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OPTIMAL CHOICE OF ANTIRETROVIRAL THERAPY REGIMEN INCLUDING PHOSPHAZIDE

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ABSTRACT — A clinical and laboratory study on selection, prescription and use of optimal antiretroviral therapy regimens for HIV patients was conducted. It was identified, that phosphazide has significant therapeutic efficacy and safety among nucleoside analog reverse-transcriptase inhibitors.

KEYWORDS — safety, phosphazide, HIV infection, therapy.

INTRODUCTION

It is known that HIV infection is one of the most complex biomedical health problems in the world. The disease causes negative consequences, signs of an emergency and long-term problems, including death [1, 2]. In Russia, there is an annual increase in morbidity, social significance and epidemiological danger, which dictates the need of new approaches to HIV/AIDS retroactions including safe and effective drug usage. According to Russian guidelines, antiretroviral therapy (ART) is carried out using the combination of at least three drugs [3, 4].

To achieve the long-term therapeutic effect of ART, it is necessary to select treatment regimens with effective and safe drugs based on the objective principles of rational drug use.

Using the expert system *AntiHIV-1* which includes the elements of the *Rational Unified Process* (RUP) software methodology, optimal and safe treatment regimen, including a NRTI class drug — phosphazide, were selected.

METHODOLOGY, MATERIALS AND RESEARCH METHODS

The medical expert system *AntiHIV-1* was created in 2017 on the basis of *Perm State Center for the Prevention and Control of AIDS and Infectious Diseases* by Federal State Budgetary Educational Institution of Higher Education *Perm State Pharmaceutical Academy* of the Ministry of Health of the Russian Federation with contribution from *Perm National Research Polytechnic University*.

Taking into account the criteria of *effectiveness* and *safety*, the safest drug of the class of nucleoside reverse transcriptase inhibitors (NRTIs) in ART regimens was determined.

MAIN CONTENT OF THE STUDY AND ANALYSIS OF THE RESULTS

In the automatic information system *AntiHIV-1* for analysis of the choice and purpose of ART, 33 used antiretroviral drugs from six classes registered in the state register of medicines were included. 25 of them were monocomponent drugs and 8 were complex (two- and three-component), they were included into the pharmacotherapeutic group J05A *Direct-acting antiviral drugs* according to the Anatomical Therapeutic Chemical Classification (ATC) classification [5].

599 medical records of patients receiving ART on an outpatient basis were analyzed, which made it possible to identify side effects and draw conclusions about the toxicity of the drugs used.

ART regimen with phosphazide were the safest one. Phosphazide is the first Russian NRTI class drug that was synthesized in the laboratory of the Institute of Molecular Biology. V.A. Engelhardt RAS [6] (Fig. 1)

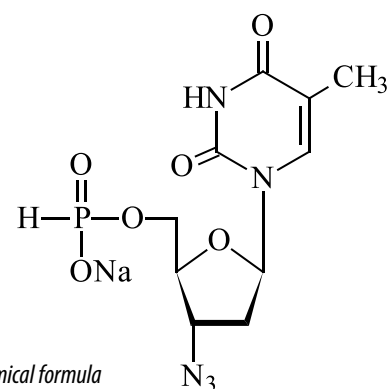


Fig. 1. Phosphazide chemical formula

High anti-HIV activity of phosphazide against HIV-1 reproduction in cultures of H9, MOLT and MT-4 lymphoblastoid cells was established (Galegov, 1988) as well as low toxic effects on tissues and organs [7, 8, 9, 10].

We had also studied its safety and low toxicity in the schemes of perinatal chemoprophylaxis of mother-to-child HIV transmission, treatment of infection and prevention of parenteral infection of medical workers in the course of their duties earlier. [11–14].

As a result, ART regimens with the least number of undesirable side reactions (ADR) from organs and systems were identified — this is a combination of 2 NRTIs + AI — tenofovir + phosphazide + dolutegravir (73 (11.8%) of 617 ADR), while the combination of abacavir + phosphazide + dolutegravir potentially causes only 8 (1.3%) ADR, which are the same for all three drugs.

Among the alternative ART regimens, phosphazide + emtricitabine + fosamprenavir (52 (8.4%) of 617 ADR), phosphazide + emtricitabine + atazanavir, and phosphazide + emtricitabine + fosamprenavir / ritonavir with five (0.8%) ADR should be marked.

The analysis of the clinical laboratory diagnostics results, changing under the influence of antiretroviral therapy drugs, revealed ART regimens, the use of which causes the least effect on the change in laboratory parameters. These are the following drug combinations recommended in the Russian Federation: phosphazide + emtricitabine + fosamprenavir, phosphazide + emtricitabine + saquinavir / ritonavir, phosphazide + lamivudine + fosamprenavir, phosphazide + lamivudine + saquinavir / ritonavir.

Among monocomponent ART drugs, phosphazide is characterized by the least number of potential manifestations of ADR — 10 ADR (1.6%).

There should be noted such ART drug regimens that do not influence the indicators of clinico-laboratory diagnostics (0 indicators of CLD (0.0%) out of 42) for the treatment of HIV infection: phosphazide + emtricitabine + atazanavir and phosphazide + lamivudine + fosamprenavir [15–17].

CONCLUSION

As a result of the use of the AIS *AntiHIV-1*, the optimal ART regimens which have the least amount of side effects were determined. All schemes include a representative of NRTI class — phosphazide, which is registered and manufactured in Russia.

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