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Comparative study of efficacy of methyldopa vs labetalol in the management of pregnancy induced hypertension in respect to maternal and perinatal outcomes

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ABSTRACT

This study was a prospective, comparative study, used to determine & compare the efficacy of treatment with methyldopa vs labetalol with respect to maternal – perinatal benefits and adverse effects. Conducted in the Department of Obstetrics and Gynaecology in Vivekananda Institute of Medical Science, Ramakrishna Mission Seva Pratishthan, a total 425 patients were taken into the study. The patients were divided into two groups by simple random sampling method. They were monitored throughout pregnancy and delivery till 7 days postpartum. The results obtained were divided in 3 sections- Effective BP control, Maternal outcome, Perinatal outcome, which were again divided into three periods – Antepartum, Intrapartum and Postpartum for better elaboration. The study revealed that labetalol helps in quicker and more efficacious control of BP in mothers developing gestational hypertension with chances of developing preeclampsia – eclampsia syndrome.

Keywords: PIH, Methyldopa, Labetalol

INTRODUCTION

Hypertensive disorders are the most common medical complications of pregnancy, affecting 5% to 10% of all pregnancies[1] and accounts for approximately a quarter of all antenatal admissions. These disorders are responsible for approximately 31% maternal mortality in developing countries of which 24.7% is due to eclampsia.[2] Despite years of research in this field however, there remains lack of consensus on the classification / definition of hypertensive disorders of pregnancy, the blood pressure at which antihypertensive therapy needs to be initiated, what constitutes an appropriate antihypertensive agent in pregnancy and the maternal-fetal-risk-benefit ratio of treatment. This study is used to determine & compare the efficacy of treatment with methyldopa vs labetalol with respect to maternal – perinatal benefits and adverse effects.

MATERIALS AND METHODS

The study was a prospective, comparative study conducted in the Department of Obstetrics and Gynaecology in Vivekananda Institute of Medical Science, Ramakrishna Mission Seva Pratishthan, Kolkata from 1st November, 2009, to 31st October, 2011. Total 425 patients were taken into the study out of which 25 got themselves delivered outside and amongst the rest half were allotted in one group named. 'L' and the other half were allotted in group 'M'. The patients were divided into two groups by simple random sampling method. Patients receiving labetalol were allocated in Group L.

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Patients receiving methyldopa were allocated in Group M. The eligibility criteria includes singleton pregnancy of ≤ 34 weeks with BP ≥ 140/90 mm Hg on 2 separate occasions 6 hrs apart for the first time in pregnancy with no evidence of proteinuria and no history of chronic hypertension, diabetes, all immunization, epilepsy, kidney disease, SLE or any other serious medical condition.

RESULT AND ANALYSIS

We used the SPSS software version 16 for analyzing the relevant data. Categorical Variables like Incidence of side effects and complications were analyzed using number (%) and compared across groups using Chi Square Test for independence of attributes. Continuous variables like Blood Pressure, Heart Rate etc were measured as mean ± variance and compared across groups using unpaired t test. 95% confidence interval in difference of mean for these parameters across the 2 groups was also observed. In our entire analysis a P-value of less than 0.05 was considered statistically significant.

After starting both the groups on their respective drug preparations control was achieved in Group L at around 1 week and in Group M at around 2 weeks. This was found to be statistically significant with P value of <0.001 (95% C.I: -1; -0.99). The blood pressure at initiation of labour in both the groups was 134/94 mm Hg with MAP of 107 mmHg, which was not significant. Statistical Significance was achieved when BP during labour and 1 hr after delivery was compared with *P* value for MAP readings <0.001(95%C.I.:-15.53;-13.63) and *P* value for MAP <0.001(95%C.I.-6.29;-4.14 respectively in the labetalol group. Similarly during postpartum period upto 48 hours on analysis the MAP was significantly lower with *P* value<0.001(95%C.I: -6.63;-5.46) in the labetalol group Table 1- A,B,C.

Table 1A Effective Control of BP (Antepartum)

	GROUP L	GROUP M	P value (95% C.I)
	Mean ± SD	Mean ± SD	
SBP at Admission (mmHg)	150.52 ± 5.97	149.9 ± 6.25	0.311(-0.58;-1.82)
DBP at Admission (mmHg)	119.92 ± 4.7	119.73 ± 4.31	0.674(-0.7;-1.08)
MAP at Admission (mm Hg)	130.12 ± 3.7	129.77 ± 3.48	0.330(0.36;-1.06)
Control Achieved at (Weeks)	1 ± 0	2 ± 0.07	<0.001(-1;-0.99)

Table 1B Effective Control of BP (Intrapartum)

		Group L	Group M	P Value (95% C.I)
		Mean ± SD	Mean ± SD	
Initiation of Labour	SBP (mm Hg)	134.86 ± 3.25	134.61 ± 3.16	0.427 (-0.38;0.89)
	DBP (mm Hg)	93.97 ± 2.58	94.03 ± 2.61	0.817 (-0.57;0.45)
	MAP (mm Hg)	107.6 ± 2.03	107.56 ± 1.96	0.822 (-0.35;0.44)
During Labour	SBP (mm Hg)	149.66 ± 6.45	170.63 ±6.33	<0.001 (-22.23;-19.710)
	DBP (mm Hg)	100.25 ± 6.2	111.63 ± 6.84	<0.001 (-12.67;-10.1)
	MAP (mm Hg)	116.72 ± 4.7	131.3 ± 4.95	<0.001 (-15.53; -13.63)
1 hr after Delivery	SBP (mm Hg)	145.43 ± 3.4	154.25 ± 8.95	<0.001 (-10.16; -7.49)
	DBP (mm Hg)	100.22 ± 6.18	103.63 ± 8.71	<0.001 (-4.89; -1.93)
	MAP (mm Hg)	115.29 ± 4.35	120.5 ± 6.37	<0.001 (-6.29; -4.14)

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Table 1C Effective Control of BP (Postpartum)

		GROUP L	GROUP M	P value (95% C.I)
		Mean ± SD	Mean ± SD	
1st DAY	SBP (mm Hg)	144.52 ± 9.66	136.22 ± 3.94	<0.001 (6.85 ;9.75)
	DBP (mm Hg)	94.99 ± 3.1	99.52 ± 6.07	<0.001 (-5.48 ; -3.59)
	MAP (mm Hg)	111.5 ± 3.71	111.75 ± 4.36	0.527 (-1.05 ; 0.54)
2nd DAY	SBP (mm Hg)	135.98 ± 3.49	150.01 ± 7.62	<0.001 (-15.2 ; -12.86)
	DBP (mm Hg)	93.03 ± 3.35	95.09 ± 3.12	<0.001 (-2.69 ;-1.42)
	MAP (mm Hg)	107.35 ± 2.59	113.39 ± 3.32	<0.001 (-6.63 ; -5.46)

In our study, incidence of headache and drowsiness were statistically significant with *P* value <0.001 in case of Group M receiving methyldopa which was seen in 50% and 30% cases respectively Fig-1.

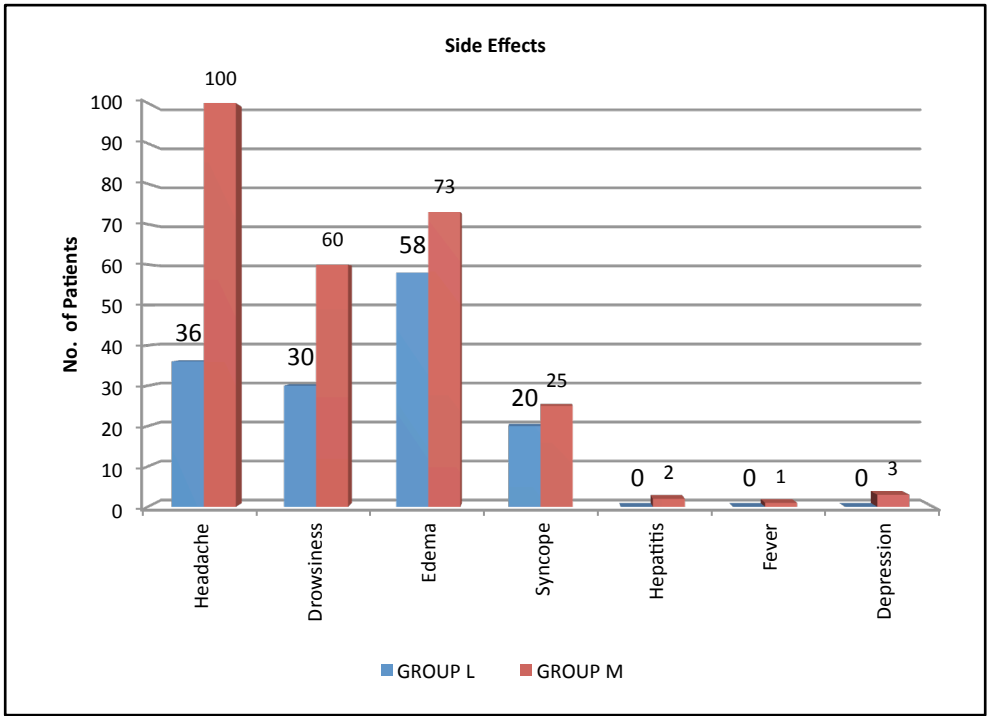

Fig 1: Frequency of Side Effects

The gestational age on admission were divided into 3 groups where duration of pregnancy in labetalol group was upto 36wks vs 32.8wks in the methyldopa group in the 28-30wks group,and in the 34-36wks group, the patients on labetalol delivered around 38wks vs 37wks in the methyldopa group Fig-2 this was found to be significant P<0.001.

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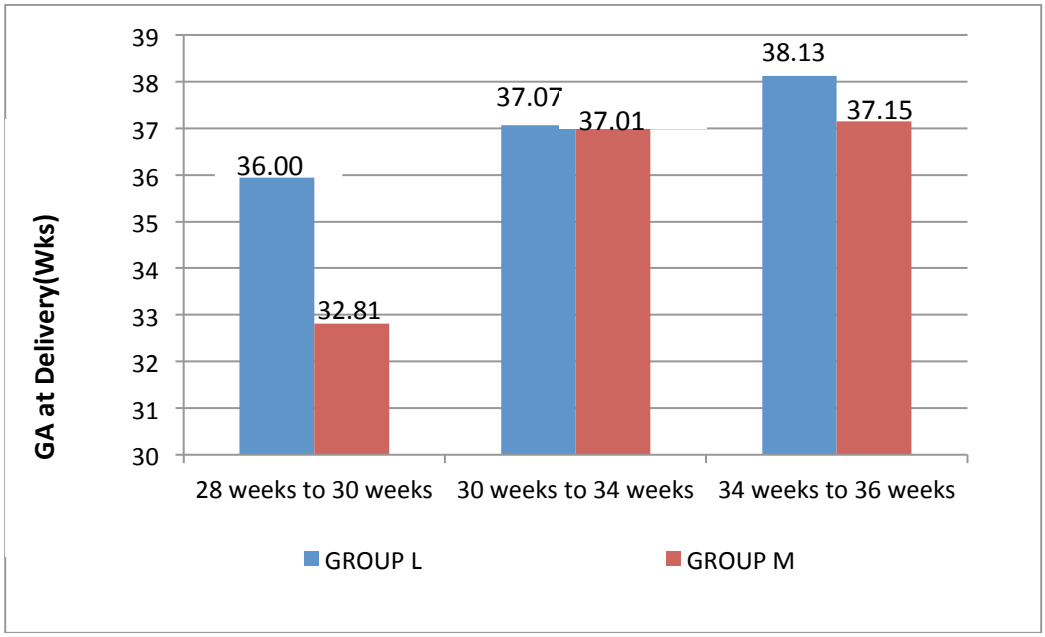

Fig 2: Duration of Pregnancy (in Weeks)

In Group L patients went into labour beyond 37 weeks and in Group M beyond 36 weeks. This difference was found to be statistically significant with P value <0.001. In Group L out of 200 patients 60 (30%) went into spontaneous labour, and rest were induced of which 120 (60%) had to undergo section. In Group M out of 200 patients 20 (10%) went into spontaneous labour, the rest were induced of which 160 (80%) underwent section. The difference of both these groups were found to be statistically significant with P value<0.001. The indications for caesarean section pertaining to this study were only analyzed. In Group L the incidence of severe PIH was 5% where as in Group M it was 24% respectively. This difference was found to be statistically significant with P value 0.023 and 0.007 respectively.

The incidence of SGA babies in Group L was 22% and in Group M was 19% .The Apgar score was <8 at 5 mins in 3% of Group L babies and 4% of Group M babies. About 13% of Group L babies were kept at NICU for more than 9 days and in Group M, it was about 15%.The incidence of preterm babies in Group L was about 11% and in Group M was about 13%. The mean birth weight in Group L was 1.8 kgs and in Group M was 1.7 kgs. However none of the parameters of live born babies were statistically significant Table 2

Table 2 Summary of Live Births

	GROUP L	GROUP M	p value
	N (%)	N (%)	
Small for Gestational Age	44 (22)	37 (19)	0.384
Apgar Score <8 at 5 mins	6 (3)	8 (4)	0.586
NICU Admission for >9 days	26 (13)	30 (15)	0.564
Born before 37 weeks	22 (11)	26 (13)	0.538

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There were 4 stillbirths in the methyldopa group and 2 neonatal deaths in the labetolol group in both of which extra anti-hypertensive drugs were added for BP control.

DISCUSSION

A number of oral medications are in use for lowering blood pressure, however in this prospective study labetalol was compared with methyldopa with the intention of recording the maternal and perinatal outcomes followed by their comparison and thus to determine which drug has an edge over the other. While analyzing the blood pressure details in our study effective control of BP in Group L was achieved at approximately 1 week and in Group M at 2 weeks (Table-1A, B, C) Similarly in the study by A.M.El-Qarmalawi et al[3] 81.4% patients receiving labetalol had a significant fall in MAP (P<0.005) to below 103.6mmHg compared with 68% in patients getting methyldopa. However the duration of therapy was similar in both the groups. In a study by G.D.Lamming et al,[4] the average MAP in both groups was the same before treatment. There was a highly significant fall in MAP in the group treatment with labetalol (P<0.001) but no significant fall in the group tested with methyldopa (P> 0.05).The daily average BP of each group until delivery also indicates that BP control was better in the group treated with labetalol.

Analysis of maternal outcome in our study reveals that majority of the pregnancies went beyond term (37weeks) in Group L when compared against Group M (Fig-2). This was statistically significant. (P<0.001). Side effects of methyldopa were also more frequently observed headache (50%) and drowsiness (30%) - however none were life threatening. Incidence of these side- effects were significantly less in Group L (P<0.001) (Fig-1). In our study on observation in the intrapartum period it was found that in Group L out of 200 patients, 60 (30%) went into spontaneous labour, 70% were induced of which 10% delivered vaginally and 120(60%) had to undergo caesarean section with maximum indications being for severe PIH (5%). But in Group M out of 200 patients, 20(10%) went into spontaneous labour, 90% were induced of which 10% delivered vaginally and 160(80%) underwent caesarean section which was significant (P<0.001) amongst which significantly most were due to severe PIH (15%)(P<0.001). In the study by A.M.El-Qarmalawi et al,[3] side effects were more frequent in the methyldopa group, however the gestational age at delivery were more or less similar in both the groups.

More patients though needed induction of labour and emergency caesarean sections in the methyldopa group due to uncontrolled BP; with more number of patients going into spontaneous labour in the labetalol group. However in the study by Plouin et al,[5] there were no significant difference in mode of delivery in both the groups; neither did the gestational age at birth differed in both the groups. Side effects were mild with frequency of significant proteinuria similar in both groups. While comparing the perinatal outcome in our study almost the same proportion of babies were preterm with low Apgar scores <8 in 5 mins with NICU admission for more than 9 days in both the group of patients receiving labetalol and methyldopa(Table-2),and there were 2 neonatal deaths and 4 stillborns. In El-Qarmalawi *et al*'s[3] study as regards the fetal/neonatal outcome, there was no significant difference between the two groups. In Plouin et al 's[5] study there were 4 stillbirths in methyldopa group and the live-born baby's mean birth weight and gestational age at birth were quite similar in both the groups. In the Cochrane review of Antihypertensive drug therapy for mild to moderate hypertension during pregnancy[6] it was found that there is no difference in the risk of the baby dying (17 trials,1130 women; RR 0.67; 95% CI 0.37 to 1.21) when any antihypertensive drug is compared with methyldopa.

CONCLUSION

Our study has revealed that labetalol helps in quicker and more efficacious control of BP in mothers developing gestational hypertension with chances of developing preeclampsia – eclampsia syndrome. With good maternal outcome with respect to development of complications, prolongation of pregnancy and maximum rate of spontaneous vaginal delivery. There were also minimum need for additional drugs in controlling BP with less development of side effects in case of labetalol. However none of the drugs had any edge over the other with respect to perinatal outcome as observed

on extensive monitoring of the fetal parameters over 48 hours in the antepartum, intrapartum and postpartum periods.

REFERENCES

1. Danforth's Obstetrics and Gynaecology, 10th ed. Gibbs, Ronald S., Karlan, Beth Y., Harey, Arthur F., Nygaard, Ingrid E. Lipincott Williams & wilkins, 2008, p-258.
2. Chhabra S, Kakani A. Maternal Mortality due to eclamptic and non eclamptic hypertensive disorders: a challenge. J Obstet Gynaecol. 2007 Jan; 27 (1): 25-9.
3. El-Qarmalawi A.M, Morsy A.H. ,Al-Fadly A, Obeid A, Hashem M. Labetalol vs methyldopa in the treatment of pregnancy–induced hypertension. International Journal of Gynecology & Obstetrics. 1995 Jan 49; 125-130.
4. Lamming G.D. Symonds E. M. use of labetalol and Methyldopa in Pregnancy Induce Hypertension. Br. J. Clin. Pharmac. 1979; 8:217S-222S.
5. Pierre-Francois Plouin, Gerard Breart, Francoise Maillard, Emile Papiernik, Jean-Pierre Relier. Comparison of antihypertensive efficacy and perinatal safety of labetalol and methyldopa in the treatment of hypertension in pregnancy: a randomized controlled trial. Br. J Obstet Gynaecol 1988; 95:868-876.
6. Abalos E, Duley L, Steyn DW, Henderson-smart DJ. Antihypertensive drug therapy for mild to moderate hypertension during pregnancy. Cochrane Database Syst Rev 2007, CD 002252.