Original Article

Comparative Outcomes of Cyclogest Pessary Versus Conservative Management in Threatened Miscarriage

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Abstract

Objective: To compare Cyclogest pessary with conservative management in women with threatened miscarriage with regard to pregnancy continuation rate, maternal morbidity and neonatal outcomes.

Methodology: This prospective cohort study was conducted from January 1, 2022, to December 31, 2022, at the Department of Obstetrics and Gynecology, Hayatabad Medical Complex, Peshawar. Participants were grouped according to clinical management into two groups. Cyclogest Group (n=100) - administration of 400 mg/day of vaginal progesterone (Cyclogest pessary) until 20 weeks of gestation or symptom resolution. Conservative Management Group (n = 70), women in this group received an alternative form of progesterone support (e.g., oral or intramuscular progesterone) to ensure that all participants received some form of progesterone therapy. Data were analyzed using SPSS version 25. Baseline characteristics were summarized using descriptive statistics. Statistical significance was defined as p-value ≤ 0.05.

Results: Mean age for the Cyclogest group was 28.5 ± 5.2 years and 27.8 ± 5.6 years for the conservative group (p = 0.23). Both groups were comparable in terms of gravidity, parity, and gestational age at presentation (p > 0.05). The continuation of pregnancy beyond 20 weeks was significantly higher in the Cyclogest group compared to the conservative group (87% vs. 70%, p = 0.004). The rate of complete miscarriage was lower in the Cyclogest group (13%) compared to the conservative group (30%). Maternal morbidity rates were comparable between the two groups, with no significant differences in postpartum hemorrhage, infection, or hypertensive disorders (p > 0.05).

Conclusion: Cyclogest pessary significantly improves pregnancy continuation rates in women with threatened miscarriage compared to conservative management. Further randomized controlled trials are needed to validate these findings and refine treatment guidelines.

Keywords: Threatened miscarriage, cyclogest pessary, progesterone therapy, pregnancy, management, outcomes.

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Introduction

Threatened miscarriage is a common early pregnancy complication, occurring in about 20% of pregnancies and defined as vaginal bleeding with a live intrauterine pregnancy within 20 weeks of gestation.[1] It significantly heightens maternal anxiety due to the potential risk of miscarriage. Progesterone therapy has been proposed as a treatment to reduce the risk of miscarriage, and as such, the management of miscarriage in a threatened form remains a controversial field. In some cases, the hormone progesterone, essential for sustaining pregnancy, may be lacking and result in an early pregnancy loss.[2]

Progesterone, a hormone vital for sustaining pregnancy, is critical in sustaining a suitable endometrial niche and suppressing uterine contraction. In some cases of threatened miscarriage, a deficiency in progesterone production has been regarded as a possible contributing factor.[3]. As a result, progesterone supplementation has been introduced as a therapeutic strategy, Cyclogest pessary a vaginal route of

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progesterone is one of the frequently prescribed formulation of the make.[4] Studies suggest that vaginal progesterone, such as Cyclogest, may improve pregnancy outcomes by enhancing endometrial receptivity and reducing uterine contractility, thereby potentially lowering the risk of miscarriage in cases of threatened miscarriage.[5] Its mechanism of action and localized delivery have positioned it as a potential treatment option in cases of hormonal insufficiency during early pregnancy.[6]

Conversely, conservative management comprising of observation and reassurance is often used as first line management, especially for women who are not at high risk.[7] This technique is non-invasive and does not require unnecessary medical intervention, though it may not treat the underlying hormonal deficiencies which could be a factor in those susceptible to pregnancy loss.[8] The option of conservative management or medical therapy including progesterone supplementation is commonly a clinical discretion on a case-to-case bases depending on patients expectations and evidence based guidelines availability.

In Pakistan specifically, 15-20% of clinically diagnosed pregnancies come with the prevalent obstetric issue of threatened miscarriage.[9] Consanguinity, maternal malnutrition, vitamin D insufficiency, and inadequate prenatal care are probably some of the causes of this, particularly in a place with limited resources like Peshawar. High levels of stress, viral diseases, and other endocrine disorders are also linked to an increased risk. However, there is no conventional method for managing this prevalent condition. Progesterone therapy has a substantial impact on pregnancy loss, thus more research and evidence-based treatment algorithms are necessary to maximize outcomes for both mothers and newborns.[10]

Both approaches are used widely and there is no clear consensus on the best management of threatened miscarriage. It is important to understand how Cyclogest pessary compares with conservative management in this regard, as this might have a significant impact on clinical decision making. We aim to assess the efficacy of these two strategies compared with each other, evaluating all relevant outcomes including continuation of pregnancy, maternal morbidity, and live birth rates. By providing strong evidence, the study aims to contribute to the optimization of care for women with threatened miscarriage, alleviating the physical and psychological burden that this condition represents.

Methodology

This prospective cohort study was conducted from January 1, 2022, to December 31, 2022, at the Department of Obstetrics and Gynecology, Hayatabad Medical Complex, Peshawar. The institutional review board approved the study protocol, and all patients gave written informed consent for enrolment.

The study consisted of women aged 18–40 years presenting with threatened miscarriage (vaginal bleeding before 20 weeks of gestation and a viable intrauterine pregnancy on transvaginal ultrasound). Those excluded were women with significant associated diseases, ectopic pregnancy, multiple pregnancies or in known hypersensitivity to progestogen. Sample size was calculated by using power analysis (95% confidence interval and 80% power) based on an estimated 20% difference in pregnancy continuation rates between both groups (reported in prior studies).[11,12] The sample size required was then calculated to be 170 using the formula for comparing two proportions.

Participants were grouped according to clinical management into two groups. Cyclogest Group (n=100) - administration of 400 mg/day of vaginal progesterone (Cyclogest pessary) until 20 weeks of gestation or symptom resolution. Conservative Management Group (n = 70): Women in this group received an alternative form of progesterone support (e.g., oral or intramuscular progesterone) to ensure that all participants received some form of progesterone therapy. For the purpose of reducing bias, the participants were randomly assigned into the groups to obtain an even distribution of demographic and clinical characteristics in both groups. A structured proforma was employed to record data comprising demographics (age, gravidity, parity), clinical history and details of presenting symptoms (overall duration of bleeding and its severity, abdominal pain). All ultrasonographic evaluations were performed by certified radiologists to ensure diagnostic accuracy.

The main outcome was pregnancy beyond 20 weeks of gestation. The secondary outcomes included the occurrence of complete miscarriage, preterm birth, maternal complications, and neonatal outcomes (birth weight and Apgar scores). Participants were followed every two weeks, with the endpoint being resolution of

symptoms or pregnancy outcomes. Although it was stated that progesterone treatment had been stopped at 20 weeks, the possible role of progesterone treatment on later pregnancy outcomes (notably

preterm birth) was investigated by clinical assessment and records of the progression of the pregnancy rather than by objective measurement of cervical length (not evaluated in this study).

Participants were followed up in regular intervals (every 2 weeks) until symptoms resolved or pregnancy ended. Data were analyzed using SPSS version 25. Baseline characteristics were summarized using descriptive statistics. Statistical significance was defined as p-value ≤ 0.05.

Results

The study included 170 women with threatened miscarriage, with 100 in the Cyclogest group and 70 in the conservative management group. Mean age for the Cyclogest group was 28.5 ± 5.2 years and 27.8 ± 5.6 years for the conservative group (p = 0.23). Both groups were comparable in terms of gravidity, parity, and gestational age at presentation (p > 0.05). Table I

Table I: Baseline Characteristics of Participants.

Characteristics	Cyclogest Group (n=100)	Conservative Group (n=70)	p-value
Mean age (years)	28.5 ± 5.2	27.8 ± 5.6	0.230
Mean gestational age enrolment	9.6 ± 2.3	9.4 ± 2.1	0.181
Mean gestational age at birth	37.2 ± 3.1	35.8 ± 4.2	0.015
Gravidity(mean ± SD)	3.1 ± 1.2	3.0 ± 1.3	0.453
Parity (mean ± SD)	1.4 ± 0.9	1.5 ± 0.8	0.340

The continuation of pregnancy beyond 20 weeks was significantly higher in the Cyclogest group compared to the conservative group (87% vs. 70%, p = 0.004). The rate of complete miscarriage was lower in the Cyclogest group (13%) compared to the conservative group (30%, p = 0.004). Table II

Table II: Pregnancy Outcomes.

Outcome	Cyclogest Group (n=100)	Conservative Group (n=70)	p-value
Continuation of pregnancy >20 weeks	87 (87%)	49 (70%)	0.004
Complete miscarriage	13 (13%)	21 (30%)	0.004
Preterm delivery (<37 weeks)	15/87 (17.2%)	15/49 (30.6%)	0.047

Maternal morbidity rates were comparable between the two groups, with no significant differences in postpartum hemorrhage, infection, or hypertensive disorders (p > 0.05). Table III

Table III: Maternal Morbidity

Maternal Morbidity	Cyclogest Group (n=100)	Conservative Group (n=70)	p-value
Postpartum Hemorrhage	3 (3%)	5 (7%)	0.18
Maternal Infection	2 (2%)	4 (6%)	0.12
Thromboembolic Events	1 (1%)	0 (0%)	0.99
Hypertensive Disorders	4 (4%)	3 (4%)	0.99

The mean birth weight was significantly higher in the Cyclogest group (3.1 ± 0.4 kg) compared to the conservative group (2.8 ± 0.5 kg, p = 0.02). Apgar scores at 1 and 5 minutes were comparable between groups. Table IV

Table IV: Neonatal Outcomes.

Neonatal Outcomes	Cyclogest Group (n=100)	Conservative Group (n=70)	p-value
Mean birth weight (kg)	3.1 ± 0.4	2.8 ± 0.5	0.02
Apgar score at 1 minute (mean ± sd)	7.8 ± 0.6	7.6 ± 0.7	0.12
Apgar score at 5 minutes (mean ± sd)	8.9 ± 0.4	8.7 ± 0.5	0.08
Fetal anomalies	2 (2%)	3 (4%)	0.45
Neonatal intensive care unit (NICU) admission	5 (5%)	8 (11%)	0.10

Discussion

Threatened miscarriage is a multifaceted clinical state with profound emotional and physiological consequences for affected women.[13] Progesterone treatment significantly improved pregnancy outcomes and decreased adverse outcomes related to this condition. Due to the considerable psychological burden associated with threatened miscarriage on women, the identification of an effective therapeutic option is imperative not only for physical health but also for mental well-being.

Cyclogest was associated with a higher proportion of pregnancies not past 20 weeks at follow-up (87%) compared with conservative treatment (70%). This difference was statistically significant (p = 0.004) and would suggest an advantage with vaginal progesterone use in maintaining a pregnancy following a threatened miscarriage. Our results are concordant with those of

Iqbal M et al and the authors also provide improved biological plausibility supporting the potential role of progesterone therapy in reducing miscarriage rates.[14] The results are in agreement with the classical mechanism of action of progesterone via endometrial stabilisation, immunological tolerance and inhibition of uterine contractility. Progesterone is also effective in modulating inflammatory responses and promoting vascularization, further advocating its use for sustaining early pregnancy, particularly in women with a history of first-trimester bleeding.[15]

In contrast, our findings differ somewhat from those of Shehata H et al, the beneficial impact by progesterone on such outcomes was age-specific and enhanced by recurrent pregnancy loss history.[16] This difference can be attributed to our population cohort that estimate was in women in whom different obstetric histories may exist such as other than patients with recurrent pregnancy loss. These differences might also be attributable to differences in dosage, route of administration, and gestational age at which treatment was begun. Understanding how various characteristics of individual patients interact with the use of progesterone therapy and impact outcomes will require further research and may hold the key to personalized treatment plans that ensure improved response to progesterone therapy.

The association is even stronger when we observe that the rate of complete miscarriage was lower in the Cyclogest group (13% vs. 30%; p = 0.004), sustaining its protective role, likely against hormonal deficiency leading to pregnancy loss. The low miscarriage rate seen in the Cyclogest group supports the findings from a study by Tetruashvili N et al, who concluded that progesterone may be helpful in preventing pregnancy loss, especially amongst women at high risk of miscarriage.[17] These findings more than ever support the use of progesterone therapy in clinical practice for women who have luteal phase defects or have had previous pregnancy losses.

The current study further confirms these findings for better neonatal outcomes with higher birth weights (3.1 ± 0.4 kg in Cyclogest group vs. 2.8 ± 0.5 kg in conservative group, p = 0.02) due to a logical common correlation between progesterone therapy with better fetal growth and development. This difference could be due to progesterone's physiological role in promoting placentation and nutrient transfer. The rate of preterm deliveries (presented as the percentage of continuing pregnancies) during our study was 17.2% in the Cyclogest group against 23.4% in the conservative group. Consistently we report on placental development and function being stimulated after progestogen supplementation to ensure fetal health.[18] The precise mechanism are still being investigated but one study found that progesterone may inhibit the expression of pro-inflammatory cytokines as well as maintain cervical competence, therefore preventing spontaneous preterm labor.[19]

While Apgar scores at 1 minute (7.8 ± 0. 6 vs. 7.6 ± 0.7, p = 0.12) and at 5 minutes (8.9 ± 0.4 vs. 8.7 ± 0.5, p = 0.08) were similar between groups, higher birth weight with progesterone therapy indicates potential long-term benefit. These results highlight the need for not only considering short-term pregnancy outcomes but also including neonatal health metrics to assess treatment efficacy. The changes in birth weight may have downstream effects on growth trajectories during infancy, an important developmental period characterized by increased susceptibility to risks associated with low birth weight, including a heightened risk of developing metabolic disorders and decreased neurodevelopmental skills.[20]

The current study contributes to the increasing amount of data demonstrating the effectiveness of Cyclogest pessary in cases of imminent miscarriage. Even if the results are encouraging, more extensive multicenter trials with longer follow-up periods are necessary to validate these results and improve clinical recommendations. By acknowledging the strengths and limitations of our study, we intend to influence the changing field of miscarriage care by promoting evidence-based practices catered to the need of specific patients

Conclusion

In women with threatened miscarriage, this study shows that Cyclogest pessary treatment massively increases rates of continuation of pregnancy and ultimately improves neonatal outcomes compared with that of conservative management. These results highlight the potential of progesterone therapy as a specific treatment to address issues associated with early pregnancy anomalies.

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