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INVESTIGATION PROCEDURES OF APOLIPOPROTEINS AT ARTERY HYPERTENSION PATIENTS AND EXPERIMENTAL DATA PROCESSING BY THE MULTIPLE CORRELATION METHOD

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ABSTRACT:
Some investigation procedures of apolipoproteins are presented in the framework of the paper and for the artery hypertension patients, the parameters of plasmatic lipoproteins were established. The values of APO A and APO B are expressed in function of the cholesterol value, HDL respectively LDL values and the age of the patient by the multiple correlations method.

KEYWORDS:
cholesterol, HDLc, LDLc, apolipoprotein Apo A, Apo B,
multiple correlations

1. GENERAL PRESENTATION OF INVESTIGATION MODELS

Modern studies on lipoproteins are based on ultra-centrifugation, which separates lipoprotein classes depending on volume and macro-molecular sizes.

Though exact assessment of plasma or serum density is pretty difficult as it depends on variations of total macromolecule level and of small molecule composition, it is generally estimated to have a density of 1.0063 g/ml.

Separating ultra-centrifugation accomplishes the isolation of each lipoprotein fraction. A more difficult problem is to separate exogenous kilo-microns from very low-density endogenous lipoproteins.

During preparative ultra-centrifugation there is a considerable redistribution if the salts from the upper part towards the lower part of the preparative test-tube whose density depends both on the nature and concentration of the salts and on the nature of centrifugation.

In case separation ultra-centrifugation is not followed by an analytical ultra-centrifugation, refractometry is the only assessment method of VLDL and LDL.

2. PARAMETERS ASSESSED

Plasmatic cholesterol and plasmatic tri-glycerides are a fraction of plasmatic lipids that circulate through blood vessels under the form of links with plasmatic proteins. This circulation is necessary as the different fractions of plasmatic lipids are not hydrosoluble and could result in accentuated plasma turbidity. For the plasma to have a clear and not turbid aspect, both cholesterol and tri-glycerides are linked under the form of synapses with plasmatic proteins. These links are called plasmatic lipoproteins.

Apolipoproteins A are the main protein components of high-density lipoproteins (HDL). Apo A is about 60% of the HDL proteins. It is known that Apo A supplies the structural component necessary for the formation of HDL. Apo A is also the agent responsible for the activation of lecithin cholesterol acyl-transferase (LCAT) that catalyses cholesterol esterification.

Apolipoprotein B (Apo B) is the main protein of low-density lipoproteins (LDL) covering about 90% of the LDL volume.

Calculus formulas for cholesterol and its fractions (HDLC and LDLc) are the following:

- for cholesterol

$$conc.colesterol = \frac{\Delta Asample}{\Delta As\tan dard} \times conc.s\tan dard$$

- for HDLc

$$conc.HDLc = \frac{\Delta Asample}{\Delta As\tan dard} \times conc.s\tan dard$$

- for LDLc

  conc. LDLc – conc. total cholesterol – conc. supernatant cholesterol (HDL + VLDL)

where A sample – variation of the sample absorbance
A standard – variation of standard absorbance

3. PROCESSING EXPERIMENTAL DATA

Within this study, we tested 15 patients with arterial hypertension every 3 months for the following: total cholesterol, triglycerides, HDL, LDL, APO A. APO B. Another parameter known and used in calculus is patients' age.

The bottom idea of this work is assessing by mathematical calculus apolipoproteins APO A and APO B in relation to secondary parameters easily to assess experimentally, i.e. total cholesterol, HDL and LDL, and age of the patients, as we know that experimental assessment of these parameters is difficult and costly. We have used the multiple correlation method.

We shall note the main parameters APO A (APO B) by y and secondary parameters as follows: total cholesterol by x_1, HDL (LDL) by x_2, and age by x_3. The equation of linear multiple regression of the 4 parameters can be expressed as (1).

$$Y(x_1, x_2, x_3) = a_0 + a_1 \cdot x_1 + a_2 \cdot x_2 + a_3 \cdot x_3 \qquad (1)$$

After processing experimental data after the known methodology [1], we calculated the mean square deviation of measured values y compared to values calculated with the help of regression equation Y (δ^2) and of the multiple correlation coefficient (R).

Results obtained are shown in Table 1.

Table1

Time	Ecuaţion regresion multiple liniar		σ^2	R
0	APO A	$Y=201,745+0,011x_1+0,834x_2-1,638x_3$	12,003	0,757
	APO B	$Y=-41,095-0,05x_1+0,742x_2+1,436x_3$	16,16	0,913
3 month	APO A	$Y=5,699+0353x_1+1,253x_2-0,395x_3$	19,052	0,803
	APO B	$Y=115,575+0,087x_1+0,392x_2-0,91x_3$	17.128	0,741
6 month	APO A	$Y=-11,37+0,018x_1+0,102x_2+2,477x_3$	33,414	0,410
	APO B	$Y=75,028+0,185x_1+0,198x_2-0,164x_3$	13,096	0,671

As one can see in Table 1, the values of mean square deviations and of multiple correlation coefficients are not satisfactory, therefore linear multiple regression equations cannot be applied for the calculus of main parameters APO A and APO B in relation to secondary parameters. We went on to a non-linear multiple correlation of the order 2 of the form (2):

$$Y(x_1, x_2, x_3) = a_0 + a_1x_1 + a_2x_2 + a_3x_3 + a_4x_1^2 + a_5x_2^2 + a_6x_3^2 + a_7x_1x_2 + a_8x_2x_3 + a_9x_3x_1 \qquad (2)$$

Coefficients a_0, a_1,…,a_9 are called coefficients of regression function. They are determined with the help of the least square method so that dispersion of deviation of values assessed experimentally y compared to values determined with the help of regression equation (1) be minimal. After calculating in accordance with the algorithm presented in paper [2] we got the following non-linear correlation function of the order 2.

3.1. Time $t_0=0$

Parameter APO A

$$Y = 317,899 + 1,115x_1 - 3,776x_2 - 4,654x_3 - 3,2 \cdot 10^{-3}x_1^2 - 0,022x_2^2 + 1,2 \cdot 10^{-3}x_3^2 + 0,013x_1x_2 + 0,072x_2x_3 - 7,1 \cdot 10^{-3}x_3x_1$$

The square average deviation: $\sigma^2=6,457$

The multiple correlation coefficient: R=0,936

Parameter APO B

$$Y = 959,582 - 16,482x_1 + 17,093x_2 - 5,375x_3 - 0,035x_1^2 - 0,064x_2^2 - 0,133x_3^2 + 0,101x_1x_2 - 0,36x_2x_3 + 0,31x_3x_1$$

The square average deviation: $\sigma^2=8,933$

The multiple correlation coefficient: R=0,974

3.2. Time t_1=3 month

Parameter APO A

$$Y = -256{,}831 - 0{,}876x_1 - 7{,}68x_2 + 19{,}997x_3 + 3{,}9 \cdot 10^{-3}x_1^2 - 0{,}011x_2^2$$
$$- 0{,}164x_3^2 + 0{,}024x_1x_2 + 0{,}091x_2x_3 - 0{,}026x_3x_1$$

The square average deviation: σ^2=16,895

The multiple correlation coefficient: R=0,849

Parameter APO B

$$Y = 2{,}4 \cdot 10^{-3} + 4{,}241x_1 - 10{,}74x_2 - 68{,}11x_3 - 0{,}019x_1^2 + 0{,}03x_2^2$$
$$+ 0{,}487x_3^2 + 0{,}051x_1x_2 + 0{,}108x_2x_3 - 0{,}033x_3x_1$$

The square average deviation: σ^2=10,679

The multiple correlation coefficient: R=0,908

3.3. Time t_2=6 month

Parameter APO A

$$Y = -956{,}528 + 7{,}233x_1 + 17{,}06x_2 - 2{,}076x_3$$
$$- 0{,}021x_1^2 - 0{,}045x_2^2 + 0{,}231x_3^2 - 0{,}067x_1x_2 - 0{,}367x_2x_3 - 0{,}039x_3x_1$$

The square average deviation: σ^2=20,756

The multiple correlation coefficient: R=0,824

Parameter APO B

$$Y = -256{,}119 + 1{,}236x_1 - 3{,}557x_2 + 14{,}994x_3 + 0{,}023x_1^2 - 6{,}4 \cdot 10^{-3}x_2^2$$
$$- 0{,}03x_3^2 - 9{,}5 \cdot 10^{-3}x_1x_2 + 0{,}107x_2x_3 - 0{,}131x_3x_1$$

The square average deviation: σ^2=8,865

The multiple correlation coefficient: R=0,865

4. CONCLUSIONS

The results presented in paragraph 4 show that mean square deviations of the values measured y compared to values calculated with the help of the multiple regression equation of the order 2 (Y) and multiple correlation coefficients have rather good values, which leads to the conclusion that main parameters APO A and APO B can be calculated depending on total cholesterol, HDL and LDL, and patients' age, using correlation functions Y.

From a medical point of view, the calculus method presented has first of all an economic advantage. It is known that experimental assessment of the value of apolipoproteins is very costly. Using this calculus method, parameters APO A and APO B no longer need to be determined experimentally, but they can be calculated very accurately in relation to secondary parameters whose assessment is simple and cheap.

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