

Role of Apolipoproteins B and A1 in the Development of Arterial Hypertension against the Background of Obesity

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Abstract When the values of the ApoB / ApoA1 index are above 0.46, it can be reliably assumed that a patient with obesity and AH has initial stages of atherogenesis. The role of serum lipoproteins in the development of atherosclerosis was confirmed, and that makes it possible to classify patients with obesity and hypertension as group with a high risk of cardiovascular diseases development in subsequent periods of life.

Keywords Obesity, Dyslipidemia, Prevention, Risk, Apolipoproteins A1

1. Introduction

Cardiovascular pathologies continue being the leading cause of death in all developed countries of the world [1]. In spite of all the measures taken by public health care agencies the anxiety grows around persisting high lethality rate among “young” adults aged 35-54 year old, as one of the reasons of these deaths is prevalence of obesity and diabetes mellitus in childhood [2].

Recently prevention of unfavorable clinical events in the life of middle-aged people was considered to be the basic type of prophylaxis of cardiovascular pathologies. However, researches performed within the last two decades showed that, all cardiovascular pathologies originated in young age, and the main risk factor was early atherosclerosis development [3].

Dyslipidemia is the basic factor in the development of atherosclerosis [4]. Epidemics of obesity led to appearance of a greater number of patients with deviations in lipid spectrum, i.e. patients with secondary dyslipidemia [5]. The values of serum lipids are the basic tools for the stratification of the risk in cases of dyslipidemia. Serum concentrations of low-density lipoproteins cholesterol (LDLC) and high-density lipoproteins cholesterol (HDLC) are the lipid classes most often used for that purpose. Quantitative values of LDL and HDL particles such as apolipoproteins B (ApoB) and A1 (ApoA1) can serve to be better risk markers compared to concentrations of LDLC and HDLC, and, correspondingly, atherogenic index (AI) traditionally used in

local medicine [6].

Subclinical atherosclerotic alterations in the inner membrane of vessels can be accurately determined with the help of ultra sound without invasion. Increase of the thickness of intima media complex (IMCT) is the basic marker of atherosclerotic alterations linked with the impact of various risk factors [7] and it can be used to predict unfavorable cardiovascular changes [8]. The impact of very atherogenic particles becomes the cause of the early atherosclerosis development. Multiple studies confirmed that a high concentration of LDLC was reliably linked with the increase of IMCT [7,9,10].

Later it was proved that, quantitative values of LDL and HDL particles ApoB and ApoA1 were predictors of subclinical atherosclerosis development [11].

Taking into account the prophylactic character of modern medicine the objective of our study was the assessment of the capabilities of various classes of serum lipids in the early definition of alterations in intima media complex in vessels for the prognosis of initial stages of atherogenesis with background obesity and arterial hypertension.

2. Research Data and Methods

The study involved one hundred and eleven individuals, among them 62 patients composed the basic group, while the rest 49 made up the control one. The mean age of the patients in the basic group was 42.0 ± 2.0 years old, and in the control group it was 41.3 ± 2.0 years old. Inclusion criteria for the basic group were obesity, as one of the risk factors (WHO, 2011) and arterial hypertension.

Concentrations of total cholesterol (TCC), high-density lipoproteins cholesterol (HDLC), and triglycerides (TG) were determined in blood serum sample taken in the morning after 12-14-hours fasting with the help of semi-automatic analyzer «EPOLL-20» (Austria). We used reactants made by

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«Human» (Germany).

IMCT in common carotid artery (CCA) was determined using high resolution ultra sound apparatus Philips HD 11XE at the distance of 1cm proximally from CCA bifurcation along its dorsal wall in the area of maximal thickening at the end of diastole during three cardiac cycles both on the right and the left carotid arteries [12]. For the statistical analysis we applied a mean of intima-media complex of the right and left CCA.

Statistical processing of the data was performed by means of Statistica Windows 6 software.

3. Results of the Study

The study of blood lipids' parameters revealed reliable differences between the groups (table 1).

Table 1. Blood plasma lipid spectrum parameters

Lipid profile values	Basic group (n = 62)	Control group (n = 49)
Total cholesterol (mmol/L)	5.59±1.2	3.65±0.1*
Triglycerides (mmol/L)	1.9±1.1	0.71±0.03*
LDL cholesterol (mmol/L)	3.96±1.44	1.78±1.6*
Apolipoprotein B, g/L	1.07±0.02	0.73±0.01*
HDL Cholesterol (mmol/L)	0.767±0.21	1.78±0.26*
Apolipoprotein A1, g/L	1.31±0.06	1.7±0.02*

Note: * - $P < 0.01$

Concentration of TCC in the basic group was reliably higher than that in the control one ($p < 0.001$), mostly due to the increase of atherogenic lipid fractions. At the same time mean concentration of HDLC in the basic group was below normal values ($p < 0.001$). A1 and B lipoproteins amounts were reliably different in the groups (< 0.001).

Most often registered deviations were ones in the values of HDLC (36%) and TG (26%), and that was marker disorder of lipid exchange in AH cases. Deviations in the ApoA1 concentration were registered only in 24%, and only 22% of the patients had deviations in the concentrations of TC. These data reflect the necessity of the further study of the complete lipid spectrum in the patients with obesity. Rises of LDLC and ApoB concentrations were registered in 14% of the patients of the basic group. At the same time, 17.7% of the patients (11 individuals) had normal values of the lipid spectrum. Thus, more than 80% of the patients with AH had secondary disorders of lipid exchange.

The basis of atherogenesis is sub-endothelial accumulation of particles containing LDLC [13]. Secondary dyslipidemia in cases of obesity is very atherogenic due to several reasons. Small dense particles of LDL are not effectively captured by liver with the help of LDL-receptors. Greater amount of circulating LDL particles increase the risk of accumulation in sub-endothelial matrix, while decrease in HDL amount limits reverse transport of cholesterol from tissues to liver [14,15]. Atherogenicity of

combined dyslipidemia observed in cases of obesity has its manifestation in structural and functional vascular alterations, which can be assessed without invasion according to the increase of IMCT in carotid artery. In the compared groups that parameter was reliably different ($p < 0.001$), with dominance in the basic group (0.422 ± 0.007 mm) over the control one (0.352 ± 0.009 mm). Thus, vascular alterations in obesity occur even at the early stages of AH development.

Revealing the factors reliably effecting atherogenesis we compared groups of patients with obesity and AH with different thickness of intima-media, gender, age, anthropometric parameters, and laboratory data. In spite of the absence of any reliable differences in all groups ($p > 0.05$), increase in the thickness of intima-media complex was linked with aging, BMI, and TT.

Single-factor disperse analysis in various groups revealed no reliable differences in the concentrations of lipids (TC, TG, LDLC, HDLC, ApoB, ApoA1) ($p > 0.05$). Similar results were presented in the works of other authors [18] for cholesterol fractions of serum lipids (TC, TG, LDLC, HDLC).

Markus Juonala *et al.* [11] proved the presence of reliable link between the ratio of ApoA1 and ApoB and subclinical atherosclerosis determined according to IMCT. Concentration of B and A1 apolipoproteins and their ratio serve to be the leading prognostic factors of cardiovascular morbidity and lethality [16,17].

We have chosen three variants of lipid ratio:

- atherogenic index (AI) traditionally used in local medicine [19], where $AI = (TCC - HDLC) / HDLC$;
- ApoB/ApoA1, in compliance with multiple references, possessing the best capability to predict atherosclerotic alterations [11,20];
- LDLC/ HDLC [20].

The analysis showed that, ApoB/ApoA1 ratio was reliable predictor of atherogenesis in patients with obesity and AH, and it can be used for the prognosis of alterations of vascular intima. The greatest sensitivity and specificity corresponded to the value of ApoB/ApoA1 equal to 0.46. Thus, with the values of that lipid index above 0.46, it can be reliably assumed that a patient with obesity and AH has initial stage of atherogenesis.

We demonstrated that, rise of ApoB/ApoA1 in the patients with obesity and AH is a reliable predictor of IMCT increase.

4. Conclusions

1. A1 and B apolipoproteins can be used for the assessment of initial stages of atherosclerotic intima alterations risk in patients with obesity and AH. With the value of ApoB/ApoA1 above 0.46 initial signs of subclinical atherosclerosis development can be reliably assumed.
2. Patients with the risk of secondary dyslipidemia

development, first of all those with obesity and AH, should have complete lipid screening including assessment of A1 and B apolipoproteins concentration.

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