MONOCLONAL LDL-APHERESIS IN A FEMALE PATIENT WITH FAMILIAL HYPERCHOLESTEROLEMIA

D. Nenov, A. Stoyanov, P. Chankova, V. Orbetzova, G. A. Konovalov

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Familial hupercholesterolemia (FH) results from a genetic defect of the receptors specific for low-density lipoproteins (LDL). Homozygotous forms of the disease are resistant to drug therapy. Atherosclerotic lesions first affecting coronary vessels set in rather early in such patients. That is why it is necessary to extract the lipids by means of extracorporeal methods of blood processing — e. g. plasma exchange, cascade plamapheresis, LDL-adsorption with sepharose. or precipitation with heparin, etc. when these forms of the illness are concerned Monoclonal technology based on an immune principle consisting in extraction of LDL only (because they are atherogenic) and in preservation of high-density lipoproteins (HDL) (because they are atheroprotective) seems to be the most advisable approach in this case (4).

The purpose of the present communication is to report our experience with LDL-apheresis introduction for the first time in Bulgaria and to consider some complications related to this treatment.

Material and methods

We treated a 10-year old girl, M. P. P., with homozygotous familial hypercholesterolemia. Prior to treatment, initial cholesterol level was over 40-mmol/l (in 1986)). LDL-apheresis was carried out every week for 2 years in the All-Union Institute of Cardiology, Academy of Medical Sciences of the Soviet Union, Moscow. Plasma was put through columns containing monoclonal LDL antibodies immobilized on sepharose. Plasma was obtained by centrifugation with an IBM-2997 apparatus (USA). Since September 1938, procedures were performed in the Nephrologic Clinic of the Higher Institute of Medicine in Varna. Plasma separation from blood cells was realized by means of plasma filters «Plasmaflux P-1» through two pumps. Column regeneration after LDL-apheresis was done with a solution containing glycine followed by washing with buffer solution and sterilization with solution containing sodium asyde.

Estimations of lipid profile prior to and after LDL-apheresis and of eluate was carried out by using of tests of «Boehringer» firm (GFR). Determination of osmotic resistance was done prior to LDL-apheresis.

Results and discussion

LDL-apheresis with monoclonal antibodies is an effective and highly specific therapeutic method for FH. In the course of 2-year treatment of the patient M. P. P., xanthomas located on her elbow joint have been almost completely resorbed (fig. 1 and 2).

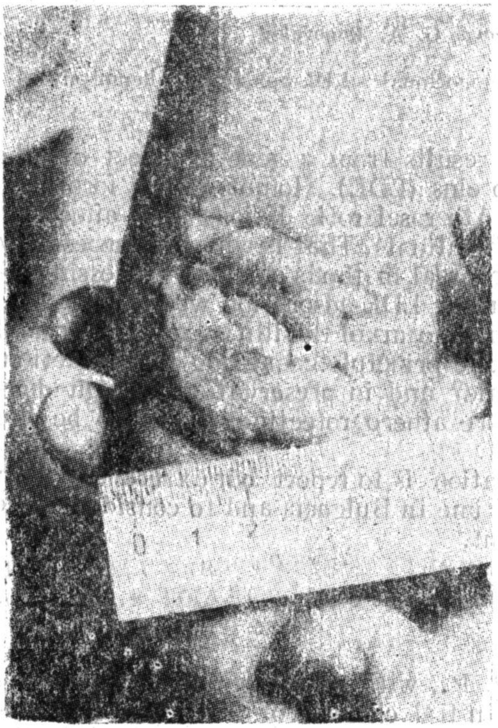

Fig. 1.

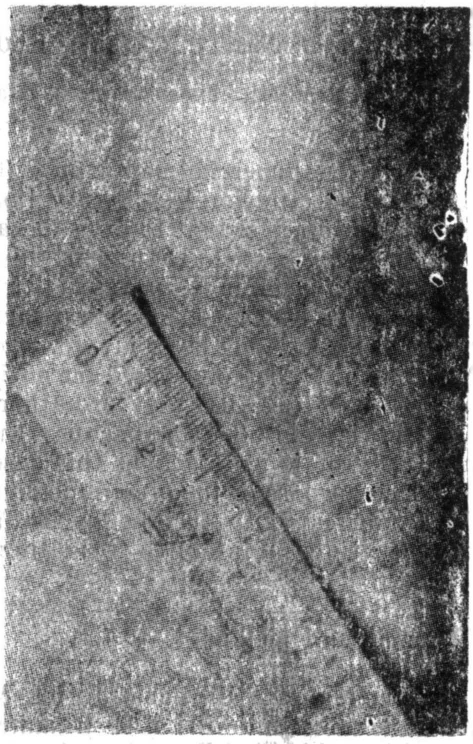

Fig. 2.

After LDL-apheresis, a considerable decrease of the total chlosterol (table 1) as well as of LDL-cholesterol, triglycerides and phospholipids and especialy of Apo B was seen (table 2). Hemolysis was often observed when «Plasmaflux P-1» filters were repeatedly applied. That was why we estimated erythrocyte osmotic resistance. It proved to be in normal limits: at the beginning — 0.50 per cent, and at the end — 0.28 per cent. We accept that the appearance of hemolysis during the repeated usage of «Plasmaflux P-1» filters is due to the stronger pressure created in them because of partial obturation from the previour plasmafiltration. A similar phenomenon, i. e. an event of consequent greater ultrafiltration has been described in cases of repeated usage of filter, durins hemodialysis. Hemolysis could be also caused by long lasting LDL-a-pheresi. itself. It is known that LDL bear about 50 per cent of serum vitamin E (1). Vitamin E plays an essential role for erythrocyte stability maintenance. It inhibits the peroxidation of polyunsaturated fatty acids which present a component of erythrocyte membrane. The increased vitamin E level induces also

Table 1

Plasma and eluate total choloesterol levels after regular treatment with LDL-apheresis

	Plasma, cholesterol in mmol/l		Decrease in %	Removed cholesterol — in mmol/l for one procedure
	prior to LDL- apheresis	after LDL- apheresis		
n	14	14	14	13
x	14.27	7.01	50.49	7.32
S	2.60	1.17	5.50	1.89
S	0.70	0.31	1.47	0.52

$P < 0.001$

alpha-tocopherol excess in the erythrocyte membrane that can reduce erythrocyte sensibility to osmotic hemolysis. Some authors (2, 6) report a successful treatment of renal anaemia with vitamin E. However, there are also opposite communications (3, 5). These data concern uremic patients on periodic hemodialysis.

As a further stage of our investigation an issue emerges concerning the determination of vitamin E level in patients with hyperlipemia treated for a long time with LDL-apheresis.

We can draw the following conclusions:

1. A successful treatment of FH patient by means of monoclonal LDL-apheresis is performed for the first time in Bulgaria.
2. A hemolysis complicating a long-lasting monoclonal LDL-apheresis treatment in FH patient is first reported.
3. It is supposed that one possible reason for hemolysis in FH patients on long-lasting LDL-apheresis could be vitamin E deficit due to extraction of LDL as bearer of 50 per cent of serum vitamin E concentration.

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Table 2

Effect of monoclonal LDL-apheresis on plasma lipoproteins in a patient with familial hypercholesterolemia

$x \pm Sx$	Total cholesterol mmol/l	HDL-cholesterol mmol/l	LDL-cholesterol mmol/l	Triglycerides mmol/l	Phospholipids mmol/l	APO-A g/dl	APO-B g/l
before	14.20±1.15	0.815±0.22	12.44±1.21	2.044±0.22	3.90±0.24	1.67±0.44	3.16±0.87
n	* 10	10	* 10	* 10	* 10	6	8
after	7.66±0.49	0.420±0.04	6.48±0.55	1.240±0.21	2.45±0.10	0.83±0.08	2.10±0.25
n	10	8	8	10	10	7	8

* — before: after with $p < 0.05$.