

Oral Labetalol Versus Oral Methyldopa for the Management Pregnancy Induced Hypertension

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ABSTRACT

Background: Hypertension is the major cause leading to maternal morbidity and mortality globally.

Aim: To compare the efficacy of oral Labetalol versus oral methyldopa for the treatment of pregnancy induced hypertension.

Methodology: This randomized controlled trial. was conducted in Department of Gynecology, Maula Buksh hospital teaching unit, Sargodha, Pakistan following the Hospital's Ethical Committee consent. Two groups with 175 females each received labetalol (at 100 twice daily) and methyldopa (at 250 mg twice daily) respectively. Continuous blood pressure monitoring was done and doses were adjusted according to requirement in first 24 hours. The effectiveness of drug was recorded 72 hours after the start of treatment in its capacity to lower the blood pressure below 140/90 mmHg. Numerical variables were presented as mean \pm SD. Achievement of blood pressure control were presented in the form of frequency and percentages. Chi square test was applied between achievements of blood pressure control by methyldopa versus labetalol with p-value \leq 0.05 as significant.

Results: In labetalol group, there were 148 (84.6%) cases who had controlled their blood pressure and in methyldopa group there were 123 (70.3%) of the cases had controlled their blood pressure. The success to control BP was higher in labetalol group when compared to methyldopa group having p-value $<$ 0.001.

Conclusion: Labetalol showed more efficacy than methyldopa in the management of pregnancy induced hypertension. Hence, oral labetalol can be an effective agent for better management of pregnancy induced hypertension.

Keywords: Hypertension, Labetalol, Methyldopa and Pregnancy.

INTRODUCTION

All Pregnancies results in high blood pressure by almost 6-10% and is the major cause leading to maternal morbidity and mortality¹. It is a leading cause of fetal growth retardation, fetal death, premature delivery and abruptio placentae². Long term health issues have also been noted with hypertension that includes chronic hypertension, retinal involvement, renal issues and neurological disorders³. Approximately 10-15% of maternal deaths seen in low and middle income countries are attributed because of pregnancy-induced hypertension⁴.

Hypertension in pregnancy can persist throughout the pregnancy and during post-partum or can appear first time after the delivery^{5,6}. According to NICE and American college of Obstetricians and Gynecologists (ACOG) , patients having blood pressure of 140/90 mm Hg should be offered treatment for hypertension^{7,8}. Eclampsia and Intracranial hemorrhage are the complications of untreated severe hypertension (\geq 160/110 mm Hg).⁶ This signifies the effective treatment of moderate to severe hypertension.

Multiple pharmacological treatments are available for the treatment of hypertension that includes oral and intravenous labetalol, intravenous hydralazine, oral nifedipine, amlodipine and methyldopa. The national institute of health and care excellence recommended to avoid usage of methyldopa and switch to alternative due to side effect of sedation, however during breast feeding it is the preferred anti-hypertensive^{9,10}. Due to increased ratio of

side effects of hydralazine; it is not used as first line drug and is better to be avoided. The ACOG committee (February 2019) recommends that oral nifedipine with immediate release should be used as first line therapy. For severe hypertension the other option is oral labetalol¹¹.

Methyldopa has been available for many years and is widely used as first line antihypertensive. However, recent studies have also shown labetalol as an effective antihypertensive but its superiority over methyldopa is still unclear. Multiple studies have been conducted to study and compare different drugs for the management of hypertension that include intravenous methyldopa, labetalol, hydralazine and immediate release oral nifedipine^{12,13}.

A study conducted by Lomte¹⁴ had shown the effect of methyldopa and labetalol on systolic and diastolic blood pressure for hypertension in time duration of 72 hours. It was noted that blood pressure falls by 50/30 mmhg with methyldopa, and 70/36 mmhg with labetalol in 72 hours. Also a study conducted by Qasim et al (2014) for control of pregnancy induced hypertension by methyldopa and labetalol showed similar results with significant fall in systolic/diastolic BP treated with labetalol as compared to methyldopa.^{15,16}

In our healthcare setting, we come across a huge group of females with hypertension in pregnancy or in the postpartum period. Due to limited resources, the best management for these patients is either labetalol or methyldopa for pregnancy induced hypertension. So, we conducted this study to compare and evaluate the effect of these medications in pregnant women with hypertension.

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The objective of the study was to compare the efficacy of oral labetalol versus oral methyldopa for the treatment of pregnancy induced hypertension.

METHODOLOGY

It was conducted in Department of Gynecology, Maula Buksh hospital teaching unit, Sargodha, Pakistan following the Hospital's Ethical Committee consent. All pregnant females (18-40 years age) with gestational week between 20 and 38 weeks (determined by last menstrual period) with pregnancy induced hypertension (>150/100 mmHg) requiring an antihypertensive medications were included in the study. Two groups with 175 females each received labetalol (at 100 twice daily) and methyldopa (at 250 mg twice daily) respectively. Continuous blood pressure monitoring was done and doses were adjusted according to requirement in first 24 hours. The effectiveness of drug was recorded 72 hours after the start of treatment in its capacity to lower the blood pressure below 140/90 mmHg. Patients with multiple pregnancies, placenta previa and pre-existing chronic kidney disease were excluded.

Statistical analysis: Data collected was analyzed by SPSS v17.0. Parameters like age, parity, BMI and gestational age were summarized as mean±SD. Qualitative variables like achievement of blood pressure control were presented in the form of frequency and percentages. Chi square test was applied with p-value ≤ 0.05 taken as significant. Data was stratified for age, parity and severity of hypertension at presentation. Chi square test (p ≤ 0.05) was applied to check statistical significance post-stratification.

Table-3: Stratification For Age, Parity And Severity Of Hypertension

Variables	Categories	Labetalol	Methyldopa	P-value
		Frequency & Percentage		
B.P control with respect to age	18-29 years	83 (83.8%)	77 (70.0%)	0.018
	30-40 years	65 (85.5%)	11 (14.5%)	0.033
B.P control with respect to parity	1-3 parity	93 (81.6%)	90 (73.8%)	0.151
	>3 parity	55 (90.20%)	32 (26.2%)	0.001
B.P control with respect to severity of blood pressure	Mild	18 (94.7%)	45 (69.2%)	0.024
	Moderate	52 (86.7%)	42 (71.2%)	0.038
	Severe	78 (81.2%)	36 (70.6%)	0.140

DISCUSSION

This study compared the role of oral labetalol and oral methyldopa for the management of pregnancy induced hypertension. Oral labetalol is more effective as compared to oral methyldopa in our study. The labetalol showed higher efficacy because it is an alpha-beta-adrenergic blocker, it is absorbed readily by oral route and achieves peak plasma concentration in only 20-60 minutes. Its therapeutic dose minimally effects the patients cardiac output. Our results are in accordance with the findings of Molvi et al. (2012) who documented better results with oral labetalol as compared to methyldopa¹⁷. They further reported that patients treated with labetalol had lower incidence of hypertension in females compared to women given methyldopa. Similarly, in a study by Qasim et al.

RESULTS

Parameters in both groups like age, parity, body mass index (BMI) and gestational-age were almost same (Table-1).

The success to control BP was higher in labetalol group when compared to methyldopa group with p-value<0.001 (Table 2).

Data was stratified for age, parity and severity of hypertension at presentation. In case of blood pressure severity, under mild, moderate and severe blood pressure condition, labetalol controlled more effectively (94.7%, 86.7% and 81.2%, respectively) rather than methyldopa group (69.2%, 71.2% and 70.6%, respectively) with insignificant p-value (Table-3).

Table-1: Demographic And Pregnancy Characteristics Among Enrolled Patients (n=350)

Characteristics	Labetalol Group	Methyldopa Group
	Mean ± S.D	
Age (years)	28.39 ± 6.11	28.14 ± 6.38
Parity	2.88 ± 1.54	2.88 ± 1.60
BMI (kg/m ²)	27.39 ± 5.71	26.92 ± 5.76
Gestational age (weeks)	28.71 ± 5.30	29.26 ± 5.50

Table-2: Efficacy Of Labetalol Vs Methyldopa For Pregnancy Induced Hypertension

Variables	Drugs	Frequency	%age
Blood pressure control after 72hrs	Labetalol	148	84.6%
	Methyldopa	123	77.4%
Test applied	P-value	0.001*	

*Statistically significant

(2014) it is concluded that labetalol is more efficacious with decreased fetal and maternal side effects in comparison to methyldopa¹⁵. Alike, Lamming¹⁸ reported that labetalol gave better results compared to methyldopa.

Another study shows that decrease in the systolic/diastolic Blood Pressure was quite significant with labetalol as compared to methyldopa in patients.¹⁸ Results from the study showed that labetalol was effective in lowering blood pressure in 81.4% of patients while methyldopa lowered blood pressure in 68.5% of patients.

Our study results are in accordance with the results of studies of Michal¹⁸ (92%) and lardoux's¹⁹ (82%) in controlling blood pressure with labetalol. A bundle of studies have shown the satisfactory effect of labetalol in pregnancy induced hypertension and confirmed its use with minimum maternal side effects and fetal side effects¹⁹.

Limitations: Lack of other serum markers with genetic study, limited resources and financial constrain are the limiting factors for this presented study. We confess this.

CONCLUSIONS

We concluded that both the drugs have good efficacy in stabilizing the blood pressure within 72 hours of starting the treatment. However, labetalol showed more efficacy than methyldopa in the management of pregnancy induced hypertension. Hence, oral labetalol can be an effective agent for better management of pregnancy induced hypertension. By using oral labetalol, we can further improve fetomaternal outcome by controlling pregnancy induced hypertension.

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