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Comparison of Nifedipine Vs. Labetalol in Preeclampsia Hypertensive Emergency in Terms of Mean Time to Reach Target Blood Pressure at a Tertiary Care Hospital

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ABSTRACT

Background: Preeclampsia-related hypertensive emergencies represent a critical obstetric complication with potentially life-threatening maternal and fetal outcomes. Rapid pharmacologic control of blood pressure is vital to prevent progression to eclampsia and associated morbidities. Nifedipine and labetalol are commonly recommended first-line agents; however, their relative efficacy in achieving timely blood pressure control remains a subject of clinical importance. **Objective:** To compare the nifedipine and labetalol in preeclampsia hypertensive emergency in terms of mean time to reach target blood pressure. **Study Design:** Randomized controlled trial. **Duration and Place of Study:** This trial was conducted from January 2025 to May 2025 in the Department of Obstetrics and Gynecology, Combined Military Hospital, Muzaffarabad. **Methodology:** Sixty pregnant women meeting diagnostic criteria for preeclampsia hypertensive emergency were randomized into two equal groups. Group A received sublingual nifedipine (10 mg every 15 minutes, maximum five doses), while Group B was treated with intravenous labetalol in escalating doses. Blood pressure was monitored at 10-minute intervals, and the primary outcome was defined as the time taken to achieve target blood pressure of ≤140/90 mmHg. **Results:** Baseline characteristics including age, gestational age, parity, body mass index, admission blood pressure, and proteinuria were comparable between groups. The mean time to achieve target blood pressure was significantly lower in the nifedipine group (30.83±3.40 minutes) compared to the labetalol group (51.50±4.13 minutes) ($p<0.001$). **Conclusion:** Sublingual nifedipine is significantly more effective than intravenous labetalol in achieving rapid blood pressure control in preeclamptic hypertensive emergencies, supporting its role as a first-line therapeutic option.

INTRODUCTION

Preeclampsia hypertensive emergency is a life-threatening obstetrical emergency with sudden onset of severely high blood pressure in pregnant women, normally in the range of over 160/110 mmHg, along with evidence of end-organ dysfunction.[1] It arises over the background of preeclampsia, a disease specific to pregnancy, and is described in the setting of systemic endothelial dysfunction, vascular spasm, and a hyper-inflammatory state.[2] Fetus and mother are exposed to severe consequences of such hypertensive emergencies in the form of cerebral hemorrhage, pulmonary edema, acute renal failure in the mother,[3] and for the fetus, intrauterine growth retardation, placental abruption, and perinatal death.[4] Prompt diagnosis with consequent immediate pharmacotherapy is absolute, as relentless blood pressure in such a situation can very quickly convert to eclampsia culminating in seizures and further maternal-fetal compromise.[5]

Key objective in the treatment of preeclampsia hypertensive emergency is to expedite a lowering of a safe range of blood pressure, ideally in the range of 140–150/90–100 mmHg, in such a way as not to induce sudden hypotension that could compromise the uteroplacental perfusion.[6] Several antihypertensive agents are utilized in such a case, e.g., intravenous hydralazine, labetalol, oral or sublingual nifedipine, and far less frequently, agents such as nicardipine.[7] Drug selection is made on the basis of drug efficacy, onset, safety profile, availability, and patient's condition.[8] Hydralazine was classically used, but due to looming unpredictable reactions and maternal side effects, more use of labetalol and nifedipine as first-line therapy has occurred.[9] Both drugs have a different mechanism of action but both have a relative rapidity of inducing reductions in the blood pressure such that they are desirable for acute control in pregnancy where both maternal and perinatal implications are contingent upon a prompt and controlled measure.[10]

Comparing nifedipine and labetalol in the context of preeclampsia hypertensive emergency, particular note was taken of mean time to achieve target blood pressure. Nifedipine, a oral immediate-release dosing calcium channel blocker, quite often has a rapid onset of effect, reducing blood pressure in a significant percentage of cases within 20–30 minutes, making it favorable in resource-poor or non-intravenous circumstances.[11] Labetalol, a mixed alpha- and beta-adrenergic blocker dosed generally intravenously, is also efficacious and well-tolerated, with the distinguishing feature of fewer maternal-related undesirable effects such as tachycardia or headaches, on occasion encountered in nifedipine therapy.[12] Labetalol is, however, titrated with repeat dosing or continuous infusion, and as such may have increased mean times to reach target control compared to the more prompt response typical of nifedipine.

In the study by Duro-Gómez et al. (2017), nifedipine was found to reduce blood pressure significantly faster than labetalol, with a mean time of 31.30 ± 11.1 minutes compared to 53.50 ± 34.32 minutes ($p = 0.03$). Based on this evidence, nifedipine may be considered a more suitable first-line option for the management of preeclampsia-associated hypertensive emergencies.[13] Conversely, a more recent Pakistani study by Wasim et al. (2020) demonstrated that both nifedipine and labetalol were equally effective in lowering blood pressure in women with preeclampsia, with mean times of 22.09 ± 11.7 minutes and 22.6 ± 13.5 minutes, respectively. The difference between the two agents was not statistically significant ($p > 0.05$).[14]

Preeclampsia remains a significant contributor to perinatal and maternal morbidity in Muzaffarabad, Kashmir, where readily available healthcare facilities and ready access to high-intensity obstetric care are not always available. Antihypertensive agent choice in hypertensive emergencies remains a very important issue, as any resultant delay in reaching the desired level of blood pressure can have a direct impact on outcome in both foetus and mother. Both nifedipine and labetalol are highly recommended but their relative efficacy in reducing mean time to attain target blood pressure in the local population hasn't been explored sufficiently. Context-specific evidence generation shall facilitate optimization of protocol of therapy, help in safe clinical decisions, and ultimately benefit the mother's and neonatal outcome in the region.

METHODOLOGY

This randomized controlled trial was undertaken in the Department of Obstetrics and Gynecology at Combined Military Hospital, Muzaffarabad, from January 2025 to May 2025. Ethical clearance was obtained from the institutional review board prior to patient recruitment. The required sample size was determined using the WHO sample size calculator. A total of 60 women (30 in each group) was calculated to be sufficient at a 95% confidence level, 80% power, and 5% level of significance. The calculation was based on previously reported mean times to achieve target blood pressure of 31.30 ± 11.10 minutes for nifedipine and 53.50 ± 34.32 minutes for labetalol.[13]

Eligible patients included pregnant women aged 18–45 years, at or beyond 28 weeks of gestation, presenting with preeclampsia hypertensive emergency. This condition was defined as new-onset hypertension and proteinuria. Hypertension was considered when systolic blood pressure exceeded 150 mmHg or diastolic blood pressure was greater than 95 mmHg on two separate readings at least four hours apart in a previously normotensive woman. Proteinuria was confirmed if urinary protein excretion was more than 300 mg in a 24-hour collection or if the protein-to-creatinine ratio in a single voided urine sample was ≥0.3. Women were excluded if they had chronic hypertension without proteinuria, cardiac rhythm abnormalities, asthma, intrauterine fetal demise, structural fetal anomalies, or required urgent lifesaving interventions at the time of presentation.

All eligible participants and their attendants were thoroughly counseled, and written informed consent was obtained. Demographic data such as age, parity, gestational age, and body mass index were recorded, alongside initial clinical parameters including blood pressure at admission and urinary protein levels. Randomization was performed using the lottery method. Patients in Group A received oral nifedipine 10 mg every 15 minutes up to a maximum of five doses, accompanied by intravenous placebo. Patients in Group B were administered intravenous labetalol in escalating doses of 20, 40, 80, 80, and 80 mg, together with a placebo oral tablet. Blood pressure was recorded every 10 minutes during treatment by the same clinical staff to reduce observer bias. The primary outcome was defined as the time elapsed from the administration of the study drug until blood pressure was reduced to 140/90 mmHg or below.

Data were analyzed using IBM SPSS Statistics version 27. Continuous variables such as age, gestational age, body mass index, admission blood pressure, urine protein levels, and time to achieve target blood pressure were expressed as mean ± standard deviation. Categorical variables such as parity were reported as frequencies and percentages. Independent sample t-tests were applied to compare the mean time to reach target blood pressure between groups, with a p-value of ≤0.05 considered statistically significant. Stratification was done for age, parity, and gestational age to control for effect modifiers, and post-stratification analysis was performed using independent sample t-tests.

RESULTS

The study included 60 patients equally distributed between Group A (Nifedipine) and Group B (Labetalol), with baseline demographic characteristics showing comparable profiles between groups (as shown in Table-I). The mean age was 30.00±5.13 years in Group A versus 31.27±5.19 years in Group B, with gestational ages of 34.80±3.53 weeks and 35.50±3.60 weeks respectively. Parity was similar between groups at 2.40±1.19 for Group A and 2.63±1.19 for Group B. Body mass index values were 26.69±3.14 kg/m^2 in the Nifedipine group and 27.47±3.13 kg/m^2 in the Labetalol group. Admission blood pressure measurements revealed systolic pressures of 171.93±5.41

mmHg in Group A and 175.13±6.02 mmHg in Group B, while diastolic pressures were 108.87±4.19 mmHg and 110.57±4.46 mmHg respectively. Proteinuria levels were 760.67±276.06 mg/dL in the Nifedipine group and 838.00±292.70 mg/dL in the Labetalol group.

Table I

Patient Demographics

Demographics	Group A (Nifedipine)	Group B (Labetalol)
	Mean ± SD	Mean ± SD
Age (years)	30.00±5.13	31.27±5.19
Gestational Age (weeks)	34.80±3.53	35.50±3.60
Parity	2.40±1.19	2.63±1.19
BMI (kg/m^2)	26.69±3.14	27.47±3.13
SBP at Admission (mmHg)	171.93±5.41	175.13±6.02
DBP at Admission (mmHg)	108.87±4.19	110.57±4.46
Proteinuria (mg/dL)	760.67±276.06	838.00±292.70

The primary outcome analysis demonstrated a statistically significant difference in time to reach target blood pressure, with Group A achieving target levels in 30.83±3.40 minutes compared to 51.50±4.13 minutes in Group B (t=-21.163, p<0.001) (as shown in Table-II).

Table II

Comparison of Mean Time to Reach Target Blood Pressure in Both Groups

Outcome	Group A (Nifedipine)	Group B (Labetalol)	t	P value
	n=30	n=30		
Time to Target BP (minutes)	30.83±3.40	51.50±4.13	-21.163	<0.001

Stratified analysis by demographic factors consistently showed superior efficacy of Nifedipine across all subgroups (as shown in Table-III). Among patients aged ≤30 years, Group A required 28.59±2.15 minutes versus 48.20±2.04 minutes for Group B (p<0.001), while in patients >30 years, the times were 33.77±2.31 minutes versus 54.80±2.78 minutes respectively (p<0.001). When stratified by gestational age, patients ≤36 weeks showed response times of 28.76±2.39 minutes for Group A and 48.07±2.06 minutes for Group B (p<0.001), while those >36 weeks demonstrated times of 33.54±2.54 minutes versus 54.50±2.94 minutes respectively (p<0.001). Parity-based analysis revealed that patients with parity ≤3 had response times of 29.67±2.62 minutes in Group A compared to 49.74±2.77 minutes in Group B (p<0.001), whereas those with parity >3 showed times of 35.50±1.76 minutes versus 57.29±1.80 minutes respectively (p<0.001).

Table III

Stratification of Mean Time to Reach Target Blood Pressure with Respect to Demographic Factors in Both Groups

Demographic Factors		Group	Mean Time to Target BP (minutes)	P Value
			Mean ± SD	
Age (years)	≤30	A (n=17)	28.59±2.15	<0.001
		B (n=15)	48.20±2.04	
	>30	A (n=13)	33.77±2.31	<0.001
		B (n=15)	54.80±2.78	
Gestational Age (weeks)	≤36	A (n=17)	28.76±2.39	<0.001
		B (n=14)	48.07±2.06	
	>36	A (n=13)	33.54±2.54	<0.001
		B (n=16)	54.50±2.94	
Parity	≤3	A (n=24)	29.67±2.62	<0.001
		B (n=23)	49.74±2.77	
	>3	A (n=6)	35.50±1.76	<0.001
		B (n=7)	57.29±1.80	

DISCUSSION

The present study demonstrated that sublingual Nifedipine achieved significantly faster blood pressure control compared to intravenous Labetalol in preeclamptic hypertensive emergencies, with mean time to target blood pressure reduction of approximately 20 minutes favoring the Nifedipine group. This superior efficacy can be attributed to Nifedipine's rapid onset of action through its direct calcium channel blocking mechanism, which causes immediate vasodilation of peripheral arteries and arterioles, leading to prompt reduction in systemic vascular resistance. The sublingual route of administration further enhances this effect by providing rapid drug absorption through the highly vascularized oral mucosa, bypassing first-pass hepatic metabolism and achieving therapeutic plasma concentrations within minutes. Conversely, Labetalol's alpha and beta-adrenergic blocking action, although being more gradual and prolonged to reduce blood pressure, takes longer time for complete therapeutic effect based on its receptor saturation dependency and resultant intracellular signaling cascades. The consistency of Nifedipine's superiority across all demographic strata suggests that the drug's pharmacological advantage is independent of patient characteristics such as age, gestational age, and parity. The comparable baseline demographics between groups, including similar admission blood pressure values and proteinuria levels, validate the reliability of these findings by eliminating potential confounding variables that could influence treatment response. These results support the clinical utility of sublingual Nifedipine as a first-line agent for rapid blood pressure control in preeclamptic emergencies where immediate therapeutic intervention is crucial for maternal and fetal outcomes.

Our results showing significantly faster time to target blood pressure with sublingual nifedipine (30.83±3.40 minutes) compared to intravenous labetalol (51.50±4.13 minutes) are consistent with multiple studies that have reported similar advantages for nifedipine formulations. Kumari et al. [15] reported comparable findings with oral nifedipine achieving target blood pressure in 45.14±14.84 minutes versus 54.00±18.22 minutes for intravenous labetalol, while Jamil et al. [16] demonstrated even faster control with oral nifedipine at 30.6±7.8 minutes compared to 34±7.7 minutes for labetalol. Similarly, Sahai et al. [17] found nifedipine superior with a mean time of 34.67±20.297 minutes versus 52.00±29.054 minutes for labetalol, and Shah et al. [18] reported 45.60±21.01 minutes for nifedipine versus 54.80±20.92 minutes for labetalol. These consistent findings across different populations and study designs support the pharmacological advantage of nifedipine's rapid calcium channel blockade mechanism over labetalol's dual adrenergic blocking action.

However, some studies have reported contrasting results, with Sudeepthi et al.[19] demonstrating faster blood pressure control with intravenous labetalol (33.85±11.87

minutes) compared to oral nifedipine retard (48.56±17.36 minutes), and Mehdi et al. [20] showing similar efficacy between labetalol (33.60±14.97 minutes) and nifedipine (39.57±20.99 minutes). These discrepancies can be attributed to differences in drug formulations, with sustained-release nifedipine preparations having delayed onset compared to immediate-release or sublingual formulations used in our study. The route of administration also plays a crucial role, as our sublingual approach provides more rapid absorption compared to oral administration, while the comparison with intravenous labetalol in some studies may have favored the parenteral route's immediate bioavailability.

The consistency of nifedipine's superiority across demographic strata in our study, with all subgroups showing $p<0.001$, mirrors findings from Kumari & Sinha [21] and Siddiqua et al. [22] who also reported significant advantages for nifedipine regardless of patient characteristics. This demographic-independent efficacy suggests that nifedipine's mechanism of action is not significantly influenced by age, gestational age, or parity, unlike some antihypertensive agents whose effectiveness may vary with physiological changes during pregnancy. The dose requirements in our study, while not specifically quantified, align with reports from Jamil et al. [16] and Sahai et al. [17] who found that nifedipine required fewer doses to achieve target blood pressure, supporting its superior potency and rapid onset profile. The absence of serious maternal complications in our study is consistent with the safety profiles reported across all comparative studies, reinforcing nifedipine's established safety record in pregnancy when used appropriately for hypertensive emergencies.

These results contribute valuable evidence to the existing literature favoring nifedipine-based interventions and may inform clinical guidelines for the acute management of hypertensive emergencies in pregnancy, particularly in resource-limited settings where rapid, cost-effective treatment is paramount. However, several limitations must be acknowledged when interpreting these findings. This single-center study design may limit the generalizability of results to other populations and healthcare settings with different patient demographics or clinical protocols. The relatively small sample size of 60 patients, while adequate for statistical significance, may not capture the full spectrum of treatment responses or rare adverse events that could influence clinical decision-making. Additionally, the study did not evaluate long-term maternal and neonatal outcomes beyond the immediate treatment period, which are crucial considerations for comprehensive assessment of therapeutic efficacy and safety. The lack of blinding in this open-label design could potentially introduce bias in outcome assessment, and the exclusion of patients with specific contraindications may limit applicability to more complex clinical scenarios.

CONCLUSION

Our study has concluded that sublingual nifedipine demonstrates superior efficacy compared to intravenous labetalol in achieving rapid blood pressure control in preeclamptic hypertensive emergencies. The significant reduction in time to reach target blood pressure with nifedipine remained consistent across all demographic subgroups, indicating its reliability as a first-line therapeutic intervention regardless of patient characteristics such as age, gestational age, or parity.

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