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HERPES INFECTION DURING PREGNANCY

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Abstract:
Herpes simplex virus remains one of the most common etiological factors of infectious and inflammatory diseases of the reproductive system in women. This review presents the main morphological properties of the virus, pathogenesis and clinical manifestations of herpetic infection, current data on the incidence in Russia and other countries among the entire population and pregnant women, identified risk groups for the development of herpetic infection (depending on gender, age, number of sexual partners, etc.). The most frequent complications of pregnancy and childbirth in this group of patients (severe forms of gestosis, antiphospholipid syndrome, thrombophilia, premature rupture of fetal membranes, spontaneous termination of pregnancy, etc.) are described, as well as data on intrauterine fetal malformations (ventriculomegaly, corpus callosum dysgenesis, porencephaly, microcephaly, hydrocephalus and microphthalmia, etc.) possible ways of transmission of infection from mother to child during gestation and after childbirth are analyzed. The currently accepted approaches to the diagnosis and treatment of pregnant women with herpes virus infection, as well as indications for natural delivery or caesarean section, are described.

Keywords: herpes virus, spontaneous abortion, intrauterine malformations, genital herpes, pregnancy.

INTRODUCTION

Currently, there is an increase in the frequency of herpetic infection in the structure of sexually transmitted infections. Women of reproductive age are most often infected with the herpes simplex virus, which makes the problem of intrauterine vertical transmission to the fetus and infection of newborns relevant in the work of an obstetrician-gynecologist. It has also been established that the herpes simplex virus leads to the development of various obstetric complications and increases the risk of intrauterine malformations.

The aim of the work is to analyze modern literature sources devoted to the ideas about the influence of herpetic infection on fetal development, to reveal the features of the course of the gestation period in patients with herpes simplex virus.

Infections of the female reproductive system remain one of the most pressing problems in the work of an obstetrician-gynecologist. The most common etiological factors of infectious and inflammatory diseases of the genital organs are Candida spp., Trichomonas spp., Chlamydia spp., N. gonorrhoeae, Gardnerella spp., which can cause discomfort to patients, cause infertility and complications of the gestational period [1]. Among viral agents, Herpes simplex virus (HSV) 1 and 2 play a leading role in the structure of morbidity [2].

Currently, herpes virus infection in women and its effect on the course of pregnancy and childbirth attracts the attention of many researchers. HSV 2 is the most common cause of genital herpes and is transmitted mainly by sexual route. HSV 1 is already being registered in

childhood and is usually transmitted through non-sexual contacts [3]. It should be noted that the structure of genital herpes has changed in some developed countries; for example, in the USA, the herpes simplex virus 1 serotype is the main cause of genital herpes, especially in young people [4].

Women of reproductive age are most often infected with herpes simplex virus, which makes the problem of intrauterine vertical transmission to the fetus and infection of newborns relevant in modern health care [4]. The analysis of observations shows that the primary infection of the mother with HSV infection is one of the main factors in the development of genital herpes in a child. A woman who first acquired the herpes simplex virus during, and not before, pregnancy increases the risk of HSV transmission to a child many times. Also, risk factors for intranatal and neonatal infection include the use of skin electrodes in the fetus and the age of the mother less than 21 years [2].

Herpes viruses 1 and 2 serotypes are DNA-containing, belong to the Alphaherpesvirinae subfamily of the Herpesviridae family [5]. The entrance gate for both representatives is the mucous membrane or damaged skin cells; they migrate through the nervous system and remain latent in it. HSV 1 is found mainly in the ganglia of N. trigeminus, causing orophasial lesions, and HSV 1 - in the ganglia of the lumbosacral region. HSV 1 and 2 can cause an infectious-inflammatory process in both the oral region and the genital tract [6].

In recent decades, the proportion of genital herpes in the structure of sexually transmitted infections has increased. For example, in the USA HSV 2 is registered in every fifth adult, in Russia the frequency is about 5 cases per 100 people, in African countries the highest infection rates are 30-80% of women and 10-50% of men have this infection [5-7]. At the same time, in our country, most patients are asymptomatic carriers and do not know about the possibility of viral release and infection of other people [6]. It has been established that gender and age are risk factors for the development of genital herpes. The prevalence of herpes virus infection is low in children and adolescents (0.1 and 9.4 cases per 100 thousand people. accordingly), the peak of morbidity in the Russian Federation is observed at the age after 20 years and at 35-40 years [3, 8]. Women have higher incidence rates of genital herpes, but the number of sexual partners has a greater impact on the risk of developing the disease [9, 10]. In addition, economic well-being, alcohol abuse and/or drug addiction, early onset of sexual activity, sexual behavior and the presence of bacterial vaginosis may increase the risk of infection of women before pregnancy [4, 11].

About 20% of pregnant women are infected with HSV-2 and about 1-5% acquire genital herpes during pregnancy [12]. The danger of genital herpes during gestation is due to the high frequency of spontaneous termination of pregnancy, premature birth, congenital and neonatal herpetic infections, delay in fetal development [13]. Herpetic infection is also associated with an increase in the incidence of thrombophilia and antiphospholipid syndrome due to damage to the endothelium of HSV blood vessels. When women are infected with HSV 2 in the third trimester, the risk of infection of the newborn is up to 50-75%, in the first trimester - about 1-3% [2]. This is due to the fact that in the case of primary infection with the herpes virus at the end of the gestation period, the time before childbirth is not enough to produce the antibodies necessary to suppress the replication of the virus [1]. Intrauterine transmission of HSV from

mother to fetus is rare; more than 85% of perinatal transmission occurs during childbirth. Studies have shown that HIV co-infection with HSV significantly increases the risk perinatal transmission of HIV, primarily in women with a confirmed diagnosis of genital herpes during pregnancy. With common forms of herpes infection in the mother, transplacental infection can reach 50% [14].

A newborn with genital herpes can also be infected with HSV-1, which accounts for almost a third of all new diagnoses [8]. A growing proportion of genital herpes infection caused by HSV-1 suggests that there is currently a risk of transmission of HSV-1 to a newborn during pregnancy in young girls [4]. At the same time, HSV-1 decreased in childhood, so that more young people are HSV-seronegative when they become sexually active [14]. This explains the observed increase in newly detected HSV-1 infection of the reproductive system in this age group.

Genital herpes is asymptomatic in most cases [15]. Clinical manifestations of this disease occur 2-21 days after infection and include: rash and ulceration of the external genitalia and cervix, dyspareunia, dysuria, vaginal discharge, local lymphadenopathy [16]. Vesicular and ulcerative lesions of the inner surface of the thigh, buttocks, perineum and/or perianal zone are also observed. Both men and women with primary infection may have systemic manifestations, such as fever, headache and myalgia (38% in men, 68% in women), sometimes meningitis and vegetative neuropathy, leading to urinary retention, mainly in women [7, 8]. Herpetic meningitis is found in 40% with primary HSV-2, in 12% with primary HSV–1 and in 1% of patients with a recurrent course of the disease. At the same time, systemic manifestations may be the only symptoms of the disease. It was established that the presence of antibodies to serotype 1 of the herpes virus can facilitate the course of subsequent acquisition of serotype 2 [1]. The most dangerous during gestation is primary HSV infection, which leads to more serious complications in pregnant women compared to non-pregnant women. In particular, the incidence of acute gingivostomatitis and herpetic vulvovaginitis increases [2]. As a result, patients may have disseminated skin lesions, internal organ damage (hepatitis, encephalitis, meningitis, thrombocytopenia, leukopenia and coagulopathy) [6, 9]. Despite the fact that the common form of HSV infection is rare during gestation, the mortality rate for it is about 50%. In pregnant women in the third trimester with primary infection of the mucous membranes, the risk of not only transmission of HSV to a child during vaginal childbirth increases, but also the development of common forms of herpetic infection [2, 8].

Relapses of herpetic infection are characterized by a shorter (7-10 days) and lighter course and in the overwhelming majority of cases are caused by HSV 2 [2]. Asymptomatic phases between clinically pronounced outbreaks of genital herpes are dangerous, since the herpes virus can periodically reactivate in infected cells of the sensory ganglia and migrate through neuronal axons back to the mucous membrane of the genitals without clinical signs or symptoms [1]. This mechanism is known as asymptomatic virus division; most of the sexual transmission of HSV occurs during these asymptomatic periods. In addition, it has been shown that asymptomatic discharge is more often detected in women with HSV 2, compared with women with HSV 1 [7, 8]. Recurrent genital herpes is the most common cause of neonatal infection (the route of transmission is through the birth canal). During cesarean section surgery, the risk

of infection of the child is significantly reduced. Transmission of HSV to women with asymptomatic viral discharge is an urgent problem, since newborns in most cases acquire an infection, and diagnosis and treatment in this case are carried out untimely [7].

When the fetus is infected in the antenatal period, various developmental disorders may occur. The literature describes cases of brain formation disorders, the most common are ventriculomegaly, corpus callosum dysgenesis, porencephaly, microcephaly, hydrocephalus and microphthalmia, which can be detected at the stage of prenatal diagnosis [13]. Also, against the background of a herpetic infection in the mother, anemia in the fetus, liver and cardiovascular system abnormalities may develop (these disorders occurred mainly in HSV 2) [2]. After birth, this group of children has chorioretinitis, herpetic keratitis, anencephaly, porencephaly, cerebellar abnormalities, cerebral hemorrhages, intra-cranial calcification. Postnatal infection in most cases is associated with HSV 2 (81%) [13]. Modern observations also show that there is no correlation with the time and type of HSV infection: as with other congenital infections (CMV, rubella, toxoplasmosis), the risk increases with infection in the early stages of pregnancy, but the appearance of HSV in the last trimester does not exclude the possibility of severe consequences for the fetus [1].

Diagnosis of herpes virus infection in pregnant women is complicated due to the possible presence of only systemic manifestations, unexpressed local symptoms, or complete absence of clinical manifestations [5]. In addition, there are symptom-free periods with continued viral release between periods of exacerbation. HSV infection can be identified directly upon detection of the virus (the contents of the vesicles, smears, prints, PCR) or by the analysis of specific serum antibodies to the virus [10, 16].Difficulties for diagnosis arise when a pregnant woman is suspected of herpetic hepatitis. The gold standard of verification is a liver biopsy followed by histological examination. In hepatitis caused by HSV, hemorrhagic necrosis, inflammation and enlargement of nuclei (frosted glass) with marginalized chromatin are pathognomonic [14]. However, invasive follow-up is associated with a high risk of uncontrolled bleeding due to blood clotting disorders. Empirical treatment is recommended for this group of patients, as well as diagnosis by determining specific IgM antibodies and PCR in the presence of fever and an increase in the level of hepatic transaminases according to biochemical blood tests [19].Treatment of pregnant women with primary genital herpes or its recurrence is carried out with acyclovir or valacyclovir in recommended doses [22, 23]. Since acyclovir and valacyclovir are not officially approved for the treatment of patients, patients should be informed about possible side effects. Randomized studies have shown that therapy with acyclovir and valacyclovir from the 36th week of pregnancy to delivery significantly reduces the frequency of clinical manifestations and the intensity of virus release during childbirth, thereby reducing the need for cesarean section and, probably, the risk of vertical transmission [22].If genital herpes occurs in the first or second trimesters of pregnancy, it is recommended to conduct a virological study from the 32nd week of gestation. If two studies are negative and there are no signs of active herpetic infection on the genitals, then it is possible to conduct natural delivery [12, 7]. Women who had an episode of recurrent genital herpes a few weeks before the expected date of delivery are recommended to undergo therapy with acyclovir or valacyclovir during the last 4 weeks of gestation, as well as a virological

examination of cervical-vaginal secretions from the 36th week of pregnancy. In the absence of clinical manifestations and positive test results for the detection of the virus, a planned caesarean section is performed [1, 18].All patients with recurrent herpetic infection at the stage of pregnancy planning are recommended to carry out comprehensive pre-gravidar preparation [4, 5]. The study showed that the use of recombinant human interferon, anticoaulants, antiplatelet agents and antioxidants reduces the incidence of severe forms of gestosis, thrombophilia, antiphospholipid syndrome, fetoplacental insufficiency, premature rupture of fetal membranes and the threat of termination of pregnancy [6].

Conclusion

Thus, based on all of the above, it can be concluded that herpes virus infection is an urgent problem in the work of an obstetrician-gynecologist. Against the background of HSV infection, the frequency of various complications of the course of gestation and childbirth, as well as the formation of fetal malformations, increases. It is necessary to carry out timely diagnosis and treatment of this group of patients not only during pregnancy, but also at the stage of planning by pregravidar preparation, which will improve the prognosis for mother and child.

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