Original Research Article

Role of Labetolol in hypertension in pregnancy in comparison with Nifedipine in terms of fetomaternal outcome

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Abstract

Background: Hypertensive disorders complicate 5-10% of all pregnancies and together they form one member of the deadly triad, along with haemorrhage and infection that contribute greatly to maternal morbidity and mortality rates.

Materials and methods: Antihypertensive drugs taken into the study were Tab. Labetolol, 100-300 mg three times a daily, max dose 2400 mg per day and T. Nifedipine, 10 mg three times a day, max dose 120 mg per day. The study was a randomised control clinical trial, the study period started from Nov 2014 to June 2016, in the Department of Obstetrics and Gynecology, KGH, Andhra Medical College, Visakhapatnam, India.

Results: Age distribution, Gravidity, Gestational age at the time of admission, Distribution of cases as per type of hypertension, Duration of therapy before delivery in study group, Changes in blood pressure, Maternal side effects in the study group, Mode of delivery, APGAR score of the babies at the time of delivery were tabulated.

Conclusion: Labetolol gave good control of BP with single agent, when the dose was titrated appropriately, till the BP was controlled. The control of BP was consistent with labetolol, and also could be used for longer duration without any additional therapy whereas with nifedipine, control of BP was inconsistent and required additional medication for proper control of BP.

Key words

Labetalol, Nefidipine, Hypertension, Pregnancy.

Introduction

Hypertensive disorders complicate 5-10% of all pregnancies and together they form one member of the deadly triad, along with haemorrhage and infection that contribute greatly to maternal morbidity and mortality rates [4]. Hypertensive disorders are important causes of premature delivery, intrauterine growth restrictions and IUD [1]. Maternal complications include those that attribute to excessive increase in BP, such as stroke, acute cardiac decompensation and acute renal failure. According to WHO, in developed countries 16% of maternal deaths were due to hypertensive disorders [4]. The incidence of pre-eclampsia is commonly cited to be about 5%. Although remarkable variations are reported from 5-15%. Although the incidence of both the developing countries and developed countries is similar, the severe form of disease and complications are more in developing countries due to inadequate antenatal care. In India it is about 7-10%. An ideal antihypertensive should maintain cardiac, renal, cerebral and uteroplacental perfusion. It should not increase the heart rate or plasma volume. It should not have side effects on both foetus and mother. Labetolol is a competitive antagonist at both alpha and beta adrenergic receptor sites. It is non selective for β1 and β2 receptors, but selective for α receptors. Nifedipine is a calcium channel blocker of dihydropyridine group, belonging to L type of voltage sensitive calcium channels. Main action is on the arterioles, causing decrease in peripheral resistance resulting in the blood pressure fall. It has a mild natriuretic action, but significant diuresis does not occur.

Materials and methods

Antihypertensive drugs taken into the study were Tab. Labetolol, 100-300 mg three times a daily, max dose 2400 mg per day and T. Nifedipine, 10 mg three times a day, max dose 120 mg per day.

The study was a randomised control clinical trial, the study period started from Nov 2014 to June 2016, in the Department of Obstetrics and Gynecology, KGH, Andhra Medical College, Visakhapatnam, India.

Criteria of selection of cases

Inclusion criteria

- Gestational hypertension
- Pre-eclampsia
- Chronic hypertension
- Chronic hypertension with superimposed pre-eclampsia

Exclusion criteria

- Eclampsia
- Patients with heart disease, bronchial asthma, renal diseases.

Methods of study

Before starting treatment, the baseline investigations like complete hemogram, renal function tests, liver function tests, opthalmoscopic examination, foetal surveillance tests (cardiotocogram, total obstetrical scan) were done. We divided the patients into four groups depending upon the gestation age.

- Less than 24 weeks,
- 24-28 weeks,
- 28-34 weeks,
- More than 34 weeks

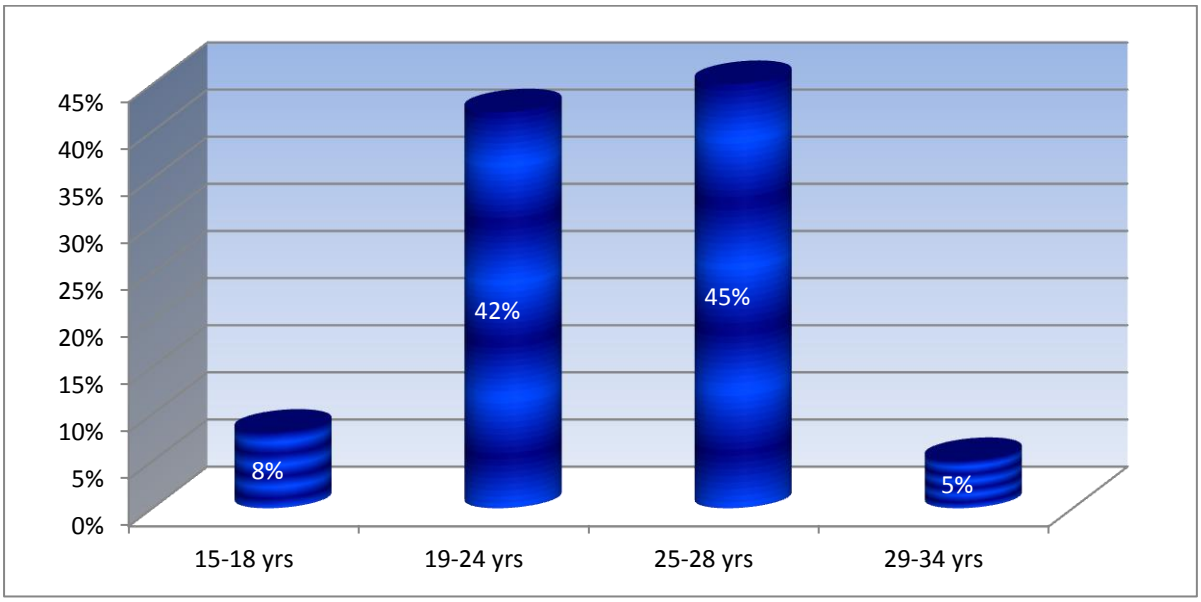
After administration of the drug, BP monitoring, side effects of the drug, foetal outcome and maternal outcome were evaluated. BP and pulse rate were recorded every 6^{th} hourly, patients were monitored for side effects. Fetal heart rate was also monitored. Urine examination was done on alternate days, ultrasound done once weekly. If BP control was not achieved with initial dose of the drug within 48 hrs, dose was increased.

Results

Age distribution was as per **Chart – 1.** Gravidity was as per **Table – 1.** Gestational age at the time

of admission was as per **Table – 2.** Distribution of cases as per type of hypertension was as per **Table – 3.** Duration of therapy before delivery in study group was as per **Table – 4.** Changes in blood pressure were as per **Table – 5.** Maternal side effects in the study group were as per **Table – 6.** Mode of delivery was as per **Table – 7.** APGAR score of the babies at the time of delivery was as per **Table – 8.**

Chart - 1: Age distribution.



Discussion

Labetolol is an effective drug in control of hypertension in pregnancy. A study by G.D. Lamming and E.M. Symonds on Labetolol proved that Labetolol is a useful drug in the treatment of PIH.

Table - 1: Gravidity.

Gravida	No. of cases	%
Primi	47	47%
Second	30	30%
Third	12	12%
Fourth	4	4%
Fifth	1	1%
Sixth	1	1%

Table - 2: Gestational age at the time of admission.

Gestational age	No. of cases	%
<24	1	1
24-28	10	10
28-34	43	43
>34	46	46

Table - 3: Distribution of cases as per type of hypertension.

Type of hypertension	No. of cases	%
Gestational hypertension	34	34%
Mild pre-eclampsia	17	17%
Severe pre-eclampsia	35	35%
Chronic hypertension	4	4%
Chronic hypertension with superimposed pre-eclampsia	5	5%
Recurrent pre-eclampsia	5	5%

A study by A.El Qarmalwi proved that Labetolol is well tolerated. It proved that Labetolol gives more efficient control of BP, may have beneficial effect on renal functions with fewer side effects.

In the present study Labetolol gave good control of HTN while having fewer side effects and beneficial effect on renal function by decreasing proteinuria.

A randomised double blind study of hemodynamic evaluation of patients taking Labetolol and Nifedipine with pre eclampsia by Scardo J.A et al revealed that Nifedipine group has increase in heart rate where as Labetolol had no effect. Mean arterial BP was lowered significantly in both the groups.

Table - 4: Duration of therapy before delivery in study group.

Duration	Labetolol		Nifedipine	
	No. of cases	% of cases	No. of cases	% of cases
5 days-1 week	2	4%	2	4%
1 week-2 weeks	34	68%	38	76%
3 weeks-4 weeks	8	8%	8	16%
5weeks-6weeks	4	4%	0	0%
7weeks-8weeks	2	2%	2	4%

Table - 5: Changes in blood pressure.

	Labetolol		Nifedipine	
	Before treatment	After treatment	Before treatment	After treatment
Mean systolic blood pressure	162	128	160	136
Mean diastolic blood pressure	105	90	104.8	88
Mean arterial pressure	126	102	122	94

Table - 6: Maternal side effects in the study group.

Side effects	Nifedipine	Labetolol
Headache	4	0
Nausea, vomiting	0	0
Palpitations	6	0
Tachycardia	7	0
Orthostatic hypertension	7	0
Dizziness	0	0
Any other	0	0

Table - 7: Mode of delivery.

Duration	Labetolol		Nifedipine	
	No. of cases	% of cases	No. of cases	% of cases
Vaginal	40	40%	33	33
A. Spontaneous	15	15%	5	5%
B. Induction	23	23%	28	28%
C. Outlet foreceps	2	2%	1	1%
Cesarean section	12	12%	17	17%
A. Elective	5	5%	8	8%
B. Emergency	5	5%	9	9%

Table - 8: APGAR score of the babies at the time of delivery.

APGAR score	Labetolol		Nifedipine	
	No. of cases	% of cases	No. of cases	% of cases
10	30	60%	28	56%
6-8	11	22%	13	26%
4-6	2	4%	2	4%
2-4	3	6%	4	8%
2-0	4	8%	3	6%

Nifedipine and Labetolol are equally efficacious in the control of HTN in the present study. A randomised double blind study trial of oral nifedipine and Labetolol on HTN in pregnancy by Vermillion ST et al opined that both are efficient in the management of PIH. Nifedipine controls HTN more rapidly. Blood pressure control by Nifedipine is rapid where as Labetolol was slow in action.

Labetolol was found to have favourable effect on Bishop Score of Cervix. It was proved in 2 studies By A.M.El. Qarmalwi [5] and G.D. Lamming and E.M. Symonds [9].

A study by Tarek Z.K.Mahmoud, et al. on effect of Labetolol on the fetoplacental circulation and the fetal outcome stated that Labetolol as an effective drug in controlling BP, Doesn't have any adverse effect on the umbilical artery flow velocity waveform, No neonatal problems were directly attributed to the drug, fetal outcome was satisfactory.

A study by G.D. Lamming and E.M. Symonds on the Labetolol proved Labetolol is a useful drug in the treatment of PIH and it also lowers BP satisfactorily and does not seem to have any detrimental effects on the fetus.

A study by Sibai et al found that mean prolongation of pregnancy with Labetolol was 22 days. In the present study pregnancy was prolonged for a mean of 23 days. Labetolol when compared with other antihypertensive is safe and efficacious.

Comparative study of Labetolol with other anti hypertensive drugs by B.N.C. Prichard and D.A. Richards gave following conclusions (**Table – 9**):

- Pharmacological and Hemodynamic profile of Labetolol is different from other drugs in that reduced BP and peripheral vascular resistance is not accompanied by changes in resting heart rate and cardiac output.
- Its efficacy as an anti hypertensive is comparable with other drugs like Nifedipine and Methyldopa.
- It produces no greater burden of side effects than other anti hypertensive drugs.

Conclusion

The present study is a randomised control study conducted at King George Hospital. The study shows the highest incidence of preeclampsia in age group of 19-28 years. The maximum incidence is in primis at term gestation. Most common type of HTN is pre-eclampsia. In the present study efficacy of nifedipine and labetolol are compared. Labetolol gave good control of BP with single agent, when the dose was titrated appropriately, till the BP was controlled. The control of BP was consistent with labetolol, and also could be used for longer duration without any additional therapy whereas with nifedipine, control of BP was inconsistent and required additional medication for proper control of BP. The patients who were treated with Labetolol were found to have favourable cervix and had spontaneous vaginal deliveries resulting in less maternal morbidity. Nifedipine often resulted in

complications like tachycardia and palpitations, while labetolol group had very few side effects. Both the drugs were found to be safe for the foetus.

Table – 9: Comparison of various studies.

Studies	Conclusion
Scardo J.A., et al. [7]	• Nifedipine group had increase in heart rate where as labetolol had no effect • Mean arterial BP were lowered significantly in both groups • Both drugs are efficient in the management of PIH • Nifedipine controls HTN more rapidly
A.M.EL. Qarmalwi [5]	Labetolol was found to have fewer side effects
B.N.C Prichard and D.A Richards	Labetolol was found to have fewer side effects
Present study	Labetolol gave good control of hypertension, have fewer side effects

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