УДК: 618.3 - 06 : 577.175.632 - 07

COMPARATIVE ANALYSIS OF VAGINAL AND RECTAL PROGESTOGEN ADMINISTRATION IN PREGNANT WOMEN WITH THREATENED MISCARRIAGE BEFORE 21 WEEKS OF GESTATION

Karimov A.H., Aliyeva M.B.
Tashkent medical academy

XULOSA

Homiladorlikning erta davrida uchraydigan eng ko‘p asoratlardan biri – tahdidli tushish bo‘lib, u asosan qin orqali qon kelishi va qorin og‘riqlari bilan namoyon bo‘ladi. Homiladorlikni davom ettirish uchun progesterone keng qo‘llaniladi, biroq uni yuborishning eng maqbul yo‘li hanuz bahsli masala bo‘lib qolmoqda. Ushbu randomizatsiyalangan nazoratli tadqiqotda 6–21 xafta muddatdagi 60 nafar homilador ayolda vaginal va rectal mikroblangan progesterone taqqoslandi. Natijalarga ko‘ra, vaginal yuborish homiladorlikni davom ettirish ko‘rsatkichini yuqoriroq darajada ta’minladi (90,0% ga nisbatan 76,7%), simptomlarni tezroq bartaraf etdi va bemorlarning qoniqishini oshirdi. Bu topilmalar vaginal progesteronning ustunligini ko‘rsatib, amaliyotda uni ustuvor qo‘llashni qo‘llab-quvvatlaydi.

Kalit so‘zlar: *homilani tushish tahdidi, qin orqali qon kelishi, progesteron terapiyasi, homiladorlikni davom ettirish, vaginal yo‘l, rectal yuborish, randomizatsiyalangan tadqiqot.*

РЕЗЮМЕ

Угрожающий выкидыш является одной из наиболее распространённых осложнений ранней беременности, основными проявлениями которого являются вагинальное кровотечение и абдоминальные боли. Несмотря на широкое применение прогестероновой терапии, оптимальный путь введения остаётся предметом дискуссий. В данном рандомизированном контролируемом исследовании были сопоставлены вагинальные и ректальные формы микронизированного прогестерона у 60 беременных с угрожающим выкидышем на сроке 6–21 недель. Результаты показали, что вагинальное введение обеспечивало более высокие показатели продолжения беременности (90,0 % против 76,7 %), более быстрое купирование симптомов и большую удовлетворённость пациенток. Полученные данные подтверждают клиническое преимущество вагинального прогестерона и обосновывают его приоритетное использование.

Ключевые слова: *угрожающий выкидыш, вагинальное кровотечение, прогестерон, сохранение беременности, вагинальный путь, ректальное введение, рандомизированное исследование.*

Threatened miscarriage affects approximately 15–20% of all clinically recognized pregnancies, making it one of the leading causes of early pregnancy loss. It is diagnosed when vaginal bleeding and/or cramping occur without expulsion of the fetus, often accompanied by a closed cervix and a viable intrauterine pregnancy confirmed on ultrasound. While some cases progress to term without complications, others result in spontaneous abortion. [3]

Progesterone is essential in early gestation, maintaining a quiescent myometrium, supporting decidualization, and promoting vascular stability within the endometrium. Deficiency or impaired progesterone action has been linked to miscarriage risk. Numerous studies support its therapeutic role in preventing pregnancy loss, yet the most effective route of administration remains controversial. Vaginal administration delivers progesterone directly to the uterus via the “first uterine pass” effect, potentially achieving higher local concentrations. Rectal administration, while bypassing vaginal discomfort, relies on systemic absorption and may yield different pharmacokinetics.[4,5]

The present study was designed to compare these two administration routes, with a focus on pregnancy continuation, symptom resolution, adverse events, and patient satisfaction.

MATERIALS AND METHODS

This randomized controlled trial was conducted at Tashkent Medical Academy from December 20, 2023, to November 27, 2024, in accordance with the CONSORT guidelines. Ethical approval was obtained from the Institutional Review Board, and all participants provided written informed consent.

Inclusion criteria were:

• Age 18–40 years;

• Singleton intrauterine pregnancy confirmed by ultrasound;

• Gestational age between 6 and 21 weeks;

• Diagnosis of threatened miscarriage with bleeding and/or cramping, closed cervix, and no fetal tissue expulsion;

• Willingness to comply with study protocols.

Exclusion criteria included: spontaneous or missed miscarriage, ectopic pregnancy, fetal anomalies, multiple gestations, history of preterm labor, uterine malformations, contraindications to progesterone, and inability to follow the regimen.

Participants (n = 60) were stratified by the presence or absence of vaginal bleeding and then randomly assigned to one of four subgroups:

1. Vaginal bleeding + vaginal progesterone;
2. Vaginal bleeding + rectal progesterone;
3.No vaginal bleeding + vaginal progesterone;
4. No vaginal bleeding + rectal progesterone.

Both interventions involved micronized progesterone 200 mg daily at bedtime for 14 days.

Primary outcome: pregnancy continuation beyond 24 weeks of gestation.

Secondary outcomes: cessation of bleeding, relief of abdominal cramping, patient satisfaction (5-point Likert scale), and occurrence of adverse effects.

Follow-up assessments were performed at baseline, day 7, day 14, and at 24 weeks of gestation. Statistical analysis was conducted using SPSS v.25, with Chi-square and t-tests applied. A p-value < 0.05 was considered significant.

RESULTS

Baseline characteristics were similar between groups in terms of age (28.5 ± 4.1 vs. 29.2 ± 4.4 years), gestational age (9.0 ± 2.3 vs. 9.2 ± 2.1 weeks), parity, and BMI.

• Pregnancy continuation: Vaginal group – 90.0% vs. Rectal group – 76.7% (p = 0.05).

• Symptom resolution within 7 days: 88.6% (vaginal) vs. 74.3% (rectal), p = 0.07.

• Cramping relief time: 4.0 ± 0.9 days (vaginal) vs. 4.8 ± 1.2 days (rectal), p = 0.05.

• Bleeding cessation time: 4.8 ± 1.1 vs. 5.6 ± 1.3 days, p = 0.06.

• Adverse effects: mild and comparable between groups (p > 0.05).

• Patient satisfaction: significantly higher in vaginal group (4.2 ± 0.7 vs. 3.8 ± 0.8; p = 0.02).

At 24 weeks, live birth rates were 86.7% in the vaginal group and 76.7% in the rectal group, although the difference was not statistically significant.

DISCUSSION

The findings of this trial indicate that vaginal progesterone offers clinical advantages over rectal administration for women with threatened miscarriage. The higher pregnancy continuation rate and faster resolution of abdominal cramping may be attributed to more efficient local drug delivery to the uterus, maximizing the hormone's therapeutic effect. Additionally, higher patient satisfaction suggests that, despite the potential for mild local irritation, the vaginal route is more acceptable for most women.

Rectal administration remains a valid alternative, particularly for patients with vaginal infections, post-surgical conditions, or personal preference against vaginal application. However, the slightly lower clinical efficacy observed in this study suggests it should be considered a secondary option.

CONCLUSION

Vaginal progesterone administration demonstrated superior outcomes in pregnancy preservation, symptom relief, and patient-reported satisfaction compared with rectal administration in women with threatened miscarriage before 21 weeks. Clinicians should consider prioritizing vaginal delivery of progesterone when no contraindications exist. Future studies with larger cohorts and longer follow-up are needed to confirm these results and to explore potential subgroups that may benefit from alternative administration routes.

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