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A Comparative Study of Vaginal Micronized Progesterone and Oral Dydrogesterone in Threatened Abortion

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ABSTRACT

Introduction: Threatened abortion, characterized by vaginal bleeding and abdominal pain in early pregnancy, requires effective management to improve pregnancy outcomes. Progestogens such as vaginal micronized progesterone and oral dydrogesterone are commonly used, yet limited comparative research exists to inform their optimal use. This study evaluates the efficacy and safety of these treatments in managing threatened abortion.

Methods: This prospective observational study, conducted at Saraswathi Institute of Medical Sciences, Hapur, U.P., included pregnant women with clinically and sonographically confirmed threatened abortion (≤24 weeks gestation). Participants were divided into two groups: one receiving 200 mg of vaginal micronized progesterone twice daily and the other 10 mg of oral dydrogesterone twice daily. Data collection included demographic details, bleeding episodes, and obstetric outcomes. Statistical analysis was performed, with significance set at $p < 0.05$.

Results: Baseline characteristics, including age and gestational parameters, were comparable between groups. Pregnancy continuation rates were 89.0% and 84.0% for oral dydrogesterone and vaginal progesterone, respectively ($p = 0.30$). Adverse effects were similar across groups, with no statistically significant differences.

Conclusion: Both oral dydrogesterone and vaginal progesterone demonstrated comparable efficacy and safety profiles in managing threatened abortion. The choice of treatment may depend on patient preferences and clinical circumstances.

Keywords: Threatened abortion; progesterone; dydrogesterone; pregnancy outcomes; vaginal bleeding

INTRODUCTION

Threatened abortion, characterized by vaginal bleeding and abdominal pain in early pregnancy, presents a significant clinical challenge. Progestogens, including vaginal micronized progesterone and oral dydrogesterone, have shown promise in managing this condition by supporting endometrial receptivity, preventing uterine contractions, and modulating the maternal immune response.[1] These hormones are believed to reduce the risk of miscarriage and improve pregnancy outcomes. However, there is limited research comparing the efficacy, safety profiles, and optimal dosages of vaginal versus oral formulations in threatened abortion. This study aims to fill this gap by conducting a comparative analysis of vaginal micronized progesterone and oral dydrogesterone, with a focus on their effectiveness and impact on pregnancy outcomes.[2]

While both forms of progestogens are used to manage threatened abortion, direct comparisons between them are scarce. Understanding the differences between vaginal micronized progesterone and oral dydrogesterone is essential for refining clinical guidelines and improving patient care. This research will help guide clinicians in choosing the most appropriate intervention, contributing to personalized, evidence-based care for patients facing threatened abortion.[3]

By addressing the clinical uncertainties surrounding these treatments, this study has the potential to improve maternal and fetal well-being, thereby enhancing the management of threatened abortion. This study is crucial in advancing scientific understanding and informing clinical practice, ensuring that hormonal therapies are optimized for better pregnancy outcomes in threatened abortion cases.

This study aims to fill the gap in research by comparing the efficacy, safety, and impact of vaginal micronized progesterone and oral dydrogesterone in managing threatened abortion. Given the clinical uncertainty surrounding the choice of progestogen, this research seeks to provide evidence-based insights to guide clinicians in making informed, personalized treatment decisions for better patient care.

MATERIALS AND METHODS

The study was conducted at the Department of Obstetrics and Gynaecology at Saraswathi Institute of Medical Sciences, Hapur, U.P., after obtaining approval from the Institutional Ethical Committee and informed consent from all participants. The study period extended from August 2022 to July 2024 and was designed as a prospective, observational study. Data were collected from pregnant women attending the institute, with inclusion criteria including those diagnosed with clinically and sonographically confirmed threatened abortion at 24 weeks of gestation or less. Exclusion criteria included a history of more than one previous abortion, presence of an incompetent cervix, fetal anomalies after 18 weeks, congenital uterine malformations, fibroids, genital tract infections, trauma, or ultrasound findings of abnormal gestational sacs or fetal bradycardia.

Each participant underwent detailed history-taking, physical examination, relevant blood investigations, and ultrasonography (TAS/TVS) to assess gestational age, gestational sac, yolk sac, fetal bradycardia, and the presence of subchorionic hematoma. Systematic random sampling was employed to divide the participants into two groups. The first group received 200mg of micronized vaginal progesterone twice daily, while the second group was administered 10mg of oral dydrogesterone twice daily. All women were advised to rest and maintain hydration. Follow-up was carried out until 28 weeks, with the primary obstetric outcomes recorded, including continuation of pregnancy, episodes of bleeding or spotting with or without abdominal pain, and the number of pregnancies ending in missed or spontaneous abortion.

The sample size was calculated using a prevalence of 20% based on a previous study by Sivasane et al. [4], a standard error of 5.6%, and a required sample size of approximately 200. Statistical analysis was conducted with continuous data presented as mean ± standard deviation, and dichotomous data presented as frequencies and percentages. Univariate analysis of dichotomous variables was performed using the Chi-square test,

with Yates correction applied where necessary. A p-value of less than 0.05 was considered statistically significant.

RESULTS

Table-1 compares the mean values of three clinical parameters-age, period of gestation, and number of days of bleeding between two treatment groups: Oral Dehydrogesterone and Vaginal Progesterone. The mean values for both groups are similar for all parameters, with age (29.62 ± 2.50 vs. 29.93 ± 2.68), period of gestation (29.30 ± 3.23 vs. 29.08 ± 3.25), and number of days of bleeding (4.73 ± 2.23 vs. 5.22 ± 1.92) showing no significant difference. The p-values indicate that there is no statistically significant difference between the two groups for these variables, suggesting that the characteristics of the groups are comparable.

The distribution of first bleeding across different gestational age intervals (6-10 weeks, 11-15 weeks, 16-20 weeks, and 21-24 weeks) is similar between the two groups, with a p-value of 0.86 indicating no significant difference. Regarding treatment initiation, a higher proportion of women in the Oral Dehydrogesterone group (77.8%) started treatment early (6-10 weeks) compared to the Vaginal Progesterone group (22.2%). However, the overall p-value of 0.07 suggests no significant difference between the groups in the timing of treatment initiation. (Table 1)

Spotting was more common in the Vaginal Progesterone group (54.5%) compared to the Oral Dehydrogesterone group (45.5%), making up 66.0% of the total cases. Moderate bleeding was more frequent in the Oral Dehydrogesterone group (58.8%) than in the Vaginal Progesterone group (41.2%), accounting for 34.0% of all cases. The p-value of 0.07 suggests that the difference in bleeding types between the two groups is not statistically significant. (Table 3)

Overall, 44.7% of participants in the Oral Dydrogesterone group and 55.3% in the Vaginal Progesterone group reported adverse effects, but the difference was not statistically significant (p = 0.40).

Table 1: Comparison of Demographic and Clinical Parameters Between Treatment Groups

Parameter (Mean±sd)	Oral Dehydrogesterone	Vaginal Progesterone	Total	p-value
Age	29.62 ± 2.50	29.93 ± 2.68	29.78 ± 2.59	0.399
Period of Gestation	29.30 ± 3.23	29.08 ± 3.25	29.19 ± 3.24	0.632
No. of Days of Bleeding	4.73 ± 2.23	5.22 ± 1.92	4.98 ± 2.09	0.098

Table 2: Comparison of Gestational Age at First Bleeding and Treatment Initiation Between Treatment Groups

Parameter	Oral Dehydrogesterone	Vaginal Progesterone	Total	p-value
Gestational Age at Which First Bleeding Occurred				
6-10 weeks	14 (53.8)	12 (46.2)	26 (13.0)	0.86
11-15 weeks	20 (47.6)	22 (52.4)	42 (21.0)	
16-20 weeks	24 (46.2)	28 (53.8)	52 (26.0)	
21-24 weeks	42 (52.5)	38 (47.5)	80 (40.0)	
Gestational Age at Which Treatment Started				
6-10 weeks	14 (77.8)	4 (22.2)	18 (9.0)	0.07
11-15 weeks	20 (43.5)	26 (56.5)	46 (23.0)	
16-20 weeks	24 (45.3)	29 (54.7)	53 (26.5)	
21-24 weeks	42 (50.6)	41 (49.4)	83 (41.5)	

Figures in the parenthesis indicate percentage.

Table 3: Type of vaginal bleeding reported among treatment groups

Type of Vaginal Bleeding	Oral Dehydrogesterone	Vaginal Progesterone	Total	p-value
Spotting	60 (45.5)	72 (54.5)	132 (66.0)	0.07
Moderate	40 (58.8)	28 (41.2)	68 (34.0)	

Figures in the parenthesis indicate percentage.

Table 4: Adverse effect among treatment groups

Adverse Effect	Oral Dehydrogesterone	Vaginal Progesterone	Total	p-value
Adverse Effects	21 (44.7)	26 (55.3)	47 (23.5)	0.40
Nausea	17 (53.1)	32 (100)	49 (24.5)	0.70
Vomiting	7 (43.8)	9 (56.3)	16 (8.0)	0.60
Vaginal Irritation	5 (33.3)	10 (66.7)	15 (7.5)	0.17
Headache	4 (40.0)	6 (60.0)	10 (5.0)	0.51
Fatigue	10 (40.0)	15 (60.0)	25 (12.5)	0.28

Figures in the parenthesis indicate percentage.

Table 5: Outcome among treatment groups

Outcome	Oral Dehydrogesterone	Vaginal Progesterone	Total
Incidence of Miscarriage	11 (11.0)	16 (16.0)	27 (13.5)
Continuation of Pregnancy	89 (89.0)	84 (84.0)	173 (86.5)

Figures in the parenthesis indicate percentage.
P value 0.30 (non – significant)

Common adverse effects included nausea, vomiting, vaginal irritation, headache, and fatigue. Nausea was more common in the Vaginal Progesterone group, with 100% reporting it, but this difference was not statistically significant (p = 0.70). Similarly, other adverse effects such as vomiting, vaginal irritation, headache, and fatigue showed no significant differences between the two groups (p-values ranging from 0.17 to 0.60). (Table 4)

The incidence of miscarriage was 11.0% in the Oral Dehydrogesterone group and 16.0% in the Vaginal Progesterone group, with a total of 13.5% across both groups. However, the difference in miscarriage rates between the two groups was not statistically significant, as indicated by the p-value of 0.30. The continuation of pregnancy was observed in 89.0% of participants receiving Oral Dehydrogesterone and 84.0% of those receiving Vaginal Progesterone, with a total of 86.5%. Again, no significant difference was found between the two treatment groups regarding the continuation of pregnancy. (Table 5)

DISCUSSION

In our study, the choice of medication for managing threatened abortion showed no significant variation across age groups. Participants aged ≤25 years predominantly received oral dydrogesterone (57.1%) compared to vaginal progesterone (42.9%), while in the 26–30 years age group, oral dydrogesterone was used in 50.9% of cases versus 49.1% for vaginal progesterone. Similarly, participants aged 31–35 years showed a near-equal distribution (48.2% vs. 51.8%, respectively). The chi-square analysis (χ^2 = 0.28, p = 0.8) confirmed no association between age and medication choice, aligning with findings by Parveen et al. (2021), who observed no significant age difference between oral dydrogesterone and vaginal progesterone users (30.57 ± 3.42 years vs. 31.14 ± 3.27 years; p = 0.3223).[5] Other studies, including Kale et al. (2021) and Das et al. (2022), reported similar findings.[6,7]

Gestational age at bleeding showed a comparable distribution between groups in our study. In cases of bleeding at 6–10 weeks, oral dydrogesterone was used in 53.8% of cases, while 46.2% received vaginal progesterone. Similar distributions were observed for gestational ages of 11–15 weeks (47.6% vs. 52.4%), 16–20 weeks (46.2% vs. 53.8%), and 21–24 weeks (52.5% vs. 47.5%). Verma et al. reported analogous trends across gestational ages.[8]

Regarding treatment initiation, oral dydrogesterone was favored in the 6–10 weeks group (77.8%), whereas vaginal progesterone predominated at 11–15 weeks (56.5%). For later gestational ages, the treatments were evenly distributed. These patterns are consistent with Parveen et al., who noted no significant efficacy differences between oral dydrogesterone and vaginal progesterone for managing threatened abortion across gestational ages (p = 0.7642).[5]

In our study, no significant difference was found in mean age or gestational period between the groups. The mean age of oral dydrogesterone users was 29.6 ± 2.5 years,

and for vaginal progesterone users, it was 29.9 ± 2.7 years (p = 0.399). Mean gestational periods were 29.3 ± 3.2 weeks and 29.1 ± 3.3 weeks, respectively (p = 0.632). The mean bleeding duration was 4.7 ± 2.2 days for oral dydrogesterone and 5.2 ± 1.9 days for vaginal progesterone, with no significant difference (p = 0.098). Sadaf et al., however, reported significantly shorter cessation of bleeding with oral dydrogesterone compared to vaginal progesterone (7.0 ± 0.9 days vs. 9.2 ± 0.8 days; p = 0.001).[9]

Miscarriage rates in our study showed a similar trend to previous studies. Qing et al. noted miscarriage rates of 43.5% and 56.5% for oral dydrogesterone and vaginal progesterone, respectively, while Parveen et al. reported 9.2% vs. 26.5% (p = 0.0164).[5,10] A meta-analysis by Lee et al. highlighted a lower miscarriage rate in oral dydrogesterone users compared to controls (11.7% vs. 22.6%; OR: 0.43, p = 0.001), whereas no significant difference was seen with vaginal progesterone (p = 0.30) [59]. Similarly, Wang et al. reported a reduced miscarriage risk with oral dydrogesterone (RR: 0.55).[11]

Pregnancy continuation rates in our study were 51.5% for oral dydrogesterone and 48.6% for vaginal progesterone. Comparable findings by Qing et al. (88.4% vs. 84.9%; p > 0.05) and Verma et al. support these outcomes.[8,10]

Regarding adverse effects, no significant difference was noted in our study (p = 0.40). Vaginal progesterone users reported slightly more adverse effects (55.3%) than oral dydrogesterone users (44.7%). Kale et al. and Das et al. similarly observed minimal adverse effects with either medication.[6,7] Conversely, Siew et al. reported more drowsiness among vaginal progesterone users, while Ikechebelu et al. found significantly higher vaginal irritation rates in the vaginal progesterone group (24.7% vs. 4.9%).[12,13]

Conclusion

The study found no significant differences in age, period of gestation, or bleeding duration between the Oral Dydrogesterone and Vaginal Progesterone groups, indicating comparable baseline characteristics. Gestational age at first bleeding and timing of treatment initiation were also similar between groups. Adverse effects, including nausea and vaginal irritation, were reported in both groups without significant variation. Pregnancy outcomes, including miscarriage rates and continuation of pregnancy, were comparable between the two groups. Overall, both treatments demonstrated similar efficacy and safety profiles in managing threatened abortion.

Authors Contribution

NN: Study conception, design, data collection, data analysis, interpretation, and manuscript preparation.; **US:** Study design and manuscript preparation.; **KK:** Data analysis and interpretation.; **PY:** Data collection, analysis, and interpretation.; **DO:** Data collection, analysis, and interpretation

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