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Influence of Infectious Factors on Changes in Hormonal Indicators in Women in the Early Period of Miscarriage

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***Abstract*---**The work studied the influence of infectious factors on changes in immunological and hormonal parameters in women who have a full pregnancy without infections of the genitourinary system and women with an infection of the genitourinary system and have miscarriages in the early stages of up to 12 weeks of pregnancy. It was concluded that in women in early pregnancy, the presence of infections of the genitourinary system, with insufficient corrective effect of protease inhibitors and TGF-?1. The formation of a pronounced pro-inflammatory immune response is possible, which can contribute to an imbalance of sex hormones. It manifests itself in a slight decrease in prolactin, FSH, LH, but at the same time a pronounced and reliable decrease in the value of progesterone and an increase in the level of estradiol. Thus, all this can contribute to the unfavorable course of early pregnancy and the development of miscarriages.

***Keywords*---**early pregnancy, genitourinary system, inflammation, interleukins, miscarriage, protease inhibitors, sex hormones.

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Introduction

According to the available data, the inflammatory process of the organs of the reproductive system without infection does not lead to significant changes in the systemic level of the studied hormones. In the presence of an infectious agent, a hormonal imbalance may be observed, as a result of these disorders, a change in the hormonal background is possible (Guskova et al., 2020). In the experiment, changes in the nature of the secretion of placental hormones were studied in sheep infected with C. psittaci and in control animals that were injected with saline. It was found that infection of sheep with C. psittaci was associated with changes in the synthesis of placental steroids and prostaglandins. It has been suggested that a premature decrease in progesterone and a premature increase in estradiol and prostaglandin E 2 concentrations contribute to the onset of preterm labor in sheep infected with C. Psittaci (Azenabor et al., 2007).

Trophoblast infection can disrupt the biosynthesis of cellular cholesterol, thus depleting the substrate pool for the synthesis of estrogen and progesterone. This defect can disrupt the function of the trophoblast during implantation and placentation, as a result, affect the consequences of pregnancy (Azenabor et al., 2007). Rats receiving hormonal treatment showed marked changes in their susceptibility and immune responses depending on the hormone treatment received. Rats infected after genital contact with chlamydial infection and receiving progesterone developed severe inflammation, while rats receiving estradiol remained uninfected and showed no signs of inflammation. Thus, the hormonal environment during genital infection can play an important role in determining both susceptibility and immune responses (Kaushic et al., 2000).

Numerous studies have examined the effect of hormones on infectious diseases, and there is now a lot of data regarding the more specific action of sex hormones, estrogen and progesterone, on urogenital infections. The interactions between these hormones and the immune system are complex, and variations in the hormonal effect between species further complicate the true picture in humans. Therefore, it is difficult to draw general conclusions (Sonnex, 1998). Objective to study: the influence of infectious factors on changes in immunological and hormonal parameters in women in the early stages of miscarriage (Baudouin et al., 2004; Rajasekaran et al., 1995).

Material and methods. The work examined 38 women who were divided into 2 groups. Group 1 included 20 women with a full pregnancy and full delivery, who had no infections of the genitourinary system before pregnancy. Group 2 included 18 women who had miscarriages at 12 weeks of gestation and also had infections of the genitourinary system before pregnancy (Chlamydia trachomatis, Ureaplasma urealyticum, Mycoplasma hominis). In the blood of women before pregnancy, at 6 and 12 weeks of pregnancy, the following parameters were determined by ELISA: pro-inflammatory - interleukin-1β (IL-1) and tumor necrosis factor-α (TNF-α), and anti-inflammatory - interleukin-10 (IL- 10) with the use of test systems of ZAO "Vector-Best" Russia, also transforming growth factor-β1 (TGF-β1) using test systems "DRG" Germany. In addition, the protease inhibitors α-1-anti-trypsin and α-2-macroglobulin were determined using test systems "Sentinel" Italy. In addition, in the blood of women before pregnancy, at 6

and 12 weeks, the indicators of sex hormones were determined by the ELISA method: prolactin, FSH, LH, progesterone, estradiol using test systems of OOO "HEMA" (Koiwa et al., 1997; Anson et al., 2005).

Results and Discussion

The data obtained showed (Table 1) that in women of group 1 and group 2, the value of TNF-α in the blood was significantly at a higher level at 6 and even higher at 12 weeks of gestation compared with similar results before pregnancy.

Table 1
Changes in the parameters of pro-inflammatory (TNF-α, IL-1β), anti-inflammatory (IL-10) interleukins, TGF-β1 and protease inhibitors in the blood of women of the surveyed groups

Investigated indicators	Group	Before pregnancy	6 weeks pregnant	12 weeks pregnant
IL-TNF pg / ml	1	6,2±0,8	9,7±1,2*	11,9±1,5 *
	2	19,5±2,2º	38,8±4,3* º	48,1±5,1 * º
IL-1β pg / ml	1	3,7±0,4	7,2 ± 0,9*	10,1±1,2*
	2	14,9±1,7 º	26,5 ± 3,1* º	33,6±3,7* º
IL-10 pg / ml	1	9,3±1,2	7,4±0,8	5,9±0,7*
	2	4,2±0,6 º	2,7±0,4* º	2,1±0,3* º
TGF-β1 ng / ml	1	32,6 ± 4,5	49,8 ± 5,7*	58,6±7,3*
	2	21,3 ± 1,9 º	14,5 ± 1,7*º	11,4±1,5* º
α -1-anti-trypsin	1	136±14,8	179±18,6	198±21,4*
mg / dl	2	71±8,0º	49±5,2* º	38±4,1* º
α -2 -macro-	1	284±30,6	297±31,6	315±33,9
globulin mg / dl	2	231±25,3	210±22,9 º	196±21,4 º

Note: 1 - women who have a full pregnancy without infections of the genitourinary system; 2 - women who have miscarriages with an infection of the genitourinary system.
* - Significantly different values to the indicators before pregnancy.
º - Significantly different values to the indicators of group 1.

At the same time, the level of TNF-α in women in group 2 was significantly and reliably higher than in women in group 1. Similar changes in indicators were noted according to the results of a study in the blood of IL-1β in women of groups 1 and 2. At the same time, when studying IL-10 in women of both groups 1 and 2, there were opposite changes in the blood compared with the indices of TNF-α and IL-1β. The results obtained for IL-10 in women of group 1 decreased insignificantly at 6 weeks of gestation and significantly at 12 weeks of gestation, and also significantly at 6 and 12 weeks of gestation in women of group 2. Nevertheless, in women of group 2 before pregnancy, at 6 and 12 weeks of pregnancy, it was found that all IL-10 indicators were significantly and reliably lower than similar results in women of group 1 (Table 1). In addition, it was found that in women of group 1 a significant increase at 6 weeks of gestation and even more at 12 weeks of gestation in blood TGF-β1 values, compared with similar results before pregnancy. Also, TGF-β1 in women of group 2 had opposite

changes and did not significantly decrease at 6 and 12 weeks of gestation compared to those before pregnancy. At the same time, in women of group 2, the results of TGF-β1 at 6 and 12 weeks of gestation were significantly lower than the same results of group 1 (Table 1). According to the results of the study of protease inhibitors, a greater change in α -1-anti-trypsin in women of group 2 was revealed, which was expressed in a significant decrease in this indicator before pregnancy, as well as at 6 and 12 weeks of gestation compared with the same results for women in group 1. In addition, there was a significant decrease in α -1-anti-trypsin at 6 and 12 weeks of gestation compared to similar results before pregnancy. Changes in α-2-macro-globulin were observed to a lesser extent. So in women of group 1, at 6 weeks of gestation and even more at 12 weeks, there was a slight increase in α-2-macro-globulin in relation to the results before pregnancy. At the same time, in women of group 2 at 6 and 12 weeks of pregnancy, there was an insignificant decrease in this indicator, compared with the results before pregnancy in the same group. Nevertheless, in women of group 2, all results before pregnancy, at 6 and 12 weeks of pregnancy were significantly lower than those of women in group 1 (Table 1) (Wise et al., 1999; Burnett, 1995).

As a result of the study of sex hormones, it was found (Table 2) that in women of group 1 and group 2, the value of prolactin levels in the blood was not significantly higher at 6 weeks of gestation and even higher at 12 weeks of pregnancy in relation to the results before pregnancy. At the same time, the results of prolactin in women in group 2 were not significantly less similar data than in women in group 1. Similar changes were noted according to the results of FSH blood tests in women of groups 1 and 2. It was also noted in women of both groups 1 and 2, the level of FSH was not significantly higher at 6 and 12 weeks of gestation compared to pre-pregnancy rates (Khayif, 2021; Titko et al., 2021).

Table 2
Changes in sex hormone indicators in the blood of women of the surveyed groups

Investigated indicators	Group	Before pregnancy	6 weeks pregnant	12 weeks pregnant
Prolactin (mIU / L)	1	439±49,2	457±52,1	469±51,6
	2	421±46,7	445±48,5	458±47,3
FSH (mEd/l)	1	8,3±1,0	9,7±1,1	10,9±1,3
	2	7,5±0,8	8,5±1,0	9,8±1,1
LG (mEd/l)	1	6,1±0,7	7,3±0,9	7,9±0,8
	2	5,4±0,6	6,2±0,8	7,1±0,9
Progesterone (nmol / l)	1	3,8±0,4	4,8±0,6*	5,3±0,7*
	2	3,4±0,28	3,1±0,30 º	2,5±0,23* º
Estradiol (nmol / l)	1	0,54±0,05	0,75±0,07*	0,84±0,09*
	2	0,59±0,06	0,93±0,08*	1,19±0,11* º

Note: 1- women without urinary tract infections; 2 - women with an infection of the genitourinary system.
* - Significantly different values to the indicators before pregnancy.
º - Significantly different values to the indicators of group 1.

Also, FSH in women in group 2 was not significantly lower than those in women in group 1. The results of the LH study were similar to the changes in the parameters of both prolactin and FSH (Table 2). At the same time, the study of progesterone in the blood showed more pronounced changes in comparison with prolactin, FSH and LH. In addition, in women of group 1 with a normal pregnancy, there was a significant increase in this indicator by 6 and even more at 12 weeks of pregnancy in relation to the results before pregnancy of the same group. At the same time, in women of group 2 with miscarriages and infections of the genitourinary system, there was an unreliable decrease in progesterone at 6 weeks and a significant decrease at 12 weeks of gestation in relation to the results before pregnancy (Fatimah et al., 2021; Vocroix, 2021). Nevertheless, the indicators of progesterone in women of group 2 at 6 and 12 weeks of pregnancy were significantly and reliably lower than those of women in group 1. The conducted studies of estradiol also revealed pronounced changes that were manifested in women of group 1 in a significant increase in this indicator by 6 and even more at 12 weeks of pregnancy in relation to the results before pregnancy. Similar, but more pronounced changes were noted in women of group 2, which were expressed in a significant increase in estradiol at 6 and even more at 12 weeks of gestation in relation to the results before pregnancy. At the same time, in women of the 2nd group, the indicators before pregnancy and at the 6th week of pregnancy were not significantly higher, and at the 12th week of pregnancy, they were significantly higher than the same results of women of the 1st group (Table 2) (Pasquier, 1995; Verthelyi, 2001).

The obtained results show that in women in early pregnancy, the presence of infections of the genitourinary system, with insufficient corrective effect of protease inhibitors and TGF-β1. The formation of a pronounced pro-inflammatory immune response is possible, which can contribute to an imbalance of sex hormones (Nyandra & Suryasa, 2018; Layuk et al., 2021). Manifested in a slight decrease in prolactin, FSH, LH, but at the same time a pronounced and significant decrease in the value of progesterone and an increase in the level of estradiol. Thus, all this can contribute to the unfavorable course of early pregnancy and the development of miscarriages. In addition, research results show a pronounced relationship between infectious inflammation and sex hormones. In this case, the arising imbalance of sex hormones can be considered as an adaptive mechanism for infectious inflammation. Therefore, the use of hormone therapy, especially progesterone, can lead to an increase in the infectious and inflammatory process and contribute to an increase in the possibility of miscarriages in early pregnancy (Kanda & Watanabe, 2005; Ornoy et al., 2006).

Conclusion

In women in early pregnancy, the presence of infections of the genitourinary system, with insufficient corrective effect of protease inhibitors and TGF-β1. The formation of a pronounced pro-inflammatory immune response is possible, which can contribute to an imbalance of sex hormones. Manifested in a slight decrease in prolactin, FSH, LH, but at the same time a pronounced and significant decrease in the value of progesterone and an increase in the level of estradiol. Thus, all this can contribute to the unfavorable course of early pregnancy and the

development of miscarriages (Wira et al., 2015; Leaver et al., 1989; Ratten et al., 2021).

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