

HEMOSTASIS INDICATORS IN WOMEN WITH COVID-19

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Abstract. The main group included 20 women who had COVID-19 and had menstrual irregularities that arose after the disease. The main group consisted of 2 subgroups: a subgroup of patients who had mild COVID-19 (n=10) and a subgroup of patients who had severe COVID-19 (n=10). The control group included 10 women who did not have COVID-19 and did not have menstrual irregularities. In patients from both groups, hormonal parameters, hemostasis status were assessed, Doppler ultrasound of the basal and spiral arteries of the endometrium and ovarian arteries was performed.

Keywords: coronavirus infection, hemostasis, COVID-19, reproductive period, menstrual function, Dopplerometry, hemodynamics, thrombosis.

INTRODUCTION

Although women tolerate COVID-19 more easily than men, the possible consequences of the disease on reproductive health cannot be ignored [6–8]. Currently, the impact of COVID-19 on women's reproductive health is not well understood. It is assumed that the pathogen can have a direct impact on women's menstrual and reproductive functions by affecting the angiotensin-converting enzyme 2 receptors, which are widely expressed in the ovaries and uterus. Specific interactions between the reproductive system and SARS-CoV-2 infection are believed to occur at the ovarian/endometrium level. Severe vasoconstriction of endometrial spiral arterioles and activation of the coagulation system form pathological menstrual blood loss.

MATERIALS AND METHODS

SARS-CoV-2 infection may affect the hypothalamic-pituitary-ovarian-endometrium axis, leading to changes in the menstrual cycle. There is a reciprocal relationship between the hypothalamic-pituitary-adrenal axis, which mediates the stress response, and the hypothalamic-pituitary-ovarian axis, whereby activation of one axis leads to suppression of the other. Chronic stress suppresses estrogen production, which contributes to menstrual cycle irregularities and anovulatory cycles [1]. Stress-related menstrual cycle disorders represent a spectrum of disorders that include secondary amenorrhea (absence of menstruation for 3 months or more, provided that the menstrual cycle was previously regular) and a rarer form, primary stress-induced amenorrhea, so it is necessary to assess the potential impact of COVID-19 on the reproductive system [2].

RESULTS AND DISCUSSION

A comprehensive examination of all patients included an assessment of blood hormone levels, ultrasound and Doppler examination of the pelvic organs with an assessment of endometrial and ovarian hemodynamics, and determination of hemostasis system parameters.

In patients from the control group, blood samples were taken to determine hormone levels from days 3 to 7 of the menstrual cycle; in patients from the main group, blood samples were taken without regard to the menstrual cycle phase, since the menstrual cycle was disrupted from a delay to amenorrhea.

The studies were performed on a Toshiba Aplio ultrasound Doppler apparatus using a multi-frequency (3.5–5 MHz) transabdominal sensor. The ultrasound examination was performed in a horizontal position. Hemodynamic parameters were determined in the spiral and basal vessels of the endometrium, as well as in the ovarian artery on both sides. Hemodynamics were assessed by the level of systolic blood flow (V), diastolic blood flow (V), systolic-diastolic ratio (S/D), as well as by peripheral circulation indicators: resistance index (RI) and pulsatility index (PI).

The average age of patients in both groups was 28.5 ± 1.28 years. Women had no bad habits that would have a negative impact on ovarian function. In the control group, 7 women (70%) had a history of childbirth, in the main group - 8 (40%). All patients from the main group noted menstrual cycle disorders after COVID-19: the cycle was irregular, with a tendency to delay the next menstruation from several days to several weeks. The duration of the menstrual cycle in the control group was 28.3 ± 1.21 days, and in the main group - 53.1 ± 0.84 days, i.e. 1.9 times more ($p < 0.05$). There was a tendency for a longer menstrual cycle in patients with severe COVID-19. If after mild COVID-19 the duration of the menstrual cycle reached 43.4 ± 0.51 days, then after severe COVID-19 — 57.3 ± 1.25 days. In patients of the control group the number of ovulatory cycles reached 100%. In patients who had mild COVID-19 the proportion of anovulatory cycles was 25.8%, and in patients who had severe COVID-19 — 77.8%. Menstrual discharge had pathological signs — there was a tendency to oligomenorrhea, in 92% of cases there was spotting.

Secretion of follicle-stimulating hormone (FSH) is known to increase rapidly at the beginning of the follicular phase of the menstrual cycle, so that basal hormone secretion values are several times higher than those in the luteal phase of the cycle. FSH stimulates proliferation of granulosa cells and promotes transformation of the stromal tissue surrounding the follicle into a theca cell layer, thus regulating differentiation and organization of steroid-producing tissues of the follicle. Adequate development of the follicle and realization of its steroidogenic activity are necessary prerequisites for ovulation [3]. In the control group, the FSH concentration at the level of increasing estradiol was 5 [4] IU/l. The FSH level in patients of the main group was higher against the background of decreasing estradiol. During a normal ovulatory cycle, the frequency and amplitude of luteinizing hormone (LH) pulses change in accordance with the phase of the menstrual cycle. At times close to ovulation, peak values of LH and FSH are recorded - synchronized in time, but with varying degrees of increase in concentration [2]. In the main group, the LH indicator had a stable level, which did

not change depending on the phase of the menstrual cycle and did not depend on the severity of COVID-19. In the control group, the LH level was 6.75 [6.6; 6.9] IU / l.

CONCLUSION

When analyzing the parameters of hormonal levels, hemostasis, and hemodynamic parameters in the pelvic organs of women in the reproductive period who have had COVID-19, menstrual cycle disorders were revealed. The multifactorial impact of coronavirus infection on the reproductive organs dictates the need for an in-depth study to more fully understand the impact of SARS-CoV-2 infection on women's menstrual function.

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