Comparison of Efficacy of Labetalol and Methyldopa in Patients with Pregnancy Induced Hypertension

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Research Article

Abstract: Despite developments in health services, maternal mortality is still very high in India. Pregnancy induced hypertension and its complications still rank amongst major cause of maternal mortality in semi urban setups like us. Antihypertensive drugs are often used to lower blood pressure and also help in reducing maternal and fetal complications. Hence, this study was planned to assess and compare efficacy of labetalol and methyldopa in controlling blood pressure in patients with pregnancy induced hypertension and study maternal and perinatal outcome in rural Indian population. **Methods:** 180 patients with pregnancy induced hypertension were divided into two groups randomly. After randomization, group a received methyldopa 250 mg tid and group B received labetalol 100 mg tid. Mean arterial pressure (MAP) was calculated according to formula – systolic BP+2 diastolic BP/3. Patients were subjected to 6 hourly BP monitoring. Comparison of two drugs was done daily by calculating MAP of two groups. Following observations were made as regards fall in BP with labetalol/methyldopa, time required to control BP, onset of labour spontaneous/induced, Bishop Score at induction of labour, side effects of drugs. **Results:** Significant fall in MAP was seen in patients receiving labetalol. Mean time required controlling BP in group A was 42.22 hrs and in group B it was 36.97 hrs. Mean Bishop Score at induction in present study in group A was 8.27 and in group B was 9.33 with a statistically significant $\rho < 0.05$. 33.33% patients went in spontaneous labour in group a while in group B 23 patients (48.94%) patients went in spontaneous labour. **Conclusion:** The freedom from maternal and fetal side effects, the efficient hypotensive action indicates that labetalol is suitable for use during pregnancy.

Keywords: Pregnancy, Hypertension, Labetalol, Methyldopa, Efficacy.

Introduction

Maternal mortality rate is high in India despite progress and development in health services. The analysis of causes of maternal deaths highlight the fact that majority of these deaths are preventable. Hypertensive disorders seem to complicate approximately 10% of pregnancies and are important causes of maternal and fetal mortality and morbidity[1]. Globally around 6-8% of pregnancies are complicated by hypertension[3]. Hypertension is the most common medical problem encountered during pregnancy[2]. It is said that preeclampsia and eclampsia contribute to death of a woman every 3 minutes worldwide[2, 4]. Today, though oral medications are available and widely used for the treatment of PIH, the physicians still have to deal with many challenges. Antihypertensive drugs are often used to lower blood pressure with the aim of preventing its progression to adverse outcomes for the mother and the baby. The risk of developing severe hypertension is reduced to half by using antihypertensive medications[5]. Severe hypertension is treated to prevent severe maternal complications[6]. Methyldopa, labetalol and long acting nifedepin are acceptable oral antihypertensive agents in pregnant women with mild to moderate hypertension. This study was planned to assess and compare efficacy of labetalol and methyldopa in controlling blood pressure in patients with PIH and to study maternal and perinatal outcome in rural Indian population.

Aims and Objectives

1. Comparison of efficacy of labetalol and methyldopa in controlling blood pressure in patients with PIH.
2. To study maternal and perinatal outcomes in both the groups.

Methods

This study was conducted in the Department of Obstetrics and Gynecology Government Medical College, Latur. Over a period of 1 yr. (Sept. 2011- Sept. 2012) after taking ethical committee clearance.

Population being investigated: Pregnancy induced hypertensive women after 20 wks of pregnancy at Govt. Medical College, Latur over a period of 1 yr. from Sept. 2011- Sept.2012

Sample Size: 180 Patients of PIH of which 90 were given labetalol and 90 were given Methyldopa. Patients were selected for the study by subjecting to following

1. History
2. Clinical examination – general and systemic examination.

Indusion Criteria: Diagnosed PIH patients based on criteria BP more than 140/90 mmHg on two separate occasions 6 hrs apart, proteinuria 1+ dipstick in two midstream urine samples collected 4 hrs apart and gestational age more than 20 wks of pregnancy.

Exclusion Criteria:
Multi fetal pregnancy, eclampsia and women with preexisting or concurrent medical disorders like diabetes mellitus, cardiac disease, renal disease, thyrotoxicosis, hemophilia and chronic hypertension. Patients were divided into two groups randomly. After randomization, group A received methyldopa 250mg tid and group B received labetalol 100mg tid. Mean arterial pressure (MAP) was calculated according to formula systolic BP+2 diastolic BP/3[8]. Patients were subjected to 6 hrly BP monitoring. Comparison of two drugs was done daily by calculating MAP of two groups. If there was no fall in BP even after 48 hrs of drug therapy, dose of the drug was doubled. Response in lowering BP was assessed over a period of 7 days. Observations were made as regards fall in BP with labetalol/methyldopa, time required to control BP, average dose of drugs required to control BP, onset of labour spontaneous/induced, Bishop score at induction of labour and side effects of drugs. The results thus obtained were subjected to standard statistical analysis and analyzed using the Chi-square test. A ρ value of less than 0.05 was considered statistically significant.

Results

I. According to figure 1, among total 180 patients, maximum number of patients i.e. 92 belonged to age group 15-24 yrs, 48 patients (53.33%) in group A and 44 patients (48.89%) in group B. The mean age of the patients in group A was 24.41 yrs and in group B was 24.84 yrs. The mean age was statistically non significant in both the groups.

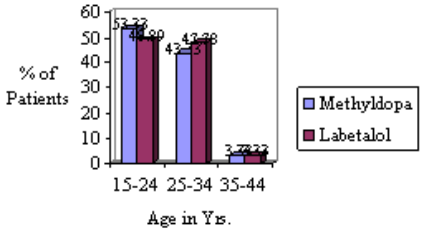

Figure 1: Age wise Distribution of patients in both the Groups

II. Figure 2 states that in present study 102 patients were primigravidae, 53 patients (58.89%) in group A and 49 patients (54.44%) in group B. The difference between the two groups was statistically non significant.

Table 1*:* Comparison of MAP in both groups of Day 1 and Day 7

	Group	N	Mean(mmHg)	Std. Deviation	Mean Difference	Z-value	ρ-value
Day 1	Methyldopa	90	109.86	2.91	0.37±0.42	0.88	0.37NS,ρ>0.0
	Labetalol	90	109.49	2.78			
Day 7	Methyldopa	90	98.15	3.44	1.24±0.46	2.68	0.008,S,ρ<0.05
	Labetalol	90	96.90	2.70			

Table 2: Comparison of Time to control BP in both the groups.

Group	N	Mean(hours)	Std. Deviation	Std. Error Mean	Z-value	ρ-value
Methyldopa	90	42.22	3.04	0.32	11.74	0.000,S,ρ<0.05
Labetalol	90	36.97	2.94	0.31		

III. Table 1 Shows comparison of MAP in both the groups on Day 1 and Day 7. In the present study, the MAP in patients treated with methyldopa on admission was 109.86 mmHg while on day 7 it reduced to 98.15mmHg with a statistically significant ρ value <0.05, With labetalol, the MAP on admission was 109.48 mmHg which reduced to 96.90 mmHg on day 7. Reduction in MAP was statistically significant. On comparing the two drugs, MAP on admission were comparable but on day 7 significant falls in MAP was seen in patients receiving labetalol.

IV. Table 2 shows comparison of time to control BP in both the groups. In the present study, the mean time required controlling BP in group A was 42.22 hrs and in group it was 36.97 hrs. The difference between the two groups was statistically significant with labetalol showing earlier control of BP than methyldopa.

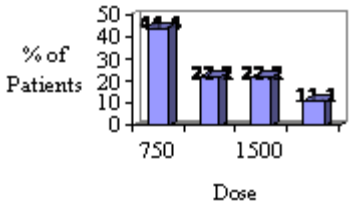

Figure 3: Distribution of Patients according to dose in methyldopa group

V. Figure 3 shows the mean dose required to control BP in group A was 1111.11mg. In group A, 40 patients (44.4%) required dose of 750 mg/day to achieve optimal BP control. Out of the remaining 40 patients, 20 patients (22.2%) required a dose of 1000 mg/day to achieve optimal BP control while remaining 20 patients (22.2%) required a dose of 1500 mg/day. 10 patients had to take 2000 mg/day to achieve optimal BP control.

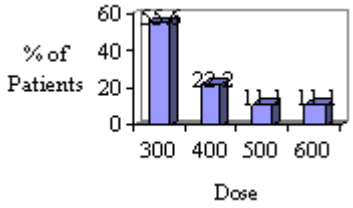

Figure4: Distribution of Patients according to dose in labetalol group

VI. Figure 4 says in group B the mean dose required was 382.22 mg. 50 patients (55.6%) had their BP controlled with 300mg/ day. 20 patients (22.2%) required a dose of 400mg/day. Of remaining 20 patients, 10 patients (11.1%) required a dose of 500mg/day 600mg/day. and 10 patients (11.1%) required dose of

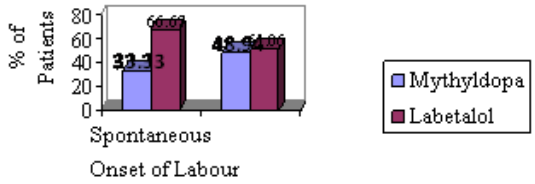

Figure 5: Distribution of patients according to onset of labour who delivered vaginally

VII. Figure 5 in the present study 9 patients in group a went in spontaneous labour while 18 patients were induced. In group B 23 patients went in spontaneous labour and 24 patients were induced these values were found to be statistically significant. Thus rate of spontaneous labour was more in patients treated with labetalol. This may be accounted to the fact that labetalol has ripening effect on the cervix.

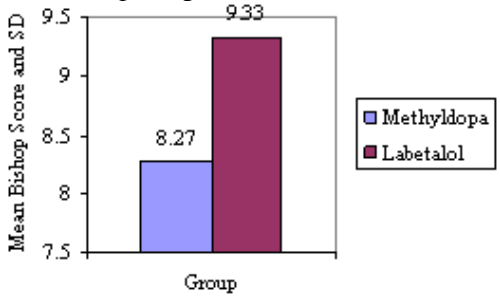

Figure 6: Comparison of Bishop Score in both the groups

VIII. Figure 6 depicts comparison of Bishop Score in both the groups. Mean Bishop score at induction in present study in group A was 8.27 and in group B was 9.33 with a statistically significant $\rho<0.05$.

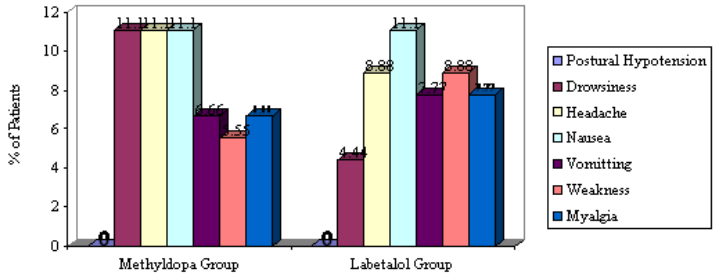

Figure 7: Distribution of patients according to side effects

IX. Figure 7 shows distribution of patients according to side effects. In the present study, most common side effect observed was headache. 10 patients in group A and 8 patients in group B had this symptom. The other side effects included drowsiness, more in patients treated with methyldopa, weakness, more in patients treated with labetalol. The incidence of side effects such as nausea, vomiting, myalgia was similar in both the groups.

Discussion

Among the total 180 patients in the present study, maximum number of patients in both the groups, group A and group B were in the age group of 15 to 24 years. Gravidity distribution showed maximum patients of PIH as primigravidae in both the groups. In the present study, the MAP in patients treated with methyldopa on admission was 109.86 mmHg, while on day 7 it reduced to 98.15 mmHg, with a statistically significant ρ value <0.05. With labetalol, the MAP on admission was 109.48mmHg which reduced to 96.90mmHg on day 7. Reduction in MAP was statistically significant. On comparing the two drugs, MAP on admission were comparable but on day 7, significant fall in MAP was seen in patients receiving labetalol. According to a study conducted by Lamming *et al*, the average MAP in both groups was same before treatment. There was a highly significant fall in MAP in the group treated with labetalol (ρ<0.00) but no significant fall was noted in the group treated with methyldopa (ρ>0.05)[8]. In a similar study conducted by El Qarmalawi *et al*, 81.4% patients in labetalol group had a significant fall in MAP as against 68.5% in patients taking methyldopa[8]. In the present study, the mean time required to control BP in group A was 42.22 hours and in group B it was 36.97 hours. The difference between the two groups was statistically significant with labetalol showing earlier control of BP than methyldopa. In a study conducted by Sanders *et al*, the average time to achieve optimal BP control was similar in both the groups[10]. DJ. Cruickshank, *et al*[11] observed that Labetalol did control the blood pressure in 45 of the 51 treated women (88%) within 24hrs. The rapid control of blood pressure with oral labetalol achieving a satisfactory response in 88% (45/51) of cases within 24 h is an obvious advantage. It is interesting that several other workers have found similar response rates – Lardoux's group 82%, CA Michael 92%[12, 13]. Marked fall of both systolic and diastolic pressure generally between 24 and 48 hours from the start of using methyldopa was noticed by S.F.Hans[14]. The mean dose required to control BP in group A was 1111.11mg. In group A, 40 patients (44.4%) required a dose of 750mg/day to achieve optimal BP control. Out of remaining 40 patients, 20 patients (22.2%) required a dose of 1000mg/day to achieve optimal BP control while remaining 20 patients (22.2%) required a dose of 1500mg/day, 10 patients had to take 2000mg/day to achieve optimal BP control. In group B the mean dose required was 382.22mg, 50 patients (55.6%) had their BP controlled with 300mg/day. 20 patients (22.2%) required a dose of 400mg/day. Of remaining 20 patients, 10 patients (11.1%) required a dose of 500mg/day and 10 patients (11.1%) required a dose of 600mg/day. In a study conducted by Sanders *et al* maintenance doses for labetalol and methyldopa averaged 810 mg/day and 1183mg/day respectively. In present study average dose of labetalol required to achieve optimal BP control was much less than in above mentioned study, but for methyldopa doses were comparable[10]. Lardoux's group found that the average daily dose of labetalol required for satisfactory blood pressure control was 600mg[12]. In the present study, 9 patients in group A (33.33%) went in spontaneous labour while 18 patients (66.67%) were induced. In group B, 23 patients (48.94%) went in spontaneous labour and 24 patients (51.06%) were induced. These values were found to be statistically significant with ρ<0.05. Thus the rate of spontaneous labour was more in patients treated with labetalol. This may be accounted to the fact that labetalol has ripening effect on the cervix. The observation made by Qarmalawi *et al* suggest higher incidence of spontaneous onset of labour in the labetalol group[9]. Lamming *et al* too reported a higher incidence of spontaneous labour in the labetalol group[8]. Mean Bishop Score at induction in present study in group A was 8.27 and in group B was 9.33 with a statistically significant ρ<0.05. Lamming *et al* reported a higher Bishop score of 10 in patients treated with labetalol as compared to a mean Bishop score of 7.1 in patients treated with

methyldopa[8]. In the present study, most common side effects observed was headache. 10 patients in group A and 8 patients in group B had this symptom. The other side effects included drowsiness, more in patients treated with labetalol. The incidence of side effects such as nausea, vomiting, myalgia was similar in both the groups. Study conducted by Verma *et al* states that adverse events observed were lower in the labetalol treated group compared to the methyldopa group[15]. In a study by Qarmalawi *et al*, patients receiving methyldopa complained of side effects such as drowsiness (22.22%), headache (14.8%), nasal congestion (7.4%), postural hypotension (5.6%) [9]. 6 patients in labetalol group complained of dyspnoea, no other side effects were noticed.

Conclusions

Present study showed that labetalol is more advantageous than methyldopa in terms of better and quicker control of blood pressure. The chances of spontaneous onset of labour were greater in the labetalol group than in the methyldopa group. Those patients on labetalol, who required induction of labour were noted to have a better Bishop score at the time of induction. The freedom from maternal and fetal side effects, the efficient hypotensive action and consequent improved perinatal mortality in a condition usually accompanied by high fetal loss, indicate that labetalol is suitable for use during pregnancy. The only limiting factor in use of labetalol is economic constraints among rural population of India.

Funding

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Ethical Approval

The study was approved by the Institutional ethics committee.

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