REVIEW ARTICLE

FEATURES OF HIV/AIDS PHARMACOTHERAPY IN PREGNANT WOMEN

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ABSTRACT

The article under consideration describes the main ways to reduce the likelihood of transmission of infection from mother to fetus, emphasizes the features of therapy for women during pregnancy and proposes methods and approaches for treating this disease.

The above data speak in favor of an integrated approach to the treatment and prevention of HIV infection. An important role is played by the earliest possible initiation of drug therapy. The combination of these aspects can reduce the number of viruses in the mother's blood, contribute to overall health maintenance and make pregnancy, as well as the process of childbirth, safer. At the same time, in each specific clinical case, it is required to consider the risk/benefit ratio as a determining aspect and, taking into account a wide range of features-from the mother's diet and the presence of concomitant anomalies, to changing the dosage regimen and replacing drugs.

KEY WORDS: HIV and AIDS therapy, pregnancy, features of pharmacotherapy during pregnancy

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INTRODUCTION

Optimal drug pharmacotherapy during pregnancy is an important issue. As is known, colossal changes occur in woman's body during pregnancy affecting a wide range of factors. Anatomy, physiology, mental and cognitive functions, as well as the processes of pharmacokinetics and pharmacodynamics of drugs are undergoing changes. As a rule, the use of most drugs during this period is associated with great risks and should be carried out only in the case of superior health benefits to the unborn child or mother. The human immunodeficiency virus is nothing more than a long-term progressive anthroponous disease of an infectious nature, characterized by damage to human immune cells. This infection can develop during contamination with the corresponding virus with a further transition to acquired human immunodeficiency syndrome (AIDS). AIDS, first recorded in the United States in 1981, has now been spread across the globe. According to the WHO, there are currently more than 10 million people around the world affected by this disease. In addition, both the rate of spread of this disease and the frequency of its occurrence in the population are increasing every year, since every day around the world up to 9000 young people under the age of 25 are infected with HIV, almost half of whom are pregnant women [1]. Therefore, at present, the efforts of many scientific centers are aimed at studying this problem and finding appropriate approaches for treating and correcting the symptoms of AIDS and HIV during pregnancy. Accordingly, the purpose of this research was to study the characteristics of pharmacotherapy of HIV and AIDS during pregnancy.

REVIEW AND DISCUSSION

Due to the change in physiology and anatomy during pregnancy, the treatment of this disease is particularly difficult in the case of pregnant women.

DRUG THERAPY FOR HIV AND AIDS DISEASES AND ITS FEATURES DURING PREGNANCY

One of the main problems in HIV infection is to preserve not only the health of the mother and the fetus, but also to study the prerequisites for the development of negative symptoms, as well as to prevent the appearance of abnormalities throughout the entire period of postnatal development of the child, which constitutes a number of certain difficulties, since, as a rule, the most dangerous clinical manifestations of AIDS are the appearance of opportunistic infections, the development of autoimmune processes and malignant neoplasms. Therefore, another difficulty in the treatment of this anomaly lies in the fact that the specialist who prescribes the appropriate drug therapy during pregnancy must know every helix of each DNA and every feature of patient: the duration of treatment, the drugs used as well as the occurrence of unwanted drug reactions and the presence of concomitant diseases [2]. So, any detail that is insignificant at first glance, for example, insufficient mother's nutrition, can seriously aggravate the progression of HIV infection. It was found that vitamin A deficiency is associated with a more rapid development of the disease in HIV-infected women, an increase in the frequency of HIV transmission from mother to child, and

higher concentrations of the virus in milk in the case of breastfeeding. Research results show that pregnancy itself does not accelerate the course of HIV infection. However, the impact of HIV on mothers is not limited to the period included in the maternal mortality rates. Thus, there is an evidence that the mortality rate of HIV-positive women is high in the postpartum period, as they may be more susceptible to postoperative complications. These include higher rates of ectopic pregnancy, early abortion, development of bacterial pneumonia, urinary tract infection and other infectious lesions. In addition, among the aspects that increase the risk of infection during pregnancy, the following can be distinguished:

- A large number of pathogenic viruses in the bloodstream (especially in the last trimester and immediately before childbirth)
- Low immune status (less than 200 cells/ml)
- Exacerbation of chronic disease
- Prolonged labor (more than 4 hours)
- Abnormalities in the development of the placenta

But even with a favorable childbirth and the birth of an HIV-negative child, infection from the mother is still possible due to breastfeeding. Accordingly, the best option for such an outcome would be the option of a balanced diet with milk formulas [2]. In further studies of the child's health, it should be kept in mind that during the first days of the child's postnatal development, his HIV tests may be positive, since the mother's antibodies are still in his blood, and it will be possible to reliably accurately say about the fact of transmission of the virus from mother to child only closer to one and a half years of life. According to research, until recently, HIV-positive women were recommended to terminate their pregnancy, but progress is not standing still, and now the woman's desire to give birth is a decisive aspect. So, according to the available literature data, the infection of a child in the case of an HIV-positive mother occurs in 15% of all cases [4]. It is known that HIV infection is a complex disease that brings negative symptoms to almost all structures and functions of the body [5]. Accordingly, the optimal solution for the treatment of such an anomaly would be to use a similar integrated approach, including during pregnancy. So, according to the literature, the greatest efficiency in the treatment of HIV infection lies in the complex use of different groups of drugs. As a rule, antiretroviral therapy will have a clinically significant effect in the case of a combination of drugs of three classes, which are taken at least 2 times a day [6-7]. Currently, drug therapy for AIDS is a lifelong treatment, which imposes certain difficulties in its application, especially during pregnancy. An integrated approach is a combined use of three or more antiretroviral drugs with different targeting to reduce HIV replication in the body as much as possible, which makes it possible to reduce the dose of the drug administered to the body and reduce the likelihood of adverse drug reactions. Thus, it was found that the incidence of preeclampsia is lower in HIV-infected women who do not receive antiretroviral treatment than in women receiving treatment [8]. One of the main drugs currently used is azidothymidine which was invented in 1986. Its mechanism of action is based on disruption of the process of reverse transcription of viral RNA components. Currently, it is not used during pregnancy, but didanosine is used instead (as with azidothymidine intolerance) [9].

TYPICALLY, HIV THERAPY INCLUDES SEVERAL UNDERLYING PRINCIPLES

- The less drugs the patient receives, the less the frequency of taking is; as well as the element of dependence on food intake.
- The more accurately the patient follows the doctor's prescriptions, the better the clinical effect are, since skipping the drug can not only aggravate the development of symptoms of the disease, but also develop resistance of the virus.
- In the event of the appearance of a resistant strain, the drug must be replaced with another.
- It is advisable to start treatment earlier for all groups of the population. As a rule, therapy begins when the level of CD4 lymphocytes reaches 500 or less cells / μl.
- It is very important to immediately start treatment in children under the age of 5 years, while for children over 5 years old it is proposed to apply the same principle as in adults.
- To reduce the likelihood of vertical transmission from mother to fetus, it is necessary to start immediately in pregnant and lactating women with the possibility of discontinuation of therapy after the end of the period of vertical transmission of HIV infection, and continuation of therapy in women who meet the general criteria for starting therapy.

The existing literature indicates the favorable use of the efavirenz-based regimen in pregnant women, indicating that such therapy does not pose additional risks to the fetus. However, efavirenz is usually not used at the early stages of pregnancy, namely during the first trimester [10].

In our country, the combination of tenofovir, efavirenz and emtricitabineor lamivudine is considered the drug of choice for the treatment of this anomaly, which corresponds to one of the internationally accepted treatment regimens "all in one, once a day" [11].

As a rule, 5 classes of drugs are currently used for drug therapy:

(1) Drugs-nucleoside reverse transcriptase inhibitors-abacavir, didanosine, zidovudine, lamivudine, stavudine, tenofovir, phosphazide.
(2) Combination drugs-nucleoside reverse transcriptase inhibitors-abacavir + zidovudine + lamivudine, zidovudine + lamivudine + nevirapine, efavirenz.
(3) Drugs-protease inhibitors, ritonavir, indinavir, nelfinavir, atazanavir, tipanavir, darunavir.
(4) Drugs-nucleoside reverse transcriptase inhibitors-nevirapine, etravirine, efavirenz.
(5) Drugs-protease inhibitors, combination agents, integrase inhibitors, fusion inhibitors, receptor inhibitors–

(a) Integrase inhibitors-raltegravir
(b) Fusion inhibitors-enfuvirtide
(c) Receptor inhibitors-maraviroc [12-14].

It should be understood that in connection with a cascade of physiological changes during pregnancy, it is possible both a decrease in the effectiveness of a number of drugs, with a complete loss of the positive therapeutic effect, and the appearance of negative symptoms. For example, according to the literature, in the second and third trimesters of pregnancy, the effectiveness of darunavir and ritonavir decreases due to the acceleration of their elimination processes. At the same time, no adverse drug reactions have been registered that occur when they are taken during pregnancy, neither in mothers, nor in children [15, 16 and 18]. Similar results were obtained in a study of the effects of tenofovir, nevirapine and efavirenz on the health of pregnant women: apart from mild anemia in mothers and a slowdown in Neutrophils activity in infants up to 3 months of postnatal development, no side effects were noted [16,17]. However, there are a number of medicines that are not recommended when planning a pregnancy in the case of HIV treatment. These drugs include dolutegravir, cobicistat and zidovudine, which have a teratogenic effect [19-20]. At the same time, the birth of healthy, HIV-negative children is a very likely outcome, which, as a rule, is achieved by the correct selection of drug therapy and the necessary adjustment of the drug dosage regimen [17].

CONCLUSIONS

The above data speak in favor of an integrated approach to the treatment and prevention of HIV infection. An important role is played by the earliest possible initiation of drug therapy. The combination of these aspects can reduce the number of viruses in mother's blood, contribute to overall health maintenance and make pregnancy, as well as the process of childbirth, safer. At the same time, in each specific clinical case, it is required to consider the risk/benefit ratio as a determining aspect and, taking into account a wide range of features-from the mother's diet and the presence of concomitant anomalies, to changing the dosage regimen and replacing drugs.

REFERENCES

1. Eremenko N.N., Gubenko A.I., Zebrev A.I., Lysikova I.V. Modern approaches in the treatment of HIV-infected patients. Bulletin of the Scientific Center for Expertise of Medicinal Products. 2014, 2p.
2. Lukashov M.M. Features of pharmacotherapy of HIV infection in children. Biopharmaceuticalhorizons. 2019; 61:66.
3. Volokitina V.A., Bursova A.P. HIV infection and AIDS pharmacotherapy. Materials of the XI International Scientific and Practical Conference. Future Issues from the World of Science. 2015; 45:48.
4. Leshkevich O.K., Sennikova A.V. Pharmacotherapy of HIV-infected patients. Medical, social and economic aspects. 2017, 26p.
5. Dremova N.B. Analysis of the pharmaceutical market segment for antiretroviral drugs for the treatment of HIV infected patients. Pharmaco economics. Modern pharmaco economics and pharmaco epidemiology. 2009, 3p.
6. Johnson D. Features of pregnancy with HIV infection. Armenian medicine. 2012; 52(1) : 116-124.
7. Sokolova T.N., Kasparov A.E., Kovalenko L.V. et al. Features of the course of HIV infection and the mechanisms of the formation of pathology of pregnancy in residents of the subarctic region. Ulyanovskmedical and biological magazine. 2020; 20p.
8. Zabello O.G., Petrishche T.L. Features of the use of antimicrobial drugs for systemic application in the pharmacotherapy of pregnant women. Part 1. Modern problems of health care and medical statistics. 2014; 200p.
9. Boyer P.J., Dillon M., Navaie M. et al. Factors predictive of material of maternal-fetal transmission of HIV-1: preliminary analysis of zidovudine given during pregnancy and/or delivery. Jama. 1994; 271(24): 1925-1930.
10. McItyre J. Mothers infected with HIV: reducing maternal death and disability during pregnancy. British Medical Bulletin. 2003; 61(1): 127-135.
11. Kesho Bora Study Group. Triple antiretroviral compared with zidovudine and single-dose nevirapine prophylaxis during pregnancy and breastfeeding for prevention of mother-to-child transmission of HIV-1 (Kesho Bora study): a randomized controlled trial, 2011. The Lancet infectious diseases. 11(3): 171-180.
12. Volmink J., Siegfried N.L., van der Merwe L., Brocklehurst P. Antiretrovirals for reducing the risk of mother-to-child transmission of HIV infection. Cochrane Database Syst Rev. 2007; (1): CD003510. doi: 10.1002/14651858.CD003510.pub2.
13. Ntlantsana V., Hift R.J., Mphatswe W.P. HIW viraemia during pregnancy in women receiving preconception antiretroviral therapy in Kwa Dukuza-Natal. Southern African journal of HIV medicine. 2019; 20(1): 1-8.
14. Santosa W.B., Staines-Urias E., Tsivulia Matala C.O. et al. Perinatal outcomes associated with maternal HIV and antiretroviral therapy in pregnancies with accurate gestation age in South Africa. Aids. 2019; 33(10): 1623-1633.
15. Fernandez C., van Halsema C.L. Evaluating cabotegravir/riipvirine long-acting, and injectables in the treatment of HIV infection: emerging data and therapeutic potential. HIV/AIDS (Auckland, NZ). 2019; 11: 179.
16. Gupta A., Montepiedra G., Aaron L. et al. Isonazide preventive therapy in HIV –infected pregnant and postpartum women. New England Journal of Medicine. 2019; 381(14): 1333-1346.
17. Seider V., Weizsacker K., Henrich W. et al. Safety of tenofovir during pregnancy: early growth outcomes and hematologic side effect in HIV-exposed uninfected infants. European journal of Pediatrics. 2020; 179(1): 99-109.
18. Cruz Zonenshein A.C., Joan Filho E.C., Cruz M.L.S. et al. Treatment dropout after pregnancy: a study of women living with HIV in Rio de Janeiro. AIDS care. 2020; 1:7.
19. Eke A.C., Stek A.M., Wang J. et al. Darunavir pharmacokinetics with an increased dose during pregnancy. JAID Journal of Acquired immune Defincy Syndromes. 2020; 83(4): 373-380.
20. Eke A.C., Mirochink M. Ritonavir and cobicistat as pharmacokinetic enhancers in pregnant women. Expert opinion on drug metabolism and toxicology. 2019; 15(7): 523-525.

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