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New Treatment of Ureaplasmosis in Pregnant Women

G. Z. Sakhipova, B. K. Karymsakova, G. M. Kulniyazova, G. Y. Karsakova, S. A. Abdildaeva, G. Y. Kuzdenbaeva, D. O. Shamshaeva

West Kazakhstan Marat Ospanov State Medical University, Aktobe 030000, Kazakhstan

Abstract

According to WHO, approximately 60% of pregnant women experience acute or recurrent ureaplasmosis. Multiple studies show that one of the prominent causes of miscarriage associated with ureaplasmosis is cervical weakening that leads to premature dilation of the cervix and preterm birth. The population of this study included 15 pregnant women with an acute episode of chronic ureaplasmosis, out of which 2 women (13.3%) were in the 1st trimester, 10 women (66.7%) were in the 2nd trimester and 3 women (20%) were in the 3rd trimester of pregnancy. As a treatment for ureaplasmosis, all subjects received a new generation macrolide antibiotic containing josamycin-wilprafen active substance 1 tablet 3 times per day for 10 days. For 80% of the treated subjects, the natural conclusion of pregnancy was achieved with the newborns weighing 3,200 ± 100.0 g. Only 20% of the subjects had preterm labor at 32-33 weeks pregnant that resulted in live births with the newborns weighing 2,200 ± 100.0 g. The babies born to the infected mothers receiving wilprafen had no visible signs of CDF.

Keywords: ureaplasmosis, pregnancy, josamycin-wilprafen, miscarriage.

INTRODUCTION

Pregnancy is a special physiologic state that is characterized by weakened defense mechanisms of the woman's body, which may lead to activation of some "hidden" infections able to affect the course of gestation by infecting the urinary tract [1]. During pregnancy, increased progesterone reduces ureter muscle tone causing dilation of the ureters and decreased urinary output. The gravid uterus slows down urinary output by constricting the ureters. All these factors cause bacterial growth in the ureters and further spread of the bacteria into the kidneys [2]. The agents that cause infectious diseases may be classified into three groups. The first group includes TORCH infections, such as rubella, CMV, herpes and toxoplasmosis. Despite the differences in the symptoms and progression of these diseases, all of them have one common characteristic: it is highly likely that they will be transmitted to the fetus in case of initial infection. If the mother was infected during her first trimester, in 80% of the cases the virus will affect the fetus and lead to severe congenital malformations. Usually, such diagnosis means that a therapeutic abortion has to be performed [3]. By the end of the second trimester, the risk of fetal infection decreases to 25%. Infection during this time may lead to a delay in mental and physical development or epileptic seizures. The second group includes chickenpox, a childhood disease that in case of intrauterine transmission has the sequelae similar to those of TORCH infections. Nevertheless, the incidence of such sequelae is low, unless the infection develops during the 1st trimester of pregnancy. After 20 weeks, the risk is reduced to almost zero, but it increases if chickenpox is contracted several days before labor. During this period, the disease may cause the most severe complications. The third group includes influenza and acute respiratory viral infection. In this case, the major danger for pregnancy and fetus development is posed by the sequelae rather than the virus itself. It is very common for this virus to trigger acute episodes of chronic diseases, which may lead to spontaneous abortion. TORCH infections during pregnancy may cause miscarriage, premature labor or transmission of the infection to the baby [4]. Ureaplasma is mostly found in women with fertility potential, i.e. of childbearing age (18 – 38 years of age) [5]. Therefore, physicians recommend all women to check their ureaplasma status before planning for pregnancy, along with taking tests for other asymptomatic sexually transmitted infections (mycoplasmosis, chlamydiosis, candidiasis, herpes virus infection, etc.). There are two pathways to human body that ureaplasma may take: sexual intercourse with an infected individual or carrier, and birth from an infected mother, when the microbes may enter the baby's genital tracts during labor and remain there inactive throughout the lifetime. As mentioned before, for a long time after entering a woman's body (the same for pregnant women) ureaplasma remains an asymptomatic hidden infection and is mostly detected in the course of laboratory testing. Such asymptomatic form is widespread and found in about 70% of sexually active women and men. The disease starts when concentration of the microorganisms exceeds a certain threshold value and is characterized by colorless genital discharge as well as itching, burning sensation and pain during urination. Some pregnant women experience lower abdominal pain and insignificant rise in body temperature. The literature review shows that one of the prominent causes of miscarriage associated with ureaplasmosis is cervical weakening and softening of the external os resulting in its dilation and premature expulsion of the fetus [6]. According to WHO, acute or recurrent ureaplasmosis is found in about 60% of the pregnant women.

MATERIALS AND METHODS

The study was conducted on 30 pregnant women with an acute episode of chronic ureaplasmosis divided into the main and the control group. In both groups, the common complaints of the subjects were ample genital discharge, vaginal itching, burning sensation during urination, tensive pain in the lower abdomen and lower back, and vaginal discomfort that intensifies during sexual intercourse. The speculum exam showed hyperemia of the vaginal walls, yellowish-grey or ample green discharge sometimes with blood and cervicitis. The following samples were collected from all the subjects: a swab for vaginal purity analysis; vaginal, cervical and urethral samples for polymerase chain reaction (PCR); and samples from urethral mucosa, vaginal vault and cervical canal for vaginal culture. Bacterioscopic and bacteriologic tests of the vaginal discharge were performed by the traditional method. The condition of the local vaginal phagocytes was assessed based on the phagocytic activity of neutrophils that included determination of their absolute count (ANC), phagocytic index (PI) and absolute phagocytic index (API = PI ANC). The total absolute leukocyte count per 1 μL of the discharge was also taken into consideration. Vaginal biocenosis was evaluated by means of microscopy of the vaginal and cervical swabs with Gram, Romanovsky-Giemsa and Pavlovsky staining. The microscopy results were assessed according to the classification developed by E.F. Kira (1995): the 1st degree of purity is characteristic of a healthy vagina. The swab microflora includes 95% of lactobacilli; isolated leukocytes and epithelial cells may be detected. The 2nd degree of purity is similar to the 1st degree, but the swab may contain a small number of opportunistic pathogens. The 3rd degree of purity is characterized by the higher level of opportunistic pathogens as compared to Doderlein bacillus. The 4th degree of purity is characterized by a large

number of epithelial cells, leukocytes and bacterial flora; the bacilli are few or absent.

The PCR results demonstrated ureaplasma count of 10*4 and 10*5 per 1 ml of the tested sample, which meant that antibiotic therapy was required to manage the inflammatory process.

All the participating women were asked to perform preparatory activities before the test in order to ensure maximum accuracy of the results. For this purpose, the following recommendations were to be followed by the subjects in both groups:

- to abstain from any sexual intercourse for 2-3 days before the test;
- not to use any intimate hygiene products or topical medicinal products for the same period;
- not to use tampons or perform cleaning of the vaginal mucosa, including douche;
- not to perform any intimate hygiene procedures on the test day.

All the subjects received antibiotic treatment for ureaplasmosis. Concurrently, the subjects were started on Hylak forte 30 drops*3 times per day for 10 days for prophylaxis of dysbiosis, and viferon suppositories 500mg*1 time per day intrarectally for immune system reinforcement as it was very important to minimize the risk of a secondary disease. The therapy of colitis was performed with hexicon suppositories used to treat chronic exo- and endocervicitis and vaginitis [7, 8]. The product is absolutely safe for a pregnant woman and the baby, since its topically active and very poorly absorbed into the blood stream, and therefore cannot influence fetus development. At the same time, it does not disrupt the normal vaginal microflora but is effective against almost all microorganisms and protozoans that affect genitourinary tract, including ureaplasma.

Along with ureaplasmosis treatment, the subjects received the standard pregnancy-saving therapy. Considering that ureaplasma is sexually transmitted, treatment of the intercourse partner was a mandatory part of the pregnant women's therapy. The efficacy criteria for the treatment included negative results of the PCR test and vaginal culture for ureaplasmosis after 3 weeks of therapy, achievement of the 1st or 2nd degree of vaginal purity after 10 days of therapy, subsidence of the threatened miscarriage symptoms and satisfactory condition of the fetus as per the results of CTG and Doppler velocimetry after 28 weeks of pregnancy.

The subjects in the main group received a new generation macrolide antibiotic with josamycin-wilprafen active substance 1 tablet 3 times per day for 10 days [9]. The main group included 2 women (13.3%) in 1st trimester, 10 women (66.7%) in the second trimester and 3 women (20%) in the third trimester of pregnancy. The subjects experienced the following pregnancy complications: threatened miscarriage – 12 women (80%); incipient abortion – 3 women (20%): 2 women (13.3%) before 12 weeks pregnant and 1 woman (6.7%) before 22 weeks pregnant.

The control group included 15 pregnant women with an acute episode of chronic ureaplasmosis that were examined and treated according to the clinical protocol Urethral Infections during Pregnancy, Labor and Postpartum Period issued by the Ministry of Health of the Republic of Kazakhstan [9]. In this group, 11 women, i.e. 73.3% of the subjects, had threatened miscarriage symptoms before 12 weeks pregnant, and 2 women, i.e. 13.3% of the subjects, showed signs of threatened abortion between 12 and 22 weeks pregnant. All the pregnant women underwent clinical examination including urinalysis, complete blood count, urine culture, Nechiporenko test, and kidney and bladder ultrasound exam. According to the above mentioned clinical protocol, the subjects received monodose cephalosporin therapy for 3 days and amoxicillin 375-625 mg 2-3 times per day as a treatment for the lower urinary tract infections and asymptomatic bacteriuria. [10]

RESULTS

The initial vaginal purity analysis for all the subjects demonstrated the 3rd-degree purity (70%) or 4th-degree purity (30%). In particular, the 3rd-degree swab contained a small number of vaginal bacilli, multiple pathogenic bacteria and cocci and a large number of leukocytes. The swab demonstrated weakly alkaline reaction. The 4th-degree swab contained no vaginal bacilli, but a large number of leukocytes. The PCR (polymerase chain reaction) test and vaginal culture results confirmed the presence of ureaplasma in the pregnant women from both study groups.

For 80% of the subjects treated as described above, the natural conclusion of pregnancy was achieved with the newborns weighing 3,200 ± 100.0 g. Only 20% of the subjects had preterm labor at 32-33 weeks pregnant that resulted in live births with the newborns weighing 2,200 ± 100.0 g. The babies born to the infected mothers receiving wilprafen had no visible signs of congenital malformations. In the main group, ureaplasma remained in 26.6% of PCR test results and in 53.3% of vaginal culture results.

In the control group, the incidence of spontaneous abortion was 2 times higher than that of the main group. After treatment with cefalosporin, ureaplasmosis was identified by PCR method in 73.3% of the control group subjects, which was 3 times higher as compared to the main group. The vaginal purity analysis showed improvement of the vaginal biocenosis in both groups. Fetus condition as assessed by CTG and Doppler velocimetry was 2.5 times better in the main group versus the control group.

DISCUSSION

Presently, the impact of chronic genital infections on fetal development is the subject of active discussion in the scientific community. It should be noted that in the developed countries of Europe and America pregnant women who report no complaints are not tested for urea- or mycoplasma [11]. In case such tests are performed, it is done for scientific purposes only and free of charge [12]. However, in Russia and Kazakhstan the situation regarding this infection is totally different. Additional tests for ureaplasma are prescribed to almost all women and in most cases such tests are performed for a fee. It must be mentioned that this type of bacteria is found almost in all patients since in most women it is a part of the normal vaginal microflora. Nevertheless, in case of a positive result antibiotic therapy is prescribed with the mandatory requirement of treating both intercourse partners and sexual abstinence [12]. When selecting the antibiotic, macrolides are the preferred option, since they are broad spectrum non-toxic antibiotics that do not affect the fetus and have minimum impact on the intestinal microflora which means they practically do not cause dysbiosis. Therefore, the antibiotic selected for this study was wilprafen. Furthermore, wilprafen was approved for use during pregnancy by WHO and recommended by WHO Europe as a treatment for chlamydiosis, genitourinary infection, trachoma, lymphogranuloma and ureaplasma as a means of preventing intrauterine congenital malformations. The drug product is effective for the treatment of the infection-related inflammatory processes caused by the microorganisms susceptible to josamine, such as urogenital tract infections, syphilis, chlamydiosis, mycoplasmosis, ureaplasmosis and gonorrhea.

CONCLUSIONS

Summing up, use of wilprafen for treatment of ureplasmosis in pregnant women allowed to maintain pregnancy until fetal maturity was achieved. Wilprafen is one of the few antibiotics permitted for use during pregnancy due to its low toxicity and little harm for pregnant women. The absence of embryotoxic or teratogenic effect of the antibiotic was confirmed

on animals only. However, since treatment of infections during pregnancy is often necessary, wilpafren was included into the list of antibiotics permitted for use in pregnant women. Investigation of the effect ureaplasmosis has on gestation course will be continued in the course of genetic study. Laboratory prenatal diagnostics will be performed on the following fetal biological samples drawn by obstetrician-gynecologists: chorionic villi, amniotic fluid or umbilical cord blood. In order to exclude contamination of the fetal material by the mother's cells, a biological sample of the pregnant woman will be drawn as well. The fetal material used for prenatal diagnostics will be represented by a biopsy slice of chorionic villi (within 8 to 14 weeks of pregnancy) or amniotic fluid (within 16 to 21 weeks of pregnancy). After 21 weeks pregnant, the diagnostics will be performed by testing the fetal blood obtained by cordocentesis.

REFERENCES

1. Savicheva, A. M., Bashmakova, M. A., Urogenitalny chlamidioz u zhenschin I ego posledstviya: Meditsinskaya kniga [Genitourinary chlamydiosis in women and its sequelae: Medical book], NGMA, 1998.
2. Priminenie makrolida novogo pokolenia wilprafena dlya lecheniya genitalnogo chlamidioza u zhenschin: Metodicheskiye recimendatsii [Use of the new generation macrolide wilprafen for treatment of genital chlamydiosis in women: Guidelines], St. Petersburg 1997.
3. Astsaturov, O. P., Nikonov, A. P., Vulvovaginalnaya I chlamidiynaya infectsiya pri beremennosti [Vulvovaginal and chlamydial infection during pregnancy], Infektsii i antimicrobnaya terapiya [Infections and Antimicrobial Therapy], 1999, 3.
4. Kunin, C. M., Urinary Tract Infections: Detection, Prevention and Management, Williams and Wilkins, 1997.
5. Naber, K. G., Schaeffer, A. J., Heyns, C. F., Matsumoto, T., Shoskes, D. A., Bjerklund Johansen, T. E. (Eds.), Urogenital infections: Internation consultation on urogenital infections, European Association of Urology, 2010.
6. Kahn, D. V., Guide to obstetric and gynecologic urology. M. 1999.
7. Berkovitch, M., Diab-Citrin, O., Greenberg, R., Cohen, M., Bulkowstein, M., Shechtman, S., Bortnik, O., Arnon, J., Ornoy, A., First trimester exposure to amoxycillin/clavulanic acid: a prospective, controlled study, British Journal of Clinical Pharmacology, 2004, 58(3), 298-302.
8. Kolomoitseva, T. N., Kolomoiseva, G. Y., Opyt primineniya preparata Hexicon v terapii smeshannykh bakterialnogribkovykh infektsiy vlagalischa [The experience of using Hexicon drug product for treatment of the mixed bacterial infection of vagina], in Noviye tekhnologii v okhrane reproduktivnogo zdorovia: Mat. regionalnoy nauchno-prakticheskoy konferentsii [New technologies in reproductive health protection: Naterials of the regional research and practical conference], Perm 2003, pp. 60-61.
9. The management of urinary and male genital tract infections, European Association of Urology, 2007.
10. Rafalsky, V. V., Shilova, R. A., Ishchenko, A. I., Urinary tract infection in pregnancy: antibiotic resistance, analysis of the practice choice of antibacterial therapy in Russia, in Effective. pharmacotherapy in obstetrics and gynecology, St. Petersburg 2006, pp. 20-24.
11. Puil, L., Mail, J., Wright, J. M., Asymptomatic Bacteriuria in Pregnancy. Rapid answers using Cochrane Library, Canadian Family Physician, 2002, 48, 58-60, 62-64.
12. Klinichesky protocol: Infektsiya mochevykh putey vo vremya beremennosty, rodov i v poslerodovom periode [Clinical protocol: Urethral infections during pregnancy, labor and postpartum period], 2013.