LABETALOL VS. METHYLODPA IN MANAGEMENT OF PREGNANCY INDUCED HYPERTENSION

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ABSTRACT

A prospective randomised controlled trial was conducted to evaluate the efficacy and safety of labetalol over methyldopa in management of severe PIH. Twenty five subject were allocated to Group I, who received labetalol and 25 in Group II received methyldopa. Eighty percent subjects in group I and 68% in group II responded to antihypertensive therapy, the mean duration of treatment in the two groups was 21 ± 6.5 days and 18 ± 5.7 days. Labour was induced in 28% and 36% in the two groups respectively. There were 9 (36%) preterm birth in both groups. The incidence of low birth weight babies in the two groups was 48% and 44% respectively with a mean birth weight of 2.52 ± 0.61 kg. All these differences were not statistically significant. The maternal side effects were significantly more (44%) with labetalol than with methyldopa (8%).

Conclusion is drawn that though labetalol is a good antihypertensive drug. It is not superior to methyldopa in managementof PIH.

INTRODUCTION

Definitive treatment for severe pregnancy induced hypertension is termination of pregnancy, but some times that has to be deferred to achieve reasonable maturity of fetus for its optimal survival.

Though antihypertensive drugs have a definite place in lowering maternal complications and improving the perinatal outcome, till date an ideal antihypertensive drug for PIH has not been found. Methyldopa has been in vogue for long time, but its side effects particularly reduction of cardiac

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output leading to compromise in uteroplacental blood flow is not desirable. Labetalol is a promising antihypertensive drug due to its unique property of having both alpha and beta adrenoreceptor blocking action. Labetalol is of particular interest to the obstetrician because some studies have demonstrated that it does not decrease uteroplacental blood flow.

To evaluate the efficacy of labetalol as an antihypertensive and its effects on pregnancy outcome, a randomised prosopective controlled trial was conducted in the department of obstetrics and Gynae. MCH, Rohtak.

MATERIAL & METHOD

Fifty pregnant women admitted to the antenatal ward with the diagnosis of severe PIH with or without proteinurea, and between 30-36 weeks gestation were randomly allocated to two groups. The women with fulminant preeclampsia, eclampsia and other obstetric and medical complications such as APH, heart disease essential and renal hypertension or having contra indications for beta blockers were not included. Group I women received labetalol, to start with in dosage of 50 mg 8 hourly and increased by 50 mg 8 hourly after 48 hours to a maximum of 150 mg 8 hourly, depending on the response.

Group II women received methyldopa 250 mg 8 hourly with increase of 500 mg 6 hourly after 48 hours to maximum of 2.5 gms daily.

The responses was judged by lowering in SBP, DBP and MAP. Responders were those in whom DBP was maintained between 90-100 mm Hg with MAP between 105-108 mm Hg. If BP remained high even with maximum dosage after 72 hours or had rapid rise, the patients were evaluated either for addition of Ca++ channel blocker (Nifedipine) or termination of pregnancy.

The patients in both groups were monitored for BP, proteinurea, renal and liver functions, fundus changes and coagulation profile. The fetal growth and well being was monitored by gravidogram, fetal kick chart, NST and biophysical scoring with USG. Labour was induced if BP was not controlled or there was foetal compromise (IUGR). If BP was controlled and fetal growth was normal, labour was induced after 38 weeks in case spontaneous labour did not ensure.

OBSERVATIONS

1. Profile of patients in the two groups :

The patients in both the groups were matched for their age, parity, socio economic and nutritional status, the presence of proteinurea and oedema along with hypertension in these two groups was same as shown in table I.

2. Response to antihypertensive therapy in two groups :

Depending on the control of SBP, DBP and MAP, there were 5(20%) non responders in group I and 9 (36%) in group II. The average fall in SBP and DBP in two groups after 24 hours of therapy was 8 & 6 mm hg respectively. Maximum fall in BP was observed by 48 hours of commencement of therapy in responders of both groups, after that the fall was more gradual and MAP was sustained around 107 ± 3.5 and 108 ± 4.5 of therapy. The mean duration of

antihypertensive treatment in two groups was 21 ± 6.5 days and 18 ± 5.7 days.

Amongst the non responders after 72 hours Nifedipine 10 mg 8 hourly was added to 3 patients in group I and 4 patients in group II, labour was induced in one patient in group I and 2 patients in group II with Magnesium Sulphate Therapy: emergency LSCS was done in 1 patient in group 1 on account of fetal distress. Three patients in group II responded to maximum dose of 500 mg 4 hourly methyldopa.

Foetal outcome in the two groups : (Table III, IV & V)

There were 9(36%) preterm births in both two groups. The mean gestation period prolonged from 33.9 ± 4 to 36.4±36 weeks in group I and from 33.28 ± 2.8 to 35.8 ± 4.4 weeks in group II. Labour was induced in 28% cases in group I and 36% in group II. The number of low birth weight babies in group I was (48%) and that in group II (44%). The mean birth weight in two groups was 2.56 ± 0.61 and 2.61 ± 0.63 kgs respectively.

There were two neonatal deaths in group II (one due to prematurity & IUGR, and other due to I.C.H. in preterm baby) and one in group I (due to prematurity).

RENAL FUNCTION TESTS

The responders in group I showed a fall in serum uric acid and creatinine levels whereas in group II either there was no change or an increase in levels. The difference was statistically significant (Table VI).

MATERNAL SIDE EFFECTS OF DRUG

In group I, 24% women had postural

Table I

Profile of patients in two groups

			Group I	Group II
1.	Age (Mean in years)		25.28 ± 6.37	24.4 ± 6.54
2.	Parity	P0	64% (16)	52% (13)
		P1	32% (8)	40% (10)
		P2	4% (1)	8% (2)
3.	Socio Economic Status			
	(Kuppuswamy)	Class II	16% (4)	20% (5)
		Class III & IV	68% (17)	64% (16)
4.	Maternal Weight (Mean Kg.)		53.5 ± 6.3	52.6 ± 6.8
5.	Hb. gm% (Mean)		9.53 ± 0.83	9.57 ± 0.78
6.	Proteinurea (Significant)		12 (48%)	9 (36%)
7.	Oedema (Significant)		8 (32%)	10 (40%)

Table II

Response to Anti hypertensive therapy in respondents of two groups

Respondents in two groups	Mean BP before start of therapy (in mm Hg)			After 72 hours in Respondents (in mm Hg)		
	SBP	DBP	MAP	SBP	DBP	MAP
Group I 20 (80%)	155.6 ± 12.4	112.4 ± 8.4	118.5 ± 7.8	135 ± 8.4	92 ± 6.8	107 ± 3.5
Group II 16 (64%)	156.4 ± 11.8	112.8 ± 7.8	120.5 ± 6.6	138.4 ± 7.8	92.5 ± 6.4	108 ± 4.5

hypotension (8%) each had headache & bradycardia and one woman developed skin rash, whereas in group II only two women showed skin rashes and two complained of drowsiness, the difference was statistically significant.

DISCUSSION

Plouin et al 1988 Michael 1986 Lamming and Symonds 1979 compared labetalol with methyldopa in PIH and observed a highly significant fall in MAP in the group treated with labetalol, whereas in present study we observed that though there were 80% responders with labetalol as compared to 64% with methyldopa, the difference was not significant statistically. The fall in SBP, DBP and MAP in responders of both the groups was equal indicating that both are equally effective in control of B.P. Same was the observation of more et al 1983 and Sibai et al 1983 Whiteland reported that there were more induction for non responders with methylodpa whereas Redman and Qunsted 1982 reported more inductions with labetalol, but in present study we observed that there was no difference for need for induction with two drugs. Walker et al 1982 showed that, the patient of PIH where labetalol was used showed better renal functions from the first of treatment, same was our observation with fall in mean S creatinine from 1.02 ± 0.3 to 0.78 ± 0.25 mg % and no change in S.uric acid level whereas with methyldopa both the values increased from pretreatment levels (Table VI).

In present study we did not observe any significant difference, in incidence of prematurity, IUGR, birth weight and condition of newborns of two groups.

Table III

Period of gestation at the start of therapy and delivery in two groups

Period of Gestation in weeks.	Start of therapy		At Delivery	
	Group I	Group II	Group I	Group II
30 - 32 weeks	4 (16%)	8 (32%)	-	-
32+ - 34 weeks	6 (24%)	7 (28%)	3 (12%)	4 (16)
34+ - 36 weeks	15 (60%)	10 (40%)	6 (24%)	5 (20%)
37 weeks onwards	-	-	16 (64%)	16 (64%)
Mean gestation in weeks	33.9 ± 3.4	33.28 ± 2.8	36.4 ± 3.6	35.8 ± 4.4

Table IV

Nature of labour in two groups

	Group I	Group II
Spontaneous	16 (64%)	15 (60%)
Induced	7 (28%)	9 (36%)
Elective LSCS	1 (4%)	1 (4%)
Emergency LSCS	1 (4%)	0

Table V

Birth weight of Newborns in two groups

Weight in gms.	Group I	Group II
Upto 2000	4 (16%)	2 (8%)
2001 - 2499	8 (32%)	9 (36%)
2500 - 3000	9 (36%)	10 (40%)
3001 and above	4 (16%)	4 (16%)
Mean birth weight in (Kg)	2.56 ± 0.61	2.61 ± 0 63

3 babies in Group I & 2 in Group II were IUGR & rest were preterm.

Table VI

Renal function tests in responders of two groups before and after therapy

	Serum creatinine in mg%			Serum uric acid in mg%		
	Upto 1	1.1 - 1.8	Mean	Upto 6	6.1 - 8.5	Mean
Group I						
- Before therapy	19 (76%)	6 (24%)	1.02 ± 0.3	13 (52%)	12 (48%)	5.6 ± 2.8
- During therapy	22 (88%)	3 (12%)	0.78 ± 0.25	11 (44%)	14 (56%)	5.6 ± 2.6
Group II						
- Before therapy	17 (32%)	8 (32%)	0.86 ± 0.42	8 (32%)	17 (68%)	5.6 ± 2.46*
- During therapy	12 (48%)	13 (52%)	1.20 ± 0.36	6 (24%)	19 (76%)	7.2 ± 2.68

* Difference Statistically significant with p value of < 0.001

Minor maternal side effects were reported in 44% with labetalol and only 16% with methyldopa. Though none except one with methyldopa required termination of therapy, one patient on methyldopa who developed some rashes drug was stopped and she was managed with nifedipine.

From present study we conclude that though labetalol is quite effective and sage anti hypertensive drug for PIH but methyldopa is as equipotent as labetalol.

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