

Original Research

Comparative evaluation of efficacy and safety of methyldopa and labetalol in pregnancy induced hypertension

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ABSTRACT:

Introduction: Hypertension is a common medical problem encountered during pregnancy and is associated with increased risk of adverse outcomes. Aim of our study was to compare efficacy and safety of Labetalol and Methyldopa in controlling blood pressure in patients with PIH and pre-eclampsia. **Methods:** A comparative, prospective observational, single center study was conducted for 1 year in women with PIH. Group A included 100 patients treated with Labetalol while Group B included 100 patients who were given Methyldopa. Response in lowering of BP was assessed over a period of 7 days. **Results:** Labetalol treated group of patients showed significant fall from 143.50±7.30mmHg/101.30±3.93 (systolic/diastolic) on 1st day to 126.10±5.49 mmHg/87.40±5.62 mmHg (systolic/diastolic) 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. Author found that MAP in Labetalol group reduced from 115.226±4.17 mmHg to 100.17±4.43 mmHg on day 7 while in Methyldopa group had MAP on admission 115.99±4.38 mmHg and on day 7 it reduced to 103.27±2.99mmHg which is highly significant. **Conclusions:** Labetalol controls systolic and diastolic blood pressure more rapidly and effectively than Methyldopa. Safety profile and adverse effects of Labetalol and Methyldopa are similar to each other.

Key Words: Labetalol, Methyldopa, Pregnancy induced hypertension

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INTRODUCTION

Hypertension is the most common medical problem encountered during pregnancy. Hypertension complicates up to 10% of all pregnancies and is associated with increased risk of adverse fetal, neonatal and maternal outcomes, including preterm birth, diabetes, chronic hypertension, perinatal death, acute renal or hepatic failure, antepartum

haemorrhage, postpartum haemorrhage and maternal death.¹ The risk of developing severe hypertension is reduced to half by using antihypertensive medications. Methyldopa is centrally acting adrenergic antagonist that acts by stimulating central alpha 2 receptors leading to decrease in sympathetic activity with resultant arterial dilatation and reduction in BP. Labetalol is a combined alpha and beta blocker, it has

arteriolar vasodilator effect that results in lower peripheral vascular resistance with little or no decrease in cardiac output. In the recent times there has been a shift towards the use of Labetalol for same purpose. The purpose of this study is to evaluate the comparative effectiveness of Methyldopa and Labetalol monotherapy in patients with pregnancy-induced hypertension.

MATERIAL AND METHODS

We conducted a comparative, prospective, observational single centre study conducted in women with pregnancy induced hypertension admitted in Obstetrics and Gynaecology Department in a tertiary care center for a period of one day after obtaining the ethical clearance. We included 200 patients of pregnancy induced hypertension who were divided into two groups i.e. Group A and Group B of 100 patients each. Subjects were divided into four categories: Gestational hypertension, Preeclampsia and eclampsia syndromes, Chronic hypertension, Preeclampsia superimposed on chronic

hypertension.³ The All patients diagnosed PIH as per NHBPEP i.e. BP more than 140/90 mmHg on two separate occasions 6 hours apart, with or without proteinuria (1+ dipstick in two midstream urine samples collected 4 hours apart) and after 20 weeks of pregnancy till term. We excluded Women with pre-existing or concurrent medical disorders Group A of 100 patients were given Labetalol 100mg TDS and if there was no fall in BP within 48 hours i.e. MAP < 106mmHg doses were doubled and were escalated up to 1.2gm/day in divided doses as per required.¹³ Group B of another 100 patients were given Methyldopa 250mg QID and if there was no fall in BP within 48 hours i.e. MAP< 106mmHg doses were doubled and increased up to maximum of 3 gm/day in divided doses.¹⁴ Observations were made as regards in fall of BP with each drug. Monitoring of systolic and diastolic BP was done 6 hourly, comparison of systolic and diastolic BP and mean arterial pressure was done on day 1 of admission and on day 7 after treatment with each drug in respective group.

RESULTS

In Methyldopa group, there were 52 (52%) patients in the age range of 21-25 years, while in Labetalol group, there were 51 (51%) cases. There were 47 (47%) cases from Methyldopa group in the age range of 26 - 30 years, while 45 in the Labetalol group. **Table 1**

Table 1: Demographics of the two groups

Patient details	Levels	Groups (Mean±SD)		P-value*
		Drug I: Methyldopa	Drug II: Labetalol	
Age (years)	21 - 25	52	51	0.3959 (NS)**
	26 - 30	47	45	
	> 30	1	4	

The difference between mean systolic and diastolic blood pressure was statistically insignificant on the day of admission for both the groups. Mean systolic blood pressure after treatment for the group treated using Methyldopa was 129.20±4.86mmHg, while it was 126.10±5.49mmHg for the group treated using Labetalol. The difference between the means was statistically highly significant with p-value <0.0001. **Table 2**

Table 2: Mean and SD for systolic and diastolic blood pressure between the groups before and after treatment

Blood pressure	Levels	Groups (Mean±SD)		P-value*
		Drug I: Methyldopa	Drug II: Labetalol	
Systolic				
	Pre	145.20±7.17	143.50±7.30	0.0983 (NS)
	Post	129.20±4.86	126.10±5.49	< 0.0001 (HS)
P-value**		< 0.0001 (HS)	< 0.0001 (HS)	
Diastolic				
	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

Also, the mean diastolic blood pressure seven days after treatment for the group treated using Methyldopa was

90.50±3.30mmHg, while it was 87.40±5.62mmHg for the group treated using Labetalol. The difference between the means was statistically highly significant with p-value <0.0001 For Methyldopa and Labetalol treatment groups, the difference between mean systolic and diastolic blood pressure before and seven days after treatment was statistically highly significant with p-value <0.0001 as obtained using paired t-test

Table 3 shows that the fall in systolic BP after 48 hours of starting treatment in Methyldopa group was by 2.1mm Hg whereas in patients treated with Labetalol systolic BP falls by 5.2mmHg. The diastolic BP falls by 3.8mmHg after 48 hours in group treated with Methyldopa and it falls by 7.8mmHg in Labetalol treatment group. Thus systolic and diastolic BP falls more rapidly in patients treated with Labetalol.

Table 3: Mean difference in fall of BP

Blood pressure	Duration	Groups (Mean fall in mmHg±SD)		P value
		Drug I: Methyldopa	Drug II: Labetalol	
Systolic	48 hours	2.1±1.47	5.2±2.99	<0.0001
Diastolic	48 hours	3.8±2.21	7.8±3.48	<0.0001

The MAP for patients in Methyldopa group was 115.99±4.38mmHg on day 1, while it was 115.226±4.17mmHg for patients in Labetalol group. The difference between means was statistically insignificant with p-value of 0.2093. However, on day 7, the mean MAP for patients in the group treated with Methyldopa was 103.27±2.99mmHg, while it was 100.17±4.43mmHg for patients treated using Labetalol. Thus the difference was statistically highly significant with p-value <0.0001 as obtained using t-test for independent samples. **Table 4**

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

MAP	Groups		P-value*
	Drug I: Methyldopa (n=100)	Drug II: Labetalol (n=100)	
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 provides the descriptive statistics for bishop score at the time of spontaneous onset of or induction of labour in the two treatment groups. The difference between means was statistically significant.

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

Bishop score	Groups		P-value*
	Drug I: Methyldopa (n=100)	Drug II: Labetalol (n=100)	
Mean ± SD	7.96±1.89	8.23±1.95	0.0232 (S)

DISCUSSION

There was reduction on the Labetalol and methyldopa group systolic/diastolic BP on day 7, Similar results were shown by study conducted by Qasim et al.⁴ Statistically significant reduction in systolic/diastolic BP was observed in case of Labetalol treated group. Study conducted by El Qarmalawi et al says that Labetalol provides more efficient control of BP than Methyldopa in treatment of hypertension in pregnancy.⁵ In our study we found that MAP difference in patients treated with Labetalol and Methyldopa were highly significant with p value of <0.0001. In study conducted by Jinturkar A et al MAP in patients treated with Methyldopa on admission was 109.86 mmHg while on day 7 it is reduced to 98.15mmHg with statistically significant p value of <0.05.⁶ With Labetalol MAP on admission was 109.48mmHg which reduced to 96.90mmHg on day 7

after treatment and this was statistically significant. This study also quoted that significant fall in Mean Arterial Pressure was seen in patients treated with Labetalol. Similar results were interpreted in a study conducted by Subhedar et al.⁷ In a similar study conducted by El Qarmalawi et al, 81.4% patients receiving Labetalol had significant fall in MAP as against 68.5% in patients taking Methyldopa.⁵ We found that systolic and diastolic BP falls more rapidly in patients treated with Labetalol as compared to Methyldopa. We also noted that Labetalol is more effective than Methyldopa in controlling blood pressure in patients with pregnancy - induced hypertension. Marked fall of both systolic and diastolic pressure, generally between 24 and 48 hours from the start of using Methyldopa, was noticed by Hans SF.⁸ Whereas in a study conducted by Jinturkar A et al, the mean time required to control BP in

Methyldopa group was 42.22 hours and in Labetalol group it was 36.97 hours.⁶ The difference between the two groups was statistically significant with Labetalol showing earlier control of BP than Methyldopa. Similar results were seen in study conducted by Subhedar et al.⁹ It is in accordance with the study conducted by Cruickshank DJ et al which observed that Labetalol had rapid control of BP in 88% of patients.¹⁰ Another study by Lardoux's also showed rapid fall in BP in 82% of patients treated with Labetalol while it was seen in 92% patients treated with Labetalol in study conducted by Michael et al.^{11,12}

CONCLUSION

Hypertensive disorders during pregnancy are a major cause of morbidity and mortality worldwide. Antihypertensive medications play an important role in managing maternal blood pressure. In our study we found that Labetalol controls systolic and diastolic blood pressure more rapidly and effectively than Methyldopa. The chances of spontaneous labour and normal vaginal delivery are more in Labetalol, thus Labetalol has ripening effect on cervix.

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