OPEN ACCESS
Scholars International Journal of Obstetrics and Gynecology
Abbreviated Key Title: Sch Int J Obstet Gynec
ISSN 2616-8235 (Print) |ISSN 2617-3492 (Online)
Scholars Middle East Publishers, Dubai, United Arab Emirates
Journal homepage: https://saudijournals.com

Original Research Article

Relation Between Labetalol and Methyldopa in Treatment of Pregnancy Induced Hypertension

Layla Khayrun Nahar[1*], Nazma Haque[2], Afroza Kutubi[3], Ratu Rumana[4], Shikha Gangoly[5], Sabina Akhter[6], Nowshin Yesmin Tonny[7], Saira Khan[8]

[1]Indoor Medical Officer (IMO), Department of Obstetrics and Gynaecology, Dhaka Medical College Hospital, Dhaka, Bangladesh
[2]Professor & Head, Department of Obstetrics and Gynaecology, Dhaka Medical College, Dhaka, Bangladesh
[3]Professor & Head, Department of Obstetrics and Gynaecology, Sir Salimullah Medical College (SSMC), Dhaka, Bangladesh
[4]Professor (Ex), Department of Obstetrics and Gynaecology, Sir Salimullah Medical College (SSMC), Dhaka, Bangladesh
[5]Professor, Department of Obstetrics and Gynaecology, Dhaka Medical College, Dhaka, Bangladesh
[6]Assistant Registrar, Department of Obstetrics and Gynaecology, Sylhet MAG Osmani Medical College Hospital, Sylhet, Bangladesh
[7]Indoor Medical Officer (IMO), Department of Obstetrics and Gynaecology, Mugda Medical College Hospital, Dhaka, Bangladesh
[8]Associate Professor, Department of Paediatrics, HM Samorita Medical College, Dhaka, Bangladesh

DOI: 10.36348/sijog.2022.v05i10.010 | **Received:** 14.09.2022 | **Accepted:** 25.10.2022 | **Published:** 29.10.2022

***Corresponding author:** Layla Khayrun Nahar
Indoor Medical Officer (IMO), Department of Obstetrics and Gynaecology, Dhaka Medical College Hospital, Dhaka, Bangladesh

Abstract

Background: Hypertensive disorder is the most common medical problem encountered in pregnancy with a high perinatal and maternal mortality & morbidity. Worldwide about 76,000 pregnant women die each year from preeclampsia and related hypertensive disorders. ***Objective:*** To assess the relation between labetalol and methyldopa in treatment of pregnancy induced hypertension. ***Methods:*** This study was hospital based comparative prospective study was conducted at Dept. of Obstetrics & Gynaecology, Dhaka Medical College Hospital, Dhaka, Bangladesh from January to June 2021. The study consisted of 100 patients with pregnancy induced hypertension attending outpatient department and admitted in ANW, or who directly came to labour room. These patients were randomly selected on lottery basis after they fulfilled the inclusion criteria. Total patients were taken for the study and divided into 2 groups of 50 patients in each group. ***Results:*** A total 100 patients were included. The mean age in Group I was 24.4±4.55 years and in Group-II, 23.95±4.28 years. Maximum number of patients was between 19- 24 years in both the groups. In Group-I, 26 (52%) patients and in Group-II, 25 (50%) patients were in this age group. The maximum age in the Group I was 34 years and 35 years in the Group-II. The minimum age was 17 years in both the groups. The inter group difference was not statistically significant (p>0.05) thus the two groups were comparable by age. At baseline no significant difference was seen in SBP in both treatment groups. However after 8 days post testament SBP of women was significantly lower in Group-I patients as that of Group-II patients. i.e. Group-I: 123.41 vs. Group-II: 126.62, p- value=0.009. At baseline no significant difference was seen in DBP in both treatment groups. However at 8th day post treatment DBP of patients was significantly lower in Group-I patients. i.e. 77.18 vs. Group-II 79.64, p-value=0.005. For SBP more effective control was seen in women whose parity was 3-4 and for DBP notable difference was seen in women whose parity was 1-2. The control of systolic blood pressure was more effective in patients with normal body mass index and for Diastolic blood pressure (DBP) more effective control was seen in patients who were obese. On comparison methyldopa significantly causes more drowsiness, headache and nasal congestion and the incidence of Postural hypotension and dysponea in both groups were not significantly different. The patient who required additional drugs to control the uncontrolled hypertension. In Group I, 2 (4%) patients and in Group II, 3 (6%) patients did not respond with starting drug. The inter group difference was not statistically significant (p>0.05). ***Conclusion:*** Labetalol had less maternal adverse effect compared to methyldopa but fetal outcome was not observed in this study. Labetalol and methyldopa are equally efficacious in controlling blood pressure in new onset hypertension in pregnancy. This study is just a step in this long way. Therefore, labetalol can be considered positively in the treatment of pregnancy induced hypertension.

Keywords: Labetalol, Methyldopa, Hypertension.

INTRODUCTION

Hypertensive disorder is the most common medical problem encountered in pregnancy with a high perinatal and maternal mortality & morbidity [1]. Worldwide about 76,000 pregnant women die each year from preeclampsia and related hypertensive disorders.

Fetal mortality rate is thought to be on the order of 5,00,000 per annum [2]. PIH is responsible for approximately 31% maternal mortality in developing countries of which 24.7% is due to eclampsia [3]. Effective control of blood pressure is key factor to reduce fetomaternal complications related to hypertensive disorders of pregnancy. 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]. Severe hypertension, conventionally defined as a BP of>160/110 mmHg, should be treated to prevent severe maternal complications [6]. Alpha Methyldopa is an α-methyl analogue of dopa, the precursor of dopamine (DA) and noradrenaline. Methyldopa is the most frequently prescribed and the agent of first choice for treatment of hypertension in pregnancy. There is extensive clinical experience and long-term follow-up data regarding children whose mothers received methyldopa during pregnancy with proven maternal and fetal safety. Methyldopa and labetalol are the two frequently used drugs for control of gestational hypertension [7]. Alpha methyldopa is centrally acting antihypertensive drug. The common associated side effects are headache, nausea, dizziness and dry mouth [8]. One of the adverse outcomes of antenatal use of alpha methyldopa is postnatal depression. The Recent United Kingdom (UK) guidelines from the National Institute of Health and Clinical Excellence (NICE) recommend oral Labetalol as the first line choice in the treatment of hypertension in pregnancy [9]. Patients receiving labetalol complained of dyspnoea, no other side-effects were noticed [10]. α-methyldopa has often been used as a control while comparing the effect of different drugs. Labetalol has also been successfully used for treatment of hypertensive disorder in pregnancy. Methyldopa is a weak antihypertensive drug that needs to be given three or four times a day and frequently requires titration and nonadherence to therapy [11].

MATERIAL AND METHODS

This study was hospital based comparative prospective study was conducted at Dept. of Obstetrics & Gynaecology, Dhaka Medical College Hospital, Dhaka, Bangladesh from January to June 2021. The study consisted of 100 patients with pregnancy included hypertension attending outpatient department and admitted in ANW, or who directly came to labour room. These patients were randomly selected on lottery basis after they fulfilled the inclusion criteria. Total patients were taken for the study and divided into 2 groups of 50 patients in each group. The cases were selected and divided into two groups Group I and Group II. Each case with odd number was selected in the Group I and each case with even no. was selected in the Group II. Group a patient were treated with methyldopa and Group II patients treated with labetalol. An elaborate history was taken. General physical examination and systemic examinations were done. For all the cases, dipstick test for urine albumin in random urine sample was done. Along with routine examination of pregnancy, liver function test, renal function test, coagulation profile was done. Ultrasonography was done in all the cases for estimation of gestational age, for placental localization, abruption, to rule out congenital anomalies, multiple pregnancy etc. If the patient was in labour, labour was monitored with partograph. The new borns were attended by pediatrician, examined and any complication noted was managed accordingly. Blood pressure record was maintained after delivery till discharge. On discharge, discharge card was given and postoperative visits after 6 weeks, 12 weeks were advised.

Inclusion Criteria:

- A singleton pregnancy.
- Patients who were booked before 20 weeks of gestation were taken up after they cross 20 weeks of gestation.
- Blood pressure exceeding 150 and 100 mm of Hg, systolic and diastolic respectively.

Exclusion Criteria:

- History of diabetes.
- Rhesus isoimmunisation.
- Cardiac Diseases.
- Asthma.
- Patients previously given anti-hypertensive drugs.
- Patients at risk of major obstetric complications- antepartum haemorrhage, malnutrition, twins, hydramnious during current pregnancy.
- The cases those were not booked before 20th weeks of pregnancy.
- The patients who came with any complications like eclampsia, IUFD, preterm labour, abruptio placentae, LVF, cerebrovascular accident, DIC and also the cases with symptoms of imminent eclampsia.
- Patients not willing to be hospitalized.

Data Analysis:

SPSS version 21 was used to enter and analysed the data. Quantitative variables like age, gestational age, BMI, baseline and after treatment SBP & DBP was calculated as mean and SD. Discrete variable like parity was also calculated as frequency. P-value≤0.05 was taken as significant. Data was stratified for age, gestational age, BMI and parity. Post-stratification, independent sample t-test was applied to compare success in stratified groups. P-value≤0.05 was taken as significant.

RESULTS

Table-1: Age distribution of patients in Group-I and Group-II (N=100)

Age	Group-I (N=50)		Group-II (N=50)	
	N	%	N	%
<18	4	8.0	5	10.0
19-24	26	52.0	25	50.0
25-30	15	30.0	16	32.0
>30	5	10.0	4	8.0
Age of patient(Mean±SD)	24.4±4.55		23.95±4.28	
Gestational age(Mean±SD)	34.9 ± 3.65		35.78 ± 3.72	

A total 100 patients were included. The mean age in groups I was 24.4±4.55 years and in Group II 23.95±4.28 years. Maximum number of patients was between 19- 24 years in both the groups. In Group I, 26 (52%) patients and in Group II, 25 (50%) patients were in this age group. The maximum age in the Group I was 34 years and 35 years in the Group II. The minimum age was 17 years in both the groups. The inter group difference was not statistically significant (p>0.05) thus the two groups were comparable by age (Table-1).

Table-2: Comparison of SBP on follow-up (Group-I: Labetalol, Group-II: Methyldopa) (n=100)

Comparison	Group-I Baseline-SBP		Group-II After 8 days-SBP	
N	50	50	50	50
Mean	149.65	151.13	123.41	126.62
SD	5.22	7.14	7.42	7.33
Minimum	139	140	110	115
maximum	160	163	135	138
p-value	**0.150**		**0.009**	

At baseline no significant difference was seen in SBP in both treatment groups. However after 8 days post testament SBP of women was significantly lower in Group I patients as that of Group-II patients. i.e. Group-I: 123.41 vs. Group-II: 126.62, p-value=0.009 (Table-2).

Table-3: Comparison of DBP on follow-up (Group-I: Labetalol, Group-II: Methyldopa) (n=100)

Comparison	Group-I Baseline-DBP		Group-II After 8 days-DBP	
N	50	50	50	50
Mean	102.56	102.51	77.18	79.64
SD	5.29	5.80	4.39	5.9
Minimum	93	93	70	70
maximum	113	113	85	90
p-value	**0.953**		**0.005**	

At baseline no significant difference was seen in DBP in both treatment groups. However at 8th day post treatment DBP of patients was significantly lower in Group-I patients i.e. 77.18 vs. Group-II 79.64, p-value=0.005 (Table-3).

Table-4: Comparison of SBP on follow-up stratified for Parity (n=100)

Parity	SBP		p-value
	Group I	Group II	
0	122.94±7.83	125.16±7.81	0.457
1-2	123.51±7.65	126.30±7.66	0.144
3-4	123.60±7.10	127.56±6.89	0.041

Table-5: Comparison of DBP on follow-up stratified for Parity (n=100)

Parity	DBP		p-value
	Group I	Group II	
0	76.76±4.93	80.83±5.99	0.055
1-2	77.09±3.99	80.54±6.50	0.012
3-4	77.60±4.66	78.16±5.18	0.675

For SBP more effective control was seen in women whose parity was 3-4 and for DBP notable difference was seen in women whose parity was 1-2 (Table-4, 5).

Table-6: Comparison of SBP on follow-up stratified for BMI (N=100)

BMI	SBP		p-value
	Group I	Group II	
Normal	120.45±7.06	125.84±7.04	0.011
Overweight	124.96±7.70	128.96±7.86	0.072
Obese	124.35±7.00	128.96±7.86	0.791

Table-7: Comparison of DBP on follow-up stratified for BMI (N=100)

BMI	DBP		p-value
	Group I	Group II	
Normal	76.59±5.01	77.00±4.14	0.209
Overweight	77.92±4.16	80.26±5.79	0.102
Obese	77.00±4.14	80.04±6.21	0.042

The control of systolic blood pressure was more effective in patients with normal body mass index and for Diastolic blood pressure (DBP) more effective control was seen in patients who were obese (Table-6, 7).

Table-8: Comparison of adverse effects of labetalol and methyldopa (N=100)

Adverse effects	Group I		Group II		p-value
	N	%	N	%	
Drowsiness	0	0	12	24	<0.001
Headache	1	2	9	18	<0.01
Nasal	1	2	7	14	<0.05
congestion	0	0	0	0	
Congestion	1	2	3	6	NS
hypotension	0	0	0	0	
hypotension	2	4	0	0	NS

In group I, patients developed drowsiness, headache, nasal congestion, postural hypotension and dyspnoea were 0 (0%), 1 (2%), 1 (2%), 1 (2%) and 2 (4%) and with methyldopa were 12 (24%), 9 (18%), 7 (14%), 3 (6%) and 0 (0%) respectively. On comparison methyldopa significantly causes more drowsiness, headache and nasal congestion and the incidence of Postural hypotension and dysponea in both groups were not significantly different (Table-8).

Table-9: Number of patients who required additional drug used in Group-I and Group-II (N=100)

Drug	Group I		Group II		p-Value
	N	%	N	%	
Uncontrolled hypertension	2	4.0	3	60.	<0.05
Mean ± SD (mg)	380 ± 259.51		1540 ± 503.45		

Table-9 shows the number of patient who required additional drugs to control the uncontrolled hypertension. In Group I, 2 (4%) patients and in Group II, 3 (6%) patients did not respond with starting drug. These cases were started on an additional drug from the other groups and delivery was expedited. Mean total dose of drugs per day required controlling BP by labetalol and methyldopa was 380 ± 259.51 mg and 1540 ± 503.45 mg respectively. The inter group difference was not statistically significant (p>0.05).

DISCUSSION

In mild to moderate gestational hypertension acceptable oral antihypertensive agents are Methyldopa, labetalol, and long-acting nifedipine [12]. In the absence of hypertensive crises methyldopa and oral labetalol are preferred drugs. Both these drugs are easily available in our country. Both drugs have been found effective in reducing blood pressure without any adverse effect on perinatal outcome. In the present study we compared labetalol with methyldopa for the management of gestational hypertension. A total 100 patients were included. In the present study fall of SBP, DBP and MAP was significant in both the groups. But the inter group difference was statistically not significant (p>0.05). The mean age in group I was 24.4±4.55 years and in Group II 23.95±4.28 years. Maximum number of patients was between 19- 24 years in both the groups. In Group I, 26 (52%) patients and in Group II, 25 (50%) patients were in this age group. The maximum age in the Group I was 34 years and 35 years in the Group II. The minimum age was 17 years in both the groups. The inter group difference was not statistically significant (p>0.05) thus the two groups were comparable by age. Results of our study showed that SBP (Labetalol: 123.41±7.42 vs. Methyldopa: 126.62±7.33, p value=0.009) as well as DBP (Labetalol: 77.18±4.39 vs. Methyldopa: 79.64±5.9, p-value=0.005) were effectively controlled in the group allocated to labetalol as compared to the group prescribed with methyldopa. Work done by Dwarkanath DSP showed similar findings in terms of control of blood pressure when comparison was done between methyldopa and labetalol. It was seen that control of blood pressure was more effective in pregnant patients who were randomised to the group receiving labatolol. Dwarkanath DSP study showed that labetalol is better than methyldopa in not only lowering blood pressure effectively but also reduction in proteinuria, achieving spontaneous labour and good BISHOP score if induction of labour was done and lesser number of fetuses develops IUGR as compared to methyldopa [9]. Patel did meta-analysis of compartive evaluation of these two drugs in pregnancy induced hypertension and concluded that labetalol was found to be better in reducing mean arterial pressure as compared to methyldopa. He further showed that drowsiness was more common in patients who received methyldopa [10]. Another study showed both drugs to be comparable in control of blood pressure in pregnancy induced hypertension. However spontaneous onset of labour was significantly more in patients who used labetalol [13]. The control of systolic blood pressure was more effective in patients with normal body mass index and for Diastolic blood pressure (DBP) more effective control was seen in patients who were obese. Mahmoud Alalfy from Egypt in his randomized trial and others reported that Labetalol has side effects on the mother and has better neonatal outcome and has a more rapid control of blood pressure as compared to methyldopa in the treatment of gestational hypertension [14, 15]. Contrary to these findings a trial conducted by Reena Rai Verma on 90 females with pregnancy induced hypertension, 45 received labetalol and 45 methyldopa, showed that control of both SBP (126±10.28 vs. 124±9.14mmHg; p-value >0.05) and DBP (78.44±8.24 vs. 77.55±5.28mmHg; p>0.05) were insignificant in both groups[16]. In this study, maternal adverse effects seen with both drugs are of known types. The frequency of occurrence of drowsiness, headache and nasal congestion were significantly less in labetalol group compared to methyldopa and postural hypotension and dysponea were similar in both groups. In labetalol treated group, headache was experienced by one (2%) patient in respect to 9 (18%) in methyldopa treated groups. No patient developed drowsiness with the treatment of labetalol compared to 12 (24%) with methyldopa. In labetalol treated group, only one patient (2%) had nasal congestion while it was 7 patients (14%) for methyldopa group. One (2%) patients developed Postural hypotension with the treatment of labetalol compared to 3 (6%) with methyldopa. In labetalol treated group, 2 (4%) patients had dysponea but in case of methyldopa no patient developed dysponea. This observation had similarity with previous study conducted by EI-Qarmalawi, [17] and Verma *et al.*, [16] said that most common maternal side-effect observed was headache that was equal in both groups which is dissimilar to my study. The number of patient who required additional drugs to control the uncontrolled hypertension. In Group I, 2 (2.66%) patients and in Group II, 3 (4%) patients did not respond with starting drug. These cases were started on an additional drug from the other groups and delivery was expedited. The inter group difference was not statistically significant (p>0.05). Another randomized controlled trial concluded that mehyldopa and labetalol both are comparable in reducing acute hypertension in pregnancy and since both are cheap drugs, their use is a good option in low resource countries [7].

CONCLUSION

Present study showed that labetalol is a bit advantageous than methyldopa in terms of better and quicker control of blood pressure. Labetalol and methyldopa are equally efficacious in controlling blood pressure in new onset hypertension in pregnancy. Labetalol significantly decreases proteinuria after treatment. Labetalol had less maternal adverse effect compared to methyldopa but fetal outcome was not observed in this study. This study is just a step in this long way. Therefore, labetalol can be considered positively in the treatment of pregnancy induced hypertension.

CONFLICT OF INTEREST

Nil.

SOURCE OF FUND

None.

REFERENCES

1. Jhansi, C., Harshi, M. Y. S., Sandeep, K., Rao, P. C., & Lakshmi, C. C. (2015). Comparison of efficacyand safety of oral labetalol and nifedipine in preeclampsia: A prospective observational study. *International Journal of Pharmacy and Pharmaceutical Sciences*, 7(9), 277- 280.
2. Chhabra, S., & Kakani, A. (2007). Maternal Mortality Due to Eclamptic and non eclamptic hypertensive disorders: a challenge. *Journal of Obsterics and Gynaecology*, 27(1), 25-29.
3. Davey, D. A., & MacGillivray, I. (1988). The classification and definition of the hypertensive disorders of pregnancy. *American Journal of Obstetrics and Gynecology*, 158(4), 892-898.
4. Sammour, M. B., El-Kabarity, H., Fawzy, M. M., & Schindler, A. E. (2011). Prevention and treatment of pre-eclampsia and eclampsia. *Journal of Steroid Biochemistry & Molecular Biology*, 97, 439–440.
5. Kenny, L., & Myers, J. (2017). Obstetrics by Ten Teachers. Boca Raton: Chapman and Hall/CRC; 169-219.
6. Al-Damluji, S. F., Al-Khalidi, A., Shaarbaf, H., & Tawfiq, N. H. (1982). A controlled comparison of the antihypertensive effects of labetalol and alphamethyldopa. *Pharmatherapeutica*, 3(2), 133-139.
7. Easterling, T., Mundle, S., Bracken, H., Parvekar, S., Mool, S., Magee, L. A., ... & Winikoff, B. (2019). Oral antihypertensive regimens (nifedipine retard, labetalol, and methyldopa) for management of severe hypertension in pregnancy: an open-label, randomised controlled trial. *The Lancet*, *394*(10203), 1011-1021.
8. Gupta, M., & Khalili, Y. (2021). Methyldopa [Internet]. Ncbi.nlm.nih.gov. 2021 [cited 10 July 2021]. Available: https://www.ncbi.nlm.nih.gov/books/NBK551671/
9. El- Qarmalawi, A. M., Morsy, A. H., Al-Fadly, A., Obeid, A., & Hashem, M. (1995). Labetalol vs. methyldopa in the treatment of pregnancy-induced hypertension. *International Journal of Gynaecology and Obstetrics*, 49, 125-130.
10. National Institute for Health and Clinical Excellence. (2014). Management of Preeclampsia. Hypertension in Pregnancy Pathway.
11. Steegers, E. A., Von Dadelszen, P., Duvekot, J. J., & Pijnenborg, R. (2010). Pre-eclampsia. *The Lancet*, 376(9741), 631-644
12. Thakur, V., Thakur, A., & Saroshe, S. (2016). Comparison of effect of nifedipine, labetalol and methyldopa in treatment of hypertension in pregnancy in a tertiary care government hospital. *International Journal of Reproduction, Contraception, Obstetrics and Gynecology*, 17.
13. Pentareddy, M. R., Shailendra, D., Prasuna, G., Subbaratnam, Y., Naresh, D., & Katta, R. (2017). Safety and efficacy of methyldopa and labetalol in controlling blood pressure in hypertensive disorders of pregnancy. *Int J Basic Clinic Pharmacol*, *6*(4), 942-947.
14. Trial, A. R., Alalfy, M., Eltaieb, E., & Soliman, M. (2018). Labetalol in Comparison to Methyl Dopa in Treatment of Gestational Hyperten-. 4(1), 1–10.
15. Babbar, K., Armo, M., & Bhanja, R. (2015). A comparative study of efficacy of antihypertensive drugs andfeto-maternal outcome in the treatment of pregnancy induced hypertension. *Int J Reprod Contraception, Obstet Gynecol*, 4(6), 1846–52.
16. Verma, R., Lahon, K., Tonpay, S. D., Kale, V. J., & Jain, D. K. (2012). A Comparative Randomised Controlled Parallel Group Study of Efficacy and Tolerability of Labetalol Versus Methyldopa in the Treatment of New Onset Hypertension during Pregnancy. *International Journal of Life Science and Pharma Research*, 2, 23–31.
17. El- Qarmalawi, A. M., Morsy, A. H., Al-Fadly, A., Obeid, A., & Hashem, M. (1995). Labetalol vs. methyldopa in the treatment of pregnancy-induced hypertension. *International Journal of Gynaecology and Obstetrics*, 49, 125-130.