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Evaluation of Oral Labetalol Versus Methyldopa in Hypertensive Disorders Complicating Pregnancy

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Abstract

Aims & Objectives: To compare the efficacy and safety of labetalol versus methyldopa in the management of preeclampsia Materials & Method:s Eligible women were randomly assigned, treated with Tab. Labetalol and Tab Methyldopa alternatively with matching distribution, 85 patients in each group. *Results:* Labetalol is very effective and has early onset of control of blood pressure control with less side effects. No fetal adverse effects were seen. *Conclusion:* Labetalol is safe. Inspite of cost, labetalol is very effective and early onset of control of blood pressure is seen. In patients on Labetalol requirement of adding other antihypertensive is much less than methyldopa.With effective control of blood pressure, prevention of eclampsia and the pregnancy can be prolonged to achieve fetal maturity.Labetalol is not associated with adverse fetal effects.

Keywords: Labetalol; Alpha Methyldopa; Preeclampsia.

Introduction

Hypertensive disorders of pregnancy complicates about 15% of all the pregnancies.

The level of blood pressure is also directly directly affects the fetal well being.

The choice of antihypertensive drug is dependent on its efficacy on oral administration and its freedom from maternal and fetal side effects.

Methyldopa which was commonly used antihypertensive has lost its popularity because of the high incidence of side effects and prolonged onset of action.

Labetalol is shown to be effective in treatment of essential hypertension as well as gestational hypertension.

Aims & Objectives

- To study the effectiveness of labetalol in controlling hypertension in pregnancy.
- To study the maternal and perinatal outcomes.

Material & Methods

The study was conducted in MGM Medical College & Hospital for a period of 2 years from January 2011 to December 2013.

Inclusion Criteria

Patients diagnosed to have preeclampsia i.e, blood pressure >140/90 mm Hg with warning signs and symptoms and proteinuria Gestational age from 20 weeks to term

Exclusion Criteria

Patients who were on other antihypertensives A total of 170 patients of preeclampsia were included in the study. They were alternately assigned to the labetalol and methyldopa 85 in each group.

On admission detailed history was taken and examination was done.

Blood pressure was recorded using Korotkoff V sound for determining diastolic blood pressure. After the diagnosis of preeclampsia was done, written

informed consent was taken and the trial group was treated with either labetalol or methyldopa.

Group A received Labetalol 100mg BD and group B received methyldopa 250 mg TDS. Dose was increased if required till satisfactory BP control (140/90mm Hg) was achieved

Maximum dose for labetalol was 200 TDS and for methyldopa it was 500 QID.

If blood pressure did not decrease even after increasing the dose, additional antihypertensive was added. Investigations included complete blood count, Kidney Function Tests, Liver function tests, fundoscopy, NST, Ultrasound, and Doppler.

Decision to continue with conservative management or to intervene was made depending on the maternal and fetal indications.

The side effects if any were noted and the neonatal outcome was assessed.

Results

The mean age in the labetalol groups was 24.5years and in methyldopa group was 24.3years.

As seen in the table, maximum patients were multigravida in both the groups.

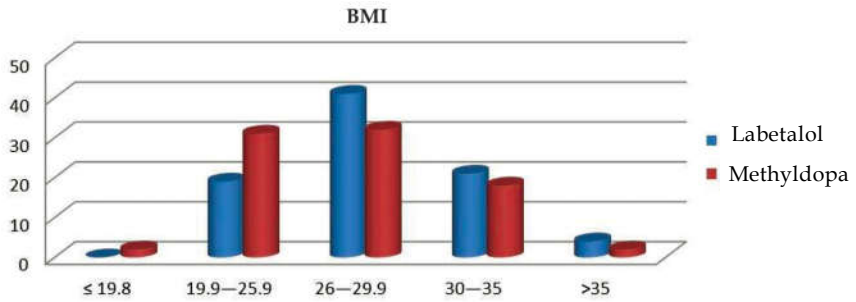
Most patients belonged to 33-37 weeks gestational age in both groups. Minimum gestational age at presentation was 22weeks in both groups.

Table 1: Age distribution

Age-Group	Labetalol		Methyldopa		Total	
	No.	%	No.	%	No.	%
≤20	19	22%	15	18%	34	20%
21-25	37	44%	39	46%	76	45%
26-30	22	26%	23	27%	45	26%
31-35	07	8%	08	9%	15	9%
Total	85	100%	85	100%	170	100%
Mean ± SD	24.56±4.03		24.37±4.11		24.63±4.02	

Table 2: Gestational age and Obstetric history

Gestational Age	Lobetalol				Methyldopa			
	Primi	%	Multi	%	Primi	%	Multi	%
<30	03	11%	10	17%	04	16%	10	17%
30-32	04	14%	11	20%	04	16%	12	20%
33-37	15	53%	20	35%	09	36%	21	35%
>37	06	22%	16	28%	08	32%	17	28%
Total	28	100%	57	100%	25	100%	60	100%



BMI: 69% patients were with BMI above26kg/m2, with maximum in range of 26-29.9kg/m2in both groups

There is no significant difference in distribution of cases in relation to severity of hypertension.

Table 3: Severity of hypertension

PREECLAMPSIA	Lobetalol		Methyldopa		Total		Chi- square value	p-value
	No.	%	No.	%	No.	%		
Eclampsia	07	09%	06	7%	13	8%		
Severe	31	36%	28	33%	59	35%	0.393	P=0.822
Mild	47	55%	51	60%	98	57%		NS
Total	85	100%	85	100%	170	100%		

Table 4: Time required for control BP in Days

Time Required for control BP in Days	Lobetalol		methyldopa		Total		Chi- square value	p-value
	No.	%	No.	%	No.	%		
<48hrs	40	47%	24	28%	64	37.65%	8.02	P=0.018 S
48-72hrs	32	38%	36	43%	68	40%		
>72hrs	13	15%	25	29%	38	22.35%		
Total	85	100%	85	100%	170	100%		

Table 5: Need for Additional Drug:

Drug	No. of women with controlled B.P.on single drug		No. of women required Additional Drug		Total		Chi-square value	p-value
	No.	%	No.	%	No.	%		
Lobetalol	78	92%	07	8%	85	100%	0.994	0.319 NS
methyldopa	74	87%	11	13%	85	100%		

Table 6: Mode of delive:ry

Mode of Delivery	Labetalol		Methyldopa		Total		Chi-square value	p-value
	No.	%	No.	%	No.	%		
Spontaneous Vaginal	26	31%	25	29%	51	30%		
Induced Vaginal	16	19%	10	12%	26	15%		
LSCS	43	51%	50	59%	93	55%		P=0.381
Total	85	100%	85	100%	170	100%	1.93	NS

Table 7: Indication of induction

Indication	Lobetalol (n=16)		Methyldopa (N=10)		Total (N=26)		Chi-square value	p-value
	No.	%	No.	%	No.	%		
Fullterm	8	50%	3	30%	11	42%	2.55	P=0.110 NS
Uncontrolled Htn	1	6%	2	20%	3	11%	0.882	P=0.348 NS
Antepartum Eclampsia	1	6%	2	20%	3	11%	0.882	P=0.348 NS
Iud	1	6%	2	20%	3	11%	0.882	P=0.348 NS
Oligohydromni Os	2	12%	4	40%	6	23%	1.58	P=0.209 NS
Iugr	5	31%	3	30%	1	4%	0.24E-04	P=0.961 NS
Abnormal doppler	3	19%	1	10%	4	15%	0.271	P=0.603 NS

Table 8: Indication of LSCS

Indication of LSCS	Lobetalol (n=43)		Methyldopa (n=50)		Total (n=83)		Chi- square value	p-value
	No.	%	No.	%	No.	%		
Prev. LSCS	06	14%	07	14%	13	16%	0.314	P=0.996NS
Unfavrable cervix	05	12%	02	04%	07	8%	1.66	P=0.198NS
Failure of induction	05	12%	00	0%	05	6%	5.49	P=0.019 S
Uncontrolled hypertension	03	7%	17	34%	20	23%	6.65	P=0.010 S
Antepartum eclampsia	03	7%	02	4%	07	8%	0.361	P=0.548 NS
Antepartum hemorrhage	03	7%	03	6%	06	7%	0.321E-01	P=0.858 NS
Malpresentation	10	23%	09	18%	18	21%	0.259	P=0.611NS
Fetal distress	08	18%	08	16%	15	18%	0.777	P=0.780 NS
Oligohydromnios	03	7%	09	18%	12	14%	1.95	P=0.163 NS
IUGR	00	0%	01	02%	01	1%	0.852	P=0.356 NS
Abnormal Doppler	00	0%	01	02%	01	1%	0.854	P=0.356 NS

Early control of blood pressure was seen in labetalol group.

Patients who required additional drug were significantly more in methyldopa group i.e.13% of patients compared to labetalol group patients which was 8%. The additional drug used was Nifedipine 10-20mg b.d. in both the groups.

There was no significant difference in the type of delivery in both the groups.

In labetalol more patients reached full term compared to methyldopa. Oligohydromnios was seen more in methyldopa group. Only 6% patients in

labetalol group had to be terminated due to uncontrolled hypertension verses 20% in methyldopa group.

Only 7% of patients had to be terminated due to uncontrolled hypertension in labetalol group compared to 34% in methyldopa group. Oligohydramnios was more in methyldopa group.

The ratio of average for gestational age to small for gestational age babies in both group is similar. IUD in both groups had occurred prior to starting the treatment with antihypertensive.

Table 9: fetal outcome

Fetal outcome		Lobetalol		Methyldopa		Total		Chi-square value	p-value
		No.	%	No.	%	No.	%		
Live	AGA	50	59%	51	60%	101	59%		
	SGA	30	35%	25	29%	55	33s%	0.362	P=0.547 NS
	Total	80	94%	76	89%	156	92%		
Death		05	6%	09	11%	14	8%	1.25	P=0.264 NS

Discussion

The present study was conducted in the Department of OBGYN, MGM Medical College & Hospital, Aurangabad . The efficacy of both the drugs labetalol and alphamethyldopa is assessed.

Age

The mean age of women in the labetalol group was 24.56 and in the alphadopa group was 24.3.This is in contrast to the findings of a large database study wherein there was a linear relationship between the age and incidence of PIH [1].

Parity

In this study, about 57% of the women in the labetalol group and 60%in the methyldopa group were multigravida. Parity distribution shows maximum patients of PIH with multigravida in both groups and there was no significant difference between groups in terms of parity distribution. This finding is in contrast to previous studies [2] and is due to randomize selection of cases in a small study sample.

Gestational Age

In this study, maximum patients belonged to 33-37 wks in both the groups. . In a study by Verma et al [3], most patients with PIH (68.88% in labetalol group and 71.11% in methyldopa group) belonged to 33-37 weeks gestational age and there was no statistically significant difference between groups. This finding in our study makes the groups comparable. This finding of the most common gestational age at which PIH developed is supported by other studies [4].

BMI

69% patients were with BMI above26kg/m^2 with maximum in range of 26-29.9 kg/m^2, making them high risk for preeclampsia. The relationship between maternal weight and the risk of preeclampsia is progressive. It increases from 4.3 percent for women with a body mass index (BMI) <20 kg/m^2 to 13.3 percent in those with a BMI> 35 kg/m^2 [5].

Control of Blood Pressure

Both labetalol and methyldopa significantly reduce the Blood pressure. However, control of BP by labetalol is much faster when compared to methyldopa (47% within 48hrs and 43% within 72hrs). Between two groups control of blood pressure is more significant in Labetalol group. Which is comparable with the study of Reena Verma et al (2012) [3]. Study of El-Qarmalawi AM says that labetalol provides more efficient control of BP than methyldopa in the treatment of hypertension in pregnancy [6]. Hypertensive crisis and eclampsia did not occur in any groups after commencement of antihypertensive treatment.

Need For Additional Antihypertensives

Need for the additional drugs for control of blood pressure was comparatively less (8%) in Labetalol group versus methyldopa group (13%). This is comparable with the study of P F Plouin et al (1988), where additional drugs requirement was 13% in labetalol & 26% in methyldopa group [2].

Type of Delivery

In this study 19% of the deliveries were induced and 31% were spontaneous in labetalol group. In methyldopa group 12% of the patients had induced

deliveries and 29% were spontaneous. In study of Pasker-de Jong PCM et al, 2010 [7], reported induced labour to be somewhat more frequent in the labetalol than in the methyldopa treated group.

But in study of G D Lamming et al (1979) and A.M. El-Qarmalawi et al (1995) [6,8] spontaneous delivery were more in labetalol when compared to methyldopa group and induced delivery were more in methyldopa group. Frequency of LSCS similar in both the groups, a similar finding of P F Plouin et al (1988), Magee et al. [2].

Perinatal Safety

50% of patients were terminated for full term pregnancy in labetalol group whereas it was only 30% in methyldopa group. Uncontrolled hypertension was indication for induction in 6% patients in labetalol group while in methyldopa group it was 20% for. Incidence of IUGR was similar in both groups. Oligohydramnios was seen less in labetalol group (12%) as opposed to methyldopa group (40%). About 94% of the patients in labetalol group and 89% in the methyldopal group had no associated morbidity.

About 35%of the babies in labetalol group and 29% in methyldopa group had Intra Uterine Growth retardation. But on birth need for NICU admission was less(32%) in labetalol group, whereas it was more (44%) in methyldopa group.

IUD in both groups had occurred prior to commencement of treatment. In a study by Redman et al, he found that two babies born to women assigned to labetalol died but no deaths were reported in methyldopa group.

The perinatal outcome was almost same in the study group as per the findings of this study. Plouin et al [2] have also observed similar findings in a similar study.

Conclusion

Hypertensive disorder of pregnancy is one of the major causes of maternal and fetal mortality and morbidity.

Yet as long as its cause remains unknown, its prophylaxis will be uncertain.

Inspite of cost, labetalol is very effective and early onset of control of blood pressure is seen.

In patients on Labetalol requirement of adding other antihypertensive is much less than methyldopa.

With effective control of blood pressure, prevention of eclampsia and the pregnancy can be prolonged to achieve fetal maturity.

Labetalol is not associated with adverse fetal effects.

The chances of spontaneous onset of labor were greater in the labetalol group when compared to methyldopa group.

At proper doses of ensuring blood pressure control, labetalol found to be safe for the newborn with lesser requirement of NICU admissions.

To conclude, labetalol is safe, quicker control of blood pressure, advantageous than methyldopa with fewer side effects, and in prolongation of pregnancy in hypertensive disorder of pregnancy.

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