Low-Density Lipoprotein Subfractions during Abdominal and Gluteofemoral Obesity

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Subfractional spectrum of plasma low-density lipoproteins in people with normal body weight and patient with obesity was studied by gradient electrophoresis (3-12%) in polyacrylamide gel. Low-density lipoprotein subfractions in fasting patients with abdominal and gluteofemoral obesity were primarily presented by small particles (compared to people with normal body weight). The composition of low-density lipoprotein subfractions underwent most pronounced changes in patients with abdominal obesity after single fat load.

Key Words: *low-density lipoproteins; particle size; obesity*

Low-density lipoproteins (LDL) are the major class of blood plasma lipoproteins that transport synthesized and alimentary cholesterol (CH) to tissues. Blood plasma LDL are heterogeneous particles differing in size, density, chemical composition, physicochemical and immunological properties, and metabolic characteristics [2,4,12]. The cause of LDL heterogeneity remains unclear. The presence of various LDL subfractions and their structural heterogeneity are related to genetic, metabolic, and biological characteristics and effects of lipolytic enzymes and proteins carrying esterified CH [4,8,10,11,14].

The size and properties of LDL particles are determined by molecular ratio between lipid and protein components. The decrease in the lipid/protein ratio is accompanied by an increase in the density and reduction in size of particles [4,12]. Small, dense, and multiply modified LDL are highly atherogenic [2,4,8]. As differentiated from native LDL, modified particles circulate in the blood for a long time and undergo oxidation due to reduced affinity for specific receptors and ability to interact with arterial wall proteoglycans and other receptors (*e.g.*, scavenger receptors on macrophages) [3,4,10]. Prospective epidemiologic studies showed that the risk of coronary heart disease in patients increases by 3 times when LDL subfractions are primarily presented by small dense particles [8].

Recent data indicate that high plasma level of atherogenic dense LDL is the symptom of insulin resistance (metabolic syndrome) [14].

Excessive body weight (*e.g.*, abdominal obesity) is a key factor that determines the development and course of insulin resistance and associated metabolic disorders [1,5,7]. During abdominal obesity adipose cells are resistant to the antilipolytic effect of insulin, which alters carbohydrate and lipid metabolism and affects fibrinolysis and endothelial function [5]. It remains unclear whether or not obesity is an independent risk factor. Metabolic changes observed during postprandial hyperlipidemia contribute to the development of cardiovascular and atherosclerotic diseases [9]. Particular attention is given to abdominal obesity related to decelerated clearance of triglyceride-rich lipoproteins after food load [6] associated with high ratio of small LDL in the plasma [9].

Here we studied LDL subfractions in patients with abdominal and gluteofemoral obesity after dietary fat load.

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MATERIALS AND METHODS

We examined 42 people (16 men and 26 women, 20-65 years) with normal body weight (n=9) and abdominal (n=24) or gluteofemoral obesity (n=9). Candidates were selected by the body weight index (BWI) and waist/hip ratio (W/H): normal body weight, 18.5 kg/m^2<BWI<25 kg/m^2; abdominal obesity, BWI≥25 kg/m^2, W/H>0.95 (men), W/H>0.80 (women); gluteofemoral obesity, BWI≥25 kg/m^2, W/H≤ 0.95 (men), W/H≤0.80 (women). Single standard meal (fat load) was given after 12-h starvation. The patients received emulsified fat (33% cream, 65 g per 1 m^2 body surface) and 50 g wheat bread. Energy value of this breakfast was 1300 kcal. The patients did not feed for the next 6 h. The blood was taken from the cubital vein 3 or 6 h after fat load. Blood plasma was analyzed at the day of sampling.

The composition of plasma LDL subfractions was studied by native gradient electrophoresis (3-12%) in polyacrylamide gel [13] using ICN Pharmaceuticals Inc. plates (catalogue No. 821619). The procedure was followed by densitometric scanning and data processing on an Amersham Pharmacia Biotech device with Image Scanner and Image Master TotalLab. 1d software. The standard mixture of high-molecular-weight proteins (HMW Native Marker Kit, Amersham Pharmacia Biotech) and lipoprotein standards isolated from the plasma by centrifugation were used for calibration. The size of standard LDL particles was estimated by electron microscopy study by the method of negative staining. LDL subfractions were assayed in the fasting state and 3 or 6 h after a food load. Samples taken from the patient were analyzed in 1 series (1 plate).

RESULTS

LDL subfractions obtained by densitometry of electrophoretograms of plasma samples were differently heterogeneous (Table 1). In people with normal body weight the number of LDL subfractions did not exceed 3. The spectrum had symmetrical shape with single major peak. Otherwise, it included two minor peaks positioned on either side of the major peak. The size of particles in subfractions varied from 210 to 278 Å. Slight asymmetry of the major peak in some samples was related to the presence of a small arm in the range of particles larger than the major peak. We observed 3 types of reactions in LDL subfractions 3 h after fat load: no changes in the composition of LDL; minimal shift of the major peak toward small or large particles; shift in the spectrum toward small particles due to disappearance of large particles. It should be emphasized that the size of particles remained practically unchanged. The composition of LDL in people with normal body weight returned to the initial state 6 h after fat load.

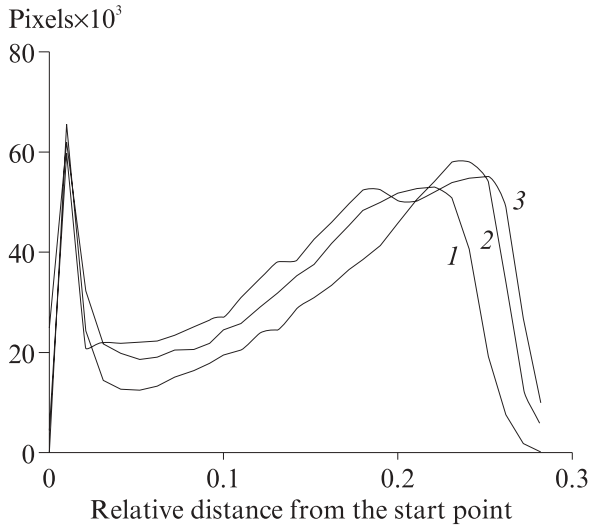

Fig. 1. Superposition of densitograms obtained after electrophoresis of plasma samples from patient with abdominal obesity in the fasting state (*1*) and 3 (*2*) or 6 h after fat load (*3*).

The number of LDL subfractions in patients with abdominal obesity before fat load was greater than in people with normal body weight (by 3-5, Table 1). In these patients major peak particles were smaller than in people with normal body weight. The major peak was shifted toward small particles 3 h after a fat load (Fig. 1). The average difference estimated from the sum of pairwise differences was 1.80±0.55 Å (d±σd). These changes persisted 6 h after fat load (2.10±0.87 Å).

TABLE 1. Plasma LDL Subfractions in People with Normal Body Weight and Patients with Various Forms of Obesity in Fasting State and after Single Fad Load

Group	Number of LDL subfractions	Particle size in subfractions, Å	Average size of major subfraction particles ($\bar{X}\pm S_x$)		
			fasting state	after 3 h	after 6 h
Normal weight (n=9)	1-3	210-278	244.0±7.5	243.0±8.4	242±8
Abdominal obesity (n=24)	3-5	205-300	227±10*	225.0±10.6*$^+$	225.0±9.9*$^{++}$
Gluteofemoral obesity (n=9)	3-4	205-300	230±11**	228.0±10.3**	230.0±11.4***

Note. *p<0.001, **p<0.01, and ***p<0.05 compared to people with normal body weight; ^+p<0.01 and ^{++}p<0.05 compared to the fasting state.

The size of LDL particles was similar in patients with gluteofemoral and abdominal obesity. However, in patients with gluteofemoral obesity LDL subfractions were less heterogeneous (3-4 peaks). In these patients major peak particles were smaller than in people with normal body weight and did not differ from major subfraction particles in patients with abdominal obesity. As differentiated from patients with abdominal obesity, the size of particles in patients with gluteofemoral obesity remained practically unchanged in the postprandial state.

Our results indicate that LDL subfractions in fasting patients with abdominal and gluteofemoral obesity are characterized by considerable heterogeneity and primarily presented by small particles (compared to people with normal body weight). The increase in the ratio of small dense particles in LDL subfractions indicates that patients with obesity are at high risk of cardiovascular diseases. Alimentary lipemia in patients with abdominal obesity is accompanied by most pronounced changes in LDL subfractions. In these patients the major peak of LDL is shifted towards small atherogenic particles.

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