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THE EFFECT OF ANTIRETROVIRAL DRUGS ON CARBOHYDRATE METABOLISM

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ABSTRACT

It's no secret that with the development of information technology, many ethical problems of biom Human immunodeficiency virus infection is one of the most common diseases on earth. The use of antiretroviral therapy in patients with this infection prolongs the life of patients and reduces the risk of serious complications. However, this category of patients has cases of type 2 diabetes mellitus, which is associated with the natural course of the disease and the use of antiretroviral therapy. In our study, we studied the cases of carbohydrate metabolism and insulin resistance in patients with human immunodeficiency virus.

Key words: antiretroviral therapy, diabetes mellitustype 2, human immunodeficiency virus.

INTRODUCTION

Topicality. The evolution of antiretroviral drugs and their introduction into medicine have completely changed the clinical prospects of HIV-infected people (2,7). The use of these drugs over the past 25 years has significantly reduced the mortality of patients from this disease (6). Lipopolysaccharides circulating in the blood, proliferating cytokines, and intracellular mechanisms activate serine kinase, resulting in serine phosphorylation in IRS-1 insulin receptors. This leads to a decrease in the control of insulin distribution (1,3).

Translocation of lipopolysaccharides and an increase in their serum levels cause innate and adaptive activation of the immune system. In macrophages and many tissues, lipopolysaccharides bind and activate with TLR4, which causes

insulin resistance and systemic inflammation, causing the JNK and NF-kB chain. In addition, lipopolysaccharides cause an increase in adipose tissue and an increase in body weight. An increase in the amount of lipopolysaccharides even as a result of endothelial dysfunction and metabolic disorders in HIV-infected people causes a deeper destabilization of the process (5,8).

It is known that there is a relationship between the activation of the immune system and insulin resistance, which is involved in the control of carbohydrate metabolism and dyslipidemia. Activation of the immune system causes chronic inflammation, which is consistent with the severity of the disease in patients who received and did not receive antiretroviral therapy. This is once again evidenced by the high level of proliferating cytokines in the blood serum of HIV-infected people (FNO, IL-6 and IL-1ß) (4).

In patients infected with HIV, but not receiving antiretroviral therapy, there is marked insulin resistance, increased levels of lipopolysaccharides and cytokines in blood serum, liver, hypothalamus, muscles, blood vessels and adipose tissue. Due to the effect of ART, the level of lipopolysaccharides and cytokines decreases.

It is noteworthy that the constant activation of the immune system and insulin resistance increase the risk of developing obesity, dyslipidemia, cardiovascular diseases, neurocognitive disorders, bone conditions and oncogenic diseases not related to HIV. The development of these complications depends on hereditary and environmental factors, each case can aggravate another condition and increase the risk of HIV infection by several times (9).

Obesity and visceral adiposition are often observed in patients receiving ART. Such obesity occurs as a result of inflammatory and metabolic reactions. Although a decrease in muscle mass is observed in HIV-infected people, the accumulation of adipose tissue is also observed in patients with normal TVI.

Recently, it is known that when monitoring HIV-infected people, there is an excess of body weight by 60-70%. This indicates harmful metabolic disorders with a predominance of visceral obesity among patients (10). Thus, lifestyle changes and pharmacological procedures are aimed at eliminating the aforementioned metabolic disorders. The study of insulin resistance in the body of an HIV-infected person, factors of predisposition to the development of type 2 diabetes mellitus is one of the urgent problems of modern medicine.

The aim of the survey: to study the effect of various groups of antiretroviral drugs on carbohydrate metabolism.

Materials and methods of research: 134 HIV-infected patients aged 18 years and older were taken for the study. Patients of the third and fourth stages of HIV infection (acquired immunodeficiency virus) were taken for examination in a

specialized infectious diseases hospital at the Research Institute of Virology and the Republican AIDS Control Center. Exclusion criteria: patients with type 1 and type 2 diabetes mellitus, patients at the stage of AIDS (acquired immunodeficiency syndrome), under the age of 18, over the age of 70, who had cirrhosis of the liver, autoimmune and acute inflammatory diseases, chronic alcoholics, unspecified hemoglobinopathies (taking into account the effect on glycated hemoglobin), patients with severe concomitant somatic diseases were not examined.

All patients underwent physical examination, including waist circumference, hip circumference, abdominal index, body mass index; laboratory tests (biochemical blood analysis: glucosanaccharide, glycated hemoglobin, insulin, Homa index). All patients received medications as part of ART, tests to determine the amount of CD4 viral load.

All the examined patients took the drug according to several schemes as an antiretroviral drug. Of these, patients in group 1 took nevafirenz (EFV) from the group of nucleoside reverse transcriptase inhibitors (RTNI) (lamivudine (ZTC), zidovudine (AZT), abacovir (ABC), Tenofovir (TDF)) in addition to drug 2 from the group of nucleoside reverse transcriptase inhibitors (RTNI). Additional protease inhibitors were applied to drug 2 from the group of reverse transcriptase nucleoside inhibitors (RTNI) in group 2 patients. Patients of group 3, in addition to drug 2 from the group of reverse transcriptase nucleoside inhibitors (RTNI), use the drug nevirapine (NVP) from the group of reverse transcriptase nucleoside inhibitors (RTNI). The results were analyzed in the context of all groups according to the duration of taking the drug ART.

Results: Group 1 patients comprise 85 people, 52 are recipients who have been taking ART for about 6 years, and 33 for more than 6 years.

Table 1

Clinical description of patients in the Group 1 according to the duration of ARVT

Indicators	**ARVT up to 6 years n=52**	**ARVT more than 6 years n=33**
Age, years	42,8±1,18	46.1±1.23
Duration of HIV, year	6.0±0.48	11.6±0.46
Waist circumference, cm	102.7±1.94	97.7±1.89
Hip circumference, cm	104.5±1.43	102.7±1.73
Abdominal intex	1.0±0.02	1.0±0.02
Body Mass Index	24.4±0.63	24.8±0.63
CD4	248.5±28.5	353.6±22.5*
Viral load	585.746±32.9	3078±1076**

Note: * - reliability level ($p<0.05$), ** - reliability degree ($p<0.01$).

According to Table 1, the patients did not differ sharply in abdominal index and body mass index. In those who took ART for more than 6 years, you can see a significant difference in viral load ($p<0.01$) and the number of CD4 lymphocytes ($p<0.05$). To study the indicators of carbohydrate metabolism in patients of this group, liver glycemia, glycated hemoglobin, liver insulin and the Homa index were studied (Table 2).

Table 2

Indicators of carbohydrate metabolism and insulin resistance in patients of Group 1

Indicators	**ARVT up to 6 years n=52**	**ARVT more than 6 years n=33**
Hyperemia	5.1±0.19	5.1±0.19
Glycated hemoglobin	5.8±0.12	5.9±0.12
Insulin resistance	16.5±0.59	17.8±0.51*
HOMA index	3.7±0.18	4.0±0.16

Note: * - reliability level ($p<0.05$)

In group 1 patients, there was no significant difference in glycemia and glycated hemoglobin, however, in patients who received ART for more than 6 years, the insulin content significantly increased.

There were 23 patients of the 2nd group, including 12 men and 11 women. The clinical characteristics of patients are presented in the following table (Table 3):

Table 3

Clinical description of patients in the group 2 according to the duration of ARVT

Indicators	**ARVT up to 6 years n=9**	**ARVT more than 6 n=14**
Age, years	47,8±1,14	43.0±1.11
Duration of HIV, year	8.9±0.82	10.0±0.34
Waist circumference, cm	95.9±2.30	93.0±1.9
Hip circumference, cm	104.4±1.20	96.4±3.5
Abdominal intex	0.9±0.02	1.2±0.18*
Body Mass Index	24.4±0.40	24.9±0.62
CD4	331.0±21.9	339.6±29.8
Viral load	8939.3±114.9	1274.8±127.6**

Note: * - reliability level ($p<0.05$), ** - reliability degree ($p<0.01$).

We can see that the abdominal index increased in group 2 patients who took antiretroviral drugs for more than 6 years. This led to the fact that taking medications reduced the viral load from 8939.3±114.9 to 1274.8±127.6 ($p<0.01$). The results of carbohydrate metabolism indicators are shown in Table 4.

Table 4

Indicators of carbohydrate metabolism and insulin resistance of Group 2 patience

Indicators	ARVT up to 6 years n=9	ARVT more than 6 n=14
Hyperemia	6.5±0.14	6.4±0.12
Glycated hemoglobin	6.3±0.15	7.0±0.10*
Insulin resistance	21.9±0.63	22.0±0.52
HOMA index	6.4±0.23	6.3±0.24

Note: * - reliability degree (p<0.05).

In group 2 patients, there was a slight increased severity of carbohydrate metabolism disorders. At the same time, it was noted that spring glycemia is higher than the standard indicators, regardless of the duration of ART. The use of protease inhibitors in group 2 patients reliably showed that the glycated hemoglobin index was higher (P<0.05) in the group with an ART duration of more than 6 years. The Homa index, however, did not differ much in the groups by the duration of ART.

Group 3 patients are recipients of the neurotransmitter nevirapine from the group of non-nucleoside reverse transcriptase inhibitors in addition to nucleoside reverse transcriptase inhibitors as an antiretroviral agent. This group included 13 patients, of which 5 were women and 8 were men.

Table 5

Clinical description of patients in the group 3 according to the duration of ARVT

Indicators	ARVT up to 6 years n=5	ARVT more than 6 years n=8
Age, years	31.6±1,38	40.3±0.38
Duration of HIV, year	9.8±0.44	12.8±0.61
Waist circumference, cm	101.6±1.69	101.6±1.49
Hip circumference, cm	106.4±0.67	105.5±1.96
Abdominal intex	1.0±0.01	1.0±0.02
Body Mass Index	25.3±0.37	25.6±0.47
CD4	197.4±18.1	368.7±25.9**
Viral load	7758.2±2136.7	1975.0±420.9**

Note: ** - reliability degree (p<0.01).

In group 3 patients, taking these drugs led to a significant increase in the number of CD4 lymphocytes (p<0.01), a decrease in viral load (p<0.01) from 7758.2±2136.7 to 1975.0±420.9.

Table 6

Carbohydrate metabolism and insulin resistance indicators in the group 3 patients

Indicators	ARVT up to 6 years n=5	ARVT more than 6 n=8
Hyperemia	5.6±0.13	5.5±0.11
Glycated hemoglobin	6.3±0.11	6.2±0.10
Insulin resistance	19.8±0.53	19.8±0.34
HOMA index	4.9±0.20	4.9±0.15

Indicators of glycemia and insulin resistance in patients of group 3 did not significantly differ in the duration of ART.

The results show that the indicator of non-oligoglycemia is higher in patients of the 2nd group. This differs from other groups more closely related to the action of protease inhibitors used in this group. In patients of all groups, a sharp excess of the Homa index over the normative indicators (≤ 2.7) was revealed. This means that patients develop insulin resistance conditions regardless of the duration of ART, body mass index, etc.

Conclusion.

1. The antiretroviral drugs used in the whole group led to an increase in the number of CD4 lymphocytes and a reliable decrease in viral load.

2. Patients of group 2 who were treated with additional protease inhibitors of group 2 from the group of reverse transcriptase nucleoside inhibitors (RTNI), compared with other groups, had higher glycaemia.

3. The Homa index, which characterizes insulin resistance in all groups, recorded results sharply exceeding the normative ones.

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