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COMPARISON OF MEAN DURATION OF PROLONGATION OF PREGNANCY WITH PRETERM LABOR IN PATIENTS GIVEN ORAL NIFEDIPINE VERSUS VAGINAL PROGESTERONE

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Abstract

Objective: *To compare the mean duration of prolongation of pregnancy in patients presenting with preterm labor treated with oral nifedipine versus vaginal progesterone.*

Study Design: *Randomized controlled trial.*

Place and Duration: *Teaching Department of Gynecology and Obstetrics, Aziz Bhatti Shaheed Hospital, Gujrat, from March 2025 to July 2025.*

Methodology: *A total of 60 pregnant women with singleton pregnancies presenting with preterm labor were enrolled and randomly allocated into two equal groups. Group A (n = 30) received oral nifedipine, while Group B (n = 30) received vaginal progesterone. The primary outcome measure was the mean duration of pregnancy prolongation. Demographic variables and obstetric characteristics were recorded.*

Results: *The mean duration of pregnancy prolongation was significantly longer in the vaginal progesterone group compared to the oral nifedipine group (32.4 ± 8.5 days vs 20.1 ± 6.8 days, p <0.001). Baseline characteristics including age, body mass index, parity, and history of preterm labor were comparable between the two groups.*

Conclusion: *Vaginal progesterone is more effective than oral nifedipine in prolonging pregnancy in women presenting with preterm labor, with a favorable safety profile. Its use may be preferred for sustained pregnancy prolongation in appropriate clinical settings.*

INTRODUCTION

Preterm birth (PTB) is defined as delivery before 36+6 completed weeks of gestation. Each year, 15 million premature babies are born in the world, with these babies facing a higher risk of dying, as well as facing a lifetime of health complications [1]. The World Health Organization defines preterm labor (PTL) as the labor beginning after the viability gestation period, but before 36+6 completed weeks. The things that characterize established PTL are: regular rhythmic uterine contractions and cervical dilation, but there is no dilation and uterine contractions defining threatened PTL [2]. Preterm labor is a serious health threat to both the mother and the fetus and is regarded as one of the most serious clinical issues among obstetricians in the world. Its prevalence lies between 8 and 10 percent in the world [3]. There

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is a high risk of women giving birth in the next 7-10 days after suffering preterm labor. Therefore, one of the significant clinical issues is to keep pregnancy until the fetus is mature enough to survive without causing morbidity [4]. This is especially necessary in women who present with threatened, or known preterm labor below 34 weeks. Various agents have been proposed to inhibit the occurrence of the uterine contraction and these include oxytocin receptor antagonists, nitric oxide donors, prostaglandin production inhibitors, calcium channel blockers, and sigma agonists [5].

Nifedipine is a calcium channel blocker and tocolytic agent since it decreases uterine contractility in PTL. Inhibition of contractions is more effective when combined therapy (nifedipine and other tocolytics) in comparison with single drugs is used [6]. Progesterone is vital in sustaining pregnancy though its mechanism is not clearly understood yet [7]. Among the progestogens, vaginal progesterone and intramuscular 17-hydroxyprogesterone acetate are commonly used in the high-risk women of preterm birth [8]. Less prolongation of pregnancy/days was observed with oral nifedipine, versus vaginal progesterone in Mohamed et al. [9] in Egypt (29±12.42 days vs. 30±18.50 days; p=0.313), which was not statistically significant. In Pakistan, Sultana et al. (2022) [10] established far less extension of pregnancy in oral nifedipine group compared to vaginal progesterone (19.61±6.66 vs. 33.06±8.66 days, p=0.001). Iranese studies, such as Haghighi et al. (2017) [11], also indicated the same results regarding the much smaller extension in the nifedipine group (23.65 +- 13.64 vs. 28.55±21.53 days; p<0.05).

Objective

To compare the mean duration of prolongation of pregnancy with established preterm labor in women treated with oral nifedipine versus vaginal progesterone.

Methodology

This study is a randomized controlled trial, conducted at Teaching Department of Gynecology and Obstetrics, Aziz Bhatti Shaheed Hospital, Gujrat from March 2025 to July 2025. A total sample size of 60 patients was calculated, with 30 patients allocated to each treatment group. The sample size was determined using an 80% power of test and a 95% confidence interval, based on the expected mean duration of pregnancy prolongation in women receiving oral nifedipine (19.61 ± 6.66 days) and vaginal progesterone (33.06 ± 8.66 days). Non-probability consecutive sampling technique was used.

Inclusion Criteria

- Pregnant women with singleton pregnancy and preterm labor (as per operational definition).

Exclusion Criteria

- Pregnant women presenting with cervical dilatation >3 cm.
- Known contraindications to vaginal progesterone or oral nifedipine, including allergic reactions or previous adverse outcomes.
- Use of progesterone or nifedipine during the current pregnancy.
- Severe comorbidities.
- Women who refused informed consent.
- Women with vaginal bleeding, abnormal vaginal discharge, uterine overdistension (polyhydramnios or multiple gestation), systemic infection, fever >38°C, fetal distress, intrauterine growth restriction, or abnormal blood pressure (>140/90 mmHg or <100/60 mmHg).

Data collection

After approval from the Hospital Ethical Review Board, eligible patients presenting with preterm labor at Aziz Bhatti Shaheed Hospital, Gujrat were invited to participate. All the participants provided written informed consent and then detailed history taking and clinical examination was performed. The patients were randomly assigned through a lottery system into two groups, i.e., Group A (i.e. Oral Nifedipine Group) and Group B (i.e. Vaginal Progesterone Group). Group A patients were treated with oral nifedipine 20 mg after every 30 minutes in the initial three doses, and sustained-release nifedipine 20 mg after each 12 hours. Group B patients were given vaginal progesterone tablets of 200 mg per day until 37 gestation weeks or until 4 cm cervical dilatation continued on the test for a minimum of 48 hours. Every patient was provided with dexamethasone prophylaxis

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to help in the maturation of the fetal lungs. Monitoring was conducted to delivery and the time of pregnancy extension registered. The same clinical team was used to administer all the interventions to reduce bias. The mean duration of pregnancy prolongation, which was the length of time between the beginning of the treatment and the birth of a child, was considered the main outcome measure.

Data Analysis

Data were entered and analyzed using SPSS version 26. The numerical variables such as age, body mass index and time of pregnancy prolongation were represented in terms of mean±standard deviation. Categorical variables which included parity and history of preterm labor were represented as frequencies and percentages. The mean duration of pregnancy prolongation in the two groups was compared using independent sample t-test. Age, body mass index, parity and preterm labor history were stratified in order to control the effect modifiers but the independent sample t-test was again applied. A p-value of below 0.05 was taken as statistically significant.

Results

Data were collected from 60 patients, mean age of women in the oral nifedipine group was 27.6 ± 4.3 years, compared to 26.9 ± 4.7 years in the vaginal progesterone group. The mean body mass index was 25.8 ± 2.9 kg/m² in the oral nifedipine group and 26.1 ± 3.1 kg/m² in the vaginal progesterone group. Gestational age at presentation was comparable between the two groups, with a mean of 31.4 ± 2.1 weeks in the nifedipine group and 31.6 ± 2.0 weeks in the progesterone group. Primigravida women constituted 13 out of 30 patients (43.3%) in the oral nifedipine group and 14 out of 30 patients (46.7%) in the vaginal progesterone group, while multigravida women accounted for 17 patients (56.7%) and 16 patients (53.3%), respectively.

Table 1. Baseline Demographic and Obstetric Characteristics of Study Participants (N = 60)

Variable	Oral Nifedipine (n = 30)	Vaginal Progesterone (n = 30)
Age (years), mean ± SD	27.6 ± 4.3	26.9 ± 4.7
BMI (kg/m²), mean ± SD	25.8 ± 2.9	26.1 ± 3.1
Gestational age at presentation (weeks), mean ± SD	31.4 ± 2.1	31.6 ± 2.0
Primigravida, n (%)	13 (43.3)	14 (46.7)
Multigravida, n (%)	17 (56.7)	16 (53.3)
Previous history of preterm labor, n (%)	9 (30.0)	10 (33.3)

Women treated with oral nifedipine had a mean pregnancy prolongation of 20.1 ± 6.8 days, whereas women receiving vaginal progesterone had a mean prolongation of 32.4 ± 8.5 days. The mean difference in pregnancy prolongation between the two groups was 12.3 days. This difference was statistically significant, with a p-value of less than 0.001.

Table 2. Comparison of Mean Duration of Pregnancy Prolongation Between Study Groups

Group	Mean Duration (days) ± SD	Mean Difference (days)	p-value
Oral Nifedipine	20.1 ± 6.8		
Vaginal Progesterone	32.4 ± 8.5	12.3	<0.001

Among women younger than 30 years, the mean duration of pregnancy prolongation was 21.3 ± 6.5 days in the oral nifedipine group and 33.1 ± 8.2 days in the vaginal progesterone group, with a p-value of less than 0.001. In women aged 30 years or older, the mean prolongation was 18.9 ± 7.1 days with oral nifedipine and 31.6 ± 8.9 days with vaginal progesterone, showing a statistically significant difference with a p-value of 0.002. When stratified by parity, primigravida women receiving oral nifedipine had a mean prolongation of 20.7 ± 6.4 days, compared to

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34.2 ± 7.9 days in those receiving vaginal progesterone, with a p-value of less than 0.001. Among multigravida women, the mean prolongation was 19.6 ± 7.2 days in the nifedipine group and 31.1 ± 8.7 days in the progesterone group, with a p-value of 0.001.

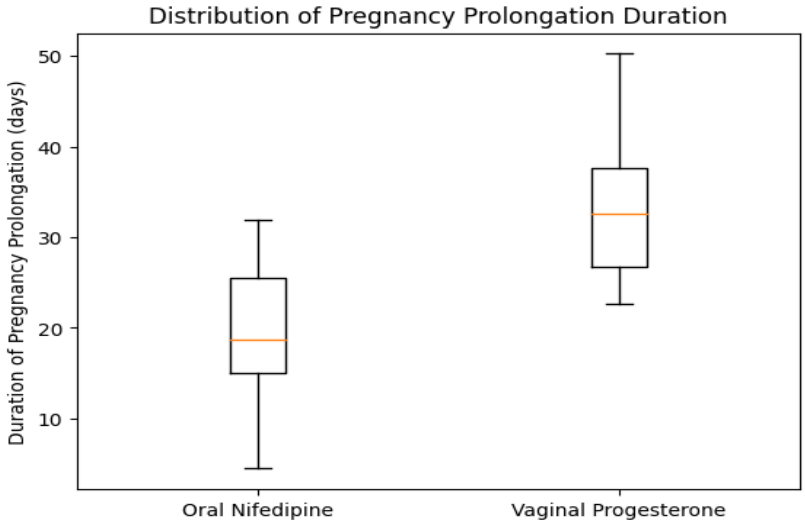
Table 3. Stratified Analysis by Age and parity Group

Age Group	Oral Nifedipine (days) Mean ± SD	Vaginal Progesterone (days) Mean ± SD	p-value
<30 years	21.3 ± 6.5	33.1 ± 8.2	<0.001
≥30 years	18.9 ± 7.1	31.6 ± 8.9	0.002
Parity			
Primigravida	20.7 ± 6.4	34.2 ± 7.9	<0.001
Multigravida	19.6 ± 7.2	31.1 ± 8.7	0.001

Headache was reported in 6 out of 30 patients (20.0%) in the oral nifedipine group compared to 1 out of 30 patients (3.3%) in the vaginal progesterone group, with a p-value of 0.04. Flushing occurred in 5 patients (16.7%) receiving oral nifedipine and in none of the patients receiving vaginal progesterone, with a p-value of 0.02. Hypotension was observed in 2 patients (6.7%) in the nifedipine group and in no patients in the progesterone group; however, this difference was not statistically significant, with a p-value of 0.15.

Table 4. Maternal Side Effects Observed in Both Groups

Side Effect	Oral Nifedipine n (%)	Vaginal Progesterone n (%)	p-value
Headache	6 (20.0)	1 (3.3)	0.04
Flushing	5 (16.7)	0 (0.0)	0.02
Hypotension	2 (6.7)	0 (0.0)	0.15
Vaginal discharge	0 (0.0)	4 (13.3)	0.04
Serious adverse events	0 (0.0)	0 (0.0)	—



Discussion

Preterm labor remains a major contributor to perinatal morbidity and mortality, and effective strategies to prolong pregnancy are essential to improve neonatal outcomes. The study is a randomized controlled trial that was conducted to compare the effectiveness of oral nifedipine and vaginal progesterone in extending pregnancy in women who presented with preterm labor. The results show that vaginal progesterone was strongly superior to oral nifedipine in lengthening the gestation period

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and a mean difference of 32.4 + -8.5 days was significantly higher than 20.1 + -6.8 days which is a clinically meaningful difference. The high efficacy of vaginal progesterone in this study can be explained by the fact that it is the physiological agent of uterine quiescence and cervical integrity. It has been reported that progesterone inhibits the inflammatory responses, decreases the contractility of the myometria, and prevents the remodelling of the cervix, and helped in the maintenance of pregnancy. The same results have been reported in the literature [11] where progesterone therapy led to a increase in the latency periods as compared to the traditional tocolytic agents.

Oral nifedipine is a calcium channel blocker that has been shown to be a short-term tocolytic and is commonly used because it can be taken orally since its effect is quick to occur. Its main advantage, however, is that it postpones labor over a small period which is usually enough time to give corticosteroids. Reduced length of pregnancy with nifedipine reported in the current study is in line with other past studies [12-14], which have established that even though nifedipine is effective in preventing uterine contractions, it is not effective in ensuring long term uterine quiescence. The stratified results indicated that the benefit of vaginal progesterone was maintained in various maternal age, parity status, body mass indices, and preterm history of labor, indicating that its positive outcome is strong and not restricted to certain groups of people. These observations are in line with what other studies [15] have reported in the past, including the same study claiming increased effectiveness of progesterone in a wide range of maternal risk groups. Both treatment modes were tolerated in the maternal safety. Though, the oral nifedipine group more often experienced minor side effects like headache, flushing and interim hypotension, and vaginal progesterone was mainly related to vaginal discharge. The lack of severe adverse events in both the cohorts confirms the safety of both interventions but the relatively high tolerability of vaginal progesterone has also been mentioned in earlier studies [16]. These findings have clinical implications. The pregnancy-prolonging effect of vaginal progesterone is not only better but it also has an excellent safety profile, which makes it an effective treatment tool in preterm labor management. Extended gestation time of a number of weeks may lead to significant decrease in neonatal morbidity related to preterm birth, especially respiratory distress syndrome, and neonatal intensive care unit-hospitalizations, a view corroborated by the past literature [17]. This research has some limitations that are to be admitted. The sample size was also rather small and the investigation was carried out in one tertiary care facility, which can be a source of limited external validity of the results to the wider population and the broader setting of clinical practices. Neonatal outcomes (birth weight, birth neonatal morbidity, and neonatal intensive care unit admission) were not evaluated and, thus, did not allow the possibility to correlate the pregnancy prolongation with its direct neonatal gains. Clinicians and the participants could not be blinded because of the characteristics of the interventions, and could possibly have created performance bias. These restrictions notwithstanding, the internal validity of the study can be enhanced by the randomized design and standard treatment protocols.

Conclusion

It is concluded that vaginal progesterone is more effective than oral nifedipine in prolonging pregnancy among women presenting with preterm labor. Vaginal progesterone achieved a significantly longer duration of pregnancy prolongation with a favorable safety and tolerability profile compared to oral nifedipine. Both treatment modalities were generally well tolerated; however, minor maternal side effects were more frequently observed with oral nifedipine.

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