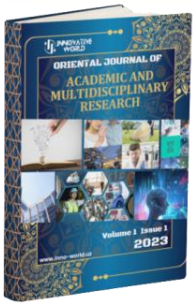

THE PROBLEM OF ADDICTED MISSING OF PREGNANCYIN EARLY STAGES OF PREGNANCY

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ANNOTATION:

A literature review is devoted to the problem of early pregnancy loss. The modern classification is presented, the issues of the etiology and pathogenesis of this complication, the criteria for diagnosis and differential diagnosis, as well as the standards of therapy and the possibilities of prevention are highlighted.

According to the definition of the World Health Organization, spontaneous miscarriage (abortion) is understood as spontaneous expulsion of an embryo or fetus weighing up to 500 g from the uterine cavity within 22 weeks of pregnancy [4;17]. A habitual miscarriage is considered to be a woman's history of 3 or more spontaneous abortions up to 22 weeks in a row. Spontaneous miscarriage (SPV) is the most common complication of early pregnancy, with an incidence ranging from 8 to 20%. Up to 80% of miscarriages occur in the first 12 weeks of pregnancy [2]. After 15 weeks, the overall risk of PWV is 0.6%, provided the fetus has a normal karyotype [13]. Preclinical termination of pregnancy occurs even more often and reaches 26% [10]. In 2003, the study confirmed that in the population the frequency of preclinical pregnancy loss is 26%, and after confirmation of pregnancy - 8% [12]. According to the timing of occurrence, an early spontaneous abortion is distinguished - up to 12 weeks and a late spontaneous abortion - from 12 to 22 weeks of pregnancy. ICD 10 structures SPV into: O03 Spontaneous abortion; O02.1 Failed miscarriage; O20.0 Threatened abortion; N96 Habitual miscarriage and O26.2 Medical care for a woman with recurrent miscarriage.

Currently, a large number of risk factors for PWV development have been identified, but the most significant and proven ones are [14]:

1. Mother's age: the risk of PWV at the age of 20 to 30 is 9-17%, at the age

of 35 - 20%, at the age of 40 - 40% and at the age of 45 - 80%.

2. A history of one miscarriage increases the risk of subsequent PWV to 20%, after two consecutive miscarriages up to 28%, and up to 43% after three or more miscarriages.

3. Smoking more than 10 cigarettes a day is associated with an increased risk of pregnancy loss (OR: 1.2–3.4). The mechanism of the negative effect of tobacco is not fully understood, but it may be associated with its vasoconstrictor and antimetabolic effects.

4. Alcohol: the risk of PWV is increased in women who consume alcohol more than 3 times a week during the first 12 weeks of pregnancy [7].

5. The use of non-steroidal anti-inflammatory drugs (NSAIDs) during conception may be associated with an increased risk of miscarriage [14]. NSAIDs disrupt the implantation processes by blocking the activity of prostaglandins in the decidual tissue [1].

6. An increase in body temperature above 37.8 oC or more may increase the risk of early termination of pregnancy, however, these data are not fully confirmed.

7. A low plasma folate level (≤2.19 ng / ml (4.9 nmol / L)) is associated with an increased risk of PWV between 6 and 12 weeks of gestation, but only with a normal fetal karyotype [18]. There is no evidence that vitamin supplementation prevents miscarriage [9].

8. Maternal weight: BMI less than 18.5 or greater than 25 kg / m2 is associated with an increased risk of infertility and PWV [16; 13].

Etiology of PWV. Traditionally, it is customary to distinguish 5 main reasons for early termination of pregnancy. These are genetic, anatomical, infectious, endocrine and immunological (auto- and alloimmune) factors. In addition, idiopathic termination of pregnancy is distinguished, which develops in the case when the immediate cause of the miscarriage could not be established [11]. In the case of PWS, in terms of up to 8 weeks, in 1/3 of observations, anembryonia is detected and in 2/3 of cases, frozen (undeveloped) pregnancy [8]. In the overwhelming majority of cases, the cause of the formation of a non-developing pregnancy is chromosomal abnormalities or the action of teratogens. Chromosomal abnormalities Chromosomal abnormalities are responsible for about 50% of all miscarriages. Most of them are represented by aneuploidies. It has been proven that the shorter the gestational age at which PWV occurred, the higher the likelihood that the cause of the miscarriage is a chromosomal pathology.

The frequency of karyotype abnormalities in the fetus with anembryony reaches 90%, with abortion at 8–11 weeks, 50%, and with PWV at 16–19 weeks, it does not exceed 30% [8]. The most common types of chromosomal abnormalities detected in the study of the karyotype of abortions are autosomal trisomy (52%), monosomy on the X chromosome (19%) and polyploidy (22%). Most chromosomal abnormalities in the embryo occur de novo. Genetic abnormalities are not investigated in routine cytogenetic analysis, and therefore, their frequency and prevalence has not been established. Congenital anomalies are also factors leading to early termination of pregnancy.Congenital anomalies or malformations can be caused by genetic or chromosomal abnormalities, formed under the influence of external factors and teratogens. The anatomical causes of PWV include congenital or acquired anomalies of the uterus (intrauterine septum, bicornuate uterus, submucosal leiomyoma, intrauterine synechiae) [9].

In studies of infectious agents, a role in the development of PWV of a newly emerging acute inflammatory process caused mainly by viruses (listeria monocytogenes, toxoplasma gondia, parvovirus B19, rubella virus, herpes simplex virus, cytomegalovirus, lymphocytic choriomeningitis virus) and leading to the formation of primary placental insufficiency, fetal malformations and abortion [11]. Endocrinopathies (thyroid dysfunction, diabetes mellitus, polycystic ovary syndrome) can also contribute to the development of PWS due to the formation of an inadequate luteal phase and insufficient decidual transformation of the endometrium [3]. Immunological causes of PWS are mainly associated with the development of thrombophilic complications and hypercoagulability due to congenital or acquired thrombophilia and disorders of the immune system (for example, systemic lupus erythematosus, antiphospholipid syndrome), which lead to immunological rejection of the embryo or fetus or the formation of placental insufficiency. Idiopathic termination of pregnancy is PWV of a structurally normal embryo / fetus in apparently healthy women.As noted above, genetic abnormalities are not found on standard tests and appear to be one of the causes of unexplained pregnancy losses.

Clinical manifestations and diagnosis of PWV. The main clinical manifestations of termination of pregnancy are pain syndrome of varying severity, spotting from the genital tract, the nature of which depends on the duration of pregnancy and the reasons for the termination of pregnancy, and hypertonicity of the myometrium. Traditionally, there are several stages of

spontaneous abortion in the early stages. Threatened abortion is characterized by minor or moderate pulling pains in the lower abdomen and in the sacrum, scanty bloody discharge. In this case, the size of the body of the uterus corresponds to the period of pregnancy, the tone of the uterus is increased, the cervix is not changed, the external pharynx is closed. Bleeding is often painless, but may be accompanied by minimal suprapubic pain. From 90 to 96% of pregnancies with minor bleeding within 7–11 weeks with intact cardiac activity in the heart remain and are not accompanied by an unfavorable prognosis for the subsequent course of pregnancy [20]. A systematic review found an insignificant association (odds ratio ≤ 2) between the presence of bleeding in the first trimester of pregnancy and the development of adverse outcomes later (miscarriage).

A systematic review found a minor association (odds ratio ≤ 2) between the presence of bleeding in the first trimester of pregnancy and the development of adverse outcomes later (miscarriage, premature birth, premature rupture of membranes, fetal growth retardation, bleeding during labor) [14]. The prognosis worsens when bleeding is severe or develops in the second trimester of pregnancy [16]. For an abortion that has begun, more pronounced pain sensations and the presence of bloody discharge from the genital tract are characteristic. The size of the body of the uterus corresponds to the gestational age, since the ovum exfoliates in a limited area, the tone of the uterus is increased, the cervix is not changed, the external pharynx can be slightly opened [5]. With the development of abortion, cramping pains in the lower abdomen and pronounced bloody discharge appear in the course, the ovum, detached from the walls of the uterus, lobs into the dilated cervical canal. Abortion in progress can result in a complete or incomplete abortion. With an incomplete abortion, parts of the ovum are retained in the uterus, making it difficult for the uterus to contract and contributing to ongoing bleeding, the volume of which depends on the duration of pregnancy. With a complete abortion (more often it develops before 12 weeks of pregnancy), the ovum completely leaves the uterus, the uterus contracts and bleeding stops [12].

Frozen pregnancy is the lack of elimination from the uterine cavity of a dead embryo or fetus for some time.

Septic abortion - implies the development of an infectious and inflammatory process as a result of the accumulation of pathogenic microorganisms. Septic abortion, in addition to the symptoms described

above, is characterized by the appearance of fever, chills, general malaise and pain in the lower abdomen. The causative agent of the infection is usually Staphylococcus aureus, gram-negative bacteria, or some gram-positive cocci. The infection can spread and lead to the development of acute salpingitis, diffuse peritonitis and sepsis. Most spontaneous abortions are not septic [8].

Diagnosis. The main clinical sign of spontaneous abortion is the presence of vaginal bleeding. First trimester bleeding can be light, heavy, intermittent or persistent, painless, or painful.

It is necessary to take into account four main causes of bleeding in the early stages of pregnancy [2]:

1.physiological bleeding (accompanying the implantation process);

2. ectopic pregnancy;

3. Overwatch threat or overstepping overnight;

4. pathology of the cervix, vagina or uterus.

To make a correct diagnosis, it is necessary to examine the patient, ultrasound and, if indicated, to assess the level of chorionic gonadotropin in the blood. The final diagnosis of non-developing pregnancy or PWV can be made on the basis of the following criteria:

1. absence of cardiac activity in an embryo with a parietal-coccygeal size (CTE) of more than 5 mm [2];

2. absence of a yolk sac with an average diameter of the ovum of 13 mm;

3. Lack of visualization of the embryo at 6 weeks of gestation with an average ovum diameter of more than 25 mm (with transabdominal measurement) or more than 18 mm (with transvaginal measurement).If the above ultrasound criteria are identified, it is necessary to re-examine in 4-7 days.

The following ultrasound data are suspicious regarding the prospects for complications of pregnancy [17,19]:

1. Abnormal yolk sac - premature reduction (up to 10 weeks) or persistence (over 11 weeks).

2. Low fetal heart rate: with a heart rate of 60 to 80 beats per minute. in the period from 6 to 8 weeks - the probability of SPV is 100%. A heart rate of less than 100 beats per minute up to 8 weeks is associated with a high risk of PWV. It is necessary to conduct a second ultrasound in 5-7 days.

3. Small size of the ovum relative to the size of the embryo (the difference between the average diameter of the ovum and CTE is less than 5 mm) or an increase in the size of the ovum by less than 1 mm per day. The risk of

of developing PWV in such a situation reaches 78%.

4. Retrochorial hematoma - with its size exceeding 25% of the area of the ovum, the risk of PWS increases by 2 times, the risk of premature placental abruption increases by 5.7 times, the risk of premature birth by 1.65 once. It should be borne in mind that the presence of retrochorial hematoma is not an indicator of thrombophilia. If a retrochorial hematoma is detected, expectant tactics with ultrasound guidance are indicated after 1–2 weeks. The presence of a retrochorial hematoma is not.

Medical tactics. When diagnosing threatening or incipient PWS, subject to imaging of an embryo with a palpitations, hormonal therapy is indicated (dydrogesterone 20 mg per day by mouth or micronized progesterone 200-400 mg per day in the vagina) in combination with antispasmodic and hemostatic therapy. In the case of a non-developing pregnancy or incomplete spontaneous miscarriage, surgical or medical curettage is indicated. Medical curettage (according to WHO recommendations in 2007) is carried out in non-developing pregnancies using misoprostol 800 mcg in the vagina or 600 mcg sublingually once. Against the background of emptying the uterine cavity, for prophylactic purposes, short courses of antibiotic therapy are used. A short treatment regimen with the use of 100 mg doxycycline, 2 doses every 12 hours on the day of curettage, has been proven to be effective [18]. In risk groups for the development of infectious complications, prolonged use of doxycycline for 5–7 days is permissible. 2 weeks after medical curettage, the thickness of the endometrium should not exceed 15 mm according to ultrasound [15]. During the next 2 weeks (depending on the duration of pregnancy), it is possible to preserve the secretions from the genital tract. After instrumental curettage, spotting usually persists for 5-7 days. On the day of the curettage, an ectopic spiral may be installed, and combined oral contraceptives (COCs) may be started. With Rh (-) blood in a woman and with termination of pregnancy in the period from 8 to 12 weeks, the introduction of anti-Rhesusimmunoglobulin in a dose of 50-100 μg is indicated. Planning for the next pregnancy is possible in 2–3 months, but earlier pregnancy does not additionally increase the risk of repeated PWV [6].

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