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Associations of polyphenols intake and the risk of dyslipidemia in the Siberian urban population

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Aim. To identify associations of polyphenols' (PP) consumption in general, as well as their classes with the risk of dyslipidemia in the Novosibirsk population aged 45-69 years.

Material and methods. In 2003-2005, as a part of the international project HAPIEE "Determinants of cardiovascular diseases in Eastern Europe: a multicenter cohort study", a population sample (n=9360) aged 45-69 years (mean age — 57,6 years) was examined in Novosibirsk. There were 4266 men and 5094 women. For the analysis of nutrition, a Food Frequency Questionnaire (FFQ) was used (141 product names). The content of PP and their classes was evaluated using the European database Phenol-Explorer 3.6. The food habits of the population were taken into account. The determination of total (TC) and high-density lipoprotein cholesterol (HDL-C) levels were carried out by enzymatic method. Hypercholesterolemia was established at TC >5,0 mmol/L (190 mg/dL). HDL-C <1,0 mmol/L in men and <1,2 mmol/L in women were considered as HDL-hypocholesterolemia. The concentration of low-density lipoprotein cholesterol (LDL-C) was calculated with the Friedewald formula (1972): TC-HDLC-TG/5. LDL-hypercholesterolemia was established at LDL-C <3,0 mmol/L.

Results. In comparison with the low PP consumption quartile, the odds for hypercholesterolemia in the highest consumption quartile for Other PP was 20% lower (OR 1,2, confidence interval (CI 1,01-0,14), p=0,033), for phenolic acids — 20% lower (OR 1,2 (CI 1,01-1,42), p=0,04) and for stilbenes — 37% lower (OR 1,37 (CI 1,15-1,64), p=0,001). The risk of HDL-hypocholesterolemia was lower in the quartile of high general PP consumption by 18% (OR 1,18 (CI 1,002-1,4), p=0,051), of phenolic acids by 32% (OR 1,32 (CI 1,11-1,57), p=0,001) and of other PP by 20% (OR 1,2 (CI 1,01-1,41), p=0,04). In comparison with the low PP consumption quartile, the odds for LDL-hypercholesterolemia in the high consumption quartile for Other PP decreased by 16% (OR 1,16 (CI 1,002-1,355), p=0,049), for lignans — by 33% (OR 1,33 (CI 1,14-1,56), p<0,001).

Conclusion. General intake of PP and their particular classes (phenolic acids, stilbenes, and Other PP) reduces the dyslipidemia risk in Siberian population.

Key words: polyphenols, blood lipids, population, dyslipidemia.

Relationships and Activities: the study was carried out as part of State Assignment № AAAA-A17-117112850280-2 and was supported by RF President grant for leading scientific schools (№ NS-2595.2020.7).

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Cardiovascular diseases keep the lead in the global mortality patterns [1]. The main causes of cardiovascular diseases (CVD) are non-modifiable (age, sex, family history) and modifiable (smoking, sedentary lifestyle, alcohol abuse, inappropriate diet) risk factors. The results of various multicenter studies show a high prevalence of CVD and their risk factors [2, 3]. For example, the observational study ESSE-RF revealed a high prevalence of hypercholesterolemia (HCE) in Russia — 57,6% (age group 25-64 years), with an increase to 74,5% in the age group 55-64 years [4].

Researchers from different countries pay great attention to studying the effect of diet on various cardiovascular risk factors, including changes in blood lipid levels. In recent years, interest has increased in assessing the impact of polyphenols' (PP) consumption on risk factors. Large population studies demonstrated that a high content of PP in the diet reduces blood lipids (NHANES, HAPIEE, Moli-sani, PREDIMED) [5-8]. Also, a PP rich diet influenced the lipid profile. For example, consumption of cocoa and cocoa-containing products (chocolate), olives and olive oil increases high-density lipoprotein cholesterol (HDL-C), while green tea lowers total cholesterol (TC) and low-density lipoprotein cholesterol (LDL-C) [9-11].

Thus, most studies demonstrate a positive effect of PP consumption on blood lipids. The contribution of PP certain classes in the regions vary, depending on the geography and eating habits of the population, which also needs to be taken into account. However, there are still no large studies on the consumption of PP in Russia.

The aim of the study was to identify associations of polyphenols' (PP) consumption in general, as well as their classes with the risk of dyslipidemia in the Novosibirsk population aged 45-69 years.

Material and methods

As a part of the international project HAPIEE "Determinants of cardiovascular diseases in Eastern Europe: a multicenter cohort study", a population sample (n=9360) aged 45-69 years (mean age — 57,6 years) was examined in Novosibirsk. There were 4266 men and 5094 women. All participants signed informed consent. Local ethics committee approved this study. The levels of TC and HDL-C was determined by the enzymatic method using standard Biocon (Germany) kits using a biochemical analyzer Labsystem (Finland). HCE was established at TC >5,0 mmol/L (190 mg/dL). HDL-C <1,0 mmol/L in men and <1,2 mmol/L in women were considered as HDL-hypocholesterolemia. The concentration of LDL-C was calculated with the Friedewald formula (1972): TC-HDLC-TG/5. LDL-HCE was established at LDL-C <3,0 mmol/L.

Table 1

Consumption of various PP classes in groups with and without HCE

	Men				P (1-2)	Women				P (3-4)	P (1-3)	P (2-4)
	HCE- (1)		HCE+ (2)			HCE- (3)		HCE+ (4)				
	M (95% CI)*	Me (25%, 75%)	M (95% CI)*	Me (25%, 75%)		M (95% CI)*	Me (25%, 75%)	M (95% CI)*	Me (25%, 75%)			
Number of patients, n	722		3518			427		4623				
Total of polyphenols, mg	1283,4 (1236,1-1330,6)	1134 (869,2-1528)	1270,8 (1249,4-1292,1)	1118,8 (842,2-1537)		1196,7 (1137,9-1255,5)	1127 (799-1529,8)	1201,3 (1183,6-1219,1)	1064,9 (797,7-1441,5)			<0,001
Flavonoids, mg	865,5 (825-906,1)	716,3 (498,5-1108,5)	858,6 (840,2-876,9)	703,4 (494,4-1085,9)		843,8 (793,9-893,7)	748,1 (508,8-1099,6)	842,9 (827,8-857,9)	707,7 (494,7-1054,7)			
Phenolic acids, mg	277,4 (265,7-289,1)	267,4 (194,7-322,9)	272,6 (267,3-277,9)	254 (190,3-316,6)	0,045	231,8 (217-246,7)	215,7 (154,6-284,6)	235 (230,5-239,5)	203,9 (150-275,7)		<0,001	<0,001
Other polyphenols, mg	89,5 (87,2-91,8)	91,2 (72,3-109,2)	87,2 (86,2-88,3)	86,7 (66,1-107,1)	0,01	66,2 (63,3-69,1)	65,2 (43,2-86,9)	66 (65,1-66,9)	60,5 (44,6-84,2)		<0,001	<0,001
Lignans mg	43,1 (41,1-45,1)	39 (28,4-53,7)	45 (44,1-45,9)	39,5 (27,2-55,8)		47,7 (44,9-50,6)	43,5 (29,8-61,4)	50,4 (49,6-51,3)	44,5 (31-61,6)		0,003	<0,001
Stilbene mg	7,7 (7,4-8,0)	6,8 (6,7-12,1)	7,2 (7-7,3)	6,8 (6,7-7,1)	0,002	6,9 (6,6-7,2)	6,8 (6,7-7,1)	6,8 (6,7-6,9)	6,7 (6,8-7)			0,031

Note: p — Mann-Whitney U-test, * — data are standardized by age.

For the analysis of nutrition, a Food Frequency Questionnaire (FFQ) was used (141 product names). The content of PP and their classes was evaluated using the European database Phenol-Explorer 3.6. [13]. The eating habits of the population were taken into account. Dietary survey was not performed for 70 people due to technical reasons.

Statistical analysis was performed using the software package SPSS (v. 17). Normality of distribution was analyzed. We calculated age-standardized arithmetic mean value (M) and 95% confidence interval (CI). The data in the tables and text are presented as M (95% CI). Since the distribution of variables was non-normal, the medians (Me) and the interquartile range (25%, 75%) were calculated. Mann-Whitney U-test was used for the comparison of variation series of two independent groups. Risk was assessed by calculating OR (95% CI). Differences were considered significant at p<0,05.

Results

We divided all participants on the following groups: with HCE (HCE+) and without HCE (HCE-); HDL-hypocholesterolemia+ and HDL-hypocholesterolemia; LDL-HCE+ and LDL-HCE-.

We revealed that men without HCE had a higher content of phenolic acids, stilbenes and Other PPin the diet. The content of PP classes in diets of women with/without HCE was the same (Table 1). Sex differences were observed in the consumption of phenolic acids, Other PP, and lignans both in groups with and without HCE. The total amount of PP consumed was greater in men with HCE than in women.

The consumption of PP rich products characteristic of the Siberian population (cereals, pulses, white/brown bread, vegetables, potatoes, fresh fruits and berries, dried fruits, sweets (not including sugar), tea, coffee, alcohol, vegetable oil) was assessed. Men and women had different eating habits, which leads to differences in the consumption of most foods. It is worth noting that in men, the consumption of potatoes, white bread, brown bread, tea, as well as alcohol was significantly higher than in women, regardless of HCE. Women were more likely to eat fruits and berries were in all studied groups, in contrast to men (p<0,001). Alcohol consumption in HCE- men was 12,3 (10,9-13,7) ml/day, in HCE+ men — 12,8 (12,2-13,5) ml/day. In women, this parameter amounted to 2,3 (1,9-2,7) ml/day and 1,9 (1,8-2) ml/day, respectively (p<0,001).

To assess the HCE risk in relation to the consumption of PP and their certain classes, an odds ratio was calculated. We revealed that for the entire population, the odds of developing HCE in the high consumption quartile of other PP was 20% less than in the low consumption quartile: OR 1,2 (CI 1,01-

Table 2

Consumption of various PP classes in groups with and without HDL-hypocholesterolemia

	Men				P (1-2)	Women				P (3-4)	P (1-3)	P (2-4)
	HDL-hypocholesterolemia- (1)		HDL-hypocholesterolemia+ (2)			HDL-hypocholesterolemia- (3)		HDL-hypocholesterolemia+ (4)				
	M (95% CI)*	Me (25%, 75%)	M (95% CI)*	Me (25%, 75%)		M (95% CI)*	Me (25%, 75%)	M (95% CI)*	Me (25%, 75%)			
Number of patients, n	4019		222			4034		1015				
Total of polyphenols, mg	1275,2 (1255,2-1295,2)	1122,2 (847,6-1534,7)	1232,2 (1147,2-1317,3)	1110,3 (824,2-1566,2)		1207,2 (1188,2-1226,1)	1073,5 (804,7-1457,3)	1176,5 (1138,6-1214,3)	1051,6 (766,7-1420,2)		<0,001	0,045
Flavonoids, mg	860,4 (843,2-877,5)	706,6 (495,7-1087,6)	848,5 (775,5-921,6)	690,7 (490,3-1116,6)		846,6 (830,5-862,7)	712,1 (499,4-1064,6)	826,6 (790,5-860,7)	697,2 (485-1038,6)	0,04		
Phenolic acids, mg	274,6 (269,7-279,6)	257,3 (191,5-318,3)	251,1 (230-272,2)	243,7 (171,1-308,1)	0,046	237 (232,2-241,8)	206,7 (151,8-278,4)	225,7 (216,1-235,2)	201 (145,1-272,2)		<0,001	<0,001
Other polyphenols, mg	88 (87-88,9)	87,9 (68-107,3)	81,4 (77,4-85,5)	83,4 (54,7-106,8)	0,022	66,2 (65,3-67,2)	60,9 (44,9-85,2)	65,3 (63,4-67,1)	59,8 (43,6-83,3)		<0,001	<0,001
Lignans mg	44,7 (43,9-45,6)	39,5 (27,3-55,1)	43,8 (40,3-47,4)	39,1 (28,5-56,3)		50,3 (49,4-51,2)	44,4 (31-61,6)	49,8 (48-51,7)	44,3 (30,4-61,3)		<0,001	0,009
Stilbene mg	7,3 (7,1-7,4)	6,8 (6,7-7,3)	7,1 (6,6-7,7)	6,8 (6,7-7,5)		6,8 (6,7-6,9)	6,8 (6,7-7)	6,8 (6,6-7,1)	6,8 (6,7-7)			

Note: p — Mann-Whitney U-test, * — data are standardized by age.

0,14), p=0,033. In the high consumption quartile of phenolic acids, it was also 20% less: OR 1,2 (CI 1,01-1,42), p=0,04. In the high consumption quartile of stilbenes, the risk of HCE was reduced by 37%: OR 1,37 (CI 1,15-1,64), p=0,001.

Sex differences in the odds of developing HCE were identified. For men in the high consumption quartile of stilbenes, the risk was reduced by 55%, compared with the low consumption quartile: OR 1,55 (CI 1,21-1,97), p<0,001; in the high consumption quartile of Other PP, it decreases by 28%: OR 1,28 (CI 1,02-1,6), p=0,034. For women, HCE risk was independent of PP amount consumed.

Table 2 presents data for groups with/without HDL-hypocholesterolemia.

Men with HDL-hypocholesterolemia consumed less phenolic acids and Other PP. HDL-hypocholesterolemia+ women were less likely to consume flavonoids compared to the HDL-hypocholesterolemia- group. Sex differences were observed in all groups regarding the consumption of both PP in general and their certain classes, except for flavonoids and stilbenes (Table 2).

HDL-hypocholesterolemia- men had higher consumption of white bread, vegetables, coffee and alcohol compared with HDL-hypocholesterolemia+. Women without HDL-hypocholesterolemia were more likely to consume coffee, alcohol and sweets, not including sugar.

Men consumed white bread, potatoes, sweets, not including sugar and alcohol significantly more than women, regardless of the presence of HDL-hypocholesterolemia. On the contrary, women preferred fruits, berries, dried and canned fruits.

In the highest consumption quartile of PP for the entire population, the risk of HDL-hypocholesterolemia was 18% lower than in the low consumption quartile: OR 1,18 (CI 1,002-1,4), p=0,051; for women — 23% lower: OR 1,23 (CI 1,02-1,5), p=0,035. In the high consumption quartile of phenolic acids for the entire population, the risk decreases by 32%: OR 1,32 (CI 1,11-1,57), p=0,001, for women — by 27%: OR 1,27 (CI 1,04 -1,54), p=0,021. In the high consumption quartile of Other PP for the entire population, risk decreases by 20%: OR 1,2 (CI 1,01-1,41), p=0,04.

Table 3 presents the data in groups with/without LDL-HCE. Regardless of LDL-HCE, men had a high consumption of Other PP (p<0,001), while women were more likely to consume lignans (p<0,001).

We detected a high consumption of white bread, potatoes and alcohol in all groups in men compared with women. Women were significantly more likely to consume fresh fruits and berries (205,4 (189,5-221,4) g/day and 230,1 (223,9-236,2) g/day in groups

Table 3

Consumption of various PP classes in groups with and without LDL-HCE

	Men				P (1-2)	Women				P (3-4)	P (1-3)	P (2-4)
	LDL-HCE- (1)		LDL-HCE+ (2)			LDL-HCE- (3)		LDL-HCE+ (4)				
	M (95% CI)*	Me (25%, 75%)	M (95% CI)*	Me (25%, 75%)		M (95% CI)*	Me (25%, 75%)	M (95% CI)*	Me (25%, 75%)			
Number of patients, n	932		3309			667		4382				
Total of polyphenols, mg	1262,3 (1220,7-1303,9)	1124 (853-1509,9)	1275,6 (1253,6-1297,7)	1120,6 (844,5-1542,7)		1184,2 (1137-1231,4)	1098,1 (803,6-1461,9)	1203,4 (1185,1-1221,6)	1064,2 (796,9-1449,4)			<0,001
Flavonoids, mg	846,5 (810,8-882,2)	707,9 (482,2-1081,8)	863,3 (844,4-882,3)	705,5 (499,9-1089,7)		829,8 (789,8-869,8)	732,5 (501,8-1061,4)	844,9 (829,4-860,4)	708,2 (494,5-1061,9)			
Phenolic acids, mg	276,5 (266,1-286,8)	262,3 (191-321)	272,5 (267-277,9)	254,8 (190,7-316,6)		321,1 (219-243)	210,9 (155,9-280,5)	235,3 (230,7-239,9)	204,1 (149,2-276,2)		<0,001	<0,001
Other polyphenols, mg	89,1 (87,1-91,1)	89,7 (70,4-108,3)	87,2 (86,1-88,2)	86,6 (66,1-107,1)	0,022	66,6 (64,2-68,9)	66,9 (46,4-85,9)	65,9 (65-66,8)	60,5 (44,5-84,2)		<0,001	<0,001
Lignans mg	42,6 (40,9-44,3)	38,2 (27,2-53,5)	45,3 (44,4-46,2)	39,7 (27,5-56)		49,5 (47,2-51,8)	44,3 (31,1-62,1)	50,3 (49,4-51,2)	44,4 (30,9-61,5)		<0,001	<0,001
Stilbene mg	7,5 (7,3-7,8)	6,8 (6,7-12,7)	7,2 (7-7,3)	6,8 (6,7-7,1)	0,046	7,1 (6,8-7,3)	6,8 (6,7-7,1)	6,8 (6,7-6,9)	6,8 (6,7-7)	0,024		

Note: p — Mann-Whitney U-test, * — data are standardized by age.

without LDL-HCE and with LDL-HCE), compared with men (155,4 (144,5-166,3) g/day and 175,5 (169,7-181,3) g/day, respectively (p<0,001)).

The risk of LDL-HCE in the entire population was reduced by 16% in the high consumption quartile of other PP, compared with the low consumption quartile: OR 1,16 (CI 1,002-1,355), p=0,049. In men, the odds of fourth quartile of stilbene consumption decreased by 30% compared to the first quartile: OR 1,3 (CI 1,05-1,610), p=0,018; in women — by 31%: OR 1,31 (CI 1,038-1,66), p=0,024; in the entire population — by 33%: OR 1,33 (CI 1,14-1,56), p<0,001).

Discussion

This study identified associations between the consumption of PP, their certain classes and the risk of dyslipidemia in the Novosibirsk population: HCE, HDL-hypocholesterolemia and LDL-HCE. The data in the groups with/without HCE and with/without LDL-HCE obtained by us were partially consistent with the Moli-sani study, where high PP consumption was associated with lower levels of TC and LDL-C [8], and consistent with the meta-analysis of resveratrol consumption, which significantly reduced the concentration of TC and LDL-C in the blood [14]. However, there were conflicting data regarding resveratrol, where it did not affect the lipid profile [15]. It should also take into account the different stilbene sources (in particular, resveratrol) in the Novosibirsk population and in others. The main stilbene sources in Siberia for men and women are vegetables and fruits. In other populations, for example, in the Polish HAPIEE cohort, the main sources of stilbenes were alcohol (beer and wine), and in the SUN cohort, red wine and grapes [16, 17].

In people without/with HDL-hypocholesterolemia, PP in general, phenolic acids and Other PP make a greater contribution to reducing HDL-hypocholesterolemia risk. In the PREDIMED study, the level of HDL-C increased in parallel with an increase in the total urine excretion of PP [18]. However, methods for estimating the PP consumption varied. According to studies by Kim K, et al., Sohrab G, et al., an increase in the HDL-C levels was affected by the consumption of flavonoids [19, 20]. At the same time, our data did not correspond with the data of the A Nationwide Study (Polish WOBASZ II cohort): in men, a higher consumption of PP was significantly associated with low HDL-C levels (OR 1,410; 95% CI 1,080-1,842). According to the authors, the results can be explained by the eating habits of both sexes and the difference in normal ranges for HDL-C [21].

It is quite difficult to compare the results of studies with different aims. Many authors have studied specific products indicating their effect on the lipid profile. However, one cannot ignore that, although the products are sources of certain PP classes, they also contain other classes of PP and other substances. Other authors studied PP consumption in relation to the metabolic syndrome, which in turn included blood lipid parameters. A little number of researchers studied only consumption and a certain risk factor, as shown in our study.

Thus, associations of PP consumption and blood lipid profile in the Novosibirsk population were identified. Consumption of PP in general, and especially phenolic acids, stilbenes, and Other PP reduced the risk of dyslipidemia. Despite the fact that the obtained data were consistent with the other studies, there are many conflicting results for different populations, which suggests the need for further studies.

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