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METABOLIC DISORDERS IN HIV-INFECTED PATIENTS RECEIVING ANTIRETROVIRAL THERAPY

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Background

Hypertriglyceridemia, increased levels of very low density lipoproteins (VLDL), decreased levels of high density lipoproteins (HDL) and increased levels of proatherogenic apolipoproteins are typical types of lipid spectrum disorders in HIV-infected people. With the progression of HIV infection, levels of total cholesterol (TC), low-density lipoproteins (LDL) and HDL decrease, and triglycerides (TG) – increase. The most powerful influence on lipid metabolism have traditional risk factors (heredity, age, lifestyle, non - compliance with diet, smoking, alcohol abuse, low physical activity, concomitant diseases-hypertension, diabetes, obesity, etc.).
Art also contributes to lipid and carbohydrate disorders. Dyslipidemia, which occurs in 70-80% of patients from the first months of treatment, refers to early complications of treatment and most often includes hypertriglyceridemia, as well as its combination with hypercholesterolemia. In addition, drug dyslipidemia is characterized by increased LDL and VLDL levels. Insulin resistance and hyperglycemia develop in 5-46% of patients taking PI, but diabetes occurs only in 1-11% of patients, while insulin therapy is required even less frequently (except for patients with a genetic predisposition to diabetes).

The objective

Evaluation of lipid and carbohydrate metabolism in HIV-infected patients depending on antiretroviral therapy (ART) and its duration.

Patients and methods

Analysis of lipid and carbohydrate metabolism in 229 adult HIV-infected patients.The first group included 44 patients who had never taken ART. The second group included 29 patients who received ART less than 1 year. Patients of the 3rd group (156 patients) received antiretroviral therapy for 3 to 9 years. The compared groups were equivalent in terms of sex distribution, age, Smoking rate (41-44%), proportion of patients with elevated body mass index (BMI), ART regimens (55-57% received efavirenz (EFV), 31-33% - lopinavir/ritonavir (LPV/r)), i.e. the main parameters that could affect the results of the study. Median CD4 + lymphocytes in the three groups ranged from 438 to 493 cells/μl. None of the patients took lipid-lowering drugs. Among patients who took art for a long time, 8 people (5.1%) had systolic blood pressure more than 140 mm Hg. article some patients long-term treated (group 3), the scheme of ART has already been adjusted according to their lipid profile before the start of the study, and were assigned hypo cholesterol diet.
Assess changes in body composition and fasting laboratory parameters: total cholesterol, triglycerides, high density lipoprotein, low density lipoproteins, very low density lipoproteins, apolipoprotein B (APO B), atherogenic index (AI), and plasma levels of glucose, insulin, and glycosylated hemoglobin. Calculated 10-year risk of cardiovascular disease Framingham scale.

Results

During the first year of ART exacerbates lipid disorders caused by HIV, particularly affecting the level of TG and HDL. During treatment, a partial adaptation of patients to antiretroviral drugs, which helps in recovery of these indicators.
We noted a gradual increase in the level of TC in the appointment of art and increase its duration to 3-9 years. Median TC was 4.16, 4.57 and 5.26 mmol / l (in groups 1, 2 and 3, respectively, $p<0.05$) (Fig.1). Even more significant differences were obtained in the proportion of patients with exceeding the upper limit of the norm (ULN) TC was observed in 13.6%, 24.1% and 46.2% of patients in three groups, respectively. Patients who did not receive ART had an increase in TC only 1 degree, while 2-3 degree of deviation of this parameter was registered in 13.8% of patients of the 2nd group and in 23.7% of patients of the 3rd group.

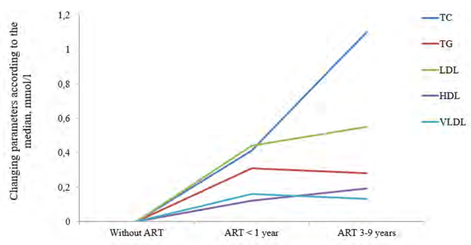

Fig.1. Changes in the median lipid metabolism in patients with HIV infection, depending on the duration of ART.

The median level of TG did not exceed normal values in all groups. The highest proportion of patients with excess of ULN was recorded among those taking ART (41.4% and 34.6% in groups 2 and 3, compared with 6.8% in group 1, $p<0.05$). At the same time, the percentage of patients with excess of ULN level of TG was significantly higher in the group of patients treated for less than a year than in patients with longer ART. Hypertriglyceridemia in the appointment of therapy can be explained by the use of LPV/r in a third of patients.

Significant differences in the average HDL level were obtained only in patients who were not treated (group 1, 1.16 mmol/l) and long-term ART (group 3, 1.35 mmol/l, $p<0.05$). However, a decrease in the level of HDL in 62% of patients who have recently started receiving ART was found, but in the group of patients with longer therapy their share decreased to 22%, which may indicate the restoration of this indicator in some patients to almost the initial values. At the same time, some patients receiving ART less than a year, recorded a significant increase in the level of HDL (mainly, it concerned patients receiving LPV/r).

IA above ULN recorded in 47.7% of patients without art and 44.8% of patients receiving art less than 1 year. In longer-term therapy, IA was elevated in 59% of patients.

LDL levels increased in the appointment of art and during treatment (median-2.46, 2.9 and 3.01 mmol/l in the 1st, 2nd and 3rd groups, respectively, $p<0.05$) (Fig.1). From one third to one half of patients had increase LDL levels above ULN. Only 1 degree of increase in LDL level was registered in the 1st group, 17.2% of patients in the 2nd group had 2 degree of change in the studied parameter, in the 3rd group-in 12.2% observed 2 degree and in 3.8%-3 degree of increase in LDL level. The levels of VLDL and ARO B changed insignificantly.Only 7-10% of patients of the 2nd group and 3-7% of patients of the 3rd group had the increase of these indicators.

None of the patients who did not receive ART had deviations from the norm.
Lipohypertrophy was detected only in 1 patient who received LPV/r for 4 years, which led to the replacement of the drug with etravirine.
In 90% of patients, the risk index for cardiovascular disease (the Framingham scale) was low (up to 10%). But with an increase in the duration of ART, the proportion of patients with average risk (10-20%) increased from 6.9% to 8.8% (Table.1). One patient who received therapy for 4 years and was obese had a high risk (more than 30%). On the basis of the obtained risk index, 14 patients were given recommendations for changing the diet and 2 patients changed the ARV scheme.

Table1. The risk index for cardiovascular disease (the Framingham scale)

The risk of cardiovascular disease	Group 1 Without ART (n=42)	Croup 2 ART < 1 year (n=29)	Group 3 ART 3-9 years (n=125)
Low (<10%), n (%).	42 (100)	27 (93,1)	113 (90,4)
Middle (10-20%), n (%)	0	2 (6,9)	11 (8,8)
High (>20%), n (%)	0	0	1 (0,8)

Men showed more significant deviations of lipid metabolism parameters than women: levels of TG (40.6% in men and 20.7% in women), LDL (58.5% in men and 37.3% in women) and VLDL (11.1% in men and 1.8% in women). Men were 1.5 times more likely to have a decrease in HDL, so their IA was higher (3.55 compared to 2.56 in women, $p<0.05$). Men were more likely to receive EFV (59.8%) and women to receive LPV/r (50.8%). In addition, the proportion of smokers among men was significantly higher than among women (53.6% and 28.8%, $p<0.001$).

Table 2. Influence of risk factors on lipid metabolism in patients with HIV infection (OR).

Parameters of lipid metabolism (OR: 95%, CI)	Risk factors				
	ART > 3 years	EFV	LPV/r	Male gender	Smoking
Increase TC	7,39 (6,47-8,31)	Not affects	Not affects	Not affects	Not affects
Increase TG	7,24 (6,02-8,46)	Not affects	3,8 (3,03-4,57)	2,4 (1,33-3,47)	Not affects
Decrease HDL	Not affects	2,01 (0,88-3,14)	Not affects	1,55 (0,11-2,99)	1,56 (0,85-2,27)
Increase LDL	1,88 (1,18-2,58)	Not affects	Not affects	Not affects	Not affects
Increase VLDL	3,26 (1,16-5,36)	Not affects	3,53 (2,12-4,94)	5,51 (3,41-7,61)	3,46 (2,26-4,66)
Increase AI	1,57 (0,9-2,24)	2,26 (1,41-3,11)	Not affects	1,84 (1-2,68)	1,67 (0,97-2,37)
Increase APO B	Not affects	Not affects	Not affects	Not affects	6,64 (4,47-8,81)

Increases the level of TC LDL, VLDL, which leads to an increase in IA. Males were significantly more frequently than women increased levels of triglycerides, VLDL, IA, and reduced HDL levels. Appointment of EFV help reduce cholesterol and improve IA and LPV/r- raise TG and VLDL. Smoking affects, albeit to a lesser extent, an increase in the concentration of VLDL apo B, IA and decreased concentrations of HDL (Tabl.2).

Disorders of carbohydrate metabolism encountered when using ART substantially less (8-10%) in combination with other risk factors lead to the development of diabetes in 1.6% of patients.EFV had a greater impact on carbohydrate metabolism than LPV/r, although the frequency of deviations from the norm was small (5-11%). Thus an adverse effect of EFV was significantly more evident among men.

Conclusion

Necessary to select ART scheme, having the least impact on lipid levels and advise patients to give up smoking. In case of apparent abnormalities in the process of therapy can correct mode of ART and / or lipid-lowering drugs to appoint. Routine screening of patients is important for timely diagnosis of impaired glucose tolerance, diabetes, insulin resistance and of corrective actions.

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