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LIPOPROTEINS AND OTHER RISK FACTORS FOR CARDIOVASCULAR DISEASE IN A STUDENT POPULATION

LIPOPROTEINI I DRUGI FAKTORI RIZIKA ZA KARDIOVASKULARNE BOLESTI U STUDENTSKOJ POPULACIJI

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Summary

Background: Cardiovascular disease (CVD) is a major cause of mortality and morbidity in many populations, especially in developed countries. The aim of the study was to analyze the lipid status in a student population at increased risk for CVD in comparison with students who are not at increased risk for CVD.
Methods: This study included 238 students from the University of Novi Sad of both sexes (126 men and 112 women), with a mean age of 22.32±1.85 years. According to the body mass index (BMI) lower and higher than 25 kg/m^2 and waist circumference (WC) of less and more than 94 cm (80 cm for females) the whole group of 238 students was divided into 2 subgroups: the group at increased risk for CVD (Group 1) and the group at lower risk for CVD (Group 2). Total cholesterol – TCH, triglycerides – TG, high density lipoprotein cholesterol – HDL-c, low density lipoprotein cholesterol – LDL-c, very low-density lipoprotein cholesterol – VLDL-c concentrations were determined and the index of atherosclerosis (IA), established risk factors RF-TCH/HDL-c ratio and non-HDL-c/HDL-c ratio were mathematically calculated.
Results: The values of TCH, LDL-c, non-HDL-c, VLDL-c and TG were significantly higher in Group 1 compared to Group 2 (P<0.001). IA, non-HDL-c/HDL-c and RF-TCH/HDL-c ratio were also significantly higher (P<0.001), while HDL-c

Kratak sadržaj

Uvod: Kardiovaskularne bolesti (KVB) glavni su uzrok morbiditeta i morbiditeta u mnogim populacijama, posebno u razvijenim zemljama. Cilj ovog rada je analiza lipidnog statusa studentske populacije sa povećanim rizikom za KVB u odnosu na studente bez povećanog rizika za KVB.
Metode: U ovu studiju je uključeno 238 studenata Novosadskog univerziteta oba pola (126 muškaraca i 112 žena), starosti 22,32±1,85 godine. Prema indeksu telesne mase (BMI) nižem ili višem od 25 kg/m^2 i obimu struka (OS) manjem ili većem od 94 cm za muškarce (80 cm za žene) cela grupa od 238 studenata je podeljena na dve podgrupe: grupu sa povećanim rizikom za KVB (grupa 1) i grupu sa smanjenim rizikom za KVB (grupa 2). U svim uzorcima krvi određivani su: ukupni holesterol (UH), trigliceridi (TG), lipoproteini velike gustine (HDL-hol), standardnim laboratorijskim metodama, dok su lipoproteini male gustine (LDL-hol.), lipoproteini vrlo male gustine (VLDL-hol.), non-HDL holesterol, indeks ateroskleroze (IA), utvrđeni faktori rizika (FR), kao i odnosi non-HDLh/HDLh dobijeni računskim putem.
Rezultati: Vrednosti UH, non-HDL-hol., LDL-hol., VLDL-hol. i TG bile su statistički značajno više u grupi 1 u poređenju sa grupom 2 (P<0,001). IA, non-HDL-hol./HDL-hol. i FR-UH/HDL-hol. bili su značajno viši (P<0,001), dok je HDL-hol. značajno niži (p<0,01) u grupi 1 u poređenju sa kon-

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was significantly lower ($p<0.01$) in Group 1 compared to controls. These results were not influenced by gender in both groups of subjects.

Conclusions: The data suggest that increased anthropometric parameters are followed by increased lipoprotein status in the group of students at increased risk for CVD and screening of the lipid status is necessary in students, especially in those who are at increased risk for CVD.

Keywords: lipid status, lipoproteins, cardiovascular disease, cardiovascular risk factors, primary prevention

trolnom grupom. Na ispitivane parametre nije uticao pol ispitanika.

Zaključak: Dobijeni rezultati ukazuju na to da su povećani antropometrijski parametri praćeni povećanim lipoproteinskim statusom u grupi studentske populacije sa povećanim rizikom za KVB i da je skrining lipidnog statusa neophodan, pogotovo kod studenata koji imaju povećan rizik za KVB.

Ključne reči: lipidni status, lipoproteini, kardiovaskularne bolesti, kardiovaskularni rizični faktori, primarna prevencija

Introduction

Cardiovascular disease (CVD) is a major cause of mortality and morbidity in many populations, especially in developed countries. Every year approximately 17 million people throughout the world die of cardiovascular disease (1, 2). It has been estimated that in the year 2020 as many as 31.5% of all deaths will be due to CVD. The most important words which are related to the benefit for patients of an early diagnosis of AMI are »Time is muscle« (3).

The multifactorial etiology of CVD is well known and results from the interactive effects of environmental and multiple genetic factors (HLA-DR class II genotype). Risk factors generally include sex, age, diet, obesity, physical exercise, cigarette smoking, hypertension, diabetes mellitus and hyperlipidemia (4).

Today, we have convincing evidence that atherosclerotic changes start in early childhood and the period of adolescence, and according to some authors as early as in the fetal period (5, 6). Primary prevention includes modification of risk factors in the prevention of coronary atherosclerosis, atherosclerosis of other localization and ischemic heart disease (IHD) (7). Many risk factors for CVD have been established. They can be categorized as modifiable risk factors, non-modifiable risk factors and »novel« risk factors. The modifiable risk factors are those that can be prevented, treated and controlled, such as: high blood pressure, abnormal blood lipids and lipoprotein subspecies, tobacco use, physical inactivity, obesity, unhealthy diet and diabetes mellitus. Non-modifiable risk factors (age, sex, family history and ethnic background) are those which cannot be influenced by the patient (8). Among the so-called novel risk factors are excess plasma levels of homocysteine, abnormal blood coagulation characteristics and inflammation – MPO, hsCRP, protein S100B, choline CD 40L, ADMA, PAPP-a, copeptin, vitamin D, GDF-15 etc. (9–13).

The rise in CVDs reflects a significant change in dietary habits, physical activity levels and tobacco consumption worldwide as a result of industrialization, urbanization, economic development and food market globalization. Imbalanced nutrition, reduced physical activity and increased tobacco consumption are the key lifestyle factors, and primary prevention must be focused on those at elevated risk and reduce risk factors through multiple economic and educational policies and programs. Underlying risk factors include atherogenic diet, overweight (BMI ≥25–29.9 kg/m^2) or obesity (BMI 30 kg/m^2), physical inactivity and genetic factors. Severe risk factors are persistent cigarette smoking, LDL cholesterol >4.92 mmol/L, blood pressure ≥140/90 mm Hg, BMI ≥30 kg/m^2 in the presence of other risk factors. Emerging risk factors are: lipoprotein (a) ≥0.3 g/L, presence of small dense LDL, apolipoprotein B level >1.4 g/L, prothrombotic state – plasma fibrinogen >3.5 g/L and PAI-1 >7 IU/L, proinflammatory state– CRP elevated in the absence of an acute inflammatory condition >3 mg/L, soluble adhesion molecules (sICAM, sVCAM), WBC count, cytokines, plasma homocysteine ≥12 μmol/L, and the presence of calcification of coronary arteries documented by computerized tomography (CT) (14).

The aim of this study was to analyze and compare the lipoprotein levels and other risk factors for cardiovascular disease (CVD) such as: BMI (body mass index), WC (waist circumference), tobacco smoking, physical activity, and coffee and Coca-Cola drinking in student population groups at lower and higher risk for CVD, in order to establish novel targets for cardiovascular prevention and to detect early symptoms and set up early diagnosis of cardiovascular disease. Our ultimate aim was to increase active participation of students in adopting a healthy lifestyle as well as to increase their responsibility for their own health.

Materials and Methods

In our study, 238 students from the University of Novi Sad, of both sexes (126 males and 112 females), with a mean age of 22.32±1.85 years, were included. They were examined during a systematic examination in the period from 2009 to 2011. All subjects filled in a questionnaire about their habits including physical activity, smoking, alcohol and red wine intake, Coca-Cola drinking, family history of CVD, diabetes mellitus or other chronic disease, etc. The blood samples for analysis were taken after

12–14 hours of overnight fast. In the blood samples taken from the subjects the following parameters were analyzed: total cholesterol concentrations (TCH), triglyceride values (TG), high-density lipoprotein cholesterol (HDL-c), low density lipoprotein cholesterol (LDL-c), and very low-density lipoprotein cholesterol concentrations (VLDL-c). TCH, HDL-c, VLDL-c and TG levels were measured using standard laboratory methods, while LDL-c was calculated by the Friedewald formula (15). Index of atherosclerosis (IA), non-HDL-c concentration and established risk factors (RF) (TCH/HDL-c) and non-HDLc/HDLc ratio were calculated mathematically. All subjects gave their informed consent for participation in the study, which was approved by the local Ethics Committee.

Statistical analyses

The data were evaluated by Student's t-test for variables with a normal distribution and Mann-Whitney U test for variables with a non-parametric distribution. The Chi square test was used for categorized variables. The relations among parameters were examined by Spearman's correlation coefficient. Calculations were performed using the statistical program SPSS for Windows Version 14.0, and a p value <0.05 was considered statistically significant.

For the clinical interpretation of lipid values, recommendations of the NCEP (ATP III), European Atherosclerosis Society (EASC) and the Yugoslav Lipid Commission were used (16).

According to the body mass index (BMI) and waist circumference (WC) the whole group of 238 students was divided into 2 subgroups: a group at increased risk for CVD (Group 1) and a group at lower risk for CVD (Group 2). The criteria for selection were BMI lower and greater than 25 kg/m^2 and WC smaller and greater than 94 cm (for male subjects) or WC<80> cm (for female subjects) respectively.

Results

The biochemical parameter values and measured anthropometric values are presented in *Table I*.

Out of the total number of students, 164 subjects comprised Group 1 – increased risk for CVD (105 males and 59 females) and 74 subjects with BMI<25 kg/m^2 and WC<94/80 cm comprised the control group (Group 2 – i.e. the group at lower risk for CVD). The average BMI value in Group 1 was 28.85±3.86 kg/m^2 and was significantly higher in comparison to Group 2 (20.5±2.07 kg/m^2) (t=–17.434, p<0.01). The average WC value in Group 2 (97.8±10.5 cm) was also significantly higher than in controls (73.7±6.85 cm) (t=–18.124, p<0.01).

Statistical processing data revealed significantly higher values of TCH (t=5.94; p<0.01), TG (t=5.64; p<0.01), LDL-c (t=5.54; p<0.001), VLDL-c (t=5.55; p<0.01) and non-HDL-c (t=6.4; p<0.001) in the group of students at increased risk for CVD, while the values of HDL-c were significantly lower in Group 1 (t=4.04; p<0.01) compared to the control group. Group 1 also had higher values of IA (t=5.66; p<0.001), a higher non-HDL-c/HDL-c ratio (t=6.46; p<0.001) and TCH/HDL-c ratio as well, compared to Group 2 (t=6.93; p<0.001). It is important to mention that all the measured lipoprotein values of the tested subjects were within the reference interval, even

Table I Statistical data for anthropometric parameters and lipid status values in the group of students at increased risk for CVD (Group 1) and students at lower risk for CVD (Group 2).

Parameters	Group 1 $\bar{x}$ ± SD N=164	Group 2 $\bar{x}$ ± SD N=74	P	Reference values	
				Females	Males
BMI (kg/m^2)	28.85±3.86	20.50±2.07	<0.01	<25	<25
WC (cm)	97.80±10.5	73.70±6.85	<0.01	<80	<94
Total cholesterol (mmol/L)	5.19±1.01	4.38±0.87	<0.01	<5.2	<5.2
Triglycerides (mmol/L)	1.29±0.63	0.83±0.41	<0.01	<1.7	<1.7
HDL-c. (mmol/L)	1.23±0.33	1.42±0.36	<0.01	>1.5	>1.3
LDL-c. (mmol/L)	3.42±1.22	2.57±0.80	<0.001	<3.5	<3.5
VLDL-c. (mmol/L)	0.58±0.28	0.37±0.18	<0.01	<0.55	<0.55
NonHDL-c. (mmol/L)	4.02±1.28	2.97±0.87	<0.001	<3.86	<3.86
NonHDL/HDL-c. (mmol/L)	3.60±1.72	2.22±0.92	<0.001	<3.25	<3.25
IA-LDL-c./HDL-c.	3.04±1.58	1.93±0.84	<0.001	<3.00	<3.22
RF-Cholesterol/HDL-c.	4.53±1.54	3.19±0.92	<0.001	<4.03	<4.50

Arithmetic mean ± 1 standard deviation (x ± SD); BMI – body mass index; WC – waist circumference; P – significance of difference between groups.

within the recommended values according to the NCEP ATP III recommendations.

Statistical processing data revealed that 82.3% (n=135) of subjects from Group 1 and 64.8% of subjects (n=48) from Group 2 had a family history of CVD, and this difference was statistically significant ($P<0.01$). The presence of a positive personal history was determined in 58 examinees of the risk group (35.4%) and 19 examinees of the control group (25.7%), but the difference was not statistically significant ($p>0.05$).

The degree of physical activity categorized as intensive or moderate was significantly lower in the risk group with a dominant »couch potato lifestyle« or sedentary lifestyle in relation to the control group ($\chi^2=7.21$; $p<0.05$). Sedentary lifestyle was associated with 33.5% students of the risk group in relation to 20.3% students in the control group. The risk group also had more smokers (36% vs. 27% in the control group) as well as a greater percentage of those who consumed alcohol (68.9% vs. 60.9%), but the difference was not statistically significant ($p>0.05$). An interesting fact was that consumption of coffee was significantly lower in the risk group (49.4% vs. 71.6% in CG), and that was statistically significant ($p<0.001$), while the consumption of Coca-Cola was more common in the risk group (72.6% vs. 60.8% in CG), but without statistical significance.

Discussion

According to the obtained results it can be concluded that students with BMI>25 kg/m^2 and WC>94 cm (for males) and WC>80 cm (for females) respectively had increased values of the risk factors for CVD such as: increased serum lipoprotein levels (TCH, LDL-c, VLDL, non-HDL-c and triglycerides) as well as increased IA, non-HDL-c/HDL-c ratio ($p<0.001$) and TCH/HDL-c ratio ($p<0.001$). The students in Group 1 had lower HDL-c values, higher frequency of family history of CVD and diabetes mellitus and present personal cardiovascular events such as higher blood pressure. Higher percentage of sedentary lifestyle and decreased physical activity were also determined in the risk group. Smoking, consuming of alcohol and Coca-Cola were not pronounced in the risk group, while consumption of coffee had a lower frequency in the risk group in comparison to the control group.

Abnormal metabolism of lipids, lipoproteins and apolipoproteins is the most important risk factor for coronary artery disease (CAD). The etiology of CVD is multifactorial and includes multiple genetic and environmental factors (17, 18).

Low concentrations of high density lipoprotein cholesterol (HDL-c) and increased plasma levels of malondialdehyde (MDA)-modified LDL-c and oxidized LDL-c have long been associated with increased risk of atherosclerosis, coronary heart disease (CHD), CAD, unstable angina and acute myocardial infarction (AMI) (19). Moreover, a high HDL-c concentration has been identified as a »negative« risk factor which reduces the risk of coronary heart disease. Indeed, each 1% increase in HDL-c concentration has been associated with a 2–4% decrease in the risk for coronary heart disease (20, 21), while an increase of LDL-c concentration of 1 mmol/L leads to increased risk for ischemic heart disease (IHD) by 57% (22). According to Rothblat and Phillips (23) HDL-c is an independent predictor of the risk for CVD.

Our data suggest that screening of the lipid status is necessary in student populations, especially for those who come from families at increased risk for CVD. The primary prevention is very important and can be achieved through lifestyle changes, promotion of a healthy way of life, as well as modifications of the risk factors with the aim of preventing atherosclerosis, and coronary heart disease, and for some students through therapeutic intervention in established clinical cases.

Recent literature suggests that the IHD could be prevented in 80% of cases by a healthy way of life, proper nutrition (intake of fruits and vegetables of more than 600 grams per day), adequate body weight (BMI<21 kg/m^2), regular physical activity, WC – waist circumference for men <94 cm and for women <80 cm, WHR <0.90 for men and <0.85 for women, no cigarette smoking and by keeping the blood pressure below 115/80 mmHg, and total cholesterol below 3.8 mmol/L (24–26). When persons of younger age are considered, it has been established that increased values of LDL-c and lower values of HDL-c are connected with higher frequency of fatty streaks and fibrous plaque in atherosclerotic lesions (27).

Epidemiological studies have shown that if the increased LDL-c appears earlier, there is higher frequency of CHD in older age. Long-term prevention of CVD and detection of risk factors in young people, especially in the student population is very important. Combination of early detection and early prevention of increased LDL-c together with lifestyle changes offer the possibility of prevention or delay of coronary heart disease. Therapeutic lifestyle changes are necessary in young people with LDL-c higher than 3.4 mmol/L, and doctors need to pay attention to the risk of smoking and apply medicaments for LDL-c higher than 4.1–5.2 mmol/L. Slowdown and regression of atherosclerotic processes are possible to achieve with modifications of lipid risk factors, changes of lifestyle habits, with diet and better physical activity and eventually by applying medicaments for the regulation of lipids, therapy of hypertension and other modifiable risk factors.

Guidelines for diagnosis of dyslipoproteinemias together with evidence-based medicine are based on the screening of the adult population under 20 years of age every 5 years with controls of total cholesterol. However, in persons at increased risk for CAD as well as with coronary disease, hypertension, diabetes mellitus, smokers and the obese control of the lipid status is recommended once a year (29). Screening of the lipid status is at least 10 times cheaper than treatment of the consequences of this disease.

NCEP ATP III recommendations from 2003 provide new expected values: for cholesterol<5.2, LDL<3.4, HDL>1.3 for men and HDL>1.5 for women, triglycerides<1.7, with the optimal values of 3.6 for THC and 2.6 for LDL-c (16).

Proper lifestyle from the earliest childhood is of key importance in the prevention of atherosclerosis. The common goal of the European Society of Cardiology (ESC) is that: not a single child born in this third millennium should die of and should not suffer from CVD before the age of 65 years. Magic numbers for better ageing in primary prevention are: 0–3–5–140–5–3–0, which implicate a healthy way of life and control of the risk factors: 0 – without smoking (neither active nor passive), 3 – 3 km of walking per day or 30 minutes of any physical activity daily, 5 – 5 daily portions of fruits and vegetables (at least 400–600 g), 140 – systolic blood pressure lower than 140 mmHg, 5 – total cholesterol less than 5 mmol/L, 3 – LDL-cholesterol less than 3 mmol/L, 0 – without obesity and DM.

Modified »magic numbers« from the ESC for secondary prevention are: 0–3–5–120–4–2–0, where differences in regard to primary prevention imply lower values for blood pressure, total and LDL cholesterol (29).

The WHO developed some simple strategies which are effective in preventing CVD and in managing the disease such as: substitution of saturated and trans fats with non-hydrogenated unsaturated fats (especially polyunsaturated fat), increased consumption of omega-3 fatty acids from fish oil or plant sources, consuming a diet rich in fruits, vegetables, nuts and whole grains and low in refined grains, avoiding excessively salty or sugary foods, avoiding smoking, at least 30 minutes of regular physical activity daily, and maintaining a healthy weight (30).

The WHO has developed a strategic plan to reduce the impact of CVD, and the major items of the plan are the following: reduce the major CVD risk factors and their social and economic determinants through community-based programs for integrated prevention, develop standards of care and cost-effective case management for CVD, global action to enhance the capacity of countries to meet the health care needs of CVD and develop feasible surveillance methods to assess the pattern and trends of major CVDs and risk factors, monitor the prevention and control initiatives and develop effective inter-country, interregional and global networks and partnerships for concerted global action (31).

These data suggest that increased anthropometric parameters are followed by an increased lipoprotein status in the group of students at increased risk for CVD and screening of the lipid status is necessary in students, especially in those at increased risk for CVD. Risk for CVD can be decreased by physical activity and balanced nutrition which cannot be replaced by any medicament.

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Conflict of Interest Statement

The authors stated that there are no conflicts of interest regarding the publication of this article.

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