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LONG-TERM RESULTS OF ART IN HIV-INFECTED PATIENTS ON THE EXAMPLE OF THE ANDIJAN REGION

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Abstract:

In the ever-evolving field of endodontics, the role of irrigation has undergone a transformative shift, becoming a cornerstone in modern root canal treatment. This abstract explores the contemporary landscape of irrigation techniques, emphasizing their pivotal contribution to the success and longevity of endodontic procedures. The article navigates through advanced irrigation solutions, including novel irrigants, activation methods, and delivery systems, shedding light on their impact on disinfection, debris removal, and biofilm disruption. Furthermore, the abstract discusses the integration of technology, such as ultrasonic and laser irrigation, into modern endodontic practices. The critical aspects of safety, efficacy, and the potential for minimizing procedural complexities are addressed, highlighting the strides made in achieving optimal root canal disinfection. Through this exploration, the abstract aims to provide insights into the current state of irrigation in modern endodontics and its implications for enhancing treatment outcomes and promoting the longevity of root-filled teeth.

Keywords: HIV infection, antiretroviral therapy, suppressed viral load, mortality

Combined antiretroviral therapy (ART), introduced into clinical practice in the late 1990s, has identified a real breakthrough in HIV medicine. ART stops the progression and provides regression of clinical manifestations of the disease, improves the quality of life of the patient, reduces the risk of HIV transmission. An achievement of modern infectology and public health is a significant increase in the availability of ART for people living with HIV (PLHIV). Since 2000, the number of PLHIV receiving ART has increased 15-fold and stands at 15.0 million at the end of 2015 [1]. In 2015 In the Russian Federation, every 3rd patient under dispensary supervision (37%) received ART, while the task was set to increase the coverage of ARV treatment to a level of at least 60% [2]. In the Northwestern Federal District in 2013, more than 18,500 PLHIV received ART, which is 88.1% of patients in need of treatment. The increase in the number of patients requiring ART in 2013 was 24.1% [3].

Despite the availability of ART in the Russian Federation, more than 27,500 HIV-infected patients died in 2015, which is 12.9% more than in 2014 [2]. The absolute majority of deaths occur in patients who do not receive specific antiviral treatment. A significant number of publications have been devoted to the analysis of the causes of late onset of ART and fatal outcomes in PLHIV, however, most of them investigate the causes that led to the onset of death in patients who did not receive ART or stopped taking it on their own [4, 5]. There are only isolated studies analyzing the causes of an unfavorable outcome in patients receiving ART [6, 7]. Fatal outcome against ART often occurs at the initial stage or when treatment is interrupted against the background of HIV replication and existing immunodeficiency, which determines the severe course of the pathological process. At the same time, the study of deaths in PLHIV with controlled HIV suppression is of particular interest.

THE PURPOSE OF THE WORK. To assess the causes of an unfavorable outcome in HIV-infected patients who are on ART and have reached an undetectable viral load.

MATERIAL AND METHODS. The analysis and processing of data on the medical histories of deceased HIV-infected patients receiving ART were carried out using a continuous sampling method. According to the results of the laboratory examination, a group was formed, which included patients who had an undetectable viral load [HIV (HCV) less than 40 copies/ml] at the time of death. In the course of the work, the medical histories of patients were analyzed, for some patients (10 people) - data from previous outpatient follow-up. The socio-epidemiological characteristics, clinical and laboratory data, schemes and terms of treatment of patients, the final clinical

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diagnosis and the results of a pathoanatomical study were studied.

RESULTS AND DISCUSSION. During the study period (25 months), 9078 patients were hospitalized with the main diagnosis of HIV infection. The mortality rate for this group of patients was 6.5% (593 people). Among the total number of deaths, it was found that in 16 (2.7%) cases, the fatal outcome occurred in patients who received ART and had an undetectable LV at the time of death.

Among the deceased patients, the ratio of men and women was approximately equal with a slight predominance of men (9 and 7 patients, respectively). The average age of the patients was 32 years with maximum values from 25 to 43 years. The period from the moment of diagnosis of HIV infection to the beginning of ART was 9.5 years.

Most of the patients (11 people) were infected with HIV parenterally, only 5 patients became infected during sexual contact. Among the patients infected with intravenous administration of psychoactive substances (surfactants), there was an equal ratio of active drug users and patients in remission (5 and 6 people, respectively). In 3 patients, the sexual path of infection (heterosexual contacts) was combined with alcohol dependence. Previously, every 4th patient was in prison. Despite their working age, the vast majority of patients (12 people) did not work.

Upon hospitalization, the following clinical diagnoses were established: 15 patients - HIV infection, stage 4B, 1 patient - HIV infection, stage 4A. According to the CDC classification, 13 patients had stage C3, 2 patients had stage C2 and 1 patient had stage B3.

Among the concomitant pathologies, chronic viral hepatitis dominated (in 11 patients), including in 7 cases - chronic viral hepatitis B+C, in 3 cases - chronic viral hepatitis C and in 1 case - chronic viral hepatitis B. Somatic diseases of the digestive organs were noted in 4 patients (chronic pancreatitis - in 3 patients, duodenal ulcer - 1 patient).

At the time of hospitalization, 9 out of 16 patients received ART prescribed at the prehospital stage. Among them, in 6 patients it was the first prescribed regimen, in 3 patients therapy was resumed in the same mode after self-termination of treatment. In the hospital, ART was prescribed to 7 patients, including 3 "naive" patients and 4 who had previously received therapy. It should be noted that almost every second deceased patient (7 out of 16 patients) had previously interrupted life-saving ART, as a rule, due to low adherence associated with drug addiction. Upon resumption of first-line ART, all of them achieved virological suppression, which reflected the continued sensitivity of HIV strains to basic ARV drugs. All patients received regimens based on two nucleoside reverse transcriptase inhibitors (NRTIs), which were used in conjunction with non-nucleoside reverse transcriptase inhibitors (NNRTIs) in 10 patients or protease inhibitors (IP) in 5 patients. One patient received a second-row scheme: 2NIOT+ IP+ coreceptor blocker. Azidothymidine (AZT) + lamivudine (3TC) was used as the nucleoside base in 6 patients, abacavir (ABC) and 3TC were used in 4 patients, 6 patients received stavudine (d4T) or didanosine (ddI) in combination with 3TC. Efavirenz (EFV) was most often used as an NNRTI, and lopinavir/ritonavir (LPV/r) was used as an IP.

At the time of the onset of ART, the median (Iu) of the absolute and relative number of CD4+ lymphocytes was 14 cells/μl (Q25 7.25; Q75 44.25) and 3.5% (Q25 1.50; Q755.75), reflecting a deep immunodeficiency corresponding to the stage of AIDS. Against the background of ART, a certain increase in the number of CD4+ cells was observed. By the time of death, the average level of CD4+ lymphocytes was 94.5 cells/μl (Q25 28.50; Q75 1 71.00) and 9.0% (Q25 4.00; Q75 2 0.75). The level of HIV HCV at the start of ART ranged from 75,000 to 500,000 copies/ml: in 5 patients it was more than 500,000 copies /ml, and in two - 75,000 and 125,000 copies/ml, in the rest there was no data on HIV HCV at the start of therapy. At the time of death, undetectable HV <40 copies/ml was registered in all patients.

Tuberculosis was the cause of death in 7 (43.7%) cases, including generalized tuberculosis in 5 patients. Death as a result of the progression of lymphoproliferative diseases (non-Hodgkin's lymphomas) was established in 4 patients. In 3 more cases, the direct cause of death was HIV-associated secondary diseases - brain toxoplasmosis and severe combined bacterial infection (in 2 patients). In 2 cases, the fatal outcome was not directly related to HIV infection - toxic epidermal necrolysis (Lyell's syndrome) and an overdose of surfactants. The majority of deaths (14 cases) occurred in the first 12 months after the start of therapy (an average of 4.5 months). 2 patients died at the 25th and 48th months of therapy (Lyell's syndrome, which arose after the replacement of effective ART at the outpatient stage, and postoperative sepsis).

Only 2 patients whose death was not directly related to HIV infection did not have opportunistic diseases at the time of death, 62.5% of patients noted the simultaneous presence of several of them. Tuberculosis and lymphomas were combined with invasive esophageal candidiasis, generalized cytomegalovirus

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infection, cryptococcosis, persistent multifocal leukoencephalopathy.

The most important predictors of the progression of HIV infection, the development of HIV-associated diseases and the onset of death in patients with ART are the low level of CD4 lymphocytes at the time of the onset of ART and their slow increase during treatment [8]. At the same time, most authors consider the presence of the AIDS stage (CD4 level <200 cells/μl) as the most significant factor of ineffective ART. From this position, the described group of patients started ART with a prognostically unfavorable low level of CD4 lymphocytes.

It is probably the slow recovery of CD4 cells that is an important negative predictor of an unfavorable outcome of the disease. Despite the relatively rapid achievement of viral suppression, a one-time adequate restoration of the normal functioning of the immune system is not ensured, which leads to a fatal outcome of the disease. An important component of individualized therapy of HIV patients is the identification of a group of patients at risk of slow recovery of relative and absolute CD4 lymphocyte values. In the presented data, the deceased patients were less socially adapted, they had more frequent use of surfactants, stay in places of deprivation of liberty, and lack of a permanent place of work. These socio-epidemiological characteristics are generally consistent with the data of other authors who have identified factors of a slow immunological response: intravenous surfactants, mature age of patients, the presence of concomitant viral hepatitis, non-homosexual transmission pathway, high blood pressure at the start of more than 100,000 copies/ml with low CD4 lymphocyte levels [9, 10].

It can be considered that the impact of these factors is more complex, since in the standard understanding of the pathological process in HIV infection, it is the social, epidemiological and clinical characteristics that determine the low level of adherence and, as a result, the virological inefficiency of ART. In conditions of HIV suppression, these factors probably have an indirect effect, predetermining late medical treatment, a high incidence of tuberculosis and severe immunodeficiency in patients, which, in turn, explains the unfavorable outcome of the disease when signs of virological, but not immunological effect of treatment are achieved. In addition, among the deceased, every second patient had previously interrupted ART, which is an extremely unfavorable factor of negative impact on the functional potential of the immune system. In such a clinical situation, the rate of increase in HIV HCV and, as a result, the decrease in CD4 cells are more significant compared to the "natural" development of the pathological process in the absence of ART.

According to the literature, the presence of concomitant chronic viral hepatitis negatively affects the recovery rate of CD4 lymphocytes, however, most sources reflect the unfavorable value of only chronic viral hepatitis C, and not mixed viral liver damage [11, 12]. In the described group of patients with HIV infection, there were 11 (68.7%) patients with viral hepatitis.

CONCLUSION. Various studies have shown that the probability of death from HIV infection increases if a patient has several opportunistic diseases. Even in regions with a wide coverage of PLHIV ART, adverse, potentially non-curable HIV-associated conditions include brain lymphoma, progressive multifocal leukoencephalopathy, a combination of lymphoproliferative diseases and opportunistic infections [10, 13]. At the same time, tuberculosis is not included in the list of opportunistic diseases that convincingly increase the risk of death in HIV-infected patients [14]. On the contrary, in the conducted study, the presence of generalized forms of tuberculosis had a significantly negative effect on the prognosis of the disease. This may be due to the recent diagnosis of tuberculosis, which increases the level of resistance of mycobacteria to first-line preventive procedures and a more severe method of treating syndromes and the immune system in patients with CD4 lymphocyte levels <50 cl/μl.

Thus, ART, used in real clinical practice, provides rapid and stable suppression of HIV in various categories of patients, including those who had previously interrupted treatment. However, despite the virological effectiveness, the restoration of the immune system is slower, while the functional insufficiency of cellular and humoral immunity in patients with HIV suppression determines the severe, potentially intractable course of opportunistic infections, especially when combined. Timely detection of new cases, early start and continuous continuation of ART ensure a favorable course of HIV infection.

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