INTRAUTERINE INFECTIONS IN THE SYSTEM "MOTHER – AFTERBIRTH – FETUS"

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Infection process in fetus begins to develop when infection agents overcome complicated immunity system, starting from mother's common immunity and then up to histohematogenous barrier between mother' blood and morphofunctional formations of afterbirth. Then the agent penetrates through the barrier, overcomes afterbirth immunity system, penetrates through the second histohematogenous barrier of the afterbirth into fetus blood and after all overcomes fetus immunity system. Nowadays there is a necessity to work out preventive measures and treatment for a fetus during all the stages of intrauterine ontogenesis as well as the technique, which would allow to block the ways of infection spread into the system Mother – Afterbirth.

Background

Earlier we revealed two independent kinds of immunity forming in neurotropic virus infection: common barrier – extraneural and rehematoencephalic barrier – cerebrospinal [1]. During pregnancy afterbirth is being formed as an organ, connecting fetus with mother. It contains amniotic capsules and fluid, placenta, and umbilical cord. Infection disease agents, penetrating into fetus, are able to overcome barriers between morphofunctional formation of afterbirth and both mother's blood and fetus blood. [2, 3]

Research works of the last years show that intrauterine infection plays an important role in pathogenesis of those conditions, which recently were not regarded as infection pathology. The term "intrauterine infections" refers to the diseases, in which the infecting takes place during pregnancy or delivery and the mother is the source of infection. The term "intrauterine infections" is usually used to describe clinical signs of fetus and newborn infection diseases, revealed in prenatal period or straight after birth. They use in practical medicine the term "intrauterine infecting" to mark the fact of intrauterine infection, which happens more often, than clinical signs of the disease develop. The frequency of intrauterine infecting according to different authors fluctuate from 6% to 53%, achieving 70 % among prematurely born babies [4, 5, 6].

The aim of the research is to establish the frequency of infecting placenta and amniotic fluid in a newborn under different urogenital and virus infections in mother.

Materials and Methods

To resolve the task we examined 402 women in birth, 394 newborns of those mothers, 8 miscarried fetuses. We took during labor 402 amniotic fluid tests and 402 placenta tissue samples of those women.

All the women in birth were divided into the following groups:

A – women without any virus or urogenital infection according to laboratory tests. 172 subjects (control group).

B – women having virus or urogenital infection agents or the signs of infecting according to laboratory tests. 230 subjects (the main group), including:

- B1 – virus or urogenital infection agents or the signs of infecting were revealed only in women in birth – 76 subjects;
- B2 – virus or urogenital infection agents or the signs of infecting were revealed in a woman in birth, amniotic fluid, and/or in placenta tissue – 66 subjects;
- B3 – virus or urogenital infection agents or the signs of infecting were revealed both in women in birth and in their newborns. May be – in amniotic fluid and placenta tissue – 88 subjects.

There were 172 non-infected subjects in control group with normal indices of specific antibodies to herpes and cytomegalia agents and the absence of the elements of these virus and urogenital infections (chlamydiae, mycoplasmosis, ureaplasmosis) after

polymerase chain reaction (**PCR**) results. In the main group 230 subjects had different levels of specific immune globulins M and G to the given infection agents as well as positive PCR results.

All the intakes were done on the basis of Krasnoyarsk Clinical Maternity Hospital № 2 from 2002 till 2005.

We examined blood serum in newborns, afterbirths and back amniotic fluid in puerperas in groups A and B by PCR technique.

Peripheral blood and smears were taken from the subjects in the first stage of delivery. At the end of the second stage straight after the birth we took the samples of back amniotic fluid. Following the afterbirth stage we performed the cutting of placenta and amnion pieces by random. In cases of operative delivery the materials were taken on the operating table.

In 1 to 3 days after delivery we took peripheral blood samples for biochemical test from newborns in their ward. At the same moment the other blood samples were taken for testing DNA agents of the mentioned infections.

The Results of the Research

We traced the character and dynamics of infecting process in women, who were coming into delivery, by means of parallel determination of immune globulins in blood serum and the revelation of virus and urogenital infections DNA in vaginal smears.

So, in group B the IgG to cytomegalovirus (**CMV**) was revealed in 89.5%, to the virus of simple herpes (**SHV**) in 79.4%. There were no M immune globulins, which are responsible for acute process or for the exacerbation in chronic process to the mentioned viruses. Vaginal smears tests (performed by PCR technique) show cytomegalia virus DNA in 19.3% puerperas and herpes virus DNA in 13.8%. So, CMV as mono agent was revealed in 2% subjects, SHV in 9%. We marked high percentage of the associations of the given viruses with the agents of urogenital infections, which achieved 23%. The combination of DNA of these two viruses in one puerpera was not revealed by us (figure 1) [7, 8].

Percentage of urogenital infection agents was significantly higher in group B.

Totally in vaginal smears of all the infected subjects in the main group the Chlamidia trahomatis DNA was revealed in 63.2% cases. We analyzed the character of chlamydiae infection condition by immune enzyme technique (**IET**). We marked the presence of Ig M and the absence of Ig G in serum test in PCR positive subjects and regarded this as primary acute chlamydiae infection, which took place in 4.6% cases. In blood serum in 12.1% women both IgM and IgG were positive, which was regarded by us as reactivation or exacerbation of chronic chlamydiae infection. In blood serum in 73.8% patients Ig M to chlamydiae was absent. At the same time we marked diagnostically meaningful IgG titers, which can be estimated as chronic course of infecting process or as latent carriaging. In 9.5% women of this group both IgM and IgG to chlamydiae agent were not found, which can be connected with the peculiarities of immune response. We should mention that among mono infections chlamydiae corresponds to 23%, being on the first place in this niche.

We found ureaplasm DNA in smears in 38.6% and IgG to this agent in 28% patients. According to our data 36.8% women show mycoplasm DNA. Ureaplasmosis as mono infection was marked in 9% and mycoplasmosis in 7% cases.

The diagrams show the dominating position of different associations of urogenital infections - 27% (figure 1). The most prevalent are: the combinations of CMV, ureaplasmosis and Chlamidia trahomatis - 7% cases; ureaplasmosis and Chlamidia trahomatis – 4%; ureaplasmosis, mycoplasmosis and Chlamidia trahomatis – 4%. This is explained by rather high prevalence of these infections in the population [9].

The fact of determining immune globulins to the given infections does not testify obligatory on the development of infection process [10]. This is confirmed by IgG

presence in control group A, where infecting process in pregnant woman and in fetus didn't develop. So in this group 9% patients showed IgG to chlamydiae, Ig G to ureaplasm 3%, Ig G to CMV – 64%, and Ig G to SHV – 73%. Ig M in A group to the mentioned agents was not revealed.

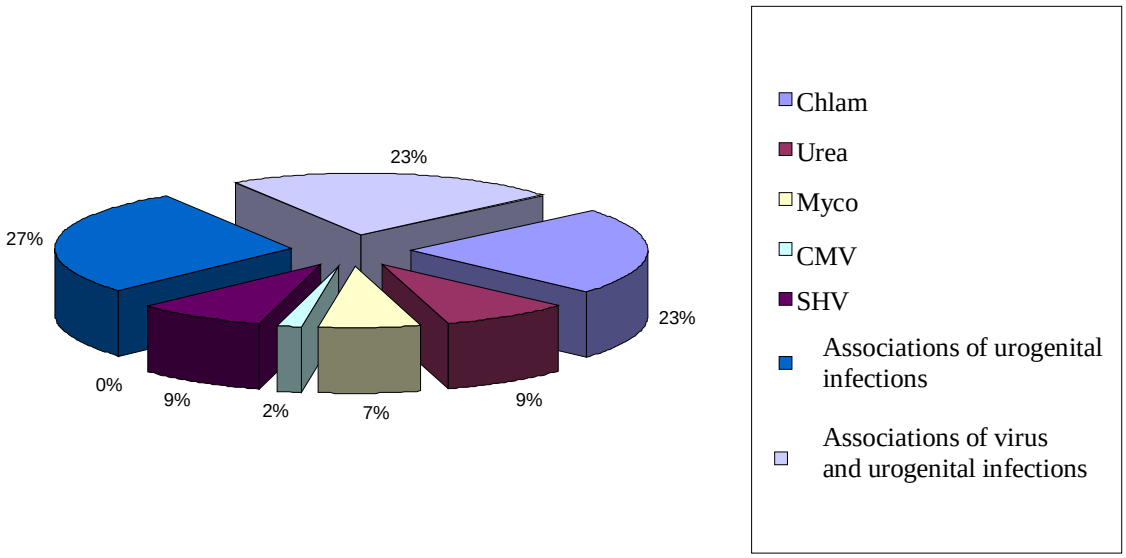

Figure 1. The prevalence of different agents of virus and urogenital infections in women of Group B (%).

We analyzed 402 afterbirths and 402 samples of amniotic fluid to reveal agent DNA of CMV, SHV and urogenital infections (chlamidiae, ureaplasm and mycoplasm). All the tests were performed by PCR technique.

We analyzed the data in details and obtained the following results. Out of 100% infected women only in 33% the infection was not distributed out of mother's organism. In two thirds of the pregnant women (67%), DNA of intrauterine infection agents were found in amniotic fluid or afterbirth or fetus (B2 and B3 groups). In 13% of the patients in the main groups, infection DNA passed fluid and placenta barriers and was recognized in newborns. In 10.4% cases infection DNA were marked in baby and in mother. In 2.6% cases infection DNA in a newborn differed from that one found in placenta and amniotic fluid (for example a newborn shows cytomegalovirus DNA but there was Chlamidiae and mycoplasm DNA in placenta and fluid).

So, in 87% mothers the infection agents passed natural barriers and went through placenta or amniotic fluid practically in 7 out of each 8 cases.

In groups B2 and B3 we revealed 43.5% cases with intrauterine infection DNA in amniotic fluid, 29% cases in placenta tissue and afterbirth cover, 27.5% cases in placenta and amniotic fluid.

Only in 10.5% cases we revealed chlamidiae DNA as mono agent. It was found in puerpera, in placenta and amniotic fluid. In 89.5% cases they were the combinations of chlamidiae, mycoplasm and ureaplasm DNA, CMV and SHV. In most cases they were different in placenta and amniotic fluid in one and the same woman.

We revealed 68% non-infected afterbirths out of 402 subjects in the main group. In 32% cases afterbirths contained DNA of the above-mentioned infections. The most prevalent were chlamidiae with the share of 19%, which made 59.4% of all the infected afterbirths. The second prevalent mono agents were SHV and mycoplasm, 3% or 9.4% of all the infections. In 2% cases we found DNA sectors to CMV in afterbirths.

We didn't reveal ureaplasm DNA in placenta (figure 2).

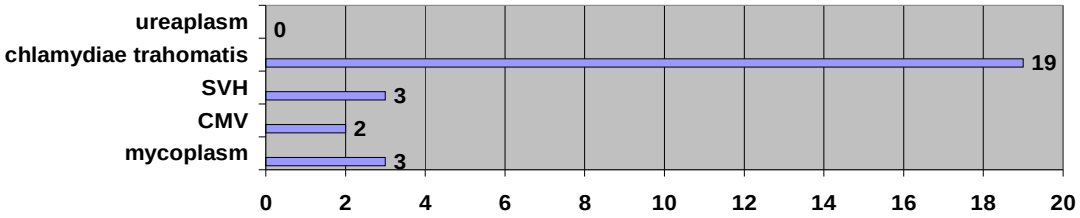

Figure 2. The results of placenta tissue tests for DNA sectors of intrauterine infections (IUI) agents in Group B patients (in %).

Only one combination of microbe associations was marked in placenta – chlamidiae and mycoplasm DNA, nearly 5%, which corresponded to 15.6% among the infected afterbirths.

57% of 402 samples of amniotic fluid in main group were not infected. Chlamidiae DNA was the most prevalent in amniotic fluid and in placenta (in 21% cases) which corresponded to 48.8% of all the infected samples. The share of mycoplasm DNA increased greatly and achieved 14% or 32.6% of all intrauterine infections. In 4% cases we revealed simple herpes virus in amniotic fluid and in 2% cases ureaplasm DNA. We didn't revealed cytomegalovirus DNA in amniotic fluid in the main group (figure 3).

So, in amniotic fluid in puerperas of the main group we marked the same associations of antigens as in placenta, i.e. chlamidiae and mycoplasm DNA but with smaller frequency of 2% cases or in 4.7% of all the infected samples [13].

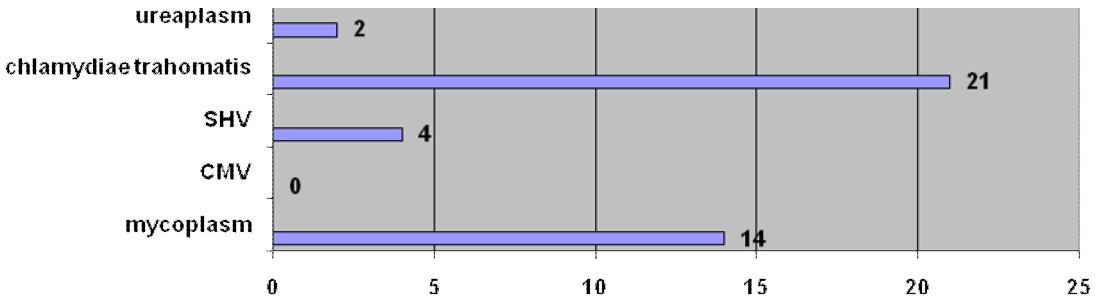

Figure 3. The results of the examination for IUI by PCR technique in amniotic fluid in Group B patients (in %).

All 394 newborns and 8 miscarriages of main group were examined by PCR technique for determining DNA specific sectors of the agents of perinatal infections - urogenital (chlamidiae, mycoplasm, ureaplasm) and virus (CMV and SHV).

According to the results of the tests there were no infected children in Group A (control group). There is no doubt, the results of Group B were the most interesting (the main group), in which all the mothers were infected and were potentially the "infection reservoir" for their babies [14, 15].

The majority of newborns of the main group (including miscarriages) were not infected according to serological test. Their share was 61.65%. The rest of the newborns had DNA fragments of one of the agents of intrauterine infection. Their share was 38.2%. It should be marked that we didn't reveal infection pathogens associations in any of the cases.

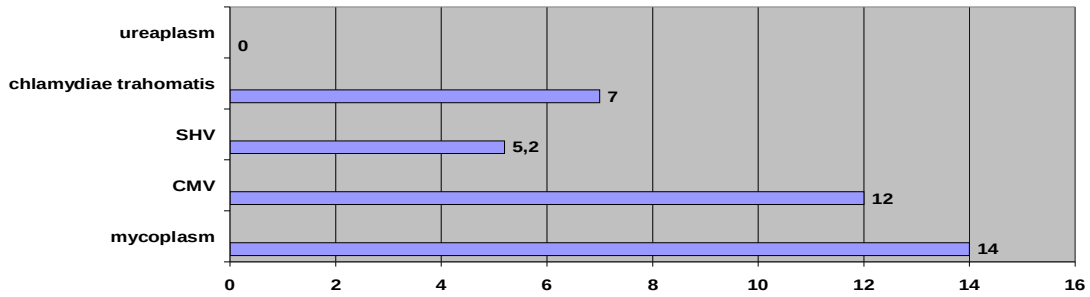

Figure 4. The results of blood serum tests in newborns for DNA sectors of intrauterine infictions agents in group B (in %).

The results of our tests for Group B newborns more often showed mycoplasm DNA. Their share was 14%. The second place in the prevalence belonged to CMV genome fragments in newborns. The share of these babies was 12%. The frequency of chlamidiae DNA in newborns was only 7 %, and SHV DNA was 5.2%. Ureaplasm DNA was not revealed at all (figure 4).

As it was mentioned above, all the IUI positive samples of blood serum in newborns contained DNA sections of representatives of some single agent. Having analyzed the share of each agent in common structure of intrauterine infection agents, taking into account DNA sectors in newborns, we received the following results: mycoplasm 36.4%, CMV 31.8%, chlamydia 18.2%, SHV 13.6%, ureaplasm 0%, associated infections 0% (figure 5).

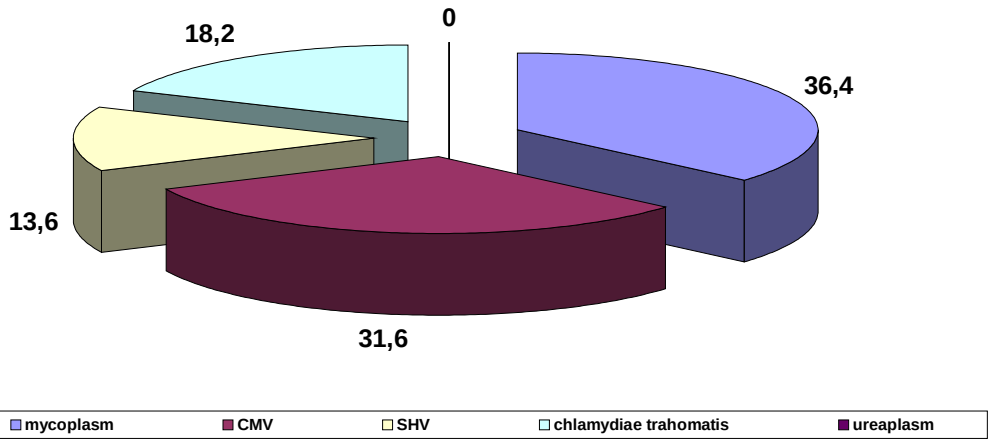

Figure 5. The shares of intrauterine infections agents in the stricture of the newborn infecting (in %).

So, having analyzed the received data, it became evident that dominating infections in puerperas are chlamydia and ureaplasm as well as different associations. In newborns mycoplasm and cytomegalia virus prevail.

So, the results of our research show that trans-placenta way of the infecting is the most typical for chlamidiae infection and less typical for cytomegalovirus or herpetic virus. For the last ones intro natal way of the infecting is more typical, which goes in conformity with researchers' generally accepted opinion [11, 12].

Conclusion

Three organisms function during pregnancy: mother, fetus and afterbirth. Each of them is developing its own immune system. But afterbirth immune system depends upon that one in a pregnant woman. Fetus protection against infection agents is provided by interactions between the developing immune system of afterbirth and immune system of mother and fetus.

References:

1. Dubov A.V. Common and cerebrospinal immunity in pantropic virus infection. – European Journal of Natural History. – 2008, № 1. – P.5 -11.

2. A.V.Dubov, N.V.Chekudaeva. The system of placenta immunity – Immunology days in Siberia. – Krasnoyarsk. – 2005. – P.108 – 111.

3. O.V.Strelskaya, A.V.Dubov. The peculiarities of infecting the system "mother-placenta-fetus-amniotic fluid". – Siberia medical magazine. – 2008. – V.23 - №3. – Issue 1. – P.117.

4. A.A.Durova. Etiology and pathogenesis of intrauterine infecting / A.A.Durova, N.G.Simakova, V.S.Smirnova // Obstetrics and Hynecology. - 1995. - №6. - P.9-12.

5. V.I.Kozlova. Virus, chlamydia and mycoplasm diseases of genitals / V.i.Kozlova, A.F.Pukhner // Guidelines for doctors. - M.: Filin, 1997. – 536 p.

6. Sterner, G. Guidelines for management of pregnant women with infections at delivery and care of their newborns / Ed. G. Sterner // Stockholm: Karolinska Inst., - 1990. -408p.

7. K.V.Orekhov. Intrauterine infections of herpetic and cytomegalovirus etiology / K.V.Orekhov, M.V.Golubeva // Actual questions of pediatrics: Collected scientific transactions. - Nalchik, 1997- P.84-91.

8. Corney, L. The current trend in genital herpes. Progress in prevention // Sex. Transm. Dis. - 1994. - V.21, N#2. - P. 38-44.

9. I.S.Sidorova. Intrauterine infections: Chlamydia, mycoplasmosis, herpes, cytomegalia / I.s.Sidorova, I.N.Chernenko // Russian bulletin of perinatology and pediatrics. - 1998.-№3.-P.7-13

10. A.V.Tsinzerling. Intrauterine infections, frequency and diagnosis / A.V.Tsinzerling, N.P.Shibalov // Arch. of pathology. - 1992. - №1. - P.24-30.

11. I.S.Sidorova. The state of fetus-placenta system in high risk of fetus intrauterine infecting / I.S.Sidorova, I.O.Makarov, N.A.Matvienko and others. // Russian bulletin of perinatology and pediatrics. - 2000. - №2. - P.5-8.

12. V.B.Tshai. Perinatal aspects of chronic and feto-placental insufficiency in intrauterine infecting: Abstract to full professor thesis/V.B.Tshai. Tomsk, 2000 – 39 p.

13. Alanen, A. Polymerase chain reaction in the detection of microbes in amniotic fluid / A. Alanen // Ann. Med. - 1998. - N°3. - P.288-295.

14. E.V.Pavlova. Clinical diagnostic criteria of intrauterine and early neonatal infecting and the infections in newborns: Abstract to MD thesis / E.V.Pavlova. - Moscow, 1987. – 19p.

15. A.V.Shabaldin. The implementation of polymerase chain reaction in diagnosis for intrauterine infections in fetuses and newborns/ A.V.Shabaldin, L.A.Balyanova, L.M.Kazakova and others. // Pediatrics. - 2000. - №3. - P.38-41.