

COMPARISON OF THE THERAPEUTIC POTENTIAL OF METHYLDOPA AND LABETALOL IN PREGNANCY-INDUCED HYPERTENSION: A QUASI-EXPERIMENTAL STUDY

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ABSTRACT

BACKGROUND: Pregnancy-induced hypertension (PIH) affects around 10% pregnancies, leading to maternal and fetal morbidity and mortality.

OBJECTIVE: This study explores the efficacy of methyldopa and labetalol in the management of PIH.

METHODOLOGY: This study was conducted in the department of obstetrics and gynecology, Health Ways Hospital, Kohat, from September 2024 to April 2025. After ethical approval, 200 PIH patients (100 in each group), aged between 20-35 years with gestational age >20 weeks and blood pressure $\geq 140/90$ mmHg were enrolled. The methyldopa group was prescribed methyldopa 250 mg thrice daily, while the labetalol group received Labetalol 100 mg thrice daily. Data was analyzed using SPSS version 26.0. A paired sample t-test was employed to find the mean difference in blood pressure between each group. Independent sample t-test was used to find the statistical differences between systolic blood pressure (SBP) and diastolic blood pressure (DBP) in both groups

RESULTS: There were significant reductions in both SBP and DBP at the 1st and 2nd follow-ups in both methyldopa and labetalol group with p-values <0.001. The independent sample t-test shows that the SBP at 1st follow-up and 2nd follow-up in the labetalol group was significantly reduced compared to the methyldopa group, with p-values of 0.03 at the first follow-up and <0.001 at the second follow-up. Regarding, the DBP reduction, while no significant differences were evident between groups at the first follow-up, the labetalol group showed a significant reduction in DBP at the second follow-up, with a p-value of 0.01

CONCLUSION: Both methyldopa and labetalol significantly reduce both SBP and DBP in PIH. However, in comparison, labetalol reduction in blood pressure is significantly higher as compared of methyldopa.

KEY WORDS: Blood Pressure, Labetalol, Methyldopa, Pregnancy-Induced Hypertension

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INTRODUCTION:

Pregnancy-induced hypertension (PIH) frequently emerges during pregnancy and creates severe dangers for the mother and fetus. The medical definition for this condition describes the development of hypertension (systolic blood pressure reaching 140 mmHg and/or diastolic blood pressure reaching 90 mmHg) after week 20 of pregnancy, but without any signs or evidence of preeclampsia. PIH represents a significant public health issue since improper treatment management creates elevated threats of severe complications for both mother and baby during pregnancy.² Within the global population of pregnancies, PIH exists in 5 to 10 per cent of cases, while remaining the main contributor to maternal and infant life-threatening complications.³ The disease prevalence is detected differently among various geographical regions and the socioeconomic standing of mothers, as well as their preexisting health conditions, including obesity, diabetes, and advanced age.⁴ An unclear origin of PIH seems to arise from the combination of effects of improper placental tissue development, dysfunctional

cellular membranes, and exuberant inflammatory responses.⁵ Multiple factors including inherited risk tendencies and changes to the immune system combined with cardiovascular problems in mothers, play an active role in the development of PIH.⁶ PIH management failure escalates into preeclampsia and eclampsia that produce greater maternal dangers, including stroke and renal failure, together with HELLP (hemolysis, elevated liver enzymes, low platelet count) syndrome.⁷ The condition of PIH generates two severe fetal complications through its actions that create intrauterine growth restriction (IUGR) and raise perinatal mortality risks.⁸ Several medications have been implemented, among which the methyldopa for treating PIH has become possible since it demonstrated secure operation over multiple decades.⁹ Labetalol has gained recognition as a leading antihypertensive drug because it combines excellent immediate benefits with superior hemodynamic results, but its potential maternal side effects and effects on newborn heart rate make healthcare providers proceed with caution.¹⁰

This study sought to determine which of the two medications,

labetalol or methyldopa, presented superior results in managing PIH-related blood pressure. The research findings offer support for medical choices regarding the antihypertensive medications that should be provided to pregnant women with PIH.

METHODOLOGY:

A quasi-experimental study was designed to achieve the study's objective. This study was conducted in the Department of Obstetrics and Gynecology at Health Ways Hospital, Kohat, from September 2024 to April 2025. The inclusion criteria are females aged between 20-35 years with gestational age >20 weeks and diagnosed with PIH with blood pressure $\geq 140/90$ mmHg¹ on two separate readings at least 4 hours apart. Patients not willing to participate in the study, having proteinuria, preeclampsia, and chronic renal or liver disorders were excluded from the study. The sample size was calculated using a web-based tool (OpenEPI)¹¹, taking the prevalence of PIH 10%, margin of error 5%, confidence level 95% and power of the study 80. We included 200 patients in our cohort, who were equally divided into two groups (100 in the methyldopa group and 100 in labetalol group). After a detailed interview, the demographics were recorded on a pre-designed proforma. The methyldopa group was prescribed Methyldopa 250 mg thrice daily, while the labetalol group received labetalol 100 mg thrice daily.¹² The first follow-up was conducted 7 days after initiation of therapy, and the second follow-up was conducted 14 days after initiation of therapy.

If a patient whose blood pressure was not reduced within two days of the initiation of therapy, the dose was doubled. Dose

escalation was performed to achieve optimal therapeutic response in accordance with standard PIH management protocols. Uncontrolled hypertension was defined, in which a patient in either group does not maintain the optimum blood pressure

Data was analyzed using SPSS version 26.0. A descriptive statistic model was applied to present the demographic characteristics of the PIH patients. A paired sample t-test was employed to find the mean difference in blood pressure between each group. An independent sample t-test was used to find the statistical differences between SBP and DBP in both groups. P-value <0.05 was considered significant.

The ethical approval was obtained from the ethical review board of Healthways Hospital, approval number HWH 149, on 16-9-2024.

RESULTS

This quasi-experimental cohort included 200 patients with PIH, who were equally divided into two groups (methyldopa and labetalol groups). The mean age of patients in the methyldopa group was 28.65±4.0 years, while in the labetalol group, it was 28.53±3.9 years. The mean BMI in the methyldopa group was 25.78±2.93, while in the labetalol group, it was recorded as 25.76±2.98. Similarly, gestational age, Hb, SBP, and DBP in both groups were comparable, with no statistically significant differences recorded in any demographic variables upon enrollment (p-value >0.05). All details are presented in Table 1.

Table 1: Demographic characteristics of participants

Variables	Drug prescribed	Mean±SD
Age (years)	Methyldopa	28.65±4.0
	Labetalol	28.53±3.9
BMI	Methyldopa	25.78±2.93
	Labetalol	25.76±2.98
Gestational age (weeks)	Methyldopa	27.78±2.08
	Labetalol	27.38±2.0
Hb (mg/dl)	Methyldopa	10.55±1.77
	Labetalol	11.05±1.84
SBP (mmHg)	Methyldopa	147.66±5.79
SBP (mmHg)	Labetalol	148.18±5.0
DBP (mmHg)	Methyldopa	96.02±3.0
DBP (mmHg)	Labetalol	95.39±2.9

To assess the effectiveness of the treatments in each group, a paired sample t-test was applied to determine the mean difference between SBP and DBP at enrollment and subsequent follow-up in the methyldopa and labetalol groups. The first follow-up was conducted 7 days after initiation of therapy, and the second follow-up was conducted 14 days after initiation of therapy. The mean SBP and DBP in the methyldopa group at

enrollment were 147.66±5.79mmHg and 96.02±3.06 mmHg, respectively. There were significant reductions in both SBP and DBP at the 1st and 2nd follow-ups, with p-values <0.001. A similar significant reduction was also observed in the labetalol group at the 1st and 2nd follow-ups (p<0.001). Further details are summarized in Table 2.

Table 2: blood pressure reduction among methyldopa and labetalol group

Methyldopa group				
Variables		Values (mean±SD)	p-value	95%CI
SBP/DBP at enrollment (mmHg)	at	147.66±5.79/96.02±3.06	-	-
SBP/DBP at 1 st follow-up (mmHg)	at 1 st	127.66±3.57/81.07±3.06	<0.001	18.67-21.32/13.9-15.9
SBP/DBP at 2 nd follow-up (mmHg)	at 2 nd	122.28±3.97/77.53±2.32	<0.001	24.03-26.72/17.7-19.2
Labetalol group				
SBP/DBP at enrollment (mmHg)	at	148.18±5.0/95.39±2.9	-	-
SBP/DBP at 1 st follow-up (mmHg)	at 1 st	124.49±4.6/81.03±3.1	<0.001	20.63-26.74/13.5-15.1
SBP/DBP at 2 nd follow-up (mmHg)	at 2 nd	118.97±2.5/76.78±2.14	<0.001	28.02-30.39/17.8-19.3

Paired sample t-test, Abbreviations: SBP; Systolic blood pressure, DBP; diastolic blood pressure

An independent sample t-test was subsequently applied to compare the mean differences between SBP and DBP in both groups. The SBP at 1st follow-up and 2nd follow-up in the labetalol group was significantly reduced compared to the methyldopa group with p-values of 0.03 at the first follow-up and < 0.001 at the second follow-up.. Regarding, the DBP reduction, while no significant differences were evident between groups at the first follow-up, the labetalol group showed a significant reduction in DBP at the second follow-up, with a p-value of 0.01. Further details are presented in Table 3.

Table 3: Comparison between blood pressure reduction among methyldopa and labetalol group

Variables	Drug prescribed	Mean±SD	p-value	95% CI
SBP at enrollment	Methyldopa	147.66±5.79	0.49	-2.03-0.99
	Labetalol	148.18±5.0		
SBP at 1 st follow-up	Methyldopa	127.66±3.5	0.03	0.18-6.1
	Labetalol	124.49±14.6		
SBP at 2 nd follow-up	Methyldopa	122.28±3.9	0.00	2.38-4.23
	Labetalol	118.97±2.5		
DBP at enrollment	Methyldopa	96.02±3.0	0.63	-0.20-1.46
	Labetalol	95.39±2.9		
DBP at 1 st follow-up	Methyldopa	81.07±3.0	0.92	-0.82-0.90
	Labetalol	81.03±3.1		
DBP at 2 nd follow-up	Methyldopa	77.53±2.3	0.01	0.12-1.37
	Labetalol	76.78±2.1		

Independent sample t-test, Abbreviations: SBP; Systolic blood pressure, DBP; diastolic blood pressure

DISCUSSION

This quasi-experimental study evaluates the efficacy of two antihypertensive drugs, methyldopa and labetalol, in the management of PIH in 200 patients equally divided into two groups. Our findings indicate that both medications significantly reduced SBP and DBP at 1st follow-up and 2nd follow-up, thus confirming their effectiveness in treating PIH.

Both groups were comparable at baseline with respect to demographics and clinical parameters, reducing the likelihood of confounding and ensuring that differences observed in blood pressure reduction were attributable to the interventions rather than baseline variability.

In our study, both methyldopa and labetalol significantly reduce both SBP and DBP, corroborating the established role of these medications in the management of PIH.⁵ However, labetalol provides a significant reduction in both SBP and DBP as compared to methyldopa, with a p-value <0.05. The differences in the effectiveness of both methyldopa and labetalol are due to differences in the pharmacodynamic profile of both drugs. The methyldopa acts centrally by antagonizing the alpha-2 adrenergic receptors, and may require a longer duration of administration to achieve full therapeutic effects, as suggested in a previous report.³ On the other hand, labetalol has a dual-action mechanism, antagonizing both alpha and beta adrenergic receptors, allowing for its rapid onset of action and greater control over hypertension.¹³ In consistent with our findings, Sultana et al also reported that labetalol is more effective than methyldopa in achieving timely blood pressure control.¹⁴ In more recent findings, Arshad et al also reported the greater efficacy of labetalol in lowering blood pressure than methyldopa.³ According to a recent network meta-analysis published on oral antihypertensive treatment during pregnancy found no significant differences were found in the primary outcome and blood pressure reduction in pregnant women using labetalol or methyldopa¹³ confirming that both methyldopa and labetalol are safe for both mother and child. In another meta-analysis by Van de Vusse et al on the pharmacokinetics of common antihypertensive drugs in pregnancy also found no fetal accumulation or adverse events related to the use of labetalol or methyldopa in PIH¹⁵ highlighting the safety of both drugs in pregnancy outcomes. Interestingly, many published reports also stated no significant response rates between labetalol and methyldopa in the management of PIH.¹⁵⁻¹⁷ Although these studies report similar efficacy between the two drugs, our findings showed a greater reduction with labetalol. This may be due to differences in receptor-blocking profiles, faster onset of action, and better hemodynamic stability offered by labetalol. Variations in patient characteristics, dosing strategies, and follow-up durations in previous studies may also explain the differing results.

CONCLUSION

Labetalol demonstrated a more pronounced antihypertensive effect than methyldopa in women with PIH, although both drugs were effective in significantly lowering SBP and DBP. Labetalol may therefore be preferred when rapid and greater blood pressure control is desired, while methyldopa remains a safe and effective alternative.

Future recommendation

Future trials should employ randomized controlled designs, longer follow-up periods, and evaluation of maternal-fetal outcomes, including neonatal health indicators, placental function, and long-term safety.

CONFLICT OF INTEREST

The authors declare no conflict of interest related to this publication

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REFERENCES

1. Afroz T, Ferdous R, Rahman MA. The safety and efficacy of labetalol vs. methyldopa in the treatment of pregnancy-induced hypertension. *Int J Gynaecol Obstet.* 2024;6(1):38-42. <https://doi.org/10.33545/26649004.2024.v6.i1a.28>
2. Aleem A, Amanullah I, Mahmood N, Tazammul M, Rashid B, Batool A. A comparative analysis of antihypertensive drugs for hypertension and gestational hypertension among women in tertiary care hospitals in Lahore, Pakistan. *Bull Pharm Med Res.* 2023;2:31-9. <https://doi.org/10.58398/0005.000011>
3. Arshad M, Farooq S, Majeed K, Khalid U, Afsheen A, Artemis P. Labetalol versus Methyldopa for Treatment of Pregnancy Induced Hypertension. *Pak Armed Forces Med J.* 2024;74(4):1024. <https://doi.org/10.51253/pafmj.v74i4.9338>
4. Ashworth D, Battersby C, Green M, McManus R. Uncertainties: Which antihypertensive treatment is better in pregnancy for mild to moderate hypertension? *BMJ.* 2022;376:e066333. <https://doi.org/10.1136/bmj-2021-066333>
5. Awaludin A, Rahayu C, Daud NAA, Zakiyah N, editors. Antihypertensive medications for severe hypertension in pregnancy: A systematic review and meta-analysis. *Healthcare (Basel).* 2022;10:325 <https://doi.org/10.3390/healthcare10020325>
6. Bade S, Sivaiah T, Padmavathi R, Chandrakala A. A comparative observational study on the efficacy of labetalol vs methyldopa on obstetric outcome in women with pre-eclampsia. *Eur J Cardiovasc Med.* 2024;14(5).
7. El-sadek SE, El-sadek AM, Ahmed AK. Labetalol versus Alpha Methyldopa for Control of Pregnancy-Induced Hypertension. *Al-Azhar Int Med J.* 2021;2(6):23-8. <https://doi.org/10.21608/aimj.2021.75967.1473>
8. Ghosh KR, Akhter S, Das AK, Naher N, Paul SR, Islam B. Outcome of labetalol and methyldopa as oral antihypertensive agent in the treatment of pregnancy induced hypertension. *Mediscope.*

2021;8(1):19-26.

<https://doi.org/10.3329/mediscope.v8i1.52200>

9. Patel R, Shah R, Lad D, Rana D, Malhotra S. Comparative evaluation of efficacy and safety of methyldopa and labetalol in pregnancy-induced hypertension: A meta-analysis. *Trop J Obstet Gynaecol.* 2020;37(1):119-25.

10. Ishikawa T, Nishigori H, Akazawa M, Miyakoda K, Noda A, Ishikuro M, et al. Risk of major congenital malformations associated with first-trimester antihypertensives, including amlodipine and methyldopa: a large claims database study 2010–2019. *Pregnancy Hypertens.* 2023;31:73-83. <https://doi.org/10.1016/j.preghy.2023.01.001>

11. Sullivan KM, Dean MA, Soe MM, Mctm M. An introduction to OpenEpi. *OpenEpi.* 2014 Aug 18.

12. Subhedar V, Inamdar S, Hariharan C, Subhedar S. Comparison of efficacy of labetalol and methyldopa in patients with pregnancy-induced hypertension. *Int J Reprod Contracept Obstet Gynecol.* 2013;2(1):27-34. <https://doi.org/10.5455/2320-1770.ijrcog20130205>

13. Hup RJ, Damen JA, Terstappen J, Haneveld MJK, Terstappen F, Magee LA, et al. Oral antihypertensive treatment during pregnancy: a systematic review and network meta-analysis. *Am J Obstet Gynecol.* 2025.

<https://doi.org/10.1016/j.ajog.2025.04.011>

14. Sultana S, Sharmin I, Parvin M, Basak S, Sharmin N, Holy M. Comparative Efficacy of Labetalol and Methyldopa in the Management of Pregnancy-Induced Hypertension. *Dinajpur Med Coll J.* 2025;18(2). <https://doi.org/10.69861/djmcj2025v18i2s6>

15. van de Vusse D, Mian P, Schoenmakers S, Flint RB, Visser W, Allegaert K, et al. Pharmacokinetics of the most commonly used antihypertensive drugs throughout pregnancy: methyldopa, labetalol, and nifedipine—a systematic review. *Eur J Clin Pharmacol.* 2022;78(11):1763-76.

<https://doi.org/10.1007/s00228-022-03382-3>

16. Nahar LK, Haque N, Kutubi A, Rumana R, Gangoly S, Akhter S, Tonny NY, Khan S. Relation Between Labetalol and Methyldopa in Treatment of Pregnancy-Induced Hypertension. *Sch Int J Obstet Gynec.* 2022;5(10):482–487.

17. Molvi SN, Mir S, Rana VS, Jabeen F, Malik AR. Role of antihypertensive therapy in mild to moderate pregnancy-induced hypertension: a prospective randomized study comparing labetalol with alpha-methyldopa. *Arch Gynecol Obstet.* 2012;285(6):1553-62. <https://doi.org/10.1007/s00404-011-2205-2>

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All the authors agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved



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