SRYAHWA PUBLICATIONS

Open Access Journal of Gynecology and Obstetrics
ISSN: 2638-5244 | Volume 6 Issue 1, 2024
https://doi.org/10.22259/2638-5244.0601002

RESEARCH ARTICLE

Assessment and Efficacy of Labetalol and Methyldopa in Controlling Blood Pressure in Patients with Pregnancy Induced Hypertension (PIH)

Jahanara Akter[1], Pervin Akter[2], Mamata Manjuri[3]

[1]Assistant professor (Obs & Gynae), OSD, DGHS, Attached: Institute of Child and Mother Health, Matuail, Dhaka, Bangladesh.
[2]Professor and Head, Department of Physiology, Bashundhara Addin Medical College, South Keraniganj, Dhaka, Bangladesh.
[3]Assistant professor (Obs & Gynae), Colonel Malek Medical College, Manikgonj, Bangladesh.

Received: 20 April 2024 Accepted: 10 May 2024 Published: 13 May 2024

Corresponding Author: Jahanara Akter, Assistant professor (Obs & Gynae), OSD, DGHS, Attached: Institute of Child and Mother Health, Matuail, Dhaka, Bangladesh.

Abstract

Background: The most frequent medical disease in pregnancy is hypertension, which contributes considerably to maternal and perinatal mortality and morbidity. It is estimated that hypertension complicates around 6-10% pregnancies. If it remains uncontrolled, it can lead to complications like pre-eclampsia, eclampsia, fetal growth retardation, abruptio placentae, premature delivery and fetal mortality as well as maternal morbidity and the mortality. Hypertension is the most common medical problem encountered during pregnancy. It is estimated that globally 6-8% of pregnancies are complicated by hypertension. The risk of developing severe hypertension is reduced to half by using antihypertensive medications.

Objective: To asses and compare the efficacy of labetalol and methyldopa in controlling blood pressure in patients with pregnancy induced hypertension.

Methods: This study was conducted in the Department of Obstetrics and Gynaecology, Shahid Syed Nazrul Islam Medical College, Kishorgonj, Bangladesh from July 2019 To June 2020. 150 patients with PIH were divided in to two groups randomly. After randomization, group A received methyldopa 250 mg tid and group B received labetalol 100mg tid. Mean Arterial pressure (MAP) was calculated according to formula systolic BP+2 diastolic BP /3. Patients were subjected to 6 hrly BP monitoring. Comparison of two drugs was done daily by calculating MAP of two groups. Following Observations were made as regards Fall in BP with Labetalol/ Methyldopa, Time required to control BP, Average dose of drugs required to control BP, Onset of labour-spontaneous/induced, Bishop score at induction of labour, Side effects of drugs.

Results: Significant fall in MAP was seen in patients receiving Labetalol. Mean time required to control B.P in groupA was 42.22 hours and in group B it was 36.97 hours. Mean Bishop score at induction in present study in group A was 8.27 and in group B was 9.33 with a statistically significant $p<0.05$. (33.33%) patients went in spontaneous labour in group A while in group B, 23 patients i.e. (48.94%) patients went in spontaneous labour.

Conclusion: The study concluded that the use of labetalol to reduce blood pressure in pregnancy induced hypertension patients is significantly effective than methyl dopa along with advantage of spontaneous onset of labour.

Keywords: Labetalol, Methyldopa, Pregnancy Induced Hypertension, Shahid Syed Nazrul Islam Medical College.

Citation: Jahanara Akter, Pervin Akter, Mamata Manjuri. Assessment and Efficacy of Labetalol and Methyldopa in Controlling Blood Pressure in Patients with Pregnancy Induced Hypertension (PIH). Open Access Journal of Gynecology and Obstetrics. 2024;6(1):17-22.

1. Introduction

The most frequent medical disease in pregnancy is hypertension, which contributes considerably to maternal and perinatal mortality and morbidity.[1] It is estimated that hypertension complicates around 6-10% pregnancies.[2] If it remains uncontrolled, it can lead to complications like pre-eclampsia, eclampsia, fetal growth retardation, abruptio placentae, premature delivery and fetal mortality as well as maternal morbidity and the mortality. Preeclampsia and eclampsia cause a woman's mortality every three minutes around the world.[3,4] Hypertensive in pregnancy occurs with an incidence of 10%4. Gestational hypertension is diagnosed as women have all of the following: BP≥140/90mmHg, no proteinuria, pregnancy of ≥ 20 weeks duration and no previous history of hypertension[5]. Methyldopa and labetalol are the two frequently used drugs for control of gestational hypertension[6]. Alpha methyldopa is centrally acting antihypertensive drug. The common associated side effects are headache, nausea, dizziness and dry mouth[7]. One of the adverse outcomes of antenatal use of alpha methyldopa is postnatal depression. It is reported that women who took alpha methyldopa for hypertension during pregnancy were more likely to develop postnatal depression[8]. Labetalol is better than methyldopa in controlling blood pressure, fetomaternal safety profile and more chances of spontaneous onset of labour[9]. If pharmacological therapy is required in pregnant women with mild to severe hypertension, labetalol, methyldopa, and long-acting nifedipine are appropriate oral antihypertensive medications.[6] Although diuretics have been demonstrated to be effective in the treatment of essential hypertension during pregnancy, they are ineffective in the treatment of pregnancy-induced hypertension. The most widely prescribed antihypertensive medicine is methyldopa, and it has been proven to be beneficial.[7] Today, though oral medications are available and widely used for the treatment of PIH, the physicians still have to deal with many challenges. Antihypertensive drugs are often used to lower blood pressure with the aim of preventing its progression to adverse outcomes for the mother and the fetus. The risk of developing severe hypertension is reduced to half by using antihypertensive medications.[6] Severe hypertension is treated to prevent severe maternal complications. Methyldopa, labetalol and long-acting nifedipine are acceptable oral antihypertensive agents if drug therapy is required in pregnant women with mild to moderate hypertension.[8] But it has a high incidence of side effects because of its central action, like postural hypotension, constipation, galactorrhoea, postpartum depression, altered sleep pattern and headache, and it takes 24 hours for complete action. NICE recommends Labetalol as a first line antihypertensive for pregnancy induced hypertension, pre-eclampsia and eclampsia, which is a nonspecific alpha and beta blocker that reduces blood pressure by peripheral vasodilation. One study concluded that labetalol is equally efficacious and better tolerated compared to methyldopa in the treatment of pregnancy induced hypertension.[8] Although labetalol is preferred over methyldopa as it is free of the above-mentioned side effects,[9-11] it is still less frequently used in our routine practice. So, the current study is designed to compare the efficacy of labetalol versus methyldopa in pregnancy induced hypertension in our population

2. Materials and Methods

This study was conducted in the Department of Obstetrics and Gynaecology, Shahid Syed Nazrul Islam Medical College, Kishorgonj, Bangladesh from July 2019 To June 2020. Total 150 patients with PIH were divided in to two groups randomly. After randomization, group A received methyldopa 250 mg tid and group B received labetalol 100mg tid. Methyldopa can lower blood pressure, and combining it with labetalol may further increase this effect. You may be more likely to experience symptoms such as dizziness, lightheadedness, fainting, flushing, headache, and heart palpitations. Patients received treatment as per the assessment of the treating obstetrician. The study was approved by the institutional ethics committee of the hospital. Informed consent was obtained from all the patients before enrollment. Medical and obstetric history was taken and physical examination was conducted at the time of initial recruitment.

2.1 Inclusion Criteria

Diagnosed pregnancy induced hypertension patients based on criteria- BP more than 140/90 mmHg on two separate occasion 6 hours apart, Proteinuria 1+ dipstick in two midstream urine samples collected 4 hours apart, and after 20 weeks of pregnancy till term.

2.2 Exclusion Criteria

Multifetal pregnancy, eclampsia, and women with preexisting or concurrent medical disorders like diabetes mellitus, cardiac diseases, renal disease, thyrotoxicosis, hemophilia and chronic hypertension attributable to hypertension during their pregnancy.

Patients were divided in to two groups randomly. After randomization, group A received methyldopa 250 mg tid and group B received labetalol 100mg tid. Mean Arterial pressure (MAP) was calculated according to formula systolic BP +2 diastolic BP /3.[12]

Patients were subjected to 6 hourly BP monitoring. Comparison of two drugs was done daily by calculating MAP of two groups. If there was no fall in BP even after 48 hrs of drug therapy, dose of the drug was doubled. Response in lowering BP was assessed over a period of 7 days. Observations were made as regards fall in BP with labetalol/ methyldopa, time required to control BP, average dose of drugs required to control BP, onset of labour-spontaneous/induced, Bishop score at induction of labour and side effects of drugs.

2.3 Data Analysis

Data statistical analysed using the SPSS version 23. Descriptive statistics were presented using charts, graphs and tables as appropriate. Quantitative variables were described using measures of central tendencies like mean and median as appropriate. Student's paired t test for within group before and after treatment. Student's unpaired t test was used for comparison of normally distributed continuous data between the two treatment groups. Categorical data were analyzed for associations using chi square test. P value <0.05 was considered statistically significant.

3. Results

Total 150 patients, maximum number of patients that is 75 patients belonged to the age group of 15 to 24 years: 40 patients (53.4%) in Group A and 37 patients (49.4%) in Group B. The mean age of the patients in Group A was 24.41yrs and in group B was 24.85yrs. The mean age was statistically non-significant in both the groups.

Table 1. *Age wise distribution of patients in both the groups (N=150)*

Age	Methyldopa (n=75)	Labetalol (n=75)
15-24 yrs	40 (53.4)	37(49.4)
25-34 yrs	32 (42.6)	35(46.6)
35-40 yrs	3 (4.0)	3(4.0)

Table 2. *Distribution of patients according to gravidity in both the groups (N=150)*

Pariy	Methyldopa (n=75)	Labetalol (n=75)
Primi	44 (59.6)	41 (54.6)
Multi	31 (41.4)	34 (45.4)

Table 2 states that in the present study, 85 patients were primigravidae, 44 patients (59.6%) in methyldopa group and 41 patients (54.6%) in labetalol group. The difference between the two groups was statistically non-significant.

Table 3. *Comparison of MAP in both the groups at Day 1 and Day 7 (N=150)*

	Group	N	Mean [mmHg]	Std. Deviation	Mean Difference	p-value
Day 1	Methyldopa	75	109.86	2.91	0.37±0.42	0.37
	Labetalol	75	109.49	2.78		$p>0.0^{ns}$
Day 7	Methyldopa	75	98.15	3.44	1.24±0.46	0.008
	Labetalol	75	90.0	2.70		$p<0.05^{s}$

Table 3 shows comparison of MAP in both the groups at Day 1 and Day 7. In the present study, the mean arterial pressure in patients treated with methyldopa on admission was 109.86mmHg, while on day 7 it reduced to 98.15mmHg, with a statistically significant *p* value <0.05. With labetalol, the mean arterial pressure on admission was 109.48mmHg which reduced to 90.0mmHg on day 7. Reduction in MAP was statistically significant. On comparing the two drugs, MAP on admission were comparable but on day 7, significant fall in MAP was seen in patients receiving labetalol.

Table 4. *Comparison of duration of control BP in both the groups (N=150)*

Group	N	Mean [hours]	Std. Deviation	Std. ErrorMean	p-value
Methyldopa	75	42.22	3.04	0.32	0.000^{S}
Labetalol	75	36.97	2.94	0.31	p<0.05

Table 4 shows comparison of duration of control BP in both the groups. In the present study, the mean time required to control BP in group A was 42.22 hours and in group B it was 36.97 hours. The difference between the two groups was statistically significant with labetalol showing earlier control of BP than methyldopa.

Table 5. *Distribution of patients according to dose in methyldopa group (N=150)*

Dose	Number	Percentage
750 mg/day	33	44.0
1000 mg/day	17	22.7
1500 mg/day	17	22.7
2000 mg/day	8	10.6

Table 5 shows the mean dose required to control BP in group A was 1111.11mg. In group A, 33 patients (44.0%) required a dose of 750 mg/day to achieve optimal BP control. Out of remaining 33 patients, 17 patients (22.7%) required a dose of 1000 mg/day to achieve optimal BP control while remaining 17 patients (22.7%) required a dose of 1500 mg/day. 8 patients had to take 2000 mg /day to achieve optimal B.P control.

Table 6. *Distribution of patients according to dose in labetalol group (N=150)*

Dose	Number	Percentage
300 mg/day	42	55.0
400 mg/day	17	22.8
500 mg/day	8	10.6
600 mg/day	8	10.6

Table 6 says in group B the mean dose required was 382.22mg. 42 patients (55.0%) had their BP controlled with 300mg / day. 17 patients (22.8%) required a dose of 400mg/day. Of remaining 17 patients, 8 patients (10.6%) required a dose of 500mg /day and 8 patients (10.6%) required a dose of 600mg /day.

Table 7. *Distribution of patients according to onset of labour who delivered vaginally (N=150)*

Onset of labour	Methyldopa	Labetalol
Spontaneous	8 (33.3)	22 (48.9)
Induced	16 (66.6)	23 (51.1)

In the present study 8 patients in group A went in spontaneous labour while 16 patients were induced. In group B 22 patients went in spontaneous labour and 23 patients were induced these values were found to be statistically significant $p<0.05$. Thus the rate of spontaneous labour was more in patients treated with labetalol. This may be accounted to the fact that labetalol has ripening effect on the cervix. These results are depicted in Table 7. The comparison of bishop Score in both the groups. Mean Bishop Score at induction in present study in group A was 8.27 and in group B was 9.33 with a statistically significant $p<0.05$.

Table 8. *Distribution of patients according to side effects*

Side effects	Methyldopa	Labetalol
Postural Hypotension	0 (0.0)	0(0.0)
Drowsiness	09 (12.0)	03 (4.0)
Headache	9 (12.0)	6 (8.0)
Nausea	9 (12.0)	09 (12.0)
Vomiting	5 (6.66)	5 (6.66)
Weakness	4 (5.33)	6 (8.0)
Myalgia	5 (6.66)	5 (6.66)

Table 8 shows distribution of patients according to side effects. In the present study, most common side-effect observed was headache. 10 patients in Group A and 8 patients in group B had this symptom. The other side- effects included drowsiness, more in patients treated with methyldopa, weakness, more in patients treated with labetalol. The incidence of side-effects such as nausea, vomiting, myalgia was similar in both the groups.

4. Discussion

Hypertensive disorders seem to complicate approximately 10% of pregnancies and are important causes of maternal and foetalmorbidity and mortality. In the present study comparison between the anti-hypertensives, labetalol and methyldopa, in terms of efficacy and safety were assessed. Among the total 150 patients in the present study, maximum number of patients in both the groups, group A [Methyldopa] and group B [Labetalol], were in the age group of 15 to 24 years. Gravidity distribution showed maximum patients of PIH as primigravidae in both the groups. In the present study, the mean arterial pressure in patients treated with methyldopa on admission was 109.86mmHg, while on day 7 it reduced to 98.15mmHg, with a statistically significant p value<0.05. Reduction in MAP was statistically significant. On comparing the two drugs, MAP on admission were comparable but on day 7, significant fall in MAP was seen in patients receiving labetalol. According to a study conducted by Lamming et al, the average MAP in both groups was same before treatment. There was a highly significant fall in MAP in the group treated with labetalol (p<0.001) but no significant fall was noted in the group tested with methyldopa (p>0.05).[12] In a similar study conducted by El Qarmalawi et al, 81.4% patients in labetalol group had a significant fall in MAP as against 68.5% in patients taking methyldopa.[13] In the present study, the mean time required to control BP in group A was 42.22 hours and in group B it was 36.97 hours. The difference between the two groups was statistically significant with labetalol showing earlier control of BP than methyldopa. In a study conducted by Sanders et al, the average time to achieve optimal B.P control was similar in both the groups.[14] D.J. Cruickshank, et al[15] observed that Labetalol did control the blood pressure in 45 of the 51 treated women (88%) within 24 hrs. In the present study, the mean time required to control BP in group A was 42.22 hours and in group B it was 36.97 hours. The difference between the two groups was statistically significant with labetalol showing earlier control of BP than methyldopa. It is interesting that several other workers have found similar response rates - Lardoux's group 82%, CA Michael 92%.[16,17] Marked fall of both systolic and diastolic pressure generally between 24 and 48 hours from the start of using methyldopa was noticed by S. F. Hans.[18] The mean dose required to control B.P in group A was 1111.11mg. In group A, 33 patients (44.0%) required a dose of 750 mg/day to achieve optimal B.P control. Out of remaining 33 patients, 17 patients (22.7%) required a dose of 1000 mg/day to achieve optimal B.P control while remaining 17 patients (22.7%) required a dose of 1500 mg/day .8 patients had to take 2000 mg /day to achieve optimal BP control. In group B the mean dose required was 382.22mg. 42 patients (55.0%) had their BP controlled with 300mg / day. 17 patients (22.8%) required a dose of 400mg/day. Of remaining 17 patients, 8 patients (10.6%) required a dose of 500mg /day and 8 patients (10.6%) required a dose of 600mg /day. In present study the average dose of labetalol required to achieve optimal B.P control was much less than in above mentioned study, but for methyldopa doses were comparable.[14] Lardoux's group found that the average daily dose of labetalol required for satisfactory blood pressure control was 600 mg.[16] In the present study, 8 patients in group A (33.33%) went in spontaneous labour while 16 patients (66.67%) were induced. In group B, 22 patients (48.94%) went in spontaneous labour and 23 patient's (51.06%) were induced. These values were found to be statistically significant with p<0.05. Thus the rate of spontaneous labour was more in patients treated with labetalol. This may be accounted to the fact that labetalol has ripening effect on the cervix. The comparison of Bishop Score in both the groups. Mean Bishop score at induction in present study in group A was 8.27 and in group B was 9.33 with a statistically significant p<0.05. Lamming et al reported a higher Bishop score of 10 in patients treated with labetalol as compared to a mean Bishop score of 7.1 in patients treated with methyldopa.[12] In the present study, most common side-effect observed was headache. 10 patients in Group A and 8 patients in group B had this symptom. The other side- effects included drowsiness, more in patients treated with methyldopa, weakness, more in patients treated with labetalol. The incidence of side-effects such as nausea, vomiting, myalgia was similar in both the groups. Study conducted by Verma et al states that adverse events observed were lower in the labetalol treated

group compared to the methyldopa group.[19] In a study by Qarmalawi et al, patients receiving methyldopa complained of side-effects such as drowsiness (22.2%), headache (14.8%), nasal congestion (7.4%), postural hypotension (5.6%).[13]6 patients in labetalol group complained of dyspnoea, no other side-effects were noticed.

5. Conclusion

This study concluded that labetalol controls blood pressure in pregnancy induced hypertension patients more effectively within short duration than methyldopa. Study also signifies that labetalol helps in spontaneous onset of labour and favourable Bishop scoring at the time of onset of labour of PIH patients.

Funding

No funding sources

Competing Interests

There are no competing interests to declare.

6. References

1. Sibai B M. Etiology and management of hypertensionand pre- eclampsia. Am J Obstet Gynecol. 2012;206:4.
2. Bramham K, Nelson-Piercy C, Brown M J. Postpartum management of hypertension. BMJ. 2013;346:1-3.
3. Giannubilo SR, Bezzeccheri V, Cecchi S, Landi B, Battistoni GI, Vitali P, et al. Nifedipine versus l abetalol in the treatment of hypertensive disorders of pregnancy. Arch Gynecol Obstet. 2012;286:637-42.
4. Khedun SM, Moodley J, Naicker T. Drug management of hypertensive disorders of pregnancy. Pharmacol Ther. 1997;7:221-58.
5. Rudra P, Basak S, Patil D, Latoo M Y. Recent advances in management of pre-eclampsia. Br J Med Pract. 2011;4(3):a433:14-20.
6. Magee, Laura A; von Dadelszen, Peter Management of Hypertension in Pregnancy, Maternal-Fetal Medicine: 2021;3;2;124-135
7. Podymow T, August P. Update on the use of antihypertensive drugs in pregnancy. Hypertension. 2008 Apr 1;51(4):960-9.
8. Verma R, Lahon K, Tonpay SD, Kale VJ, Jain DK. A comparative randomized contolled parallel group study of efficacy and tolerability of labetalol versus methyldopa in the treatment of new onset hypertension during pregnancy. Int J Life Sci Pharma Res. 2012;2(1):23-31.
9. El-Qarmalawi AM, Morsy AH, Al-Fadly A, Obeid A, Hashem M. Labetalol vs. methyldopa in the treatment of pregnancy-induced hypertension. Int J Gynaecol Obstet. 1995;49:125-30.
10. Subhedar V, Inamdar S, Hariharan C, Subhedar S. Comparison of efficacy of labetalol and methyldopa in patientswith pregnancy-induced hypertension. Int J Reprod Contracept Obstet Gynecol. 2013 ;2(1):27-34.
11. Qasim A, Siddiqui MH, Salam J, Nusrat U. Labetalol versus Methyldopa: efficacy in pregnancy induced hypertension. Gomal J Med Sci. 2014;12(4)233-6.
12. Lamming GD & Symonds EM. Use of Labetalol and Methyldopa in Pregnancy-Induced Hypertension. Br J Clin Pharmacol. 1979; 8:217S- 22S.
13. El-Qarmalawi AM, Morsy AH, al-Fadly A, Obeid A, Hashem M, et al. Labetalol vs. methyldopa in the treatment of pregnancy-induced hypertension. Int J Gynaecol Obstet 1995;49:125-30.
14. Sanders GL, Davies DM, Gales GM, Rao JG, Rawlins MD, Routledge PA. A comparative study of methyldopa and labetalol in the treatment of hypertension. Br J Clin Pharmacol 1979;8:149S-51S.
15. 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 Biol 1992;45:47-51.
16. Lardoux H, Gerard J, Blazquez G, Chouty F, Flouvat B. Hypertension in pregnancy: evaluation of the two B-blockers atenalol and labetalol. Eur Heart J 1983;4(Suppl G):35-40.
17. Michael CA. Use of labetalol in the treatment of severe hypertension during pregnancy. Br J Clin Pharmacol 1979;8:211S-5S.
18. Hans SF, Kopelman H. Methyldopa in treatment of severe toxaemia of pregnancy. BMJ 1964;1:736-9.
19. Verma R, Lahon K, Tonpay SD, Kale VJ, Jain DK. A comparative randomised controlled parallel group study of efficacy and tolerability of labetalol versus methyldopa in the treatment of new onset hypertension during pregnancy. Int J Life Sci Pharma Res 2012;2:L23-31.