e-ISSN: 0975-1556, p-ISSN:2820-2643

Available online on www.ijpcr.com

International Journal of Pharmaceutical and Clinical Research 2022; 14(9); 961-967

Original Research Article

# A Comparative Study of Labetalol vs Methyldopa in the Treatment of Hypertensive Disorders of Pregnancy

**Trishla[1], Avani Raj[2], Iftekhar Ahmed[3]**

**[1]Tutor, Department of Pharmacology, Government Medical College and Hospital, Purnea, Bihar.**

**[2]Tutor, Department of Pharmacology, Government Medical College and Hospital, Purnea, Bihar.**

**[3]Professor, Department of Pharmacology, Government Medical College and Hospital, Purnea, Bihar.**

**Received: 28-07-2022 / Revised: 26-08-2022 / Accepted: 24-09-2022**

**Corresponding author: Dr Avani Raj**

**Conflict of interest: Nil**

**Abstract**

**Background:** Pregnancy-related hypertension is a common medical issue that increases the likelihood of unfavourable consequences. The goal of this study was to evaluate the effectiveness and safety of Labetalol and Methyldopa in regulating blood pressure in PIH and pre-eclampsia patients.

**Methods:** A comparative, prospective observational study was carried out in women with PIH at the Government Medical College and Hospital in Purnea, Bihar, between April 2022 and August 2022. 100 patients in Group A received Labetalol treatment, while 100 individuals in Group B received methyldopa. Over the course of 7 days, the response in reducing BP was evaluated.

**Results:** Systolic/diastolic blood pressure in the methyldopa group on the first day was 145.20±7.17 mmHg / 101.60±4.20 mmHg, which was decreased to 129.20±4.86 mmHg / 90.50±3.30 mmHg on day 7. The labetalol treatment group of patients showed a considerable fall from 143.50±7.30 mmHg/101.30±3.93 mmHg (systolic in the Labetalol group, the author discovered that MAP decreased from 115.226±4.17 mmHg to 100.17±4.43 mmHg on day 7, while in the Methyldopa group, the author discovered that MAP decreased from 115.99±4.38 mmHg on admission to 103.27±2.99 mmHg on day 7, which is highly significant.

**Conclusions:** Compared to methyldopa, labetalol lowers systolic and diastolic blood pressure more quickly and effectively. Labetalol and methyldopa have comparable safety profiles and side effects.

**Keywords:** Labetalol, Methyldopa, Pregnancy induced hypertension



## Introduction

The most typical medical issue that arises during pregnancy is hypertension [1]. Up to 10% of pregnancies are complicated by hypertension, which is linked to a higher risk of severe foetal, neonatal, and maternal outcomes include preterm delivery, diabetes, chronic hypertension, perinatal death, acute renal failure, postpartum haemorrhage, and maternal death [2-7]. Antihypertensive medication usage cuts the risk of getting

severe hypertension in half [8]. Nowadays, a lot of people utilise labetalol. Methyldopa is an adrenergic antagonist with a central action that works by activating central alpha 2 receptors, which causes a decrease in sympathetic activity, arterial dilation, and a reduction in blood pressure.

Due to its primary functions, it frequently causes adverse effects [9]. An alpha-beta blocker with an arteriolar vasodilator action, labetalol reduces peripheral vascular resistance while having little to no effect on cardiac output. Antihypertensive medications are primarily used in PIH to prevent or treat severe hypertension and its complications (usually defined as blood pressure of 160/110mmHg) as well as to extend pregnancy as much as feasible [10].

Methyldopa has been used for a very long period to manage blood pressure. There has been a shift in recent years toward using Labetalol for the same purpose. This study compares the efficacy of methyldopa and labetalol monotherapy in treating patients with pregnancy-induced hypertension. This study's goal was to assess the effectiveness and safety of Labetalol and methyldopa in managing blood pressure in PIH and pre-eclampsia patients [11-14].

## Material and Methods

In order to conduct this study, samples were obtained from the Obstetrics and Gynecology Department of the Government Medical College and Hospital, Purnea, Bihar, where pregnant patients were admitted from April 2022 to August 2022 with pregnancy-induced hypertension. A comparative, prospective, and observational investigation was conducted.

After gaining informed agreement, pregnant women with hypertension were included in the trial after all the pregnant attendees had been checked for the condition. There were 200 patients with pregnancy-related hypertension who were split into two groups, each with 100 patients: Group A and Group B. The National High Blood Pressure Education Program Working Group determined the diagnostic and categorization criteria for the hypertensive condition during pregnancy.

The All patients were diagnosed with PIH in accordance with the NHBPEP, which requires proteinuria (1+ dipstick in two midstream urine samples taken at intervals of 4 hours), BP more than 140/90 mmHg on two different occasions, and after 20 weeks of pregnancy till term. Patients who had multifetal pregnancy, eclampsia, diabetes mellitus, cardiac diseases, renal diseases, thyrotoxicosis, haemophilia, or chronic hypertension who had undergone a clinical examination to check their systolic and diastolic blood pressure were excluded.

### Technique

After a 20-minute break, the measures were taken while seated in a chair. When the radial pulse stops, raise the cuff pressure above the systolic pressure. To calculate diastolic blood pressure, use the Korotkoff V (disappearance of the sound) method. Use Korotkoff IV if the noise continues after the cuff is deflated (muffling of the sound). Labetalol 100mg TDS was administered to Group A's 100 patients, and if there was no decrease in blood pressure within 48 hours, i.e., MAP <106mmHg, doses were doubled and escalated up to 1.2gm/day in divided doses as needed.

Methyldopa 250mg QID was administered to 100 patients in Group B, and if blood pressure did not reduce within 48 hours (MAP <106mmHg), doses were doubled and escalated up to a maximum of 3 gm/day in divided doses. With each treatment, observations were recorded regarding the fall in BP. Systolic and diastolic blood pressure were monitored six hours a day, and mean arterial pressure were compared

on the first day of admission and seven days after starting therapy with each medicine in the relevant group.

## Results

The descriptive data for the patient characteristics in the two therapy groups are shown in Table 1. In the age range of 21 to 25 years, there were 52 (52%) patients in the Methyldopa group and 51 (51%) instances in the Labetalol group. In the age range of 26 to 30 years, there were 47 (47%) instances in the methyldopa group and 45 in the labetalol group. Systolic and diastolic blood pressure averages and standard deviations for the two therapy groups before and seven days into treatment are shown in Table 2. On the day of admission, the difference between the mean systolic and diastolic blood pressures for the two groups was statistically insignificant. After therapy, the mean systolic blood pressure for the Methyldopa-treated group was 129.20±4.86mmHg, while it was 126.10±5.49mmHg for the Labetalol-treated group. With a p-value of <0.0001, the difference between the means was statistically very significant.

**Table 1: Age distribution of patients in two treatment groups**

| Age groups in years | Methyldopa (n=100) | Labetalol (n=100) | p-value |
|---|---|---|---|
| 21-25 | 52 | 51 | 0.3959 (NS) |
| 26-30 | 47 | 45 | |
| >30 | 1 | 4 | |

**Table 2: Mean and standard deviation for systolic and diastolic blood pressure in two treatment groups before and after treatment**

| Blood pressure | Levels | Methyldopa Mean±SD | Labetalol Mean±SD | p-value |
|---|---|---|---|---|
| Systolic BP | Pre | 145.20±7.17 | 143.50±7.30 | 0.0983 (NS) |
| | Post | 129.20±4.86 | 126.10±5.49 | <0.0001 (NS) |
| p-value** | | <0.0001 (HS) | <0.0001 (HS) | |
| Diastolic BP | Pre | 101.60±4.20 | 101.30±3.93 | 0.6025 (NS) |
| | Post | 90.50±3.30 | 87.40±5.62 | <0.0001 (HS) |
| p-value** | | <0.0001 (HS) | <0.0001 (HS) | |

Obtained using t-test for independent samples; ** Calculated using paired t-test; NS: Not Significant, HS: Highly Significant Additionally, the mean diastolic blood pressure was 90.50±3.30mmHg for the group treated with methyldopa seven days after therapy, compared to 87.40±5.62mmHg for the group treated with labetalol. With a p-value of <0.0001, the difference between the means was statistically very significant. Using a paired t-test, it was determined that the difference between the mean systolic and diastolic blood pressure before and seven days after therapy for the methyldopa and labetalol treatment groups was statistically highly significant with a p-value of <0.0001.

**Table 3: Mean difference in fall of Blood pressure**

| Blood pressure | Duration | Methyldopa Mean±SD | Labetalol Mean±SD | p-value |
|---|---|---|---|---|
| Systolic BP | 48 hours | 2.1±1.47 | 5.2±2.99 | <0.0001 |
| Diastolic BP | 48 hours | 3.8±2.21 | 7.8±3.48 | <0.0001 |

**Table 4: Descriptive statistics for MAP at day 1 and 7 in two groups**

| MAP | Methyldopa (n=100) | Labetalol (n=100) | p-value |
|---|---|---|---|
| Day 1 | 115.99±4.38 | 115.226±4.17 | 0.2093 (NS) |
| Day 7 | 103.27±2.99 | 100.17±4.43 | <0.0001 (HS) |

**Table 5: Descriptive statistics for Bishop Score in two treatment groups**

| Bishop score | Methyldopa (n=100) | Labetalol (n=100) | p-value |
|---|---|---|---|
| Mean±SD | 7.96±1.89 | 8.23±1.95 | 0.0232 (S) |

In the Methyldopa group, systolic blood pressure decreased by 2.1 mm Hg after 48 hours of treatment, while in the Labetalol group, systolic blood pressure decreased by 5.2 mm Hg. After 48 hours, the diastolic BP drops by 7.8mmHg in the Labetalol treatment group and by 3.8mmHg in the Methyldopa therapy group. As a result, when individuals take Labetalol, their systolic and diastolic blood pressure drops more quickly.

The mean arterial pressure (MAP) descriptive data for the two treatment groups are shown in Table 4. On day 1, the MAP for the patients in the methyldopa group was 115.99±4.38mmHg, whereas the MAP for the patients in the labetalol group was 115.226±4.17mmHg. With a p-value of 0.2093, the difference in means was not statistically significant. On day 7, however, individuals receiving methyldopa had a mean MAP of 103.27±2.99 mmHg, whereas those receiving labetalol had a mean MAP of 100.17±4.43 mmHg. Consequently, the difference was extremely significant statistically, with a p-value of <0.0001, as determined by the t-test for independent samples. Table 5 displays the descriptive statistics for the bishop score at the time of spontaneous labor's onset or at the time of labor's induction in the two treatment groups. The means differed in a statistically significant way.

## Discussion

In this trial, the majority of the 200 patients, 51 patients receiving labetalol and 52 patients receiving methyldopa were between the ages of 21 and 25. Regarding age distribution, both groups had statistically similar distributions. The majority of patients in group A receiving methyldopa and group B receiving labetalol in the study by Jinturkar A *et al*. were between the ages of 15 and 24 [15]. The mean patient age in the study by Dharwadkar *et al*. was 25.95±3.94 years for the methyldopa group and 26.65±3.73 years for the labetalol group [16].

In a study conducted by Pentareddy *et al*, the mean age of the patients in the Methyldopa group was 22.3 years while it was 23.23 years in Labetalol group and both groups were statistically comparable [17]. In Labetalol group systolic/diastolic BP on 1st day was 143.50±7.30 mmHg/101.30±3.93 respectively and was controlled to 126.10±5.49 mmHg/87.40±5.62 mmHg on day 7, while systolic/diastolic BP in methyldopa group on 1st day was 145.20±7.17 mmHg/101.60±4.20 mmHg which was reduced to 129.20±4.86 mmHg/ 90.50±3.30 mmHg on day 7.

Similar results were shown by study conducted by Qasim *et al*, in which patients treated with Labetalol systolic/diastolic BP on admission (1st day) was 150±9 mmHg/100±8 mmHg respectively and was controlled to 123±9 mmHg/79±7 mmHg on day 7th while systolic/diastolic BP in Methyldopa treated group on the day of admission (1st day) was 148±8 mmHg/102±9 mmHg which was reduced to

125±10 mmHg/82±6mmHg [18]. Systolic/diastolic blood pressure was shown to be statistically significantly lower in the Labetalol-treated group. This is consistent with the research conducted by Lamming *et al* [10]. According to a study by El Qarmalawi *et al*, Labetalol is a more effective BP-controlling medication for treating pregnancy-related hypertension than methyldopa [19].

Eighty-one patients with severe hypertension were included in a multicenter, double-blind, and parallel group trial by Wallin JD and Wilson D to compare the effectiveness and safety of Labetalol alone or in combination with furosemide vs Methyldopa in conjunction with furosemide [20]. Moreover, Labetalol significantly ($p<0.05$) reduced systolic blood pressure more than the Methyldopa regimen after six months and a year of treatment, respectively.

In our study, we discovered that MAP in patients receiving labetalol treatment was 115.226±4.17 mmHg at admission and dropped to 100.17±4.43mmHg by day 7, while MAP in patients receiving methyldopa treatment was 115.99±4.38 mmHg at admission and dropped to 103.27±2.99 mmHg by day 7. This has a p value of <0.0001 which is very significant. In a research by Jinturkar A *et al*., MAP in patients on methyldopa was 109.86 mmHg at admission but dropped to 98.15 mmHg by day 7 with a statistically significant p value of 0.05.

With labetalol, MAP was 109.48 mmHg upon admission; however, it dropped to 96.90 mmHg on day 7 after therapy, a statistically significant decrease. This study also stated that patients receiving labetalol experienced a significant drop in mean arterial pressure. In a study by Subhedar *et al*., similar outcomes were interpreted [21]. In a related study by El Qarmalawi *et al*., patients receiving labetalol experienced a significant decrease in MAP at a rate of 81.4% compared to patients on methyldopa at a rate of 68.5% [19].The average MAP in both groups was the same prior to treatment, according to a study by Lamming *et al*. However, there was no significant change in the MAP in the group treated with methyldopa while there was a highly significant decline in MAP in the group treated with labetalol ($p<0.001$) [10]. In our study, we discovered that the Labetalol group's systolic blood pressure fell by 5.2mmHg after 48 hours of treatment, compared to 2.1 mmHg for the Methyldopa group. After 48 hours, the diastolic BP drops by 7.8mmHg in the Labetalol treatment group and by 3.8mmHg in the Methyldopa therapy group.

This demonstrates that patients receiving Labetalol had faster systolic and diastolic blood pressure drops than those receiving Methyldopa. A total of 60 eligible patients were randomly assigned to receive either methyldopa (n = 30) or labetalol (n = 30) in a study by Lomte D *et al*. [22]. Methyldopa antihypertensive therapy was linked to a drop in systolic blood pressure of 50 mmHg and diastolic blood pressure of 30 mmHg at 72 hours. At 72 hours after starting Labetalol medication, systolic blood pressure was reduced by 70 mmHg, and diastolic blood pressure was decreased by 36 mmHg.

As a result, Labetalol is superior to Methyldopa at lowering blood pressure in women who have pregnancy-induced hypertension. Hans SF reported a significant decrease in both systolic and diastolic pressure, usually 24 to 48 hours after starting methyldopa [23]. In contrast, in a research by Jinturkar A *et al*., the mean time needed to control blood pressure in the methyldopa group was 42.22 hours, and the mean time needed in the labetalol group was 36.97 hours [15]. The two groups' differences were statistically different, with

Labetalol controlling blood pressure earlier than methyldopa. Similar findings were obtained in a study by Subhedar *et al*. It is consistent with the Cruikshank DJ *et al*. study, which found that 88% of patients experienced quick BP control when using labetalol [24].

While it was shown in 92% of patients treated with Labetalol in the trial conducted by Michael *et al*., a subsequent investigation by Lardoux's also revealed rapid decline in BP in 82% of patients [25,26].

## Conclusion

Worldwide, hypertensive conditions during pregnancy are a leading cause of morbidity and mortality. Medication used to treat hypertension is crucial in controlling maternal blood pressure. Labetalol regulates systolic and diastolic blood pressure more quickly and effectively than methyldopa, according to our study. Because Labetalol increases the likelihood of spontaneous labour and a normal vaginal delivery, it has a softening effect on the cervix.

## References


1. Arias F, Daftary SN, Bhide AG. Hypertensive disorders of pregnancy. In: Dasgupta S, Nasim S, Khanna M (Eds.) Practical guide to high-risk pregnancy and delivery- a South Asian perspective (3rd edn.), Elsevier Publication, New Delhi; 2008:397-439.
2. Duley L, Henderson-Smart DJ, Meher S. Drugs for treatment of very high blood pressure during pregnancy. Cochrane Database Syst Rev. 2006:CD001449.
3. Steegers EA, von Dadelszen P, Duvekot JJ, Pijnenborg R. Preeclampsia. Lancet. 2010; 376:631-44.
4. Duckitt K, Harrington D. Risk factors for pre-eclampsia at antenatal booking: systematic review of controlled studies. BMJ. 2005; 330:565.
5. Hernández-Diaz S, Van Marter LJ, Werler MM, Louik C, Mitchell AA. Risk factors for persistent pulmonary hypertension of the newborn. Pediatrics. 2007;120: e272-282.
6. Saftlas AF, Logsden-Sackett N, Wang W, Woolson R, Bracken MB. Work, leisure-time physical activity, and risk of preeclampsia and gestational hypertension. Am J Epidemiol; 2004; 160:758-65.
7. Skjaerven R, Vatten LJ, Wilcox AJ, Rønning T, Irgens LM. Recurrence of pre-eclampsia across generations: exploring fetal and maternal genetic components in a population based cohort. BMJ. 2005; 331:877.
8. Abalos E, Duley L, Steyn DW, Henderson-Smart DJ. Antihypertensive drug therapy for mild to moderatehypertension during pregnancy. Cochrane Database Syst Rev. 2007;1:CD002252.
9. Lamming GD, Symonds EM. Use of Labetalol and Methyldopa in pregnancy induced hypertension. Br J Clin Pharmac. 1979; 8:217S-222S.
10. ACOG Committee on Obstetric Practice. ACOG practice bulletin. Diagnosis and management of preeclampsia and eclampsia. Number 33, January 2002. Am College Obstet Gynecol. Int J Gynaecol Obstet. 2002; 77:67-75.
11. Williams Obstetrics: Cunningham, Leveno, Bloom, Sponge, Dashe, Hoffman, Casey, Sheffield: Obstetrical Complications: Hypertensive Disorders; ch.40:729-779.
12. Lomte D. An open label, prospective, single centre study to evaluate the efficacy of Methyldopa and Labetalol in treatment of patients with pregnancy-inducedhypertension. 2015; 4:1235-41.
13. Sushrut D, Girija. Labetalol an emerging first line drug for pregnancy induced

hypertension. Indian J Clin Pract. 2013;23;640-1.
14. Krishnachetty B, Plaat F. Management of hypertensive disorders of pregnancy. Anaesthesia Tutorial Week. 2014; 304:1-13.
15. Jinturkar A, Khedkar V, Dongaonkar D. Comparison of efficacy of Labetalol and Methyldopa in patients with Pregnancy Induced Hypertension. Int J Recent Trends Sci Techn. 2010;10(3):520-6.
16. Dharwadkar MN, Kanakamma MK, Dharwadkar SN, Rajagopal K, Gopakumar C, *et al*. Study of methyl dopa versus labetalol in management of preeclampsia and gestational hypertension. Gynecol Obstet. 2014; 4:242.
17. Pentareddy MR, Shailendra D, Prasuna G, Subbaratnam Y, Naresh DTV, Katta R. Safety and efficacy of Methyldopa and Labetalol in controlling blood pressure in hypertensive disorders of pregnancy. Int J Basic Clin Pharmacol. 2017;6;942-7.
18. Qasim A, Siddiqui MH, Salam JU, Nusrat U. Labetalol versus Methyldopa: efficacy in pregnancy induced hypertension. Gomal J Med Sci. 2014; 12:233-6.
19. El-Qarmalawi AM, Morsy AH, Al-Fadly A, Obeid A, Hashem M. Labetalol vs Methyldopa in the treatment of pregnancy-induced hypertension. Int J Gynecol Obstet. 1995; 49:125-30.
20. Wallin JD, Wilson D, Winer N, Maronde RF, Michelson EL, Langford H, *et al*. Treatment of severe hypertension with Labetalol compared with Methyldopa and furosemide. Am J Med. 1983;75(4A):87-94.
21. 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.
22. Friedlander WJ. The history of modern epilepsy: The beginning, 1865-1914. Westport, CT: Greenwood Press; 2001.
23. Hans SF, Kopelman H. Methyldopa in treatment of severe toxaemia of pregnancy. BMJ. 1964; 1:736-9.
24. Cruickshank DJ, Robertson AA, Campbell DM, MacGillivray I. Does Labetalol influence the development of proteinuria in pregnancy hypertension? A randomised controlled study. Eur J Obstet Gynecol Reprod Bio. 1992; 45:47-51.
25. Lardoux H, Gerard J, Blazquez G, Chouty F, Flouvat B. Hypertension in pregnancy: evaluation of the two B blockers atenolol and Labetalol. Eur Heart J. 1983;4(Suppl G):35-40.
26. Michael CA. Use of Labetalol in the treatment of severe hypertension during pregnancy. Br J Clin Pharmacol. 1979; 8:211S-5S.