DOI: https://doi.org/10.53350/pjmhs211592282

ORIGINAL ARTICLE

Comparison of Efficacy of Labetalol and Methyldopa in Gestational Hypertension

NAYYER SULTANA[1], RANA ABID ALI[2], UZMA ZIA[3], SHIRIN GUL[4], ABIDA RIAZ[5], TAYYABA MAJEED[6], ZAHID MAHMOOD[7]

[1]*Associate Professor Central Park Medical College, Lahore*
[2]*Senior Medical Officer Central Park Medical College, Lahore*
[3]*Assistant Professor Central Park Medical College, Lahore*
[4]*Senior Registrar Central Park Medical College, Lahore*
[5]*Associate Professor Sheikh Zayed Medical College Rahim Yar Khan*
[6]*Professor of Obs & Gynae, Central Park Medical College, Lahore*
[7]*Professor of Surgery, Lahore Medical & Dental College/Ghurki Trust Teaching Hospital, Lahore*
Correspondence to Dr. Tayyaba Majeed, Email: dr.tayyaba@hotmail.com, Cell: 0300-4315535

ABSTRACT

Aim: To compare the control of blood pressure after oral alpha methyldopa versus oral labetalol for management of gestational hypertension.
Study design: prospective, comparative, observational study.
Place & duration: The study was conducted at Department of Obstetrics & Gynecology, Central Park Teaching hospital, Lahore for six months i.e. 1st May 2018 to 31st October 2018.
Methodology: Total 150 females were included in the study from OPD after fulfilling the inclusion and exclusion criteria. Then females were randomly divided in two groups by using lottery method. In group A, females were given labetalol orally 100mg 2 times a day for 7 days. In group B, females were given 250mg methyldopa 3 times a day for 7 days. The females were followed-up in OPD after 8 days. After 8 days, females were evaluated for systolic blood pressure (SBP) & diastolic blood pressure (DBP).
Results: In this study we compared labetalol with methyldopa for management of gestational hypertension. 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 better controlled in patients received labetalol than alpha methyldopa. **Conclusion:** Labetalol is better than methyldopa in lowering blood pressure (systolic & diastolic) in women for management of gestational hypertension.
Keywords: Management, gestational Hypertension, Systolic, Diastolic, Blood pressure, Alpha methyldopa

INTRODUCTION

The Maternal mortality ratio of Pakistan is reduced to 186 deaths per 100,000 live births[1]. Although there is a decrease in MMR but it is still high as compared to developed countries[2]. One of the major contributors to MMR in Pakistan is hypertensive disorders of pregnancy[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]. 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].

Received on 11-04-2021
Accepted on 22-08-2021

A meta-analysis conducted to compare the efficacy and safety profile of alpha methyldopa and labetalol concluded that labetalol has better control of blood pressure in pregnancy and has less side effects than alpha methyldopa[10]. Another trial, conducted to compare efficacy of methyldopa and labetalol concluded that both have equal efficacy in controlling mean systolic blood pressure[11].

Resolution of gestational hypertension is necessary to prevent the female and baby from hazardous consequences. Literature has reported that labetalol can be more effective in controlling blood pressure as compared to methyldopa and can reduce the burden of unnecessary complicated pregnancies from hospitals. But controversial results have been noticed in literature. So we want to conduct this study to get local evidence. This will improve our practice as well as local guidelines for administration of labetalol for gestational hypertension.

The objective of our study is to evaluate the comparative efficacy of alpha methyldopa versus oral labetalol for control of blood pressure in gestational hypertension.

METHODOLOGY

A comparative, prospective, observational study was conducted for 6 months from 1st May 2018 to 31st October 2018 at Obstetrics & Gynaecology Department of Central Park Teaching Hospital, Lahore. Institutional approval was taken from ethical committee. A total 150 patients with

gestational hypertension presented after 20weeks of pregnancy were included in the study. The patients with multiple pregnancy, anemia, placenta previa, diabetes either gestational or present before pregnancy, pre-existing renal disease, proteinuric hypertension and severe pre-eclampsia were excluded. Informed consent was taken. Patients were allocated into two groups randomly by lottery method. In group A, females were given oral labetalol 100mg 2 times a day for 7 days. In group B, females were given 250mg methyldopa 3 times a day for 7 days. Then females were called for follow-up visit in OPD after 8 days. After 8 days, females were evaluated for systolic blood pressure (SBP) & diastolic blood pressure (DBP). Demographic details (name, age, gestational age, parity and BMI) were also noted. All this information was recorded on pre-designed proforma. SPSS version 21 was used to enter and analyze 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. Both groups were compared for mean BP by using independent sample t-test. 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

A total 150 patients were included. The mean age in group A was 26.73±4.86 and 27.32±4.46 was the mean age in group B. Mean gestational age of women in Group- A and in Group-B was 31.96±1.94 and 32.52±2.06 weeks respectively. In Group-A 22(29.3%) patients were having normal BMI, 25(33.3%) were overweight and 28(37.35%) were obese. In Group-B 23(30.7%) women were obese, 26(34.7%) were overweight and 26(34.7%) were having normal BMI. 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-A patients as that of Group-B patients. i.e. Group-A: 123.41 vs. Group-B: 126.62, p-value=0.009 (Table-1).

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-A patients. i.e. 77.18 vs. Group-B 79.64, p-value=0.005 (Table-2).

The DBP among women with gestational age 29-32 was notably lower in Group-A women. The SBP and DBP had no remarkable difference in both treatment groups among the women with 33-35 weeks of gestation (Table-3) 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).

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-5).

Table 1: Comparison of SBP on follow-up (Group-A: Labetalol, Group-B: Methyldopa) (n=150)

	Baseline-SBP		**After 8 days-SBP**	
	Group-A	**Group-B**	**Group-A**	**Group-B**
N	***75***	***75***	***75***	***75***
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	

Table-2: Comparison of DBP on follow-up (n=150)

	Baseline-SBP		**After 8 days-SBP**	
	Group-A	**Group-B**	**Group-A**	**Group-B**
N	***75***	***75***	***75***	***75***
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*	

Table 3: Comparison of change in blood pressure on follow-up stratified for Gestational age

GA	**SBP**		**p-value**	**DBP**		**p-value**
	Group-A	**Group-B**		**Group-A**	**Group-B**	
	75	***75***		***75***	***75***	
29-32	123.43±7.30	126.50±7.74	***0.088***	77.20±4.43	80.23±5.85	***0.014***
33-35	123.38±7.70	126.71±7.14	***0.057***	77.16±4.41	79.24±6.08	***0.107***

Table-4: Comparison of change in blood pressure on follow-up stratified for Parity

Parity	***SBP***		***P-value***	***DBP***		***P-value***
	Group-A	***Group-B***		***Group-A***	***Group-B***	
	75	***75***		***75***	***75***	
0	122.94±7.83	125.16±7.81	***0.457***	76.76±4.93	80.83±5.99	***0.055***
1-2	123.51±7.65	126.30±7.66	***0.144***	77.09±3.99	80.54±6.50	***0.012***
3-4	123.60±7.10	127.56±6.89	***0.041***	77.60±4.66	78.16±5.18	***0.675***

Table-5: Comparison of change in blood pressure on follow-up stratified for BMI

BMI	***SBP***		***p-value***	***DBP***		***P-value***
	Group-A	***Group-B***		***Group-A***	***Group-B***	
	75	***75***		***75***	***75***	
Normal	120.45±7.06	125.84±7.04	***0.011***	76.59±5.01	78.65±6.03	***0.209***
Overweight	124.96±7.70	128.96±7.86	***0.072***	77.92±4.16	80.26±5.79	***0.102***
Obese	124.35±7.00	124.87±6.64	***0.791***	77.00±4.14	80.04±6.21	***0.042***

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. 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 develop 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[11]. Our study has done comparison between labetalol and methyldopa only in achieving better control of blood pressure. Mahmoud Alalfy from Egypt in his randomized trial and others reported that Labetalol has less 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[13,14,15]. 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]. Nosheen Akhtar in her randomized controlled trail compared labetalol and methyldopa on mean DBP in patients with pre-eclampsia. Her findings showed that efficacy of both drugs was equal in reducing DBP and the difference was statistically not significant[17]. 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[6].

CONCLUSION

Labetalol is better than methyldopa in lowering blood pressure (systolic & diastolic) in women for management of gestational hypertension.

Conflict of interest: Nil

REFERENCES

1. Maternal mortality decreased to 186 deaths per 100,000 live births [Internet]. UNFPA Pakistan; 21 August 2020. Available from: https://pakistan.unfpa.org/en/news/maternal-mortality-decreased-186-deaths-100000-live-births
2. Tikkanen, R., Gunja, M., FitzGerald, M. and Zephyrin, L., 2021. Maternal Mortality Maternity Care US Compared 10 Other Countries | Commonwealth Fund. [online] Commonwealthfund.org. Available from: https://www.commonwealthfund.org/publications/issue-briefs/2020/nov/maternal-mortality-maternity-care-us-compared-10-countries
3. Khan, A., Izhar, V., & Amaar Viqar, M. Maternal morbidity and mortality in pakistan - an overview of major contributors. PAFMJ, 2017 June; 67(4), 635-40.
4. Sammour MB, El-Kabarity H, Fawzy MM, Schindler a. E. Prevention and treatment of pre-eclampsia and eclampsia. Vol. 97, Journal of Steroid Biochemistry & Molecular Biology. 2011. 439–440 p.
5. Kenny L, Myers J. Obstetrics by Ten Teachers. Boca Raton: Chapman and Hall/CRC; 2017. 169-219.
6. Easterling T, Mundle S, Bracken H, Parvekar S, Mool S, Magee LA et al. Oral Antihypertensive Regimens (Nifedipine Retard, Labetalol, and Methyldopa) for Management of Severe Hypertension in Pregnancy: An Open-Label, Randomized Controlled Trial. Obstetrical and Gynecological Survey. 2020 Feb 1; 75(2):81-83.
7. Gupta M, Khalili Y. Methyldopa [Internet]. Ncbi.nlm.nih.gov. 2021 [cited 10 July 2021]. Available: https://www.ncbi.nlm.nih.gov/books/NBK551671/
8. Nayak AS, Nachane HB. Risk analysis of suicidal ideations and postpartum depression with antenatal alpha methyldopa use. Asian J Psychiatr. 2018 Dec; 38:42-44.
9. Dwarkanath DSP, Shanmukh DKS. Comparison of methyldopa and labetalol in control of blood pressure in preeclampsia. Int. J. Clin. Obstet. Gynaecol. 2019; 3(5): 372-379.
10. 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. Tropical Journal of Obstetrics and Gynaecology. 2020; 37(1):119.
11. Pentareddy M, D. S, G. P, Y. S, D.T. V. N, 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(4):942.
12. Thakur V, Thakur A, Saroshe S. 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. 2016:17.
13. Trial AR, Alalfy M, Eltaieb E, Soliman M. Labetalol in Comparison to Methyl Dopa in Treatment of Gestational Hyperten-. 2018;4(1):1–10.
14. Babbar K, Armo M, Bhanja R. A comparative study of efficacy of antihypertensive drugs andfeto-maternal outcome in the treatment of pregnancy induced hypertension. Int J Reprod Contraception, Obstet Gynecol. 2015;4(6):1846–52.
15. Qasim A, Hussain Siddiqui M, Us Salam J, Nusrat U. Labetalol Versus Methyldopa: Efficacy in Pregnancy Induced Hypertension. Gomal J Med Sci. 2014;12(4):233–6.
16. 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. International Journal of Life Science and Pharma Research. 2012;2 :23–31.
17. Akhtar N, Hayat Z, Nazim F. Comparison betwen labetalol and methyldopa in the treatemnt of pre-eclampsia. 32(1):35–