Original Article
DOI: https://doi.org/10.70749/ijbr.v3i5.2337

INDUS JOURNAL OF BIOSCIENCE RESEARCH
https://ijbr.com.pk
ISSN: 2960-2793/ 2960-2807

Comparison of Nitroglycerin and Nifedipine in Preterm Labour

Mehwish Khalid[1], Shumaila Naeem[1], Faiza Sher[1], Aqsa Naeem[1]

[1]Pakistan Institute of Medical Sciences, Islamabad, Pakistan

ARTICLE INFO

Keywords: Calcium channel blockers, Nitroglycerin, Nifedipine, Preterm labour, Tocolysis.

Correspondence to: Mehwish Khalid, Pakistan Institute of Medical Sciences, Islamabad, Pakistan.
Email: mehwishkhalidpervaiz@gmail.com

Declaration
Authors' Contribution: All authors equally contributed to the study and approved the final manuscript.

Conflict of Interest: No conflict of interest.

Funding: No funding received by the authors.

Article History
Received: 13-02-2025 Revised: 16-05-2025
Accepted: 23-05-2025 Published: 30-05-2025

ABSTRACT

Background: Preterm labour, defined as the onset of persistent uterine contractions leading to cervical dilatation before 37 weeks of gestation, remains a leading cause of neonatal morbidity and mortality worldwide. Effective tocolytic therapy is essential to delay delivery, allowing interventions such as antenatal corticosteroids to enhance fetal lung maturity. Nitroglycerin and nifedipine are commonly used tocolytic agents, yet comparative data in local healthcare settings are limited. **Objective:** To compare the efficacy of nitroglycerin patch and oral nifedipine in the management of preterm labour. **Study Design:** Randomized controlled trial. **Duration and Place of Study:** The study was conducted from August 2024 to January 2025 at the Department of Obstetrics and Gynaecology, Pakistan Institute of Medical Sciences, Islamabad. **Methodology:** A total of 120 women aged 18–40 years with singleton pregnancies at 24–36 weeks gestation were randomized into nitroglycerin patch (n=60) or oral nifedipine (n=60) groups. Efficacy was defined as prolongation of pregnancy for at least 48 hours from onset of preterm labour. Maternal and fetal monitoring was performed throughout the intervention. **Results:** Oral nifedipine demonstrated higher efficacy (90.0%) compared to nitroglycerin patches (76.7%), though the overall difference was not statistically significant (p=0.299). Stratified analysis indicated significantly improved outcomes with nifedipine in women over 30 years of age (100% vs 60%, p=0.026). **Conclusion**: Both agents are effective for preterm labour management, with oral nifedipine showing superior efficacy, particularly in older women, supporting its use as a reliable first-line tocolytic.

INTRODUCTION

Preterm labour involves the initiation of persistent myometrial contractions before 37 weeks' gestation resulting in cervical dilatation and effacement and is a major cause of neonatal morbidity and mortality.[1] Etiological mechanisms are multifactorial and encompass maternal, fetal, and placental determinants such as intrauterine infection, cervical insufficiency, mutiple gestations, or chronic maternal comorbidities.[2] Pathophysiological interactions of myometrial contractility with hormonal and inflammatory mediator regulation induce activation of the uterus before term and cervix softening.[3] Early recognition and obstetric intervention are a requirement in order to optimize neonatal outcomes and avoid long-term complications such as respiratory distress syndrome, intraventricular hemorrhage, and neurodevelopmental impairment.[4]

Nitroglycerin, a smooth muscle relaxant and donor of nitric oxide, acts as a tocolytic agent during preterm labour as a method of suppressing the contraction of the myometrium and enhancing uteroplacental perfusion.[5] Nitroglycerin acts principally transdermally or sublingually.[5] Nitroglycerin induces fleeting uterine relaxation with a tendency to do so during acute preterm contraction; however, efficacy depends upon maternal hemodynamic status and gestational age.[6] Adverse effects of maternal hypotension, cephalgia, and fleeting tachycardia warrant clinical observation and repeated or continuous nitroglycerin administration because of a short half-life requiring continued or repeated administration to maintain tocolysis.[7]

Nifedipine, a calcium channel antagonist of the dihydropyridine class, is used extensively as a first-line tocolytic agent to prevent calcium-mediated myometrial contraction.[8] Given orally or sublingually, it reduces uterine contractile frequency and intensity and prolongs preterm parturition with a delay of crucial interventions like antenatal corticosteroids treatment for fetal lung maturity.[9] Evidence from randomized controlled trials and meta-analyses suggests nifedipine has fewer maternal adverse effects compared with beta-adrenergic agonists and has a superior safety profile with alternative tocolytics.[9] Its use both during the acute and maintenance phase highlights the importance of nifedipine as a cornerstone of current obstetrical practice and practice guidelines; clinicians should use nifedipine with careful

surveillance of possible complications like maternal hypotension, reflex tachycardia, and an exceedingly rare pulmonary edema.[10]

In a study by Goyal N. et al. has shown that efficacy of nitroglycerin patch was 75.3% as compare to 93.8% with oral nifedipine in the management of preterm labour.[11]

Consideration of the local healthcare conditions of Pakistan, preterm labour continues as a major cause of neonatal morbidity and mortality. Scarce comparative efficacy and safety data of routinely used tocolytics like nitroglycerin and nifedipine injectable oil induce doubt among clinicians regarding the choice of the best management approach. Carrying out this research will offer regionally applicable evidence to inform therapeutic choices, optimize maternal and neonatal outcomes, and assist in standardizing the treatment protocol at the Pakistan healthcare level.

METHODOLOGY

This randomized controlled trial was conducted at the Department of Obstetrics and Gynaecology, Pakistan Institute of Medical Sciences, Islamabad, from August 2024 to January 2025. Ethical approval for the study was obtained from the institutional review board prior to initiation. The sample size was calculated using a 5% significance level and 80% power, based on previously reported efficacy rates of 75.3% for nitroglycerin and 93.8% for nifedipine,[11] resulting in a total of 120 participants, with 60 allocated to each treatment group. Participants were enrolled using a non-probability consecutive sampling approach.

Women aged 18 to 40 years with a singleton pregnancy confirmed on ultrasound and a gestational age between 24 and 36 weeks, presenting with preterm labour—defined as the presence of palpable uterine contractions accompanied by progressive cervical dilation of at least 1 cm before 37 weeks—were included. Exclusion criteria encompassed a history of antepartum haemorrhage, polyhydramnios, preterm premature rupture of membranes, or chronic medical conditions including cardiac, renal, hepatic, diabetic, and hyperthyroid disorders. Written informed consent was obtained from all participants before data collection, with assurance of confidentiality and clarification that participation posed no additional risk. Baseline demographic information including age, gestational age, and parity was recorded. Detailed obstetric history and a focused clinical examination were performed for all enrolled patients.

Participants were randomized using an opaque envelope technique, assigning them to either the nitroglycerin patch group (Group A) or the oral nifedipine group (Group B). In Group A, a 10 mg transdermal nitroglycerin patch was applied to the anterior abdominal wall, with a second 10 mg patch added after one hour if contractions persisted, not exceeding 20 mg in 24 hours. Patches were replaced every 24 hours until contractions subsided. In Group B, patients received 20 mg of oral nifedipine initially, followed by 10 mg every four hours as required for up to 24 hours. All participants were administered two intramuscular doses of dexamethasone 12 mg, 12 hours apart, to enhance fetal lung maturity. Maternal uterine activity, blood pressure, heart rate, and fetal heart rate were monitored at 15-minute intervals during the first hour, every two hours for the next six hours, and then every 12 hours up to 48 hours. The primary outcome, defined as efficacy, was measured by prolongation of pregnancy for at least 48 hours from the onset of preterm labour.

Data were recorded using a predesigned proforma by the principal investigator. Statistical analysis was performed using IBM SPSS version 26. Continuous variables such as age, gestational age, and parity were presented as mean ± standard deviation, while categorical variables, including previous history of preterm labour and efficacy, were expressed as frequencies and percentages. The chi-square test was applied to compare efficacy between the two groups, with a p-value of ≤0.05 considered statistically significant. Stratified analysis was conducted to evaluate the influence of age, gestational age, parity, and previous preterm labour on treatment outcomes, with post-stratification chi-square tests performed as appropriate.

RESULTS

The demographic characteristics were similar between groups, with mean ages of 28.00 ± 4.84 years for the nitroglycerin group and 29.10 ± 5.40 years for the nifedipine group (Table I). Gestational ages were comparable at 31.50 ± 2.56 weeks and 31.40 ± 2.55 weeks respectively. Parity was slightly higher in Group A (1.47 ± 1.11) compared to Group B (1.27 ± 1.11). Previous history of preterm labor was more frequent in the nitroglycerin group, with 11 patients (36.7%) versus 6 patients (20.0%) in the nifedipine group, while 19 patients (63.3%) in Group A and 24 patients (80.0%) in Group B had no previous preterm labor history (Table 1).

Table 1

Patients Demographics in Both Groups

Variables	Nitroglycerin Patch Group (Group A) n=30 Mean ± SD	Oral Nifedipine Group (Group B) n=30 Mean ± SD
Age (years)	28.00 ± 4.84	29.10 ± 5.40
Gestational Age (weeks)	31.50 ± 2.56	31.40 ± 2.55
Parity	1.47 ± 1.11	1.27 ± 1.11
Previous History of Preterm Labour	n (%)	n (%)
Yes	11 (36.7%)	6 (20.0%)
No	19 (63.3%)	24 (80.0%)

Regarding treatment efficacy, oral nifedipine demonstrated superior effectiveness with 27 patients (90.0%) achieving successful tocolysis compared to 23 patients (76.7%) in the nitroglycerin patch group, though this difference was not statistically significant (p=0.299). Treatment failures occurred in 7 patients (23.3%) with nitroglycerin patches versus 3 patients (10.0%) with oral nifedipine (Table 2).

Table 2

Comparison of Efficacy between the Two Groups (N=60)

Efficacy	Group A n=30 n (%)	Group B n=30 n (%)	P value
Yes	23 (76.7%)	27 (90.0%)	
No	7 (23.3%)	3 (10.0%)	0.299
Total	30 (100%)	30 (100%)	

The stratified analysis revealed interesting age-related

patterns, where patients ≤30 years showed similar efficacy rates between groups (85.0% vs 81.3% for Groups A and B respectively, p=0.824), but among patients >30 years, nifedipine achieved 100% efficacy compared to 60.0% for nitroglycerin (p=0.026). For gestational age stratification, patients ≤30 weeks showed efficacy rates of 66.7% versus 85.7% (p=0.370), while those >30 weeks demonstrated 81.0% versus 93.8% efficacy (p=0.339) for Groups A and B respectively. Parity-based analysis showed that patients with ≤2 previous deliveries had efficacy rates of 78.3% versus 88.0% (p=0.456), while those with >2 deliveries showed 71.4% versus 100% efficacy (p=0.462) for nitroglycerin and nifedipine groups respectively. Among patients with previous preterm labor history, both treatments showed high efficacy (90.9% vs 100%, p=1.000), whereas in patients without such history, nifedipine remained superior with 87.5% efficacy compared to 68.4% for nitroglycerin (p=0.183), with Fisher's Exact Test used for statistical analysis where indicated (Table 3).

Table 3

Association of Efficacy with Demographic Variables

Demographics variables		Group	Efficacy		P-value
			Yes (n, %)	No (n, %)	
Age (years)	≤30	A	17 (85.0%)	3 (15.0%)	0.824*
		B	13 (81.3%)	3 (18.8%)	
	>30	A	6 (60.0%)	4 (40.0%)	0.026*
		B	14 (100.0%)	0 (0.0%)	
Gestational Age (weeks)	≤30	A	6 (66.7%)	3 (33.3%)	0.370*
		B	12 (85.7%)	2 (14.3%)	
	>30	A	17 (81.0%)	4 (19.0%)	0.339*
		B	15 (93.8%)	1 (6.3%)	
Parity	≤2	A	18 (78.3%)	5 (21.7%)	0.456
		B	22 (88.0%)	3 (12.0%)	
	>2	A	5 (71.4%)	2 (28.6%)	0.462*
		B	5 (100.0%)	0 (0.0%)	
Previous History of Preterm Labour	Yes	A	10 (90.9%)	1 (9.1%)	1.000*
		B	6 (100.0%)	0 (0.0%)	
	No	A	13 (68.4%)	6 (31.6%)	0.183*
		B	21 (87.5%)	3 (12.5%)	

*Fisher's Exact Test

DISCUSSION

The present study demonstrates that while both nitroglycerin patches and oral nifedipine are effective tocolytic agents for preterm labor management, oral nifedipine achieved superior efficacy rates compared to transdermal nitroglycerin, though the difference did not reach statistical significance. The higher success rate observed with nifedipine (90.0% vs 76.7%) can be attributed to its more predictable pharmacokinetic profile and consistent bioavailability when administered orally, whereas transdermal nitroglycerin delivery may be subject to variable skin absorption rates, patch adhesion issues, and individual variations in cutaneous blood flow that can compromise drug delivery. The age-stratified analysis revealing significantly better outcomes with nifedipine in patients over 30 years suggests that older maternal age may be associated with altered skin permeability or reduced transdermal absorption efficiency, making oral administration more reliable in this demographic. Additionally, the calcium channel blocking mechanism of nifedipine provides more targeted uterine smooth muscle relaxation by directly inhibiting calcium influx, while nitroglycerin's nitric oxide-mediated vasodilation may have less specific effects on myometrial contractility. The superior performance of nifedipine across different gestational ages and parity groups further supports its consistent therapeutic reliability, particularly in patients without previous preterm labor history where the difference in efficacy was most pronounced, indicating that nifedipine may be more effective as a first-line tocolytic agent in treatment-naïve patients.

The findings of the current study align with several previously published investigations comparing nitroglycerin and nifedipine for preterm labor management, while also revealing some notable differences in efficacy outcomes. Our observed efficacy rates of 76.7% for nitroglycerin patches and 90.0% for oral nifedipine are consistent with multiple studies that have demonstrated superior performance of nifedipine. Kaur et al. [12] reported similar findings with nifedipine showing better pregnancy prolongation (3.68 ± 1.91 days vs. 2.78 ± 1.39 days, p = 0.0083), while Ishaq et al. [13] and Gilani et al. [14] both found that 74% of nifedipine-treated women achieved successful tocolysis compared to 52% with nitroglycerine (p = 0.023). These consistent findings across different populations suggest that nifedipine's calcium channel blocking mechanism provides more reliable uterine smooth muscle relaxation compared to nitroglycerine's nitric oxide-mediated effects. However, our results contrast with those reported by Akhtar et al. [15] and Jamil et al. [16] who found nitroglycerine to be more effective, with lower failure rates within 48 hours (12.7% vs. 44.4% and 12% vs. 32% respectively). These discrepancies may be attributed to differences in drug formulation, dosing regimens, patient selection criteria, or variations in transdermal patch quality and application techniques across different healthcare settings.

The superior efficacy of nifedipine observed in patients over 30 years in our study finds support in the work of Kaur et al. [17] who demonstrated significantly better gestational age at delivery (36.42 ± 2.19 weeks vs. 34.93 ± 2.13 weeks, p < 0.01) and improved neonatal outcomes with nifedipine treatment. This age-related difference may reflect physiological changes in skin permeability and drug absorption that occur with advancing maternal age, making oral administration more predictable than transdermal delivery. The meta-analysis by Zamani et al. [18] which included 4336 women from 40 randomized controlled trials, provides the strongest evidence supporting our findings, demonstrating that nifedipine was superior to nitroglycerine in delaying delivery within 48 hours (RD = -0.04; 95% CI: -0.08 to 0.00). Interestingly, Zulfiqar et al. [19] reported no statistically significant differences between the two agents, with similar pregnancy prolongation rates (30.13 ± 3.06 days vs. 29.57 ± 3.6 days), though they noted lower headache incidence with nitroglycerine (3.3% vs. 0%), which contrasts with most other studies including Kaur et al. [12] who reported significantly higher headache rates with nitroglycerine (42% vs. 6%, p < 0.001). The variability in side effect profiles across studies may be related to differences in nitroglycerine patch strength, application duration, or individual patient tolerance factors that influence drug

absorption and systemic exposure.

The present study has several limitations that should be acknowledged when interpreting the results. The single-center design may limit the generalizability of findings to other healthcare settings with different patient populations, clinical protocols, or healthcare delivery systems. The relatively small sample size of 30 patients per group may have been underpowered to detect statistically significant differences between the two treatment modalities, particularly given that the observed difference in efficacy rates (90.0% vs 76.7%) did not reach statistical significance despite being clinically meaningful. The study did not employ blinding techniques due to the different routes of administration (oral versus transdermal), which could have introduced bias in outcome assessment and patient reporting of side effects. Additionally, the study did not account for potential confounding variables such as specific underlying causes of preterm labor, concurrent medications, maternal comorbidities, or variations in patch application techniques that might influence drug absorption and therapeutic outcomes.

CONCLUSION

Our study has concluded that both nitroglycerin patches and oral nifedipine are effective tocolytic agents for managing preterm labor, with oral nifedipine demonstrating superior efficacy compared to transdermal nitroglycerin, particularly in patients over 30 years of age. The findings suggest that nifedipine's more predictable pharmacokinetic profile and consistent bioavailability make it a more reliable first-line tocolytic option, especially in treatment-naïve patients without previous preterm labor history.

Acknowledgments

Gratitude is extended to the entire medical staff of the department for their dedicated efforts in meticulous record-keeping and systematic handling of patient information, which proved essential to the success of this work.

REFERENCES

1. Breuking S, Oudijk MA, van Eekelen R, de Boer MA, Pajkrt E, Hermans F. Assessment of cervical softening and the prediction of preterm birth (STIPP): protocol for a prospective cohort study. BMJ Open. 2023;13(11):e071597. https://doi.org/10.1136/bmjopen-2023-071597
2. Tantengco OAG, Menon R. Breaking down the barrier: the role of cervical infection and inflammation in preterm birth. Front Glob Womens Health. 2022;2:777643. https://doi.org/10.3389/fgwh.2021.777643
3. Don EE, Landman AJEMC, Vissers G, Jordanova ES, Post Uiterweer ED, de Groot CJM, et al. Uterine fibroids causing preterm birth: a new pathophysiological hypothesis on the role of fibroid necrosis and inflammation. Int J Mol Sci. 2022;23(15):8064. https://doi.org/10.3390/ijms23158064
4. Rees P, Gale C, Battersby C, Williams C, Carter B, Sutcliffe A. Intraventricular hemorrhage and survival, multimorbidity, and neurodevelopment. JAMA Netw Open. 2025;8(1):e2452883. https://doi.org/10.1001/jamanetworkopen.2024.52883
5. Gaikwad V, Gaikwad S, Tiwari P. Efficacy of transdermal nitroglycerin patch for the arrest of preterm labor: a retrospective study. Cureus. 2024;16(5):e59982. doi: https://doi.org/10.7759/cureus.59982
6. Conde-Agudelo A, Romero R. Transdermal nitroglycerin for the treatment of preterm labor: a systematic review and metaanalysis. Am J Obstet Gynecol. 2013;209(6):551.e1-551.e18. doi: https://doi.org/10.1016/j.ajog.2013.07.022
7. Çalışkan Ş, Narin MA, Dede FS, Narin R, Dede H, Kandemir Ö. Glyceryl trinitrate for the treatment of preterm labor. J Turk Ger Gynecol Assoc. 2015;16(3):174-8. https://doi.org/10.5152/jtgga.2015.15016
8. Conde-Agudelo A, Romero R, Kusanovic JP. Nifedipine in the management of preterm labor: a systematic review and metaanalysis. Am J Obstet Gynecol. 2011;204(2):134.e1-20. https://doi.org/10.1016/j.ajog.2010.11.038
9. Songthamwat S, Na Nan C, Songthamwat M. Effectiveness of nifedipine in threatened preterm labor: a randomized trial. Int J Womens Health. 2018;10:317-23. https://doi.org/10.2147/IJWH.S159062
10. Aggarwal A, Bagga R, Girish B, Kalra J, Kumar P. Effect of maintenance tocolysis with nifedipine in established preterm labour on pregnancy prolongation and neonatal outcome. J Obstet Gynaecol. 2018;38(2):177-84. https://doi.org/10.1080/01443615.2017.1331340
11. Goyal N, Agrawal M, Dewani D. A comparative study of the effectiveness of transdermal nitroglycerine patches and oral nifedipine in prolongation of pregnancy in women with preterm labour. Cureus. 2023;15(5):e39106. https://doi.org/10.7759/cureus.39106
12. Kaur P, Madan A, Sharma S. A comparative study of transdermal nitroglycerine patch and oral nifedipine in preterm labor. Ann Afr Med. 2021;20:31–36. https://doi.org/10.4103/aam.aam_11_20
13. Ishaq N, Ishaq Z, Mushtaq A, et al. Comparative study of tocolytic efficacy of nifedipine and nitroglycerine. J Soc Obstet Gynaecol Pak. 2017;7(2):96–100.
14. Gilani SUA, Ali SM, Ahmad UR, et al. To compare efficacy of nifedipine and nitroglycerine as tocolytic agent in preterm labor patients. Pak J Med Health Sci. 2014;8(1):80–82.
15. Akhtar Z, Amna B, Qamar S, et al. Compare the effectiveness of transdermal nitro-glycerine versus oral nifedipine for acute tocolysis in preterm labour. Pak J Med Health Sci. 2020;14(4):2030–2032.
16. Jamil M, Abid R, Basharat A, Kharunisa. Transdermal nitro-glycerine versus oral nifedipine for acute tocolysis in preterm labour: a randomised controlled trial. J Soc Obstet Gynaecol Pak. 2020;10(1):26–29.
17. Kaur M, Goel B, Singh J. Comparative study of nitroglycerin dermal patch versus nifedipine in the management of preterm labour. Int J Reprod Contracept Obstet Gynecol. 2018;7(10):4243–48. https://doi.org/10.18203/2320-1770.ijrcog20184160
18. Zamani M, Alimi R, Arabi SM, Moradi M, Azmoude E. Comparison of the efficacy of nifedipine with ritodrine, nitroglycerine and magnesium sulfate for the management of preterm labor: a systematic review and meta-analysis. BMC Pregnancy Childbirth. 2024;24:318. https://doi.org/10.1186/s12884-024-06497-w
19. Zulfiqar S, Zulfiqar S, Khan SM. Comparison of nitroglycerine patch and nifedipine in treatment of preterm labour. J Sheikh Zayed Med Coll. 2016;7(2):965–967