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Original Article

Comparison of Efficacy of Labetalol versus Alpha-methyldopa in the Management of Preeclampsia

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Abstract

Introduction: Hypertension is a common medical problem encountered during pregnancy and is associated with an increased risk of adverse outcomes. Preeclampsia is a multi-system disorder of unknown etiology, unique to pregnancy characterized by the occurrence of gestational hypertension along with proteinuria after the 20th week of pregnancy in a previously normotensive and non-proteinuric patient.

Aim: The aim of the study was to study the efficacy of oral labetalol versus oral Alpha-methyldopa in the management of preeclampsia.

Methods: Hundred patients included in this study were assigned to two groups randomly of 50 patients in each group. Group 1: Tablet Alpha-methyldopa (Aldomet) 250 mg was given thrice daily, and Group 2: Tablet Labetalol 100 mg was given twice daily. Blood pressure (BP) and proteinuria were recorded every 12th h.

Results: Significant fall in the diastolic BP after 48 h occurred only in the labetalol group ($P = 0.007$). In the Alpha-methyldopa group, there was a significant need to increase the drug dose after 48 h ($P = 0.043$). There appears to be no significant difference in induction rate between the two groups ($P = 0.585$). The mean birth weight was significantly higher ($P = 0.00$) in the labetalol group (3.11 kg) compared to the alpha methyldopa group (2.67 kg). There was no significant difference in the Appearance, Pulse, Grimace, Activity, and Respiration scores ($P = 0.090$) and rate of neonatal admissions ($P = 0.240$) in both groups.

Conclusion: Labetalol controls systolic and diastolic BP more rapidly and effectively than methyldopa. The safety profile and adverse effects of Labetalol and Methyldopa are similar to each other.

Key words: Labetalol, Methyldopa, Pregnancy-induced hypertension

INTRODUCTION

Preeclampsia is a multi-system disorder of unknown etiology, unique to pregnancy characterized by the occurrence of gestational hypertension along with proteinuria after the 20th week of pregnancy in a previously normotensive and non-proteinuric patient.[1] Gestational hypertension is defined as systolic blood pressure (BP) of 140 mm of Hg or more and Diastolic BP of 90 mm of Hg or more on two occasions, measured at least 6 h apart but within 7 days.[2] Proteinuria is defined as excretion of 0.3 g or more of protein in a 24-h urine sample or >1+ on the dipstick in a random sample after excluding urinary tract infection.[3]

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Preeclampsia complicates 2–8% of pregnancies.[4] Preeclampsia can affect virtually every organ system in the body and is a major cause of maternal and perinatal mortality and morbidity. Pre-eclampsia, when not controlled or left untreated, can lead to catastrophes like Eclampsia, Abruptio placenta, HELLP syndrome, fetal growth restriction, and intrauterine fetal death.[5] Although the definitive treatment of preeclampsia is the termination of pregnancy, aggressive treatment is necessary to ameliorate the disease progression to carry on the pregnancy till adequate fetal maturity is obtained. Therefore, oral antihypertensive drugs have a major role in the management of pre-eclampsia.[6] A comparison is

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made here between labetalol and the commonly used drug Alpha-methyldopa in the management of pre-eclampsia.

Aim

The aim of the study was to study the efficacy of oral labetalol versus oral Alpha-methyldopa in the management of preeclampsia.

MATERIALS AND METHODS

This randomized prospective comparative study was conducted at the Institute of Social Obstetrics and Government Kasturba Gandhi Hospital for Women and Children, Triplicane, Chennai, on 100 patients diagnosed with preeclampsia and admitted in the Eclampsia ward from September 2010 to August 2011.

The patients included in this study were assigned to two groups randomly of 50 patients in each group. Group 1: Tablet Alpha-methyldopa (Aldomet) 250 mg was given thrice daily and Group 2: Tablet Labetalol 100 mg was given twice daily.

Inclusion Criteria

All patients with gestational hypertension (more than 20 weeks of gestation till term), systolic BP of 140 mm of Hg or more, diastolic BP of 90 mm of Hg or more, and proteinuria (0.3 g in 24 h or more/1+dipstick or more) were included in the study.

Exclusion Criteria

Chronic hypertension, renal disease, liver disease, bronchial asthma, GDM, cardiac disease, and eclampsia were excluded from the study. Informed consent was obtained from these patients before administration of the drugs. BP was recorded every 12th h. The treatment was continued till delivery if the BP is controlled. If the BP was not controlled within 48 h, the dose of drugs was doubled. BP was measured by a mercury sphygmomanometer over the right arm in the sitting position after a period of rest for 15 min. Korotkoff phase 5 was used to define diastolic BP. Proteinuria was detected using the sulfosalicylic acid test. The period of study was 1 year. The change in BP after 48 h need for induction, and mode of termination of pregnancy, birth weight, Appearance, Pulse, Grimace, Activity, and Respiration (APGAR) score, and neonatal admissions was recorded. The results were subjected to statistical analysis using the *t*-test and Chi-square test.

RESULTS

These 100 patients were assigned to two groups at random of 50 patients in each group. Group 1 was started on tablet Alpha-methyldopa 250 mg thrice daily, and Group 2 was started on tablet Labetalol 100 mg twice daily. Most of the patients in both groups were in the age group of 21–25 years. 42% of cases in Group 1 and 38% of cases in Group 2 were in the age group of 21–25 years. About 60% of women in Group 1 and 40% of women in Group 2 were primigravidae. About 40% of women in Group 1 and 58% of women in Group 2 were multigravidae [Table 1]. The difference between the mean gestational ages between the two groups is not statistically significant, in Group 1 37.90 ± 1.93 weeks and Group 2 37.90 ± 1.59 weeks ($P = 0.910$). The difference between the mean BMI between the two groups is not significant, in Group 1 27 ± 3.28 and Group 2 27.30 ± 3.76 ($P = 0.671$).

Before drug administration, there is no statistical difference in systolic BP and diastolic BP. However, after drug administration, a significant fall in the diastolic BP after 48 h occurred only in the labetalol group ($P = 0.007$). During the time of delivery, there is no statistical difference in systolic BP and diastolic BP [Table 2].

About 36% of the cases in Group 1 needed an increase in the dose when compared to 18% in Group 2. There is a statistically significant need to increase the dose after 48 h in Group 1 compared to Group 2 ($P = 0.043$) [Table 3].

The need for induction in both Groups, 14% in Group 1 and 18% in Group 2 were induced with PGE2 gel [Table 4].

The mode of delivery in both the groups 44% of cases in Group 1 and 40% of cases in Group 2 underwent Emergency LSCS. About 36% of cases in Group 1 and 34% of cases in Group 2 were delivered by labor natural [Table 5].

The difference between the mean birth weights between the two groups is 442 g, which is statistically significant. The difference between the mean APGAR score between the two groups is 0.4, which is not statistically significant ($P = 0.090$). The need for NICU admission in both groups 10% of babies delivered in Group 1 and 4% of babies delivered in Group 2 needed NICU admission [Table 6].

DISCUSSION

Preeclampsia is an important cause of maternal mortality and perinatal mortality and morbidity. Oral antihypertensive drugs have played a major role in controlling the disease progression, preventing eclampsia and other dreaded complications, prolonging pregnancy, and reducing fetal prematurity. Although methyldopa has been used routinely

because of its safety profile, several controlled trials have suggested labetalol to be a better drug in controlling hypertension with the least side effects. A prospective study was carried out at City Hospital, Nottingham, the UK, in 1979. Nineteen patients with pregnancy induced hypertension (PIH) whose Mean arterial pressure was >103.3 mm of Hg were selected. They were randomly allocated to two groups. They were given either Labetalol 400 mg or Alpha methyldopa 750 mg daily. This dose was doubled 3 days later if satisfactory BP control had not occurred. Significant falls in BP only occurred in the group treated with labetalol, and daily BP control was better in this group. There was a higher incidence of spontaneous labor in the labetalol group and a significant difference in the Bishop score of the cervix between the two groups. There were no apparent detrimental effects on the fetus antenatally, during labor, or postpartum.[7]

In our study, the initial daily dose of labetalol was 200 mg, and the initial daily dose of alpha methyldopa was 750 mg. The dose was increased after 48 h if satisfactory BP control had not occurred. Statistically, significant falls occurred only in the diastolic BP in the labetalol group after 48 h ($P = 0.007$). There was no statistically significant difference between the need for PGE2 induction between alpha methyldopa and labetalol groups. About 86% of cases in the alpha methyldopa group and 82% of cases in the labetalol group went in for spontaneous labor. Only 5% of babies born in the alpha methyldopa group and 2% of babies born in the labetalol group required NICU admission. This difference was also not statistically significant ($P = 0.240$). A prospective study (2005) was carried out at Al-Jahra Hospital, Jahra, Kuwait, to assess the efficacy and safety of labetalol compared with methyldopa in the management of mild and moderate cases of PIH. One hundred four primigravidae with PIH were randomly allocated to receive either labetalol (Group A) or methyldopa (Group B).

The dose of the drugs was doubled every 48 h to maintain a mean arterial BP ≤103.6 mmHg. Ten patients in Group B (18.5%) developed significant proteinuria, whereas none developed proteinuria in Group A. Labetalol was quicker and more efficient at controlling BP, having a beneficial effect on renal functions and causing fewer side effects compared with methyldopa. The rate of labor induction and the cesarean section for uncontrolled PIH was less in Group A (48% and 1%, respectively) than Group B (63.0% and 5.6%, respectively). Moreover, a higher Bishop score at induction of labor was noticed in Group A. Labetalol is better tolerated than methyldopa, gives more efficient control of BP, and may have a ripening effect on the uterine cervix.[8] In our study, 44% of cases were in the alpha methyldopa group and 40% of cases in the labetalol group

Table 1: Comparison of patient characteristics

Variables	Group 1	Group 2	Total
Age group			
<20	6	6	12
21–25	21	19	40
26–30	17	20	37
>30	6	5	11
Parity			
Primi	30	21	51
Multi	20	29	49

Table 2: Comparison of BP

BP	Group 1	Group 2	*P*-value
Before drug administration			
SBP	150.6±8.6	150.2±8.2	0.813
DBP	103.40±4.78	102.40±4.78	0.275
48 h			
SBP	146.20±8.3	144.60±8.62	0.347
DBP	95±7.35	91.20±6.27	0.007
Time of delivery			
SBP	143±9.53	139.40±9.98	0.068
DBP	91.60±7.91	89.40±6.19	0.125

BP: Blood pressure, SBP: Systolic blood pressure, DBP: Diastolic blood pressure

Table 3: Comparison of dosage

Need to increase the dose	Group 1	Group 2	Total	*P*-value
No	32	41	73	0.043
Yes	18	9	27	

Table 4: Comparison of induction

Induction	Group 1	Group 2	Total	*P*-value
Nil	43	41	84	0.585
Pge2 Gel	7	9	16	

Table 5: Comparison of mode of delivery

Mode of delivery	Group 1	Group 2	Total	*P*-value
Elective LSCS	2	2	4	0.75
Elective RPT LSCS	1	4	5	
Emergency LSCS	22	20	42	
Emergency RPT LSCS	7	7	14	
Labor Natural	18	17	35	
Total	50	50	100	

LSCS: Lower segment Cesarean section

Table 6: Comparison of neonatal characteristics

Variables	6.092 mm	Group 2	*P*-value
Birth weight	2.68±0.60	3.12±0.61	<0.0001
APGAR	8.24±1.31	8.64±1.06	0.09
NICU admission	5	2	0.24

APGAR: Appearance, Pulse, Grimace, Activity, and Respiration, NICU: Newborn intensive care unit

delivered by Emergency LSCS; 36% of cases in the alpha methyldopa group and 34% of cases in the labetalol group delivered by Labor Natural. In a Randomized controlled trial (1988), labetalol was compared with methyldopa in a randomized controlled trial involving 176 pregnant women with mild to moderate hypertension. Diastolic BP below 86 mmHg was obtained in a similar proportion of women given labetalol or methyldopa. Intrauterine death occurred in four women treated with methyldopa, and the one neonatal death on day 1 occurred in the labetalol group. The average birth weight and the proportion of preterm or small-for-gestational-age babies were similar in both groups. Heart rate, BP, blood glucose, respiratory rate, and Silverman score of the babies did not differ between the two treatment groups, whether the comparison was made for all the infants or only for preterm or small-for-gestational-age. These data indicate that maternal beta-blockade with labetalol is as safe as methyldopa for the fetus and the newborn.[9] In our study, there were no reports of intrauterine deaths. There was a statistically significant increase in the mean birth weight in the labetalol group when compared to the alpha-methyldopa group (3.11 kg and 2.67 kg, respectively, $P = 0.001$).

CONCLUSION

Pregnancy-related hypertension is a leading cause of morbidity and mortality around the world. Therefore, antihypertensive drugs are crucial in the management of maternal BP. Labetalol reduces systolic and diastolic BP more quickly and effectively than methyldopa, according to our study. In addition, labetalol has a ripening effect on the cervix, increasing the likelihood of spontaneous labor and normal vaginal delivery.

REFERENCES

1. Gupte S, Wagh G. Preeclampsia-eclampsia. J Obstet Gynaecol India 2014;64:4-13.
2. Mammaro A, Carrara S, Cavaliere A, Ermito S, Dinatale A, Pappalardo EM, *et al*. Hypertensive disorders of pregnancy. J Prenat Med 2009;3:1-5.
3. Côté AM, Brown MA, Lam E, von Dadelszen P, Firoz T, Liston RM, *et al*. Diagnostic accuracy of urinary spot protein: Creatinine ratio for proteinuria in hypertensive pregnant women: Systematic review. BMJ 2008;336:1003-6.
4. Steegers EA, von Dadelszen P, Duvekot JJ, Pijnenborg R. Pre-eclampsia. Lancet 2010;376:631-44.
5. Uzan J, Carbonnel M, Piconne O, Asmar R, Ayoubi JM. Preeclampsia: Pathophysiology, diagnosis, and management. Vasc Health Risk Manage 2011;7:467-74.
6. Kattah AG, Garovic VD. The management of hypertension in pregnancy. Adv Chronic Kidney Dis 2013;20:229-39.
7. Pickles CJ, Broughton Pipkin F, Symonds EM. A randomised placebo controlled trial of labetalol in the treatment of mild to moderate pregnancy induced hypertension. BJOG Int J Obstet Gynaecol 1992;99:964-8.
8. El-Qarmalawi AM, Morsy AH, Al-Fadly A, Obeid A, Hashem M. Labetalol VS. methyldopa in the treatment of pregnancy-induced hypertension. Int J Gynaecol Obstet 1995;49:125-30.
9. Plouin PF, Breart G, Maillard F, Papiernik E, Relier JP. 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;95:868-76.

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