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Efficiency of Use of Dietary Supplement Arteroprotect® In Prevention of Cardiovascular Diseases

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Abstract: *Cardiovascular diseases are the leading cause of death in most developed countries and in many developing countries. The main cause of cardiovascular disease in 95% cases is supposed to be atherosclerosis, and the symptoms occur when the process is already at an advanced stage of disease. Present study was conducted to examine an efficiency of ARTEROprotect® (by Abela Pharm, Serbia) in prevention of cardiovascular diseases. The study was conducted by 76 doctors in primary health centers throughout the Republic of Serbia as a prospective clinical study of two groups of subjects. The study group included 4031 subjects (1785 males and 2246 females) who were taking ARTEROprotect®, while the control group consisted of 2564 subjects (1135 males and 1428 females) who were not taking it. Based on the results, dietary supplement ARTEROprotect®, used alone, could contribute to lowering levels of cholesterol, triglycerides, LDL-cholesterol; in combination with a statin it can achieve the target value of LDL- and HDL-cholesterol.*
Keywords: *cardiovascular diseases, dietary supplement, ARTEROprotect®.*

I. Introduction

Cardiovascular diseases are the leading cause of death in most developed countries and in many developing countries. Cardiovascular diseases are a significant cause of work disability and premature mortality of persons in a middle age (aged under 65 years). However, cardiovascular diseases such as ischemic heart disease, ischemic disease of cerebrovascular system and peripheral arterial occlusion can be prevented. In 95% of cases, the main cause of cardiovascular diseases is atherosclerosis and the symptoms occur when the process is already at an advanced stage of disease.

Prevention of cardiovascular disease involves a risk assessment for each patient. [1] One of the conducted studies showed the effect of co/administration policosanol (main constituent is octacosanol) and atorvastatin on decreasing the level of PCSK9 (plasma protein convertase subtilisin / kexin type 9) - a protein that controls the number of LDL receptors on the surface of the hepatocytes of the liver. [2] Specifically, it has been shown that statin increase the level of PCSK9 that destroys LDL receptors, and this creates resistance to statin. [2]

Because of the excellent safety and tolerability of policosanol, the search for lipid-lowering compounds based on policosanol is of great importance and interest, especially in children, elderly persons, and other special populations. [2] Policosanol prevents statin destruction of LDL receptors on the surface of liver hepatocyte, prevents resistance to statin. [2,3,4] Policosanol plus the conventional dose of atorvastatin might be an alternative strategy for attenuating the adverse effects of statins on PCSK9. [2] Also, the adequate intake of Vitamin K2 may contribute to coronary heart disease prevention. [5]

The present study was conducted to examine an efficiency of ARTEROprotect® (natural Vitamin K2/MK7 from Bacillus subtilis Natto 45µg with 20mg of Octacosanol, by Abela Pharm, Serbia) in a prevention of cardiovascular diseases.

II. Methods And Patients

The study was conducted as a prospective clinical study of two groups of subjects in health centers throughout the Republic of Serbia (Belgrade, Novi Sad, Nis, Arandjelovac, Kragujevac, Pancevo, Smederevo, Bor, Zajecar, etc.). The study was escorting by 76 doctors - general practitioners, specialists in internal medicine and cardiology, in accordance with the principles of good clinical practice and the Declaration of Helsinki [6]. Subjects from both groups were informed about all aspects of the research before the study, and only well-informed patients who have given their written consent for entering the study were included.

The study group included 4031 subjects (1785 males and 2246 females) who were taking ARTEROprotect®, while the control group compromised 2564 subjects (1135 males and 1428 females) who were not taking it. In a special questionnaire created for the purpose of research, at first visit, for subjects of both groups were recorded demographic data (such as gender and age), bad habits (smoking cigarettes and obesity),

diagnosis (in accordance to ICD-10) [7], medical therapy, and the value of laboratory parameters (serum levels of cholesterol, triglycerides, HDL-cholesterol and LDL-cholesterol). The check-ups were made after one to three months. On follow-up examination, once again, values of laboratory parameters were measured in subjects of both groups.

The primary data obtained entered the SPSS 17.0 and were analyzed by descriptive statistical parameters and methods for testing hypotheses. Descriptive statistical methods were represented by measures of central tendency (mean and median), a measure of variability (standard deviation and variation interval) and were expressed in percentages. The difference of numerical data were carried out by using Mann-Whitney or Wilcoxon test. For testing data of different cathegories Pearson's χ^2 test was used. Statistical significance was set on $p<0.05$.

III. Results

Concerning age, most of the respondents in study group were aged 61 to 70 years (40.3%), while in control group most subjects were in the age group of 41 to 60 years (Table 1). The study group comprised are obese patients; in contrast, there were less obese patients n the control group (Table 1). Concerning smoking cigarettes, most of the subjects in both groups did not have this bad habit (Table 1). A statistically significant difference between the groups was observed in terms of age and obesity, while it could not be said with regard to gender of the respondents and smoking cigarettes (Table 1).

Table 1. Characteristics of subjects

Characteristics	Study group n (%)	Control group n (%)	p^*
Gender:			
male	1785 (44.3)	1136 (44.3)	
female	2246 (55.7)	1428 (55.7)	0.509
Age group (in years):			
≤ 40	239 (5.9)	224 (8.7)	
41 - 60	1572 (38.9)	902 (35.2)	
61 - 70	1620 (40.3)	886 (34.6)	
≥ 71	600 (14.9)	552 (21.5)	0.020
Obesity:			
yes	2241 (55.6)	1194 (46.6)	
no	1790 (44.4)	1370 (53.4)	0.000
Smoking cigarettes:			
yes	1951 (48.4)	1168 (45.6)	
no	2080 (51.6)	1396 (54.4)	0.118
n-number of subjects; %-percent of subjects; *p**-statistical significance; *Pirson's χ^2- test			

Twenty-three subjects of the study group and 32 subjects in the control group did not have an approved diagnosis of any disease. In study group, subjects had on average 1.90 ± 0.92 diagnosis (0-6 diagnosis), and a similar finding was recorded in the control group (2.03 ± 1.11; 0-6 diagnosis) - Table 2. Most of the subjects in both groups had a diagnosis of hypertension (Table 2). However, a statistically significant difference between the groups was registered in the number of diagnoses (Table 2).

Table 2. Diagnosis of subjects

Diagnosis	Study group n (%)	Control group n (%)	p^*
X ± SD; Med (min-max)	1.90 ± 0.92; 2 (0-6)	2.03 ± 1.11; 2 (0-6)	0.003
Hypertension	3373 (83.7)	2093 (81.6)	
Heart attack	443 (11.0)	310 (12.1)	
Angina pectoris	617 (15.3)	548 (21.4)	
Coronary insufficiency	281 (7.0)	216 (8.4)	
Cerebral stroke	428 (10.6)	270 (10.5)	
Diabetes mellitus	1191 (29.5)	567 (22.0)	
Renal failure	116 (2.9)	116 (4.5)	
Family history of cardiovascular diseases	893 (22.2)	832 (32.4)	
Other	373 (9.3)	262 (10.2)	
n-number of subjects; %-percent of subjects; X-mean value; SD-standard deviation; Med-median; min-minimun; max-maximum; *p*-statistical significance; *Mann-Whitney test			

Concerning medication, 6.6% of subjects in study group, and 14.4% of respondents in control group had no medical therapy (Table 3). Most of the respondents in both groups were receiving statin with other medications (Table 3). Control review of the subjects in both groups, in most cases, was made one month after the first visit (Table 3). Statistically significant difference between the groups of subjects registered in taking the therapy, use of statin and time of control examination (Table 3).

Table 3. Therapy and control visit of subjects

Characteristics	Study group n (%)	Control group n (%)	p^*
Therapy:			
yes	3765 (93.4)	2195 (85.6)	
no	266 (6.6)	369 (14.4)	0.000
Statin:			
yes	2592 (64.3)	1467 (57.2)	
no	1379 (35.7)	1097 (42.8)	0.000
Control visit:			
after one month	2741 (68.0)	1752 (68.3)	
after two months	1151 (28.6)	565 (22.0)	
after three months	139 (3.4)	247 (9.7)	0.000
n-number of subjects; %-percent of subjects; *p*-statistical significance; * Pirson's χ^2- test			

During the first visit, values of cholesterol, triglycerides, HDL-cholesterol and LDL-cholesterol were registered in both groups. The same parameters were determined again, on a control examination (Table 4). Looking for average values of monitored laboratory parameters in the first and second (control) visit, a statistically significant difference was observed in both groups. In study group, mean values of cholesterol, triglycerides and LDL-cholesterol decreased, and of HDL-cholesterol increased, while in control group all the observed laboratory parameters decreased (Table 4).

Table 4. Values of laboratory parameters in first and second (control) visit of subjects

Laboratory parameter	Study group			Control group		
	I visit (X ± SD) mmol/l	II visit (X ± SD) mmol/l	*p**	I visit (X ± SD) mmol/l	II visit (X ± SD) mmol/l	*p**
Cholesterol	6.24 ± 0.96	5.82 ± 0.80	0.000	6.03 ± 1.10	5.71 ± 0.83	0.036
Triglycerides	2.19 ± 0.87	1.87 ± 0.72	0.000	1.91 ± 0.80	1.83 ± 0.68	0.026
HDL-cholesterol	1.55 ± 0.79	1.76 ± 0.79	0.000	1.70 ± 1.16	1.54 ± 0.60	0.000
LDL-cholesterol	3.71 ± 0.91	3.17 ± 0.80	0.000	3.64 ± 1.05	3.27 ± 0.76	0.018
X-mean value; SD-standard deviation; *p*- statistical significance; *Wilcoxon test						

Analyzing the mean value of the monitored laboratory parameters obtained in the first and the second (control) visit, compared to patients taking statin in study group, statistically significant difference was observed in all the dependent variables (Table 5).

Table 5. Values of laboratory parametersin first and second (control) visit of study group

Laboratory parameter	statin + ARTEROprotect®			ARTEROprotect®		
	I visit (X ± SD) mmol/l	II visit (X ± SD) mmol/l	*p**	I visit (X ± SD) mmol/l	II visit (X ± SD) mmol/l	*p**
Cholesterol	6.20 ± 1.00	5.77 ± 0.81	0.000	6.19 ± 0.99	5.79 ± 0.81	0.000
Triglycerides	2.13 ± 0.86	1.84 ± 0.72	0.000	2.13 ± 0.86	1.85 ± 0.72	0.000
HDL-cholesterol	1.58 ± 0.88	1.72 ± 0.77	0.000	1.58 ± 0.88	1.71 ± 0.75	0.000
LDL-cholesterol	3.71 ± 0.95	3.17 ± 0.79	0.000	3.68 ± 0.94	3.17 ± 0.79	0.000
X-mean value; SD-standard deviation; *p*- statistical significance; *Wilcoxon test						

IV. Discussion

Present study included a total of 6595 subjects, prevailling females (55.8% v. 44.2%). This data indicates that females are more frequent visitors of the Health Centers and responsive to their health. Primary health care at the Health Centers is exercise over the chosen general practitioner, who is as a rule the first health care worker with whom patients meet when they needed medical care. The data support the previous research on the territory of the Republic of Serbia who talk about significantly higher percentage of female population who have a chosen doctor at the health center. [8]

The respondents of this study were most commonly older than 40 years, which indicates that people in middle age are often prone to cardiovascular disease. Concerning cigarette smoking and obesity, the study in both groups had a lot of smokers and people who are obese. Clinical and epidemiological studies have shown that the most important etiological factors for cardiovascular diseases are smoking, physical inactivity and inadequate nutrition. [9] The obtained data correlated with the results of earlier studies, pointing to the fact that more than half of population was overweight or obese in Republic of Serbia. Also retrospective studies have shown that in the period from 2006 to 2013 the percentage of obese population increased, from 17.3% to 21.2% [9]. It is known that with an increase in waist circumference over 94cm for men and for women over 80 cm, growing health risk for cardiovascular disease. [10] On the other hand, the harm of tobacco and tobacco products

is well documented through research conducted since the mid-twentieth century as an increased risk of heart attacks, peripheral vascular disease and high blood pressure. [8]

In study group, subjects had on average 1.90 ± 0.92 diagnosis (0-6 diagnosis), and a similar finding was recorded in the control group. This data supports the previous studies have pointed the prevalence of hypertension i residents of Serbia. [8]

In study group there was a significant reduction in mean values of cholesterol, triglycerides and LDL-cholesterol, as well as an increase in mean values of HDL-cholesterol, whereas in the control group there was a

significant decrease in the mean values of all observed laboratory parameters. This indicates a significant impact ARTEROprotect® in terms of sinergistic effect with a statin. In fact, earlier studies have shown that as many as 56,2% of respondents who receive statin do not reach the target value of LDL-cholesterol [11], and the mentioned resistance is the result of an increase value of PCSK9. [12]

The results of this study can contribute prevention of elevated blood fats, which are elevated in population of Serbia. [5] Based on the results, it can be said that dietary supplement ARTEROprotect® used alone can contribute to lowering levels of blood fat, and in combination with a statin it can achieve the target value of HDL-cholesterol.

V. Conclusion

Dietary supplement ARTEROprotect® as a available "natural" product might be effective on improving serum lipids by lowering cholesterol, triglycerides and LDL-cholesterol, while raising HDL-cholesterol may considered safe and well tolerated. ARTEROprotect® with a statin also showed significant decreases in LDL levels and increases in HDL levels. However, more clinical investigations are needed to confirm the presented findings.

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