs), and 66.4% of respondents took dietary supplements throughout the survey period (while 11.6% of them were not aware of the fact because they classified supplements as OTC drugs in the questionnaire) – Table 1.

Table 1. The percentage of women using prescription drugs, non-prescription drugs and dietary supplements in the term of interview, n=146

Type of preparation	Women	
	n	%
Prescription drug	129	88.4
Non-prescription drug	65	44.5
Dietary supplement	97	66.4
Dietary supplements and drugs (together)	97	66.4

It has been found that 71.3% of surveyed women taking prescription drugs, took dietary supplements as well, while 94.8% of woman taking supplements took prescribed drugs as well. The respondents were taking one to fifteen drugs a day (most frequently 1-2), one to

five OTC drugs (most frequently 1) and one to seven dietary supplements (most frequently 2-3 different supplements a day).

The administered supplements mainly included essential fatty acids, lutein, and/or vitamins and minerals (Table 2).

Table 2. Composition of dietary supplements used by surveyed women, n=97^{1,2}

Component	Women	
	n	%
One vitamin	21	21.6
Several vitamins	30	30.9
One mineral	23	23.7
Several minerals	10	10.3
Vitamin and mineral formula	19	19.6
Fatty acids of n-3	45	46.4
Lutein	25	25.8
Herbal extracts (e.g. ginseng, ginkgo, echinacea)	10	10.3
Vitamin + Mineral formula + Herbal extracts	15	15.4
Glucosamine, chondroitin	11	11.3
Phytoestrogens	1	1.0
Other	13	13.4

¹ - as 100% accept women using supplements

² - the respondents could select more than one answer

The main reasons for taking supplements were: to boost immunity (40.2% of respondents), to support the cardiovascular system (28.9% of respondents), and to improve general health (26.8% of respondents) –Table 3.

Table 3. The expectations of surveyed women to supplements, n=97^{1,2}

Designed	Women	
	n	%
Boost of immunity	39	40.2
General health improvement	26	26.8
Support cardiovascular systems	28	28.9
The enhancement of memory and concentration	25	25.8
Vision improved	25	25.8
Improve the condition of the hair, skin, nails	25	25.8
Improving the joints	23	23.7
Improving digestive processes, liver function	20	20.6
Enhancing sleep, mood, anti-stress	20	20.6
Slim products	8	8.2
For diabetics	5	5.1
Other	7	7.2

¹ - as 100% accept women using supplements

² - the respondents could select more than one answer

The decision on taking supplements was made mainly due to the belief that supplements are required to stay healthy (37.1% of respondents), every fourth respondent claimed to feel better as a result of taking supplements, but 21.6% of them decided to use supplements because it was fashionable and advertised (responses: “they are recommended”, “all people take them”, “I was encouraged by advertisement”) – Table 4.

Table 4. The reason for applying dietary supplements given for surveyed women, n=97^{1,2}

Reason	Women	
	n	%
To stay healthy	36	37.1
I feel much better after use them	24	24.7
My diet is poor	20	20.6
They are recommended to people of my age	10	10.3
All people use supplements	5	5.1
Encouraged by advertising	6	6.2
Other	12	12.4

¹ - as 100% accept women using supplements

² - the respondents could select up to 3 answers

66% of respondents declared they had discussed taking dietary supplements with their physician (Figure 1).

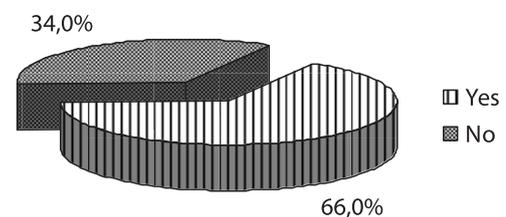


Figure 1. Percentage of respondents which consults intake of dietary supplements with physician, n=97¹

¹ - as 100% accept women using supplements

Among 92 people taking supplements and drugs, 36.9% of respondents were taking them concurrently. As to the time interval between taking dietary supplements and drugs, 60.9% kept such an interval, but only 21.8% of them waited for at least two hours (Table 5).

Table 5. The use of the time interval between these medicines and dietary supplements, n=92¹

Break	Women	
	n	%
No	34	36.9
Yes	56	60.9
<2 h	36	39.1
≥2 h	20	21.8
Non-response	2	2.2

¹ - as 100% accept women using supplements and drugs who replied about the time when they taking drugs and supplements

Less than half of respondents were aware of the fact that supplement ingredients may alter the effects of drugs, one third of respondents were convinced such an alteration is not possible, and every fifth respondent answered “do not know” (Figure 2).

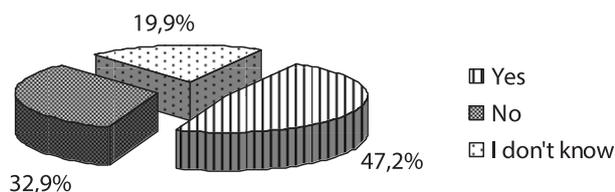


Figure 2. Distribution of answers to the question whether dietary components can alter the effect of drugs, n=146

Taking into consideration the chemical composition of the administered drugs and supplements, irrelevant time intervals between taking them, and not consulting the supplementation with a general practitioner, it has been found that the drug-supplement interactions might occur in 33 women (35.8%) under the survey (Table 6).

Table 6. The risk assessment of interactions between supplements and medicines, n=92¹

Behaviour	Women	
	n	%
Taking in the same time drugs and, dietary supplement including drugs + supplement containing ingredients with a proven track interaction	34	36.9
	22	23.9
Taking drug and supplements in an interval of <2 h including drugs + supplement containing ingredients with a proven track interaction	36	39.1
	11	11.9
In total, women exposed to interactions dietary supplements - drugs	33	35.8

¹- as 100% accept women using supplements and drugs

The most frequently taken combinations were: calcium/iron supplements along with β -blockers and levothyroxine, vitamin C with acetylsalicylic acid, ginseng extract with metformin/amlodipine, and magnesium/iron supplements with captopril (Table 7).

Table 7. The most common combined intake of medicines and supplements with the risk of interactions used without consulting a doctor by the test group of women, n=33¹

Component	Women	
	n	%
Calcium / iron + levothyroxine	13	45.5
Calcium + β - blockers	5	15.1
Calcium / iron + bisphosphonates	2	6.1
Magnesium / iron + captopril	3	9.1
Vitamin C+ acetylsalicylic acid	4	12.1
Niacin + lovastatin	2	6.1
Ginseng + metformin / amlodipine	4	12.1
Ginkgo biloba + acetylsalicylic acid	2	6.1

¹- as 100% accept women using in the same time supplements and drugs containing ingredients with a proven track interaction

DISCUSSION

There are reports available that the prevalence of dietary supplementation varies depending on the region, age of respondents, and the method of collecting data, nevertheless it concerns a significant percentage of respondents [11, 16]. In this survey, 66% percent of women were taking supplements throughout the survey period. Similar results were reported by *Kaluža et al.* [10], as well as *Saran and Duda* [17]. Dietary supplementation concerns ca. 30% of general population, however, it has been shown it is more often applied by older people, better educated individuals, and those living in big cities [15, 16].

Analysis of reasons for taking supplements has revealed that the main reason for supplementation was to boost immunity and improve health. Similar reasoning was confirmed by surveys carried out in Poland by *Pietruszka et al.* [14] and by *Sebastian et al.* [19], in the USA.

The taken supplements mainly included vitamins and minerals. Regarding the age of the surveyed women, it is surprising that only one of them was taking phytoestrogen supplements which, due to their ability to activate oestrogen receptors, may be used to prevent menopause symptoms such as bone mass decrease and hot flushes. In case of some women, they seem to be a safe alternative to the hormone substitutive therapy [2].

It has been found, based on the obtained data, that almost all the respondents who took dietary supplements, took also prescription drugs. The fact that chronically ill people often take dietary supplements and drugs at the same time has been confirmed by literature reports [10].

The study confirmed that some surveyed women were taking a number of various drugs and supplements every day (5.5% of respondents were taking ≥ 10 pills a day, most frequently 2-3 prescription drugs, 2-3 OTC drugs, and 3-4 dietary supplements), and remembered should be that except for active ingredients the drugs also include binding, glazing, dyes, and anti-oxidant agents such as: cellulose, lactose, starch, talc, silicon dioxide, polyvinylpyrrolidone, polyethylene glycol, hydroxypropyl cellulose, magnesium stearate, beeswax, Carnuba wax, titanium dioxide, red iron oxide, indigo carmine, and butylhydroxytoluene. Some of them are xenobiotics, and their detoxification burdens the liver metabolism [7].

The survey has revealed that 66% of respondents declared they had consulted taking dietary supplements with their general practitioners, however, only less than half of them were aware that supplement ingredients may interact with drugs, one third of respondents were convinced such an interaction is not possible, and one fifth answered "do not know". The problem may be in the labelling of dietary supplements - although

they look like drugs, they are just foodstuffs and their packages lack any information on undesirable effects, contraindications, or interactions that may occur when taking a given supplement along with drugs. In many cases, patients do not inform their doctors about taking dietary supplements as they believe such information is irrelevant. Information about supplement – drug interaction should be included in drug leaflets, but it seems that they were not carefully analyzed, or were incomprehensible and too vague.

Clinical observations indicate that undesirable effects and a number of complications in pharmacotherapy occur in ca. 20-50% of patients, in 5% of patients the complications are so life-threatening that they require hospitalisation [9]. One of the reasons for complications may be combining drugs with certain foods and/or dietary supplements.

The survey has shown that 76% of respondents were taking drugs with supplements at a time interval shorter than 2 hours. Taking into consideration the chemical composition of drugs and supplements, combined with irrelevant time interval between taking supplements and drugs, and the lack of any consultation about dietary supplementation with a general practitioner, it has been found that the drug-supplement interaction might occur in 1/3 of respondents. The most frequently taken combinations were calcium/iron supplements taken together with β -blockers or levothyroxine, and magnesium/iron supplements taken with captopril.

There are reports available that calcium carbonate reduces absorption of atenolol (beta-adrenergic blocker), and magnesium hampers captopril assimilation [13].

The reference data confirm frequent combination of levothyroxine and calcium supplements. It mostly concerns women after menopause [12], and may cause decreased efficiency of hypothyroidism treatment. Singh et al. [20], found that in patients taking levothyroxine along with calcium carbonate, the concentration of free and bound thyroxine significantly decreases. In vitro tests have shown that in the acidic environment levothyroxine binds calcium carbonate which may limit its bioavailability. Calcium supplements and levothyroxine should be taken separately at intervals of at least 4 hours [21]. Campbell et al. [3], revealed that also taking iron supplements and levothyroxine at the same time leads to an interaction as ferric sulphate and thyroxine form insoluble complexes.

Also the interaction between vitamin C and acetylsalicylic acid is vital. It may seem that the effect of such an interaction, namely increased excretion of vitamin C in urine, does not pose any danger to health, however, it increases the risk of renal calculi. Vitamin C is metabolised to oxalates and may increase their excretion in urine [5]. Excessive excretion of oxalate

is observed at high doses of vitamin C, i.a. delivered from dietary supplements, which contains up to 1000 mg of vitamin C per tablet, which is half the dose of Upper Level. Moreover, excess of vitamin C acidifies urine, which results in intensified crystallization of urates and cysteine salts.

An interaction also occurs between active compounds of ginseng (*Panax ginseng*) and metformin/amlodipine. The ginseng root is one of the most common plant ingredients in dietary supplements [18]. A potential danger of taking it along with drugs is caused by the biological impact of its active compounds on the activity of the CYP3A4 isoenzyme in the cytochrome P450 system which is responsible for drug metabolism [26]. As to anti-diabetic drugs, their effect may be enhanced by the hypoglycaemic impact of ginseng. While in the presence of anticoagulants, ginseng acts as an antagonist, namely it reduces blood concentration of these agents [8].

Moreover, interactions were found from taking ginkgo (*Ginkgo biloba*) supplements with tranquilizing drugs (diazepam). Active compounds of ginkgo and diazepam are both the substrates for the cytochrome P450 isoenzyme CYP3A4. Moreover, it is suggested that *G. biloba* extract may interact with benzodiazepines as a result of an antagonistic effect on GABA-A receptors. Ginkgo biloba supplements may increase the plasma concentration of nifedipine as well. Yoshioka et al. [23], reported that the peak plasma concentrations of the drug in tested volunteers increased from 30 to 60% after administering *G. biloba* extract. Moreover, more frequent headaches, dizziness, hot flushes and palpitation were observed in patients taking ginkgo extract along with drugs. Moreover, long-time taking of ginkgo supplements and acetylsalicylic acid exerts an adverse effect as they irritate the stomach mucosa and may cause gastrointestinal bleeding [6].

Interactions between drugs and dietary supplements are indeed a problem as they hamper the pharmacotherapy of many diseases. The effects of such interactions, which are so difficult to foresee, pose a real risk to health, and in some cases are even life-threatening. Therefore, it is of vital importance that, on one hand, general practitioners know about supplements taken by their patients, and on the other hand, that the patients know about possible interactions, particularly due to the increasing number of new supplements of diverse chemical composition.

CONCLUSION

The analysis of the obtained results has revealed that taking dietary supplements by the group under survey was frequent, and the risk of interactions between dietary supplements and drugs was significant.

It is recommended that doctors ask their patients about taken supplements during regular check-ups, and inform them about possible interactions between dietary supplements and drugs. Moreover, appropriate would be to change the labelling of dietary supplements, so that the packaging provides information on possible interactions between their ingredients and drugs.

Conflict of interest

The authors declare no conflict of interest.

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Received: 17.04.2016

Accepted: 27.09.2016