Section: Obstetrics and Gynaecology

Original Research Article

COMPARISON OF THERAPEUTIC EFFECTS OF LABETALOL WITH OTHER ANTI-HYPERTENSIVE'S IN CONTROL OF HYPERTENSION IN P.I.H (PREGNANCY INDUCED HYPERTENSION) IN A TERTIARY CARE HOSPITAL

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Abstract

Background: Hypertension is a common medical problem encountered during pregnancy and is associated with increased risk of adverse outcomes. Objective of this study was to compare efficacy and safety of Labetalol and Methyldopa in controlling blood pressure in patients with PIH and pre-eclampsia. **Materials and Methods:** This study was conducted in pregnant patients with pregnancy induced hypertension admitted in Obstetrics and Gynaecology Department of NMCH, Patna, Bihar, a tertiary care centre. It included 200 patients of pregnancy induced hypertension which were divided into two groups i.e. Group A and Group B of 100 patients each. The criteria for diagnosis and classification of the hypertensive disorder of pregnancy were obtained according to National high blood pressure education program working group. **Results:** 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 128.20±3.86mmHg, while it was 125.10±4.49mmHg for the group treated using Labetalol. The difference between the means was statistically highly significant with p-value. **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.

INTRODUCTION

Hypertension is the most common medical problem encountered during pregnancy.[1] 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.[2-7] the risk of developing severe hypertension is reduced to half by using antihypertensive medications.[8] Labetalol is widely used nowadays. 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. It has high incidence of side effects because of its central actions.[9] 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.

The major goal of antihypertensive medication in PIH is to prevent or treat severe hypertension (generally defined as blood pressure of ≥160/110mmHg) and its associated complications and to prolong pregnancy for as long as possible.[10] Methyldopa has been used for control of blood pressure since a long time. 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.

The objective of this study was to compare efficacy and safety of Labetalol and Methyldopa in controlling blood pressure in patients with PIH and pre-eclampsia.

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MATERIALS AND METHODS

This study was conducted in pregnant patients with pregnancy induced hypertension admitted in Obstetrics and Gynaecology Department of NMCH, Patna, Bihar, a tertiary care centre. Study was conducted between June 2022 to May 2023.

It was a comparative, prospective, observational single centre study conducted in women with pregnancy induced hypertension admitted in Obstetrics and Gynaecology Department, NMCH, Patna, a tertiary care centre of Bihar.

All the pregnant women attending antenatal clinic were screened for and hypertensive pregnant women were included in the study after obtaining informed consent. It included 200 patients of pregnancy induced hypertension which were divided into two groups i.e. Group A and Group B of 100 patients each. The criteria for diagnosis and classification of the hypertensive disorder of pregnancy were obtained according to National high blood pressure education program working group.

According to this classification patient were divided into four categories

- Gestational hypertension,
- Preeclampsia and eclampsia syndromes
- Chronic hypertension
- Preeclampsia superimposed on chronic hypertension.[11,12]

Inclusion Criteria

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.

Exclusion Criteria

Multifetal pregnancy, Eclampsia, Women with pre-existing or concurrent medical disorders like diabetes mellitus, cardiac diseases, renal diseases, thyrotoxicosis, haemophilia and chronic hypertension. The patients were clinically examined for systolic and diastolic blood pressure

Technique

The measurements were taken in the sitting position in a chair after 20 minutes rest Inflate the cuff above the systolic pressure as recognized by disappearance of radial pulse. Use korotkoff V (disappearance of the sound) to determine diastolic blood Pressure. If the sound persists when the cuff is deflated use korotkoff IV (muffling of the sound).

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

[Table 4] provides the mean and standard deviation for systolic and diastolic blood pressure in the two treatment groups before and seven days after starting treatment. 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 128.20±3.86mmHg, while it was 125.10±4.49mmHg for the group treated using Labetalol. The difference between the means was statistically highly significant with p-value

Also, the mean diastolic blood pressure seven days after treatment for the group treated using Methyldopa was 89.50±2.30mmHg, while it was 86.40±4.62mmHg for the group treated using Labetalol. The difference between the means was statistically highly significant with p-value.

[Table 5] shows that the fall in systolic BP after 48 hours of starting treatment in Methyldopa group was by 2.0mm Hg whereas in patients treated with Labetalol systolic BP falls by 5.1mmHg. The diastolic BP falls by 3.7mmHg after 48 hours in group treated with Methyldopa and it falls by 7.7mmHg in Labetalol treatment group. Thus systolic and diastolic BP falls more rapidly in patients treated with Labetalol.

[Table 6] provides the descriptive statistics for mean arterial pressure (MAP) in two treatment groups. The MAP for patients in Methyldopa group was 114.99±3.38mmHg on day 1, while it was 114.226±3.17mmHg 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 102.27±2.99mmHg, while it was 99.17±4.43mmHg for patients treated using Labetalol. Thus the difference was statistically highly significant with p-value.

[Table 7] 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 1: Distribution of patients according to age

Variable	Group (Mean±SD)		Total	P value	Significance
	Drug1: Methyldopa	Drug2: Labetalol			
21-25 years	54(52.42%)	52(54.16%)	106(53%)	0.3959	NS
26-30 years	43(41.74%)	37(38.54%)	80(40%)	0.3959	NS

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31-35 years	5(4.85%)	3(3.12%)	9(4.5%)	0.3959	NS
>35 years	1(0.97%)	4(4.16%)	5(2.5%)	0.3959	NS
Total	103(100%)	96(100%)	200(100%)	--	--

NS= Not significant, S=Significant, HS (Highly significant)

Table 2: Distribution of patients according to education

Education	Drug1: Methyldopa	Drug2: Labetalol	Total	P value	Significance
Primary	45(45%)	52(52%)	97(48.5%)	0.315	NS
Secondary	25(25%)	16(16%)	41(20.5%)		
Graduate	30(30%)	32(32%)	62(31%)		
Total	100(100%)	100(100%)	200(100%)	--	--

Table 3: Distribution of patients according to socio-economic factors

Socio-economic factors	Drug1: Methyldopa	Drug2: Labetalol	Total	P value	Significance
Lower class	50(50%)	56(56%)	106(53%)	0.215	NS
Lower middle class	14(14%)	12(12%)	26(13%)		
Upper Middle class	24(24%)	22(22%)	46(23%)		
Higher class	12(12%)	10(10%)	22(11%)		
Total	100(100%)	100(100%)	200(100%)	--	--

Table 4: Mean and standard deviation for systolic and diastolic blood pressure in two treatment groups before and after treatment

Blood pressure	Group (Mean±SD)		P value
	Drug1: Methyldopa	Drug2: Labetalol	
Systolic:			
Pre	144.20±6.17	142.50±6.30	<0.0983(NS)
Post	128.20±3.86	125.10±4.49	<0.0001(HS)
P value	<0.0001(HS)	<0.0001(HS)	
Diastolic			
Pre	100.60±3.20	100.30±2.93	<0.6205(NS)
Post	89.50±2.30	86.40±4.62	<0.0001(HS)
P value	<0.0001(HS)	<0.0001	

Table 5: Mean difference in fall of BP

Blood pressure	Duration	Groups (Mean fall in mmHg±SD)		P value
		Drug1: Methyldopa	Drug2: Labetalol	
Systolic	48 hours	2.0±4.6	5.1±2.98	<0.0001
Diastolic	48 hours	3.7±2.20	7.7±3.48	<0.0001

Table 6: Descriptive statistics for MAP at day 1 and 7 in two groups

MAP	Group		P value
	Drug1: Methyldopa (n=100)	Drug2: Labetalol (n=100)	
Day 1	114.99±3.38	114.226±3.14	0.2093(NS)
Day 7	102.2.99±1.99	99.17±3.43	<0.0001(HS)

Table 7: Descriptive statistics for Bishop Score in two treatment groups

Bishop score	Groups		P value
	Drug1: Methyldopa (n=100)	Drug2: Labetalol (n=100)	
Mean±SD	7.94±1.87	8.21±1.93	0.0232(S)

DISCUSSION

Table 1 shows the distribution of patients according to age. 96 patients receiving Labetalol and 103 patients receiving Methyldopa. Both groups were statistically comparable with respect to age distribution. Similarly in the study conducted by Jinturkar A et al, maximum number of patients in group A treated with Methyldopa and group B with Labetalol were in the age group of 15 to 24.[15] In the study conducted by Dharwadkar et al the mean age of patients for Methyldopa group was 25.95±3.94 years and for Labetalol group was 26.65±3.73 years.[16] In a study conducted by Pentareddy et al, the mean age of the patients in the Methyldopa group was 22.3 years while it was 23.23 years in Labetalol group and both groups were statistically comparable.[17]

In Labetalol group systolic/diastolic BP on 1st day was 142.50±6.30mmHg/100.30±2.93 respectively and was controlled to 125.10±4.49mmHg/86.40±4.62mmHg on day 7, while systolic/diastolic BP in methyldopa group on 1 st day was 144.20±6.17mmHg/100.60±3.20mmHg which was reduced to 128.20±3.86mmHg/ 89.50±2.30mmHg on day 7. Similar results were shown by study conducted by Qasim et al, in which patients treated with Labetalol systolic/diastolic BP on admission (1st day) was 150±9mmHg/100±8mmHg respectively and was controlled to 123±9mmHg/79±7mmHg on day 7th

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while systolic/diastolic BP in Methyldopa treated group on the day of admission (1st day) was 148±8mmHg/102±9mmHg which was reduced to 125±10 mmHg/82±6mmHg.[18] Statistically significant reduction in systolic/diastolic BP was observed in case of Labetalol treated group. This is in accordance with the study done by Lamming et al.[10] Study conducted by El Qarmalawi et al says that Labetalol provides more efficient control of BP than Methyldopa in treatment of hypertension in pregnancy.[19] In a study conducted by Wallin JD and Wilson D, Eighty-one severely hypertensive patients were enrolled in a multicenter, double-blind, parallel group study evaluating the efficacy and safety of Labetalol alone or in combination with furosemide versus Methyldopa in combination with furosemide.[20] Moreover, after six months and one year of treatment, respectively, Labetalol caused a significantly ($p < 0.05$) greater reduction in the systolic blood pressure than the Methyldopa regimen. In our study we found that MAP in patients treated with Labetalol on admission was 114.226±3.17mmHg while on day 7 it was reduced to 99.17±3.43mmHg while patients treated with Methyldopa had MAP on admission 114.99±3.38mmHg and on day 7 after treatment it is reduced to 102.27±1.99mmHg. This is 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 < 0.05.15 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 interpretated in a study conducted by Subhedar et al.[21] 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.[19] Study conducted by Lamming et al, quoted that the average MAP in both groups was same before treatment and there was a highly significant fall in MAP in the group treated with Labetalol ($p < 0.001$) but no significant fall in group treated treated with Methyldopa.[10] In our study we found that the fall in systolic BP after 48 hours of starting treatment in Methyldopa group was by 2.1mmHg 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. This shows that systolic and diastolic BP falls more rapidly in patients treated with Labetalol as compared to Methyldopa.

In a study conducted by Lomte D et al, a total of 60 eligible patients were randomized to receive Methyldopa ((n=30), or Labetalol ((n=30).[22] Antihypertensive treatment with Methyldopa was associated with reduction in systolic BP by 50 mmHg and diastolic BP by 30 mmHg at 72 hours. For the same period treatment with Labetalol was associated with reduction in systolic BP by 70mmHg and diastolic BP by 36mmHg at 72 hours. Thus 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.[23] 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.[15] 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. It is in accordance with the study conducted by Cruikshank DJ et al which observed that Labetalol had rapid control of BP in 88% of patients.24 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.[25,26]

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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