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Research Article

THE EFFECTIVENESS OF ADMINISTERING PROGESTERONE AS A MANAGEMENT FOR IMMINENT ABORTION

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ABSTRACT

Imminent abortion is defined as vaginal bleeding before 20 weeks of pregnancy without the expulsion of conception products or evidence of fetal death. This condition occurs in 20-25% of pregnancies and is associated with an increased fetal mortality rate. Progesterone plays a crucial role in preventing miscarriage through the mechanism of fetal implantation in the uterus. Research indicates that progesterone is beneficial in managing imminent abortion, whether in oral or suppository formulations. The effectiveness of progesterone is higher when administered orally compared to the suppository form.

Keywords: Imminent abortion, oral progesterone, vaginal progesterone.

INTRODUCTION

Imminent abortion is defined as vaginal bleeding before 20 weeks of pregnancy with positive results on urine and/or blood pregnancy tests. Imminent abortion may be preceded by or occur without abdominal pain, but the cervix remains closed and there is no expulsion of conception products or evidence of fetal death. Imminent abortion can progress to incomplete or complete abortion.[1] It can occur in any pregnancy regardless of the mother's age, race, comorbidities, lifestyle, or socioeconomic status. This condition occurs in 20-25% of pregnancies and is associated with an increased fetal mortality rate (15-50%). If a woman has experienced bleeding in the first trimester of pregnancy before, her risk of experiencing bleeding in subsequent first trimesters will increase.[2,3]

Based on the pathophysiology, a popular theory that can explain the occurrence of abortion is the presence of luteal defects or deficiencies. Prior to pregnancy, progesterone secreted by the corpus luteum promotes the development of a secretory endometrium characterized by immunomodulatory, paracrine, and endocrine effects that support embryo implantation. In early pregnancy, progesterone is crucial for maintaining the pregnancy, and the removal of the corpus luteum during this period (luteectomy) can lead to a decrease in progesterone levels. The role of the corpus luteum is assisted by human chorionic gonadotropin (HCG) derived from the conception products. The production of progesterone will even be replaced by the placenta after 7-8 weeks following the LH surge. In the second and third trimesters of pregnancy, progesterone maintains uterine quiescence and acts as an immunomodulator, reducing immune responses that can result in preterm labor. Low progesterone levels are suspected to be one of the causes of imminent abortion. This theory forms the basis for administering progesterone supplementation. In the management of imminent abortion, progesterone works by influencing the muscles and blood vessels of the uterus, as well as playing a role in the immune pathway.[4,5]

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THE EFFECT OF PROGESTERONE ON PREGNANCY

Progesterone plays a crucial role in preventing miscarriage by inhibiting the release of arachidonic acid and increasing sensitivity to prostaglandins and estrogen, causing smooth muscles to relax and pain to subside. Changes in muscle contractions also occur due to the expression of enzymes involved in prostacyclin production.[6,7]

Progesterone affects the blood vessels of the uterus by normalizing vascular resistance, which increases the oxygen and nutrient supply for embryo development. Efficient vascular transport depends on the capacity of uterine vessels supplied by the uterine artery. During pregnancy, the tone of the uterine blood vessels decreases, and blood flow to the uterus increases under the influence of steroid hormones such as estrogen, progesterone, and cortisol. Progesterone also induces the expression and activity of nitric oxide synthase in the uterine endothelium, which enhances blood flow and oxygenation to the uterus during pregnancy.[8]

Another effect of progesterone is to stimulate the synthesis of uterine muscle proteins called progesterone-induced inhibitory factor (PIBF) and prevent cervical dilation. PIBF is a mediator produced by sensitized lymphocytes in pregnant women under the influence of progesterone, which leads to tolerance to paternal antigens.[7] The production of PIBF by progesterone functions in immune regulation by stimulating a shift from Th1-dependent cytokine production, which is cytotoxic to pregnancy, to Th2-dependent cytokines that support pregnancy. Progesterone also increases the production of IL-10, an anti-inflammatory cytokine that provides protection during pregnancy.[5,9]

THE SAFETY OF PROGESTERONE DURING PREGNANCY

Progesterone, commonly used for the management of imminent abortion, is available in oral, injectable, and suppository formulations. Progesterone supplementation is generally performed until 10-12 weeks of pregnancy, with a vaginal dose of 400 mg/day given until the bleeding stops, or an oral dose starting at 40 mg followed by a maintenance dose of 20-30 mg/day for 7 days after the bleeding stops.[6] Meta-analyses have not found evidence of an increased risk

of congenital malformations in women using micronized vaginal progesterone. A Cochrane review on imminent abortion and recurrent pregnancy loss (RPL) did not find an increased incidence of congenital anomalies in women treated with progesterone. Randomized controlled trials have shown no increased risk of congenital anomalies, including genital abnormalities, due to progesterone exposure in early pregnancy. Clinical studies on the use of progesterone during pregnancy, whether oral or vaginal, support its tolerability and relatively minimal side effects. It is estimated that 10 million pregnant women worldwide receive dydrogesterone.[5,10]

ORAL DYDROGESTERONE IN IMMINENT ABORTION

Dydrogesterone has a similar chemical structure to endogenous progesterone, making it highly sensitive and selective to progesterone receptors. With these characteristics, this medication also minimizes side effects by avoiding binding to other hormonal receptors. Dydrogesterone has advantages over other oral preparations, such as minimal side effects, easy absorption, and better bioavailability. The metabolite of dydrogesterone, known as DHD (20-α-dihydrodydrogesterone), activates endothelial nitric oxide synthase (eNOS) and enhances nitric oxide synthase function as a regulator of blood flow and uterine oxygenation. Its metabolite does not undergo aromatization (no estrogenic effects) and does not have androgenic effects.[11]

MICRONIZED PROGESTERONE VAGINA IN IMMINENT ABORTION

Micronization is a process of reducing the particle diameter, making it only within the micrometer size range. Micronized progesterone has the same molecular structure and pharmacological effects as endogenous progesterone. A randomized controlled trial (RCT) double-blind study concluded that administering 400 mg of micronized progesterone vaginally twice a day until 16 weeks of pregnancy reduces the risk of abortion. Vaginal suppository preparations result in higher concentrations in the uterus due to the portal system, allowing direct tissue diffusion, although progesterone concentrations in the blood may be lower. Vaginal administration is considered safe and does not cause fetal developmental disorders. The drug absorption process may be reduced if administered after sexual intercourse or if it is discharged together with flowing blood.[5,9]

ORAL PROGESTERONE VS. SUPPOSITORY FORM

Various RCTs have shown that oral progesterone is more effective than progesterone suppositories in managing cases of threatened abortion. These findings are consistent with a meta-analysis of RCTs, which stated that the oral route reduces the risk of abortion better (RR 0.55; 95% CI 0.38–0.79) compared to the vaginal route (RR 0.58; 95% CI 0.28–1.12).[12] An RCT study in Pakistan stated that oral progesterone was statistically significant in preventing abortion (92%) compared to administration via the vagina (74%). Based on the study by Parveen *et al.,* the success rate of oral progesterone (200 mg twice a day) was higher (92%) compared to the administration of a 400 mg suppository once a day (92% vs. 74%) in maintaining pregnancy. The incidence of malformations or congenital abnormalities after the administration of both drugs was below 2% and there was no statistically significant difference between the oral and suppository formulations.[8]

CONCLUSION

Oral and suppository forms of progesterone have been proven effective in maintaining pregnancy and reducing the risk of miscarriage. Various randomized controlled trials (RCTs) state that the effect of progesterone is better when administered orally compared to the suppository form. The choice of progesterone administration should be based on the preference of each patient, as both formulations are equally effective and have minimal harmful side effects.

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