

Endocrinology of Miscarriage

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Abstract

Sustenance of pregnancy is a joint effort of timely events in not only the reproductive system but also the secretion of the hormones from the pituitary and the newly synthesized hormone, human chorionic gonadotrophin hormone (hCG) by the placenta. In the whole basket of events if there is a slip, then there would be a miscarriage. Miscarriage is the spontaneous loss of a pregnancy before the 20th week. About 10 to 20 % of known pregnancies end in miscarriage. Among other causes of miscarriage, low or high hormone levels in the mother are also an important factor

Keywords: factors responsible for miscarriage; cg; progesterone; thyroid

Introduction

Ovulation, conception, and sustenance of pregnancy are all a play of hormones. For any reason, if there is any imbalance in the hormonal milieu there may be problems with keeping the fetus/embryo in the uterus (1). Also, if there are structural abnormalities in the uterus viz. abnormally shaped uterus, uterine fibroids, and scar tissue in the uterus (2) that can also hinder implantation or growth of the fetus. In addition to maternal endocrine dysfunction, many other factors contribute to threatened abortion. They include embryonic or fetal chromosomal abnormalities (3) environmental (4) and immune factors (5). It is a well-established fact that progesterone plays an important role in the sustenance of pregnancy. At about 10–12 week's gestation, placental progesterone production takes over the ovaries. Historically, low levels of circulating progesterone have been associated with vaginal bleeding and impending miscarriage during early pregnancy (6).

Recurrent Pregnancy Loss

The American Society of Reproductive Medicine (ASRM) has recently redefined recurrent pregnancy loss as two or more pregnancy losses. A pregnancy loss is defined as a clinically-recognized pregnancy involuntarily ending before 20 weeks. A clinically-recognized pregnancy means that the pregnancy has been visualized on an ultrasound or that pregnancy tissue was identified after a pregnancy loss. Over one-half of patients with recurrent pregnancy loss will have unexplained recurrent pregnancy loss, which means that no specific cause could be identified in the work-up. Various treatments may be offered to these patients, but there is no universal recommendation for the treatment of these patients. Despite this, the overall chance of pregnancy is good, more than 50%, without any intervention.

Approximately 12-15% of all clinically recognized pregnancies end in miscarriage; however, it is estimated that at least 30-60% of all conceptions will end within the first 12 weeks of gestation. Up to 50% of the time, the woman doesn't even realize that she was ever pregnant. The risk of miscarriage increases with the number of previous pregnancy losses but is typically less than 50%.

Advancing maternal age is associated with an increased risk of miscarriage, which is thought to be due to poor egg quality leading to chromosomal (genetic) abnormalities. As we age, changes naturally occur in the way body systems are controlled (7)

Some target tissues become less sensitive to their controlling hormone. The amount of hormones produced may also change. Blood levels of some hormones increase, some decrease, and some are unchanged. Both men and women produce fewer hormones once they hit 30 years. Estrogen - the hormone that controls a woman's monthly cycle - begins to drop around the milestone and then takes another nosedive at 35. This can cause weight gain and lower libido (8).

Role of hormones

Hormonal imbalances of prolactin, thyroid hormone, or progesterone can result in miscarriage. In general, women in normal cases have low prolactin levels; women with hyperprolactinemia will have difficulty in becoming pregnant (9). A high enough prolactin level can inhibit the proliferation of luteinizing granulosa cells, and can also interfere with corpus luteum function resulting in luteal phase defect, as well as abnormal implantation, and embryo development (10,11). Prolactin levels reach their highest level at the time of delivery and then go back to normal around six weeks after delivery (even if a woman is breastfeeding). Serum prolactin levels during early pregnancy (5-10 weeks of gestation) were significantly higher in patients who miscarried (31.8-55.3 ng/mL) than in patients whose pregnancies were successful (12).

Poorly controlled thyroid disease (hypo- or hyperthyroidism) is associated with infertility and pregnancy loss (13-15) Excess thyroid hormone increases the risk of miscarriage independent of maternal metabolic dysfunction. Pregnant women with subclinical hypothyroidism or thyroid antibodies have an increased risk of complications, especially pre-eclampsia, perinatal mortality, and miscarriage. The presence of maternal thyroid autoantibodies is strongly associated with miscarriage and preterm delivery (16,17). There is evidence that treatment with levothyroxine can attenuate the risks Higher

TSH levels (TSH levels > 4.5 mU/L) are associated with increased risk for miscarriage and should be avoided in early pregnancy (18,19).

If it is diagnosed with hypothyroidism — or an underactive thyroid — you may be wondering if it may cause problems during pregnancy or even a miscarriage. Hypothyroidism is linked to miscarriages so it's important to be able to recognize the signs of this condition (16,17).

Progesterone is necessary for pregnancy because it gets the uterus ready to accept, implant, and maintain a fertilized egg (20). The hormone prevents muscle contractions from happening in the uterus that would cause a woman's body to reject an egg. Progesterone helps the uterus grow during pregnancy and keeps it from having contractions. Contractions in early pregnancy may lead to miscarriage. If progesterone declines, it can lead to shortening of the cervix. This can raise the risk of preterm delivery. In later pregnancy, progesterone helps the breasts get ready to make breast milk (21). These trials found that giving progestogen medication to women with recurrent miscarriages early in their pregnancy may help lower the rates of miscarriage in that pregnancy from 27.5% to 20.1% ng/mL, $P < .01$ or $P < .05$.

There are no good parameters that can be used to predict and evaluate pregnancies with bleeding during the first trimester. During the first trimester communication between the foetus and mother is controlled by many hormones in coordination. Sex steroids, including progesterone (P4) and estrogen, along with prolactin, androgen, and human chorionic gonadotrophin (hCG) sustain the pregnancy. Blood hCG and P4 levels are the main indexes that are used to diagnose and determine the prognosis in women experiencing a threatened abortion. Estradiol (E2) levels are also used in some cases. The main treatments for threatened abortion are bed rest, luteal support, and combined estrogen and P4 supplements (22). It is important to note that the use of most hormone remedies is experience-based, and full-scale individual sex hormone analyses are lacking. However, we often find that symptoms (e.g., vaginal bleeding) do not improve and may even become worse after administering standard hormone supplements.

Sex steroid metabolism depends on 3 factors: a person's genetic makeup, lifestyle and diet, and the environment. Therefore, increasing our understanding of sex hormone metabolism and interventions with it offers a significant opportunity to reduce the rate of threatened abortions. Hence, developing a non-invasive and comprehensive sex hormone test that can be used to perform a full-scale analysis of sex hormone levels and the levels of their metabolites would benefit patients. In the present study, we used quantitative liquid chromatography-mass spectrometry to compare sex hormone and sex hormone metabolite levels in the urine of women in early pregnancy with and without threatened miscarriage (23).

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