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Comparative Study of Labetalol and Methyldopa in Management of Preeclampsia

KEYWORDS

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ABSTRACT *Hypertensive disorders in pregnancy remain one of the major auses of maternal and perinatal mortality. Antihypertensive drugs are often used to lower blood pressure to prevent this adverse outcome for the mother and the fetus. Hence we carried out a prospevctive study on 110 patients .*

INTRODUCTION
Pre-eclampsia is best described as pregnancy specific syndrome that can affect virtually every organ system.

According to the criteria established by the Working group in pregnant women, hypertension is described into 4 types:

1) Gestational Hypertension: if preeclampsia does not develop and hypertension resolves by 12 week postpartum, it is designated as Transient Hypertension.
2) Preeclampsia and Eclampsia Syndrome.
3) Preeclampsia Syndrome superimposed on chronic hypertension.
4) Chronic hypertension.1

Although the outcome for most of these pregnancies is good , women with pre-eclampsia have an increased risk of developing serious problems such as renal failure , liver failure, abnormalities of the clotting system, stroke, IUGR baby, premature delivery (birth before 37 completed weeks),stillbirth or death of the baby in the first few weeks of life (Redman 1993). Therefore, there is a general consensus that she should receive antihypertensive drugs, to lower her blood pressure, and needs hospitalization. . It was once thought that lowering the blood pressure was potentially dangerous for the baby , and there were reports to support this2,3.Since 1980 , there has been an increase in the use of antihypertensive drugs by obstetrician4, and this has been associated with a reduction in maternal and neonatal death from preeclampsia , particularly in the number of maternal deaths related to cerebral pathology.

Methyldopa has been used as control while comparing the effects of different drugs. Labetalol has also been successfully used for treatment of hypertensive disorders in pregnancy. Though beta blockers have been found to be better in treating severe hypertension during pregnancy, there is insufficient evidence to support the same in case of mild hypertension in pregnancy. In this backdrop, we wanted to compare the antihypertensive drugs-Labetalol and Methyldopa in hypertension in pregnancy.

AIM AND OBJECTIVES
- Comparing the drugs Labetalol and Methyldopa in bringing down the blood pressure in cases of preeclampsia.
- To study the side effects of drugs used in mother and fetus.

MATERIAL AND METHOD
The present prospective randomized controlled study compromised of cases of preeclampsia who were outpatients as well as inpatients of antenatal ward of Obstetrics and Gynecology Department of Bharati Vidyapeeth Medical College and Hospita, Pune(Maharashtra).

INCLUSION CRITERIA:
1) All pregnant mothers diagnosed as preeclampsia with blood pressure 150/100mmHg equal or more were enrolled for the study.
2) All singleton pregnancy.

EXCLUSION CRITERIA:
1) Chronic Hypertension
2) Renal disease
3) Multiple pregnancies
4) Patient with hepatic, cardiac and renal diseases, diabetes.
5) Gestational hypertension
6) Eclampsia

Patients diagnosed with preeclampsia were selected randomly for the treatment with Labetalol or Methyldopa. Multiple drug therapy was used in whom there was uncontrolled blood pressure.

The starting dose of oral Labetalol for patients with diastolic blood pressure 100mmHg, was 100 mg BD; for 100-110mmHg, it was 100mg TID; and if >110mmHg, it was 200mg BD. Depending on the response to the treatment the dose of the labetalol was increased every 48hrs upto a maximum of 2400mg/day.

In methyldopa group, the starting dose for patients with a diastolic blood pressure of 100mmHg, was 250mg BD; 100-110mmHg, was 250mg TID- QID; and was increased to 500mg BD- QID ,up to a maximum of 2g/day.

Statistical analysis was done by applying paired 't' test for the difference in pre and post treatment values. For inter group analysis, chi-square test was applied. A P-value < 0.05 was regarded as significant with 95% confidence limit.

SAMPLE SIZE: 110 cases were included in the study withinthe period of two years (August 2010-July 2012).

OBSERVATION AND RESULT
This study included 110 patients. The patients diagnosed to have preeclampsia were studied prospectively and following observations were recorded.

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TABLE 1: Shows mean systolic blood pressure pre-and post treatment values in different groups.

Treatment	Number of patients	SBP (Mean ± SD)		p-value
		Pre treatment	Post treatment	
IV Labetalol	5	172.00 ± 13.04	164.00 ± 11.40	0.099
IV+ Oral Labetalol	22	156.73 ± 3.12	148.36 ± 8.09	< 0.001*
Oral Labetalol	27	150.00 ± 0.00	144.00 ± 7.15	< 0.001*
Oral methyldopa	29	150.00 ± 0.00	142.69 ± 5.51	< 0.001*
IV Oral + Labetalol	27	155.26 ± 3.10	147.56 ± 5.47	< 0.001*

Conclusion: By using paired test p-value <0.05 therefore there is significant decrease in the systolic blood pressure with the given treatment

TABLE 2 : Shows mean diastolic blood pressure pre and post treatment values in different groups.

Treatment	Number of patients	DBP(Mean ± SD)		p-value
		Pre treatment	Post treatment	
IV Labetalol	5	118.40 ± 7.92	102.00 ± 8.37	0.016*
IV Labetalol+ Oral Labetalol	22	107.27 ± 2.73	95.27 ± 5.11	< 0.001*
Oral Labetalol	27	100.00 ± 0.00	94.44 ± 4.65	< 0.001*
Oral methyldopa	29	100.00 ± 0.00	91.31 ± 4.29	< 0.001*
IV Labetalol + methyldopa	27	104.52 ± 2.39	96.15 ± 4.50	< 0.001*

Conclusion: By using paired test p-value <0.05 therefore there is a significant decrease in diastolic blood pressure with the treatment given.

* Significant (Paired t-test used)

TABLE 3: Comparison of side effects seen with both drugs

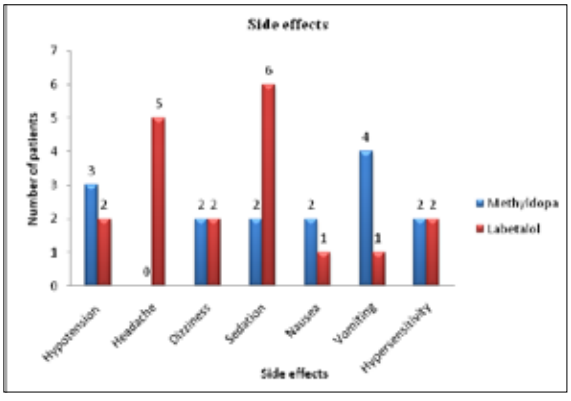

TABLE 4. Administration of Drug to the Delivery Interval

Column1	IV LABETALOL	IV + ORAL LABETALOL	ORAL LABETALOL	IV LAB. + ORAL METH.	ORAL METH.
<1Week	5	9	1	4	1
1-2week		9	6	3	2
3-4week		3	14	12	16
4-6week		1	4	2	8
>6week			2	6	2

TABLE 5 : Dose requirement for reduction in blood pressure.

FALL IN DIASTOLIC BLOOD PRESSURE	IV LABETALOL	ORAL LABETALOL	ORAL METHYLDOPA
10 mmHg	20 mg	600 mg/day	1 g/day
20 mmHg	60-80 mg	800-1000 mg/day	2g/day

DISCUSSION AND CONCLUSION:

Although antihypertensive treatment has not been shown to decrease perinatal mortality in pregnancies complicated by mild to moderate hypertension (Leather et al. 1968; Redman et al. 1976; Rubin et al. 1983)5, the administration of various antihypertensive drugs is becoming increasingly a matter of routine.

The Cochrane review on drugs for the treatment of very high blood pressure in pregnancy concluded that until better evidence is available, the choice of antihypertensive should depend on the clinician's experience and familiarity with a particular drug, and on what is known about adverse effect6.

In this study of 110 patients with preeclampsia treated with antihypertensive drugs – Methyldopa and labetalol – alone or in combination in an effort to improve perinatal outcome.

- There was no maternal mortality, eclampsia, HELLP syndrome, DIC, Renal failure, etc.
- It was concluded that the antihypertensive properties of i.v. labetalol is better than compared with oral labetalol while oral methyldopa is better antihypertensive than as compared with oral labetalol.
- Rate of normal vaginal delivery was significantly higher with methyldopa and rate of cesarean section was significantly higher with labetalol. More patients were seen delivered in both the groups at gestational age 33-37 weeks with greater frequency in methyldopa group.
- It was seen that the birth weight of majority of the babies born to the pre-eclamptic mothers were between 1.5 to 2.5 kgs and especially more in the labetalol group.
- No significant conclusion can be derived from the results of effect of labetalol and methyldopa on renal function test, liver function test, platelet counts.
- The side effects associated with these drugs included sedation and headache in the majority of the subjects and much more with Labetalol.

Thus it was concluded that I.V. Labetalol is a better drug in controlling severe preeclampsia for better maternal and fetal outcomes; while oral Labetalol is comparable to oral Methyldopa in treating and preventing adverse outcome in hypertension during pregnancy. However, the effect on fetal and maternal outcomes must be considered before selecting drugs for the treatment.

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