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EVALUATION OF ARVT LONG-TERM OUTCOMES IN HIV PATIENTS. GHOST OF LITERATURE

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Abstract
There is a growing interest in the pathogenesis, treatment, prevention of long-term complications and therapy of HIV infection. Studies of treatment complications from the cardiovascular system, kidneys, bones and adipose tissue are being conducted. These clinical problems appeared almost simultaneously with antiretroviral therapy, they continue to be important and may become even more relevant in the future. The article discusses the risk factors for the most common complications of antiretroviral therapy for HIV infection, as well as therapy for coinfection with tuberculosis, hepatitis and influenza.

Keywords: HIV infection, antiretroviral therapy, complications of antiretroviral therapy.

Introduction

The human immunodeficiency virus (HIV), when infected, affects macrophages, microglia and lymphocytes, which form the body's immune responses. This contributes to the development of acquired immunodeficiency syndrome (AIDS), which, in turn, makes the body defenseless against all kinds of secondary, including opportunistic, infections, as well as malignantly altered cells. HIV can provoke severe autoimmune conditions and neurological disorders due to direct damage to neurons and immunocompetent cells. Currently, HIV infection is widespread throughout the world, and a decrease in infection is not expected, despite educational and preventive work. The high social significance of this disease, the need of patients for social adaptation and psychological support, prompted the implementation of therapy and rehabilitation of patients under the supervision and with the support of state programs [1]. The main direction in the treatment of HIV infection is the use of drugs that reduce the ability of HIV to reproduce - antiretroviral drugs [2]. The most common antiretroviral drugs are: NIOT (nucleoside transcriptase inhibitors) of various groups: retrovir, zerit, chivid, videx, ziagen, combined drugs (trizivir, combivir); NNIOT (non-nucleotide reverse transcriptase inhibitors): viramune, stockrin, estaverine; protease inhibitors: norvir, inviraza, prezista, viracept and others; integrase inhibitors (raltegravir, dolutegravir); fusion inhibitors: fureson; receptor antagonists (maraviroc). Antiviral therapy is prescribed for life, and its success depends on the patient's discipline and following the recommendations. HIV-infected people live an average of 10-12 years, and die from both concomitant opportunistic infections and complications of antiviral therapy. The purpose of the study: to analyze the results and complications of antiretroviral therapy according to foreign studies.

Research methodology: an analysis of the literature with an emphasis on studies that take into account the risk factors of complications from the main organs and systems. Currently, various non-invasive

methods are used to study the pathogenesis and identify risk factors for the development of complications of antiretroviral therapy in HIV-infected people [2]. The results may vary depending on which modality and specific measurements are used. Some of these methods are limited for use in research settings, while others may have direct clinical applications. Some current research focuses on quantifying the contribution of risk factors associated with diseases that contribute to the risk of complications in HIV infection. We have reviewed some groups of diseases that are most common in antiretroviral therapy (ART). Results. 1. Cardiovascular complications as the most common cause of death in HIV-infected people with ART. HIV-infected patients often have elevated triglyceride levels, which is caused by both untreated HIV infection and exposure to the drug ritonavir. The independent role of triglycerides was evaluated in a large data collection study on the adverse events of antiretroviral drugs (DAD), which confirmed the role of triglyceride levels as an independent risk factor for myocardial infarction (MI) in a group of 33,308 patients and 580 cases of MI in them.

Other known risk factors for cardiovascular diseases (FR CVD), namely the levels of high-density lipoproteins (HDL) and total cholesterol (OH) increased the risk of MI in HIV-infected people [3, 13, 16]. The most common and potentially modifiable type of CVD is smoking. When analyzing the data obtained in DAD, it was confirmed that the risk of CVD was reduced in those who quit smoking 3 years after quitting smoking, compared with smokers. These results provide concrete facts to justify smoking cessation for HIV-infected people [3]. Visceral adipose tissue disorders and lipoatrophy are common problems for those who receive antiretroviral therapy (ART) for a long time. The volume of visceral fat measured by computed tomography plays a role in the development of CVD in infected patients, but this issue has not been studied well enough. The study of the relationship between CVD and visceral fat volume and general obesity in a cohort of HIV-infected people with coronary heart disease in a longitudinal study showed that there is such a connection. These results suggest that measures to reduce the amount of visceral fat promise to reduce the incidence of CVD in HIV-infected people [16].

There is great interest in the role of biomarkers in predicting CVD and other serious complications in patients receiving ART. A case-control study found a link between serum biomarkers and CVD (52 events per 2000 patients, since 1995). When analyzing blood serum samples 2-3 years before the event of MI, acute coronary syndrome, coronary revascularization, stroke or other, after adjusting for traditional cardiac risk factors, the level of D-The dimer was higher than in the control group [12]. No association has been found between the level of serum C-reactive protein (CRP) and the development of CVD in HIV-infected people with ART. Other risk factors (vascular cell adhesion molecule 1 (VCAM-1), intercellular adhesion molecule 1 (ICAM-1), amyloid A and tumor necrosis factor alpha (TNF-α) were investigated, and they were not found to be associated with cases of the disease compared with control subjects [16]. Although these results are not strong enough evidence to facilitate routine monitoring of D-dimer levels in clinical practice, they confirm earlier studies that demonstrated an association between D-dimer levels and all-cause mortality in HIV patients, and highlight the potential role of blood clotting disorders in increasing cardiovascular risk in HIV-infected patients [12].

Biomarker concentrations were correlated with Framingham risk scores (FRSs) and it was found that higher levels of high sensitivity biomarkers (hs)-CRP, interleukin-6 (IL-6) and lipoprotein-associated phospholipase A2 (Lp-PLA2) were observed in the subgroup with higher FRSs at the initial stage and in the process observations. It is unknown whether any of these biomarkers add predictive value to FRSs [3]. N-terminal pro-B natriuretic peptide (NT-proBNP) is a marker of diagnosis and prognosis of heart

failure and a predictor of CVD in the general population. In the study of the strategy of antiretroviral therapy (SMART), a case control study was conducted and it was found that higher baseline levels of NT-proBNP are predictors of CVD.

Although higher levels of amyloid P were observed in abacavir recipients at week 24, there was no consistent pattern between any of the biomarkers and abacavir exposure [10]. In an in vitro study using a human endothelial cell culture system, it was found that exposure to abacavir induces activation of the leukocyte integrin Mac-1, which then interacts with its ligand ICAM-1. This interaction between abacavir and leukocyte activation can potentially lead to accumulation of leukocytes in the endothelium. However, as noted above, no statistically significant changes in ICAM-1 levels were observed in patients treated with abacavir in vivo. A relationship was found between the activation of T cells measured by CD38+HLA-DR+ markers on CD4+ and CD8+ T cells, as well as the marker of aging of T cells (CD57+CD28 -). It was found that markers of activation and aging are associated with the elasticity of the carotid arteries and the presence of damage to the carotid arteries. Together, these studies further support the hypothesis that ongoing inflammation, as well as traditional risk factors, may contribute to the risk of developing CVD in HIV-infected patients. An in vitro study of human coronary artery endothelial cells showed that exposure to ritonavir or lopinavir plus ritonavir is associated with increased expression of the aging protein prelamin A, decreased nitrous oxide production and increased oxidative stress, which suggests a possible mechanism by which these drugs may contribute to the development of early CVD in vivo [9].

The Study to Understand the Natural History of HIV/AIDS in the Era of Effective Therapy (SUN) measured the overall carotid progression of CMM in a large 4-center study of 424 infected patients and found lower rates of progression of CMM thickness in patients who maintained the level of viral particles in blood plasma below 400 copies/ml per throughout the entire observation. Among HIV-infected patients, those who received initial reverse transcriptase inhibitor (NNRTI) therapy with a non-nucleoside analogue had lower rates of progression of CMM thickening. A combined analysis of 3 cross-sectional studies of total carotid CMM revealed male sex, old age, high low-density lipoprotein (LDL) cholesterol, smoking and prolonged exposure to ritonavir as factors associated with carotid BMI, confirming observations from earlier longitudinal studies. These data complement the information suggesting that suppression of HIV RNA levels in blood plasma and, possibly, specific antiretroviral therapy regimens may help reduce the long-term risk of developing CVD [3]. 2. Kidney diseases. Although uncontrolled HIV replication is harmful to the kidneys, antiretroviral drugs are also nephrotoxic. Several cohort studies have been aimed at clarifying the contribution of HIV treatment in general, as well as specific antiretroviral drugs, to the development or progression of renal failure [3, 13, 15]. The Centers for AIDS Research Network of Integrated Clinical Systems (CNICS) study demonstrated an improvement in glomerular filtration rate (GFR) in patients with impaired renal function at the initial stage and in those receiving ART without tenofovir or ritonavir. This improvement in the slope of the GFR was statistically significant during the first year of ART, after which the slope of the GFR became stable. In individuals with normal renal function, an initial decrease in the slope of GFR was initially observed when measured using the diet modification equation for kidney diseases.

Tenofovir with ritonavir was associated with a statistically significant initial decrease in the slope of GFR only during the first year of ART and with a stable slope of GFR after it. However, therapy with tenofovir alone does not cause statistically significant changes in glomerular filtration [13]. A Swiss

study of a cohort of HIV-infected people showed that tenofovir-containing ART was associated with a statistically significant decrease in calculated GFR in determining kidney disease compared with antiretroviral therapy without tenofovir, with an average decrease in GFR of 2.40 ml/min/1.73 m2 over an average of 2.5 years. However, the onset of ART was usually associated with an increase in GFR by 0.68 ml/min/1.73 m2 over the same time period. In a cohort of people co-infected with HIV and hepatitis B virus (HBV), tenofovir treatment lasting up to 5 years was associated with decreased renal function, as evidenced by a small but statistically significant increase in the average serum creatinine level from 0.87 mg/dl to 0.93 mg/dl (p=0.002) [18]. An independent statistically significant association of renal insufficiency was found with several antiretroviral drugs, such as tenofovir (correlation coefficient k=1.16), indinavir (k=1.12), atazanavir (k=1.21) and lopinavir (k=1.08), regardless of the method used to calculate renal insufficiency.

Although indinavir has a generally recognized association with renal insufficiency k=3.4, the association of atazanavir and lopinavir has not been previously reported. Atazanavir-related nephrolithiasis has been proposed as a possible explanation for the observed renal toxicity. Given that this was an observational cohort, it is possible that people at higher risk of CVD were preferably treated with atazanavir due to its reduced effect on lipids, which led to a sample bias. The long-term effect of the new drugs maraviroc, raltegravir, darunavir and etravirine on kidney function has not yet been studied [13].

3. Bone diseases. Osteopenia and loss of bone mineral density, fractures. Studies confirm the association between a decrease in bone mineral density (BMD) and the use of tenofovir as an initial or continuing ART.

A significant change in the BMD of the lumbar spine and hip joint was found in patients treated with tenofovir and emtricitabine, compared with treatment with abacavir and lamivudine; in patients treated with efavirenz, compared with treatment with atazanavir and ritonavir. Two-year follow-up of the French cohort revealed a high incidence of pathological bone loss over time and a high prevalence (76%) of vitamin D deficiency in this cohort. A high incidence of hip BMD loss has been described in small groups of patients with primary HIV infection and correlates with the level of HIV RNA in blood plasma [9].

A comparison of age-standardized fracture rates among HIV-infected people with population data shows that the fracture rate in the HIV-infected group was 4.3 times higher than in somatic patients over a period of time since 2002. Coinfection with hepatitis C virus (HCV), a decrease in CD4+, diabetes and substance use were recognized independent predictors of fracture risk [18]. In a cohort study of the elderly, compared with controls observed under the same conditions, HIV infection turned out to be an independent predictor of fractures only among older male veterans. A study of fracture rates in HIV-infected women compared with control subjects after an average of 79 5 years of follow-up determined that white menopausal women and kidney failure, but not HIV status, were predictors of fractures.

Among HIV-infected people, fractures were associated with AIDS, but not with CD4+ cell count or ART exposure. These studies emphasize the importance of monitoring fractures in HIV-infected people and identifying those patients who may be at greatest risk [5]. Tenofovir is increasingly being used as a component of first-line antiretroviral therapy, however, there are concerns about potential bone toxicity in the developing fetus based on animal studies.

In vitro studies suggesting that the addition of the active form of vitamin D, 1,25-dihydroxycholecalciferol (1,25-[OH]2D3), to a colony of monocytic macrophages may inhibit HIV replication. This is due to the effect of vitamin D on autophagy proteins, which are apparently necessary for the productive phase of HIV infection. Given the low cost and ease of taking vitamin D, these results indicate the need for randomized trials to explore the benefits of routine supplements [5]. 80 The prevalence of vitamin D deficiency (defined as the serum level of 25-hydroxyvitamin D [25[OH]D] < 30 ng/ml) was estimated as 72% in the SUN study. Blacks, Latinos, and people with low levels of UV exposure have a higher risk. In addition, lack of exercise and exposure to efavirenz reduce vitamin D levels. In the SUN cohort, the use of ritonavir and GFR below 90 ml/min/m2 prevent a decrease in vitamin D levels [18].

In Switzerland, a study of vitamin D levels in patients before and after ART initiation was conducted and lower levels of 25[OH]D were found in injecting drug users, while exposure to tenofovir is associated with higher levels of D. These results confirm previously published data linking efavirenz exposure to lower levels of vitamin D. [5, 9, 18]. The clinical significance of these results is still unknown.

4. Fat accumulation and lipoatrophy. Changes in body fat remain an important problem in the long-term treatment of HIV infection. With the exception of the administration of local injectable fillers and moderate effects from the withdrawal of stavudine or zidovudine, there are no treatments for lipoatrophy. It was assumed that the administration of uridine could improve the function of mitochondria and the reverse development of lipoatrophy associated with the constant exposure to analog thymidine nucleoside reverse transcriptase inhibitors [8-10]. The randomized placebo-controlled ACTG trial did not demonstrate any improvement in lipoatrophy using uridine supplementation. Unstable improvements in lipoatrophy were noted in the uridine group at the 24th week of taking the drug, and they did not persist.

In addition, the supplement was poorly tolerated by patients due to toxicity [7, 4, 15]. Assessment of changes in adipose tissue in the body within the framework of randomized ART studies is still an important means of determining the contribution of new treatment regimens to this problem. A higher lipid profile of raltegravir compared to efavirenz was demonstrated after 96 weeks of follow-up in patients randomized to receive either of these drugs in combination with tenofovir/emtricitabine. Data from a small (n=55 in the groups) study of dual-energy X-ray absorptiometry (DEXA) in the same study showed a comparable increase in the volume of limbs, trunk and appendicular fat in both groups.

Trophic disorders in HIV-infected people – loss or accumulation of fat - can be aggravated with the use of antiretroviral therapy, which, in all likelihood, leads to disorders of systemic metabolism. This problem is currently unresolved. 3. Researchers are interested in coinfections of tuberculosis, influenza, and viral hepatitis, which are most common at present due to the special social status of HIV-infected people. Despite the existing danger of severe complications, coinfections need adequate therapy that does not contradict ART. Research in this area is ongoing.

References

1. Is the end of AIDS near? 10 facts about HIV/AIDS on the eve of World AIDS Day / Medscape Infectious Diseases, 2015.

2. Ladnaya N.N., Pokrovsky V.V., Dementieva L.A., Simashev T.I., Lipina E.S., Yurin O.G. The development of the HIV epidemic in the Russian Federation in 2015: proceedings of the International Scientific-practical Con. "Actual issues of vicinexy". OTb., 2016. pp. 4-9.
3. Lioznov D.A., Konovalova N.V., Ogurtsova S.V. HIV infection in the Northwestern Federal District of the Russian Federation: an analytical review. Issue 7 / edited by A.B. Zhebrun. St. Petersburg: FBUN NIIEM im. Pasteur, 2014. 36 p.
4. Shakhgildyan V.I., Parkhomenko Yu.G., Tishkevich O.A. The structure of fatal outcomes and pathological anatomy in patients with HIV infection in Moscow // Epidemiology and infection. bol. 2004. No. 4. pp. 42-46.
5. Rakhmanova A.G., Yakovlev A.A., Dmitrieva M.I., Vinogradova T.N., Kozlov A.A. Analysis of the causes of death of HIV-infected people in 2008-2010 based on the materials of the clinical infectious diseases hospital named after S.P. Botkin, St. Petersburg // Kazan. med. journal. 2012. No. 3. S. 522-526.
6. Zakharova N.G., Dvorak S.I., Plavinsky S.L., Toropov S.E., etc. Causes of adverse outcomes in patients with HIV infection who received VAART. Part 1// HIV infection and immunosuppression. 2015. Vol.7, No. 3. pp. 48-55.
7. Yakovlev A.A., Musatov V.B., Savchenko M.A. Causes of deaths in HIV-infected patients receiving antiretroviral therapy // HIV infection and immunosuppression. 2015. Vol. 7, No. 1. pp. 84-89.
8. Moore R.D., Keruli J.S. The number of CD4+ cells 6 years after the start of highly active antiretroviral therapy in individuals with sustained virological suppression // Klinika. Infect. Dis. 2007. Vol. 44. P. 441-446.
9. Engsig F.N. Long-term mortality in HIV-positive individuals with viral suppression for >3 years with incomplete CD4 recovery // Clin. Infect. Dis. 2014. Volume 58, N 9. pp. 1312-1321.
10. Bonnet F., Lewden S., May T., etc. Opportunistic infections as causes of death of HIV-infected patients in the era of VAART in France // Scand. J. Infect. Dis. 2005. Volume 37. pp. 482-487.
11. Potter M., Odueyungbo A., Yang H., Said S. et al. The effect of hepatitis C virus replication on the progression of CD4+ T lymphocytes during HIV-HCV coinfection before and after antiretroviral therapy // AIDS. 2010. Volume 24. pp. 1857-1865.
12. Seskon A., Patterson S., Davey S., Dean E. Late initiation of combination antiretroviral therapy in Canada: a call for a national public health strategy to improve HIV treatment engagement // J. Int. AIDS Soc. 2015. Volume 18. Article number 20024.
13. Conti S., Masocco M., Pezzotti P., etc. The differential effect of combined antiretroviral therapy on the survival of Italian patients with specific diseases that determine AIDS // J. Acquir. Immunodeficiency. The syndrome. 2000. Volume 25. pp. 451-458.
14. Jave K., Buchach K., Ling Hsu, Miao-Jun Chen, etc. The risk of mortality after AIDS - the definition of opportunistic diseases among HIV-infected people - San Francisco, 1981-2012 // JID. 2015. Volume 212, N 9. pp. 1366-1375.