

Comparison between methyldopa and combination of methyldopa and nifedipine in terms of mean change in blood pressure in pregnancy induced hypertension

BILQEES AKHTAR MALIK¹, SHAHZAD BASHIR MOMINA², TAZEEN ASHRAF³

¹Assistant Professor, Department of Obstetrics & Gynecology, Combined Military Hospital Bahawalpur

²Classified Gynaecologist, Assistan Professor, Combine military Hospital Chhor / National University of Medical Science (NUMS) Rawalpindi

³Specialist Obstetrics and Gynecology, Evercare Hospital Lahore

Correspondence to: Dr. Bilqees Akhtar Malik, Email: Bilqeesmalik123@outlook.com, Cell: 03218163294

ABSTRACT

Objective: Comparison between Methyldopa and combination of Methyldopa and Nifedipine in terms of mean change in blood pressure in pregnancy induced hypertension.

Material and methods: This randomized controlled trial was conducted at Department of Obstetrics and Gynecology, Combined Military Hospital Bahawalpur from February 2020 to August 2020 over the period of 6 months. Total 80 patients with pregnancy induced hypertension as per operational definition having age 20-40 years and having gestational age ≥ 20 weeks assessed on LMP were selected.

Results: Mean age of the patients was 30.81 ± 5.670 years, mean age of patients of group A was 31.50 ± 5.809 years and mean age of group B was 30.13 ± 5.515 years. Mean gestational age was 30.17 ± 5.981 weeks, mean gestational age of patients of group A was 29.70 ± 6.329 weeks and mean gestational age of patients of group B was 30.65 ± 5.65 weeks. In group A, mean diastolic blood pressure was decrease from 101.2250 ± 4.97938 to 84.5000 ± 3.26599 and in group B from 107.7750 ± 7.18434 to 82.5000 ± 2.25320 . Comparison of mean decrease in diastolic blood pressure between group A (High dose Methyldopa) and group B (Low dose Low dose Methyldopa with Nifedipine) was done. Mean decrease in diastolic blood pressure in group A was 16.72 ± 3.935 and in group B was 25.28 ± 6.876 . Statistically significant difference of mean decrease in diastolic blood pressure between the both groups was noted with p value 0.000.

Conclusion: Results of this study showed that Low dose Methyldopa with Nifedipine combination is more effective as compared to High dose Methyldopa to reduce diastolic blood pressure in pregnant women suffering from pregnancy induced hypertension.

Keywords: Diastolic blood pressure, Methyldopa, Nifedipine, Pregnancy induced hypertension, Systolic blood pressure

INTRODUCTION

Pregnancy induced hypertension is among the common medical problem affecting upto 15-20% of pregnancies and cause of significant maternal and perinatal mortality and morbidity.¹ Pregnancy induced hypertension ultimately leads to critical condition like preeclampsia and life threatening condition like Eclampsia and HELLP Syndrome.² So it is necessary to treat pregnancy induced hypertension.³ Numerous drugs including Methyldopa, Nifedipine, Hydralazine, Labetelol have been studied for its control.⁴ Methyldopa is among the preferred drugs for control of pregnancy induced hypertension as its safety during pregnancy has long been established⁵ but it controls blood pressure in about 4 to 6 hours and has side effects of over sedation at onset and impaired mental concentration and lassitude at high doses.⁶ Nifedipine is second line therapy for control of pregnancy induced hypertension.⁷ Nifedipine has rapid onset, longer duration of action and good oral bioavailability⁸ but has side effects at high dosage.^{5,9}

Poly pharmacy is preferred over monotherapy in control of hypertension due to adverse effects associated with monotherapy and different mechanism of action of each drug. Pharmacokinetics of both drugs show that effects of both drugs are balanced.⁶

Both drugs have been studied separately and their relative efficacy has been compared, but limited literature has been found comparing the combination therapy of both drugs at low dose with high dose of first line monotherapy. So if low dose is found to be more promising than the same will be used and advocated in patients with pregnancy induced hypertension. This will further cut down the cost of medication and will benefit poor patient of our community.

OPERATIONAL DEFINITION

Pregnancy induced hypertension is defined as raised blood pressure equal to or more than 160/100 at two separate occasions, four hours apart after 20 weeks of gestation assessed on last menstrual period.

High dose Monotherapy when one drug is used for treatment, selected monotherapy is Tab. Methyldopa 750mg thrice daily.

Low dose Combination therapy when two or more than two drugs are used for treatment, selected combination therapy is Tab. Methyldopa 250gm thrice daily with Tab. Nifedipine 10gm twice daily.

Mean change in diastolic blood pressure was recorded in admitted patients at start of treatment and after 96 hours of start of treatment, these readings was recorded in diastolic blood pressure in mmHg.

METHODS AND MATERIAL

This randomized controlled trial was conducted at Department of Obstetrics and Gynecology, Combined

Received on 17-02-2021

Accepted on 15-06-2021

Military Hospital Bahawalpur from February 2020 to August 2020 over the period of 6 months. Total 80 patients with pregnancy induced hypertension as per operational definition having age 20-40 years and having gestational age ≥ 20 weeks assessed on LMP were selected.

Patients with cardiac disease and diabetes mellitus (on history), patients with renal and thyroid disease (on history) and patients taking any other antihypertensive therapy were excluded from the study.

Study is approved by the ethical committee of the institution and written informed consent was taken from every patient.

Selected patients were divided into two study group A and B. In study group, Tab. Methyldopa 750mg thrice daily was given and in group B, Methyldopa 250gm thrice daily with Tab. Nifedipine 10gm twice daily were given.

Admitted patients were monitored by recording blood pressure. Fetal monitoring was done by clinical recording of fetal heart sounds and CTG.

Outcome measures was diastolic blood pressure at the start of treatment, and blood pressure was measured 4 hours apart after start of treatment during daytime and 6 hours apart during night time and mean of diastolic blood pressure was calculated at 48 hours and then at 96 hours. Data was collected from patient file on daily basis from

daily maintained blood pressure chart and was entered on Performa.

Data was collected in from of variables and was entered and analysis was done by SPSS-17.

Mean and SD was calculated for age, gestational age mean decrease in diastolic blood pressure for both groups. Student t test was applied to detect difference between the mean decrease in diastolic blood pressure of both treatment groups. Stratification for age, gestational age was done and post stratification student t test was applied to compare the mean decrease in diastolic blood pressure. P-value of less than and equal to 0.05 was taken as significant.

RESULTS

Mean age of the patients was 30.81 ± 5.670 years, mean age of patients of group A was 31.50 ± 5.809 years and mean age of group B was 30.13 ± 5.515 years.

Mean gestational age was 30.17 ± 5.981 weeks, mean gestational age of patients of group A was 29.70 ± 6.329 weeks and mean gestational age of patients of group B was 30.65 ± 5.650 weeks.

In group A, mean diastolic blood pressure was decrease from 101.2250 ± 4.97938 to 84.5000 ± 3.26599 and in group B from 107.7750 ± 7.18434 to 82.5000 ± 2.25320 . (Table 1)

Table 1: Mean diastolic blood pressure before and after treatment of both groups

Study Group	Mean diastolic BP before treatment		Mean diastolic BP after treatment	
	Mean	SD	Mean	SD
A	101.2250	4.97938	84.5000	3.26599
B	107.7750	7.18434	82.5000	2.25320

Table 2: Comparison of mean decrease in diastolic blood pressure between group A and B

Group	n	Mean	Std. Deviation	P Value
A High dose Methyldopa	40	16.72	3.935	0.000
B Low dose Methyldopa with Nifedipine	40	25.28	6.876	

Table 3: Comparison of mean decrease in diastolic blood pressure between group A and B for age groups

Group	n	Mean	Std. Deviation	P Value
Age group 20-30 years				
A High dose Methyldopa	17	17.41	4.214	0.001
B Low dose Methyldopa with Nifedipine	22	23.91	6.640	
Age group 31-40 years				
A High dose Methyldopa	23	16.22	3.729	0.000
B Low dose Methyldopa with Nifedipine	18	26.94	6.975	

Table 4

Group	n	Mean	Std. Deviation	P Value
Gestational age 20-30 weeks				
A High dose Methyldopa	21	17.14	4.078	0.000
B Low dose Methyldopa with Nifedipine	19	23.79	6.680	
Gestational age 31-40 weeks				
A High dose Methyldopa	19	16.26	3.827	0.000
B Low dose Methyldopa with Nifedipine	21	26.62	6.932	

Comparison of mean decrease in diastolic blood pressure between group A (High dose Methyldopa) and group B (Low dose Low dose Methyldopa with Nifedipine) was done. Mean decrease in diastolic blood pressure in group A was 16.72 ± 3.935 and in group B was 25.28 ± 6.876 . Statistically significant difference of mean decrease in diastolic blood pressure between the both groups was noted with p value 0.000. (Table 2)

Two age groups were created which are age group 20-30 years and age group 31-40 years. In age group 20-30 years, mean decrease in diastolic blood pressure in study group A was 17.41 ± 4.214 and in group B was 23.91 ± 6.640 . Difference was statistically significant between the both groups with p value 0.001 In age group 31-40 years, mean decrease in diastolic blood pressure in study group A was 16.22 ± 3.729 and in group B was 26.94 ± 6.975 . Difference was statistically significant between the both groups with p value 0.000 (Table 3)

Two groups were created according to gestational age, which are 20-30 weeks and 31-40 weeks. In 20-30 weeks gestational age group, mean decrease in diastolic blood pressure in study group A was 17.14 ± 4.078 and in group B was 23.79 ± 6.680 . Difference was statistically significant between the both groups with p value 0.000 In 31-40 weeks gestational age group, mean decrease in diastolic blood pressure in study group A was 16.26 ± 3.827 and in group B was 26.62 ± 6.932 . Difference was statistically significant ($P = 0.000$) between the both groups. (Table 4)

DISCUSSION

Blood pressure fluctuation and its maintenance during pregnancy is a challenging clinical problem to clinicians. The approach to evaluation and treatment differs substantially from non-pregnant women. Anti-hypertensive agents diminish the blood pressure and antihypertensive therapy in pregnancy induced hypertension is to prevent complications due to hypertension while advancement of pregnancy. The most commonly prescribed anti-hypertensive drugs are adrenergic receptor alpha-2 agonists such as Methyldopa, calcium channel blocker Nifedipine and Labetol.¹⁰⁻¹¹

In present study, in group A, mean diastolic blood pressure was decrease from 101.2250 ± 4.97938 to 84.5000 ± 3.26599 and in group B from 107.7750 ± 7.18434 to 82.5000 ± 2.25320 after treatment. Comparison of mean decrease in diastolic blood pressure between group A (High dose Methyldopa) and group B (Low dose Low dose Methyldopa with Nifedipine) was done. Mean decrease in diastolic blood pressure in group A was 16.72 ± 3.935 and in group B was 25.28 ± 6.876 . Statistically significant difference of mean decrease in diastolic blood pressure between the both groups was noted with p value 0.000.

In one study by Jayasudha et al,¹² blood pressure was decrease from 96 ± 6.21 to 82 ± 7.14 managed with methyldopa and in combination group (methyldopa and nifedipine) blood pressure was decreased from 112.5 ± 11.05 to 85 ± 6.88 .

Togarikar et al¹³ reported use of anti-hypertensive drugs had reduced SBP and DBP significantly. After the use of methyldopa, DBP reduced from 99.6 ± 8.8 to 96.17 ± 6.4 .

Another study by Bharathi KN et al¹⁴ stated both methyldopa and nifedipine showed equal effect on reducing the blood pressure. In another study, it is found that the use of anti-hypertensive drugs had reduced the systolic and diastolic blood pressure markedly. Diastolic BP before and after treatment were 100.07 ± 11.83 mmHg and 85.19 ± 8.52 mmHg respectively after use of methyldopa.¹⁵

CONCLUSION

Results of this study showed that Low dose Methyldopa with Nifedipine combination is more effective as compared to High dose Methyldopa to reduce diastolic blood pressure in pregnant women suffering from pregnancy induced hypertension.

REFERENCES

1. Magee LA, Abalos E, von Dadelszen P, Sibai B, Easterling T, Walkinshaw S et al. How to manage hypertension in pregnancy effectively. *Br J Clin Pharmacol*. 2011 Sep;72(3):394-401
2. Lamarca B. Endothelial dysfunction. An important mediator in the pathophysiology of hypertension during pre-eclampsia. *Minerva Ginecol*. 2012 Aug;64(4):309-20
3. Ghanem FA, Movahed A. Use of antihypertensive drugs during pregnancy and lactation. *Gardiovasc Ther*. 2008 Spring;26(1):38-49.
4. Vest AR, Cho LS. Hypertension in pregnancy. *Cardiol Clin*. 2012 Aug; 30 (3):407-23
5. Jeff M. Denney, Troy Flint Porter, D. Ware Branch. High Risk Pregnancy. Autoimmune Diseases. In: David James, Philip J. Steer, Carl P. Weiner, Bernard Gonik editors, High Risk Pregnancy, 4th ed. St. Louis: Saunders, An Imprint of Elsevier; 2010. p.783.
6. Katzung BG. Basic & clinical pharmacology. New York [u.a.: McGraw-Hill Medical; 2012.
7. De Souza AR, Amorim MR, Costa AR. Nifedipine antihypertensive treatment effects in pre-eclampsia. *Acta Med Port*. 2008 Jul-aug;21 (4):351-8.
8. Rezaei Z, Sharbaf FR, Pourmojeb M, Youefzadeh-Fard Y, Motevalian M, Khazaeipour Z et al. Comparison of the efficacy of nifedipine and hydralazine in hypertensive crisis in pregnancy. *Acta Med Iran*. 2011;49(11):701-6.
9. Khan K, Zamora J, Lamont RF, Van Geijn Hp H, Svare J, Santos-Jorge C et al. Safety concerns for the use of calcium channel blockers in pregnancy for the treatment of spontaneous preterm labour and hypertension: a systematic review and meta-regression analysis. *J Matern Fetal Neonatal Med*. 2010 Sep;23(9):1030-8.
10. Abalos E, Duley L, Steyn DW, Henderson-smart DJ. Antihypertensive drug therapy to mild to moderate hypertension during pregnancy. *Cochrane Library*. 2003;1.
11. Cvijic M, Horvat M, Jernejcic P, Verdenik I, Geršak K. Analysis of the intake of drugs used in hypertensive disorders during pregnancy. *Zdrav Vestn*. 2010;79:412-8.
12. Jayasudha J, Ismail AM, Senthamarai R. Evaluation on efficacy of Methyldopa monotherapy and combination therapy with Nifedipine in pregnancy-induced hypertension. *Der Pharmacia Lettre*. 2011;3:383-7.
13. Togarikar SM. Efficacy of methyldopa versus nifedipine in mild and severe pregnancy induced hypertension. *International Journal of Reproduction, Contraception, Obstetrics and Gynecology*. 2017 Sep 23;6(10):4544.
14. Bharathi KN, Prasad KVSRRG, Jagannath P, Nalini KS. Comparison of Nifedipine with Methyldopa for Control of Blood Pressure in Mild to Moderate Pregnancy Induced Hypertension. *J Clin Diagnos Res*. 2010;4(3):2406-9.
15. Venkateshwaramurthy N, Christy J, Perumal P. Study on antihypertensives in pre-eclampsia. *Asian Journal of Pharmaceutical and Clinical Research*. 2012;201(5):3.