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Original Article

Labetalol versus Methyldopa for Treatment of Pregnancy Induced Hypertension

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ABSTRACT

Objective: To compare the mean fall in blood pressure with oral Labetalol versus Methyldopa in treating pregnancy induced hypertension.

Study Design: Quasi-experimental study.

Place and Duration of Study: Department of Gynecology, Combined Military Hospital, Bannu Pakistan, from Aug 2020-Feb 2021.

Methodology: After approval from institutional ethical committee and informed consent, sixty females with Pregnancy Induced Hypertension were included who were segregated into two groups. Group-A who took oral Labetalol 100 mg three or four times a day (up to 1200 mg per day) until the targeted blood pressure (<120/80 mmHg) was achieved. While Group-B took oral Methyldopa 250mg per day 3 to 4 up to 500 mg until targeted blood pressure(<120/80)was achieved. All patients were followed-up after one week of therapy. Primary outcome was mean fall in systolic and diastolic blood pressure after 5 days of treatment.

Results: The mean systolic and diastolic blood pressures were analogous in both Groups A and B, i.e. 152.33±6.53/100.33±4.54 mmHg versus 151.17±5.83/99.50±4.01 mmHg respectively. The mean fall in systolic BP in Group-A was 15.50±4.80 mmHg and in Group-B was 7.33±2.86 mmHg (p-value<0.0001) and mean fall in diastolic BP in Group-A was 13.17±5.80 mmHg compared to 5.50 ± 4.22 mmHg in Group-B (p-value<0.001).

Conclusion: We concluded that Labetalol is more effective in reducing blood pressure as compared to Methyldopa in Pregnancy Induced Hypertension.

Keywords: Labetalol, Methyldopa, Pregnancy induced hypertension.

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INTRODUCTION

The most prevalent disease during pregnancy is hypertension which is one of the main reasons that might result in the demise of mothers and fetuses affecting about 10% of pregnancies.[1] Preterm delivery, chronic hypertension, intrauterine fetal development retardation, perinatal death, acute renal failure, antepartum hemorrhage, postpartum bleeding, and maternal death are only a few of the consequences to mother, fetus, and neonates that are linked to hypertension.[2,3] Taking antihypertensive medication reduces the risk of getting severe hypertension by 50%.[4] The effectiveness of managing Pregnancy Induced Hypertension (PIH) can be attributed to the availability of many antihypertensive medication.[5]

PIH may classified into preeclampsia-eclampsia, preeclampsia on top of chronic hypertension, and pregnancy induced hypertension. The clinical manifestation is frequently moderate, consisting solely of mild term proteinuria and/or mild hypertension. However, in some situations, serious maternal and fetal issues such eclampsia, placentae, preterm labor, HELLP syndrome, fetal growth restriction, or even intrauterine fetal mortality, may happen.[6,7] Preeclampsia and gestational hypertension have no identified causes. Many of the related elements are recognized, though. Nulliparity, preeclampsia in a prior pregnancy, chronic hypertension in the family, chronic renal disease, antiphospholipid antibody syndrome, and hereditary thrombophilia are all risk factors for preeclampsia.[8,9]

The main objectives of antihypertensive treatment in pregnancy induced hypertension are to prolong pregnancy as much as possible and to avoid or treat severe hypertension (BP ≥160/110mmHg). Methyldopa, beta blockers, calcium channel blockers, and vasodilators are antihypertensive medications that may be taken during pregnancy safely and efficiently.

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Methyldopa has been available for many years and is frequently utilized.[7-10]

As pregnancy induced hypertension is still notorious for morbidity and mortality among a significant number of pregnant patients, our study is a quest for better antihypertensive for gravid patients since the empirical evidence obtained through our study will help us to formulate practical recommendations for better management of Pregnancy Induced Hypertension.

METHODOLOGY

After approval from Hospital Ethical Review Committee (Number. 03-005-22), the quasi-experimental study was conducted at the Department of Obstetrics and Gynecology, Combined Military Hospital, Bannu Pakistan. Sample size was calculated using WHO sample size calculator with the estimated population proportion was 10%.[10]

Inclusion Criteria: Females aged 18-45 years, presented at gestational age greater than 20 weeks and diagnosed with Pregnancy Induced Hypertension were enrolled, with PIH being labelled as blood pressure ≥140/90 mmHg on two separate occasions with time interval of 6 hours at minimum, without proteinuria (assessed by dipstick).

Exclusion Criteria: Patients with severe preeclampsia, proteinuria, chronic hypertension, on anti-hypertensive therapy or chronic renal failure were excluded.

Informed consent was taken from each patient. Two study groups were demarcated as: Group-A and Group-B (Figure). In Group-A, each patient was given an oral Labetalol 100 mg 6-hourly or 8-hourly to 1200 mg a day in divided doses until the targeted blood pressure <120/80 mmHg was achieved. While in Group-B, oral Methyldopa 250 mg was given 6-hourly or 8-hourly was increased up to 500 mg a day individed doses until targeted blood pressure was achieved (<120/80). The primary outcome was mean fall in blood pressure (both systolic and diastolic) which was measured after 5 days of treatment by subtracting mean post-treatment blood pressure from pre-treatment blood pressure.

Data was documented on a predesigned proforma and was analyzed using Statistical Package for Social Sciences (SPSS) version 26.0. Mean±SD was calculated for quantitative variables, and frequency and percentages were calculated for qualitative variables. Comparisons were made by independent t test. The *p*-value of ≤0.05 was considered statistically significant.

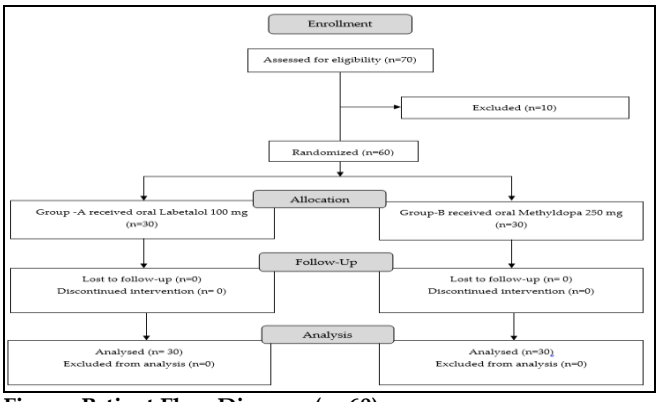

Figure: Patient Flow Diagram (n=60)

RESULTS

Age range of respondents in this study was from 18-45 years with mean of 31.63±5.87 years. In Group-A was mean age was 31.33±5.98 years and in Group-B it was 31.93±5.85 years. Mean gestational age was 29.02±3.45. Mean BMI was 29.69±2.97 kg/m² (Table–I).

Table-I: Demographics of the Respondents (n=60)

Variables		Study Groups	
		Labetalol-Group (n=30) Mean±SD	Methyldopa-Group (n=30) Mean±SD
AGE (Years)		31.33±5.98	31.93±5.85
Gestational Age (Weeks)		28.83 ± 3.46	29.30±3.45
BMI (kg/m²)		29.73±3.05	29.67±2.95
		Frequency (%)	Frequency (%)
Age Range (Years)	Age 31-45 Years	12(40%)	11(36.7%)
	Age 18-30 Years	18(60%)	19(63.3%)
Gestational Age Range (Weeks)	>28	13(43.3%)	11(36.7%)
	≤28	17(56.7%)	19(63.3%)
Parity	Primi	07(23.3%)	6(20%)
	Multi	23(76.7%)	24(80%)
Living Area	Rural	17(56.7%)	18(60%)
	Urban	13(43.3%)	12(40%)

The primary outcome was mean fall in blood pressure in both study groups. The mean pre-treatment systolic BP in Group-A was 152.33±6.53 mmHg, which was reduced to 136.83±7.48 mmHg, showing the mean fall in SBP as 15.50±4.80 mmHg while mean pre-treatment systolic BP in Group-B was

151.17±5.83 mmHg, which was reduced to143.83±5.68 mmHg, showing mean fall in systolic BP as 7.33±2.86mmHg (*p*-value<0.001). The mean pre-treatment diastolic BP in Group-A was 100.33±4.54 mmHg, which was reduced to 87.17±4.29 mmHg, showing mean fall in diastolic BP of 13.17±5.80 mmHg. The mean pre-treatment diastolic BP in Group-B was 99.50±4.01 mmHg, which was reduced to 94.0±5.78 mmHg after treatment, showing mean fall in diastolic BP of 5.50±4.22 mmHg (*p*-<0.001, Table– II).

Table-II: Comparison of Blood Pressure Before and After Medication (n=60)

Variables		Group-A (n=30)	Group-B (n=30)	*p*-value
		Mean±SD	Mean±SD	
SBP Before (mmHg)		152.33±6.53	151.17±5.83	0.471
Fall in SBP (mmHg)		15.50±4.80	7.33±2.86	0.001
SBP After (mmHg)		136.83±7.48	143.83±5.68	0.001
Fall in DBP (mmHg)		13.17±5.80	5.50±4.22	0.001
		Frequency (%)	Frequency (%)	
SBP Before (Range) mmHg	140-150	18(60%)	19(63.3%)	
	>150	12(40%)	11(36.7%)	
DBP Before (Range) mmHg	90-100	21 (70%)	24 (80%)	
	>100	9(30)	6(20)	

**SBP: Systolic Blood Pressure, DBP: Diastolic Blood Pressure*

DISCUSSION

The most typical medical issue that arises during pregnancy is hypertension.[12] There is a wide array of comorbid condition attributable to Pregnancy Induced Hypertension (PIH) including preterm birth, gestational diabetes, hypertension, perinatal mortality, renal compromise, hepatic failure and obstetric hemorrhage (antepartum and post-partum), all of which can adversely affect up to 10% of all pregnancies. Antihypertensive medication usage cuts the risk of getting severe hypertension in half. Nowadays, a lot of people utilize Labetalol. Methyldopa is an adrenergic antagonist with a central action that works by activating alpha 2 receptors, which causes a diminution in sympathetic activity, vasodilation predominantly arterial, and a drop in blood pressure. Due to its primary functions, it frequently causes adverse effects.[13-16] An alpha-beta blocker with an arteriolar vasodilator action, Labetalol reduces peripheral vascular resistance while having little to no effect on cardiac output.[17-19] This study was done to examine the average blood pressure drop caused by Labetalol against Methyldopa when treating pregnancy-related hypertension. We found that Labetalol was more effective at lowering blood pressure, than Methyldopa.

Labetalol was found to be responsible for mean reduction in systolic/diastolic blood pressure of 16.2± 3.548/11.9±3.46 mmHg, whereas Methyldopa caused a fall of 8.3±4.56/5.9±3.007 mmHg in one study.[11] This is line with our findings. Subhedar *et al*. found that MAP in individuals receiving Methyldopa treatment decreased from 110 mmHg upon admission to 98 mmHg approximately in a weeks' time. however, on 8th day onwards partitures taking Labetalol experienced a considerable drop in MAP.[20] Lamming et al., indicated that the mean MAP in both study groups was comparable prior to therapy but in group receiving Labetalol, MAP decreased significantly (*p*-< 0.05). [21]

In a related study, El Qarmalawi *et a*l. found that partitures taking experienced a substantial decrease in mean blood pressure at a rate of 81% compared to 69% in the Methyldopa group.[22] Cruickshank *et al.* found Labetalol successful in reducing blood pressure in eighty eight percent partitures within twenty-four hours. There is no denying the benefit of oral Labetalol's quick blood pressure control, which produces a good response in 88 percent (45/51) of cases within 24 hours.[23] It's intriguing that several other researchers have discovered comparable response rates, including CA Michael (92%) and Lardoux's group (82%).[21-25]

LIMITATIONS OF STUDY

Since the patients were not admitted, their compliance couldn't be observed directly. The lack of compliance could have resulted in bias.

CONCLUSION

We concluded that mean fall in blood pressure with Labetalol is higher as compared to Methyldopa in pregnancy induced hypertension and can be favored.

Conflic of Interest: None.

Authors Contribution

Following authors have made substantial contributions to the manuscript as under:

MA & SF: Study design, drafting the manuscript, approval of the final version to be published.

KM & UK: Data acquisition, data analysis, data interpretation, critical review, approval of the final version to be published.

AA & PA: Conception, data acquisition, drafting the manuscript, approval of the final version to be published.

Authors agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

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