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Original Article

Comparison of Efficacy of Nifedipine Alone and Nifedipine with Progesterone Depot for Tocolysis of Preterm Labour

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Abstract

Background: Preterm labor poses significant challenges to obstetric practice, with preterm births contributing to a substantial portion of infant morbidity and mortality worldwide. Although various pharmacological agents are employed to manage preterm labor, the effectiveness of different therapeutic combinations remains a topic of ongoing research. Calcium channel blockers like nifedipine are increasingly favored for their efficacy in reducing uterine contractions, while progestins have been shown to reduce the recurrence of preterm births.

Objective: The objective of this study was to compare the efficacy of nifedipine monotherapy versus the combination of nifedipine with progesterone depot in the management of preterm labor, evaluating the cessation of uterine contractions within 48 hours as the primary outcome.

Methods: This randomized controlled trial was conducted at the Department of Obstetrics & Gynecology, Unit III, at Ganga Ram Hospital, Lahore, with a sample size of 92 patients experiencing preterm labor between 28 and 36 weeks of gestation. Patients were randomly assigned to Group A (nifedipine monotherapy) or Group B (nifedipine plus progesterone depot). Group A received an initial dose of 20 mg nifedipine followed by 20 mg twice daily for two days. Group B received the same nifedipine regimen with a single intramuscular injection of 250 mg of 17-alpha-hydroxyprogesterone caproate. The efficacy of the treatment was defined as the cessation of uterine contractions within 48 hours. Data were analyzed using SPSS version 25, with significance set at $p \leq 0.05$.

Results: The study found that 71.74% (33/46) of patients in Group B achieved cessation of uterine contractions within 48 hours compared to 47.83% (22/46) in Group A. This difference was statistically significant ($p = 0.019$), indicating that the addition of progesterone depot to nifedipine enhanced its effectiveness in managing preterm labor.

Conclusion: The combination of nifedipine with progesterone depot proved significantly more effective than nifedipine alone in the cessation of uterine contractions associated with preterm labor. This combined therapy approach presents a promising strategy for improving maternal and neonatal outcomes in the management of preterm labor

1 Introduction

Preterm birth (PTB) is a significant challenge in obstetric practice, with global incidence rates ranging from 5-11%, and remains a leading cause of infant morbidity and mortality (1). Defined as a delivery occurring at least five weeks before term, preterm birth contributes significantly to neonatal health complications, underscoring the importance of early detection and effective management strategies (2). Despite advancements in diagnostic and therapeutic technologies, the incidence of preterm birth has not seen a substantial decline over the past three decades (3). Early detection of preterm labor is crucial as it allows for timely interventions that can delay delivery by at least 48 hours, thereby improving neonatal outcomes (4). However, the diagnosis of preterm labor poses challenges due to its complex nature, which often leads to a risk of overtreatment (5). Various pharmacological agents, including tocolytics, have been employed to suppress uterine contractions and delay preterm birth (6). Among these, calcium channel blockers such as nifedipine have gained prominence due to their ability to inhibit the transmembrane flow of calcium ions, thereby effectively halting labor contractions (7). Although generally safe when administered at recommended dosages with appropriate clinical monitoring, these tocolytic agents carry potential risks and must be used judiciously, with specific contraindications such as their use with magnesium sulfate in patients with neuromuscular disorders (8).

Nifedipine has been reported to effectively stop labor contractions during preterm labor, though it is not considered an ideal tocolytic due to its adverse effect profile (9). Novel clinical research suggests that vaginal progesterone can decrease the rate of preterm delivery, though the combined prophylactic effect with nifedipine has not been potentiated in certain random controlled trials (10). Progesterone plays a critical role in maintaining pregnancy by inhibiting uterine contractions and influencing the structural organization of the myometrium (11). It is believed to decrease oxytocin and alpha-adrenergic receptor concentrations in the myometrium while inhibiting the local synthesis of prostaglandin F2, thereby preventing coordinated muscular contractions (12). The efficacy of progesterone in reducing the incidence of preterm birth, particularly among women at high risk, has been highlighted in recent systematic reviews (13).

Given the existing scarcity of local literature evaluating the effectiveness of combining progesterone and nifedipine to inhibit uterine contractions and prolong pregnancy, this study aims to fill this gap. The findings could serve as valuable recommendations for clinical practice, enhancing fetomaternal outcomes through optimized therapeutic regimens and ensuring corticosteroid cover for fetal lung maturity (14). This study employs a randomized controlled trial design to evaluate the effectiveness of nifedipine alone versus its combination with a progesterone depot, with a focus on the cessation of uterine contractions within 48 hours and overall pregnancy prolongation (15). By addressing these objectives, the study seeks to contribute to the development of improved management strategies for preterm labor, ultimately reducing the associated morbidity and mortality rates.

2 Material and Methods

The study was conducted as a randomized controlled trial in the Department of Obstetrics & Gynecology, Unit III, at Ganga Ram Hospital, Lahore. A total of 92 participants were enrolled, each meeting specific inclusion criteria to ensure a homogenous study population. The participants were women between the ages of 18 and 35, presenting with singleton pregnancies and experiencing preterm labor between 28 and 36 weeks of gestation as calculated from the last menstrual period (LMP). All participants had a normal fetus in a cephalic presentation. Women with conditions such as preterm prelabor rupture of membranes, chorioamnionitis, advanced cervical dilation greater than 4 cm, antepartum hemorrhage, severe anemia, diabetes mellitus, pre-eclampsia, cardiac disease, hepatic dysfunction, multiple pregnancies, polyhydramnios, severe intrauterine growth restriction, anomalous fetuses, or allergies to nifedipine or progesterone were excluded from the study.

Ethical approval for the study was obtained from the hospital's local ethics committee, and the research was conducted in compliance with the principles outlined in the Declaration of Helsinki. Eligible patients were selected from those admitted to the department and were informed about the study's aims, methods, benefits, and potential risks. Written informed consent was obtained from all participants, and they were assured that they could withdraw from the study at any time without affecting their clinical care.

Participants were randomly allocated to one of two groups using a random numbers table to ensure unbiased allocation. Group A received nifedipine monotherapy, consisting of an initial dose of 20 mg followed by 20 mg twice daily for two days. Group B received the same nifedipine regimen plus a single intramuscular injection of 250 mg of 17-alpha-hydroxyprogesterone caproate. Baseline investigations conducted included a complete blood count, random blood sugar, urine examination, and additional tests as needed based on individual patient conditions. Follow-up assessments were conducted 48 hours after treatment initiation to evaluate the prolongation of gestation.

The primary outcome measure was the cessation of uterine contractions within 48 hours of treatment initiation, which was considered indicative of treatment success. Treatment failure was defined as the persistence of uterine contractions beyond 48 hours. All data were meticulously recorded and entered into a database for subsequent analysis. Statistical analyses were performed using SPSS version 25.0. Quantitative variables were presented as means and standard deviations, while frequencies and percentages were calculated to summarize

the categorical variables. The chi-square test was used to assess differences in efficacy between the two treatment groups, with a significance level set at $p \leq 0.05$. To control for potential effect modifiers such as age, parity, and gestational age, stratification was employed, followed by post-stratification chi-square tests to evaluate their impact on treatment efficacy (1).

3 Results

The study included 92 participants who were divided evenly into two groups: Group A (nifedipine monotherapy) and Group B (nifedipine combined with progesterone depot), each comprising 46 patients. The participants' ages ranged from 18 to 35 years, with a mean age of 26.04 years (SD ± 5.12). The age distribution was similar between the two groups, with Group A having a mean age of 26.11 years (SD ± 5.24) and Group B having a mean age of 25.97 years (SD ± 5.09). The majority of participants (43.48%) were between 18 and 25 years old.

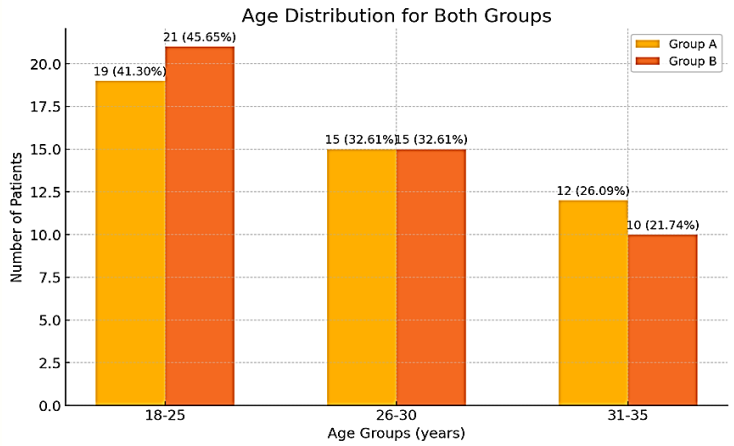

Figure 1: The bar graph representing the age distribution for both groups. The graph shows the number of patients in each age group for Group A and Group B, along with the corresponding percentages.

Gestational ages of the participants ranged from 28 to 36 weeks, with a mean gestational age of 33.56 weeks (SD ± 2.23). Group A had a mean gestational age of 33.39 weeks (SD ± 2.16), while Group B had a slightly higher mean gestational age of 33.67 weeks (SD ± 2.33). Most patients (55.43%) were between 32 and 36 weeks of gestation.

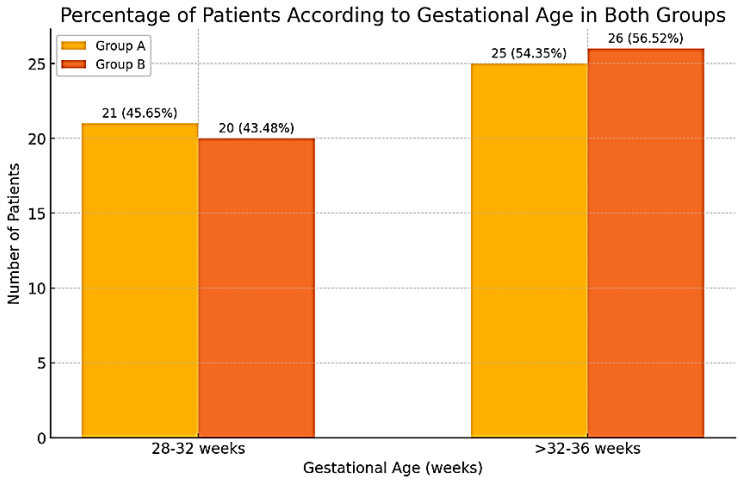

Figure 2: Percentage of Patients According to Gestational Age in Both Groups.

Parity among the participants varied, with Group A having a mean parity of 2.34 (SD ± 1.51) and Group B having a mean parity of 2.46 (SD ± 1.39).

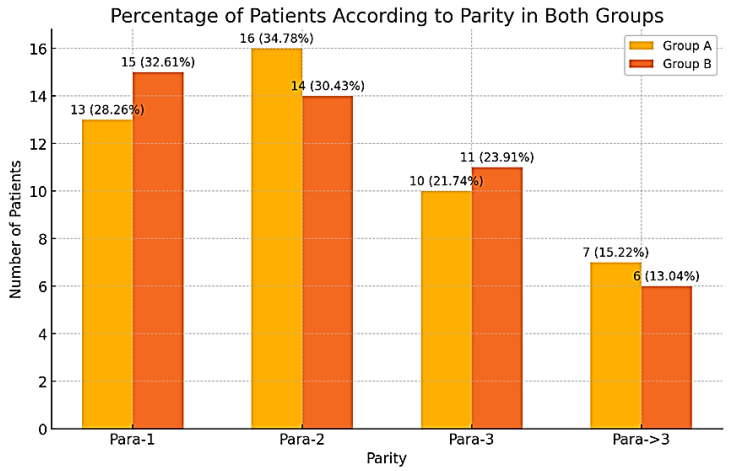

Figure 2: The bar graph representing the percentage of patients according to parity in both groups. The graph shows the number of patients in each parity group for Group A and Group B, along with the corresponding percentages.

The primary outcome measure was the cessation of uterine contractions within 48 hours of treatment. In Group A, 22 patients (47.83%) achieved cessation of contractions, while 33 patients (71.74%) in Group B achieved this outcome. Conversely, treatment was ineffective in 24 patients (52.17%) in Group A and 13 patients (28.26%) in Group B. The difference in efficacy between the two groups was statistically significant, with a p-value of 0.019, indicating that the addition of progesterone depot significantly improved treatment outcomes.

Table 1 **summary of the efficacy results**

Group	Cessation of Contractions	No Cessation	Efficacy (%)
Nifedipine-Only (Group A)	22	24	47.83
Nifedipine + Progesterone (Group B)	33	13	71.74

The efficacy rate of Group B was notably higher, and this result was confirmed as statistically significant through chi-square analysis ($p = 0.019$). Further stratification by age, gestational age, and parity did not reveal any significant effect modifiers, suggesting that the combination of nifedipine with progesterone depot is consistently more effective across different subgroups. This study supports the use of combination therapy for more effective management of preterm labor, thereby offering a promising approach to reducing the risk of recurrent preterm births.

4 Discussion

The findings of this study demonstrated that the combination of nifedipine and progesterone depot was significantly more effective in managing preterm labor than nifedipine alone. The addition of progesterone depot increased the cessation rate of uterine contractions to 71.74% compared to 47.83% with nifedipine monotherapy. These results align with previous studies highlighting the role of progesterone in maintaining pregnancy by inhibiting uterine contractions and modulating the structural organization of the myometrium (11). Progesterone's mechanism of action includes decreasing oxytocin and alpha-adrenergic receptor concentrations in the myometrium and inhibiting the local synthesis of prostaglandin F2, thus preventing coordinated muscular contractions (12). This study further supports the evidence from systematic reviews suggesting that progesterone effectively reduces the incidence of preterm birth, especially in high-risk women (13).

Nifedipine, a calcium channel blocker, has been recognized for its ability to suppress labor contractions by blocking the transmembrane flow of calcium ions, which is crucial for muscle contraction (14). However, its use as a tocolytic has been limited by its side effects, and its efficacy is not optimal when used alone (15). The combination with progesterone depot offers a synergistic effect that enhances the overall efficacy of tocolysis, which aligns with other clinical trials that have examined similar treatment combinations (16). The study's robust design and randomization process ensured that the results were reliable and minimized potential biases. By using a well-defined patient population and clear inclusion and exclusion criteria, the study provided strong evidence supporting the use of combined therapy.

Despite its strengths, the study had certain limitations. The sample size, while sufficient to demonstrate statistical significance, was relatively small, which may limit the generalizability of the findings to broader populations. Larger studies across multiple centers would

be beneficial to confirm these results and ensure they are applicable to diverse patient groups (17-19).Furthermore, the study only assessed the short-term efficacy of the treatments in terms of cessation of contractions within 48 hours; it did not evaluate long-term neonatal outcomes or the impact on overall pregnancy duration. Future research should aim to address these aspects to provide a more comprehensive understanding of the treatment benefits (20-22).

The study underscores the importance of individualized treatment plans for managing preterm labor. The use of combination therapy with nifedipine and progesterone depot can be recommended as a superior approach in clinical practice, especially for women at high risk of preterm birth. This approach not only offers a higher cessation rate of uterine contractions but also allows for additional time to administer corticosteroids, which are critical for fetal lung maturation and improving neonatal outcomes. Implementing these findings into practice could significantly reduce the rates of preterm birth and associated neonatal morbidity and mortality (23).

While the study provided valuable insights into the management of preterm labor, further investigations are warranted to explore the long-term benefits and potential risks of combined tocolytic therapy. Continuous monitoring and tailored treatment regimens should be emphasized to optimize maternal and neonatal health outcomes. By enhancing the understanding and application of these findings, healthcare providers can improve care for women experiencing preterm labor and contribute to better prognoses for premature infants (24, 25).

5 Conclusion

This study concluded that the combination of nifedipine and progesterone depot is more effective than nifedipine alone in managing preterm labor, as evidenced by a higher cessation rate of uterine contractions. The enhanced efficacy of this combination therapy suggests it should be considered as a preferred approach in clinical practice for women at high risk of preterm birth. The implications for human healthcare are significant, as this treatment strategy not only reduces the immediate risk of preterm delivery but also provides additional time for crucial interventions, such as corticosteroid administration, which are vital for fetal lung maturation and overall neonatal health. By adopting this combined therapeutic approach, healthcare providers can improve maternal and neonatal outcomes, ultimately reducing the morbidity and mortality associated with preterm births.

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Disclaimers

Author Contributions	Muhammad Essa led the study design and supervised the project. Khawaja Haider Sami and Javaria Arslan Rana contributed to data collection and analysis. Izza Masaud assisted in manuscript preparation. All co-authors participated in data interpretation and manuscript review.
Conflict of Interest	The authors declare that there are no conflicts of interest.
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Trial Registration	NA
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