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Original Research Article

Evaluation of the Effectiveness of Intravenous Labetalol and Oral Nifedipine for Managing Severe Hypertension during Pregnancy

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Abstract:

Background and Objectives: Hypertension is the most frequently encountered medical disorder in obstetric practice & remain a major cause of maternal, fetal & neonatal morbidity & mortality. The present study was undertaken to compare the time taken to reach the therapeutic goal of blood pressure after using intravenous labetolol & oral nifedipine in severe hypertension during pregnancy, To compare the efficacy and safety of the IV labetolol and oral nifedipine.

Materials and Methods: Sixty women with hypertensive crisis were randomized to receive either oral nifedipine 10 mg or intravenous labetolol 20 mg in equal numbers. Oral nifedipine was given 10 mg stat followed by 10 mg every 30 minutes up to a maximum of 50 mg. Intravenous labetolol was given 20 mg stat followed by 40 mg 10 minutes later then two more doses of 80 mg every 10 minutes up to a maximum of 220 mg. The primary outcome was the number of doses required to achieve target blood pressure (BP) and time required to reduce the mean arterial pressure by 25%. Secondary outcomes analysed included additional drugs required.

Conclusion: Oral nifedipine & intravenous labetolol regimens are equally effective in the management of severe hypertension in pregnancy; Nifedipine needs fewer doses to reach target BP and cost effective with the advantage of oral administration. Whereas labetolol needs less time to us reach target BP and appropriate drug in patients with eclampsia.

Keywords: Severe hypertension, severe preeclampsia, Nifedipine, Labetolol.

Introduction

Hypertensive disorders complicating pregnancy are common and form one of the deadly triad, along with hemorrhage and infection, which contribute greatly to maternal morbidity and mortality. The disorder affects approximately 5 to 10 % of pregnancies and is a significant cause of maternal and fetal morbidity and mortality. [1] It has been estimated that worldwide each year 1,50,000 to 8,00,000 women develop pre-eclampsia, up to 1,50,000 women have eclamptic convulsions and 90 percent of these women are from developing countries [2]. Berg and Colleagues (2003) reported that almost 16 percent of pregnancy related deaths were due to complications of pregnancy related hypertension particularly severe hypertension [1,3]. Though etiology of pre-eclampsia is still unknown and although it is not preventable, many deaths from the disorder can be prevented.

High blood pressure is a sign, not a disease reflecting an increase in cardiac output or more commonly increase in total peripheral resistance. Correct management of the individual pregnant with hypertension will therefore, depend upon correct identification of the underlying hypertensive disorder and its appropriate management [4]. Complications of hypertension are the third leading cause of pregnancy related deaths. Preeclampsia is associated with increased risk of placental abruption, acute renal failure, cerebrovascular and cardiovascular complications, disseminated intravascular coagulation and maternal death. Majority of these conditions are preventable. There are still no definitive guidelines as to when hypertension in pregnancy should be treated and which agents should be used as first or second line drug treatment. In order to decide which patients with hypertension during pregnancy should be treated one needs to identify those patients at higher risk and in need for closer monitoring [4]. Whereas the definitive treatment of severe hypertension is antihypertensive drug therapy, the definitive treatment of preeclampsia is delivery. (Natali A.Y. Chung et al.) The only definitive "cure" for preeclampsia is delivery, either vaginal or cesarean (c-section). Inducing labour is the treatment of choice for women who have reached a gestational age of at least 37 weeks. In all cases, the

consensus is that all women with preeclampsia should be delivered by 40 weeks, and the use of induction drugs and cervical ripening agents is common. For women who have not reached 37 weeks, treatment focuses on allowing the baby to mature as much as possible before inducing labour. The goal of preeclampsia treatment is to avoid progression of the disease and / or complications.

There is no single reliable, cost-effective screening test for preeclampsia and there are no well-established measures for primary prevention. Management before the onset of labor includes close monitoring of maternal and fetal status [5].

Objectives

To know the prevalence of hypertension in the study group.
To note the complications of the drug in the study group.
To assess the fetal outcome

Material and Methods

This study is completely inpatient based. Primary data was generated by studying patients admitted for the management of preeclampsia at Nalanda Medical College and Hospital Patna, Bihar. Study duration is of 10 months.

Inclusion Criteria

- All women, primigravida or multigravida with gestational age > 28 weeks with severe hypertension with BP ≥ 160 mmHg systolic and ≥ 110 mmHg diastolic.
- Latest blood pressure recording prior to enrolment must fulfill the criteria of severe hypertension.
- Singleton pregnancies.

Exclusion Criteria

- Medically associated conditions- Heart failure, asthma, heart rhythm abnormality, diabetes in pregnancy etc,
- Chronic hypertension,
- Non pregnancy related hypertension,
- Atherosclerotic cardiovascular disease and those at risk of atherosclerotic cardiovascular disease,
- Allergy to nifedipine or labetolol.

A total number of 60 pregnant women with severe hypertension were included in the study and were assigned alternatively in labetolol or nifedipine group with 30 cases in each group. On admission brief history was taken, examined and investigated. Blood pressure was recorded using mercury sphygmomanometer with patient in 15 degree left lateral recumbent position. Korotokoff V sound was used for determining diastolic blood pressure. After diagnosis trial group was started with either labetolol or nifedipine. BP was measured by non-invasive BP cuff and all patients were on continuous monitoring. Group A received labetolol 20 mg slow IV over 5 minutes as a stat dose and repeated every 10 minutes as 40,80 and again 80 mg until target blood pressure is reached or a total dose of 220 mg and group B received tablet 10 mg stat dose and 10 mg repeated every 30 minutes upto total dose of 50 mg. If blood pressure does not decrease even after the dose to maximum, cross over treatment done with other anti-hypertensive agent and treatment is considered as failure.

Investigations included complete hemogram, platelet count, renal and liver function tests, urine albumin, 24-hour urine protein, and coagulation profile in selective cases, fundoscopy, NST, ultrasound and Doppler in some cases. Patients with gestational age less than 35 weeks were given steroid prophylaxis to help lung maturity. Those patients with impending eclampsia were given prophylactic $MgSO_4$ and eclampsia patients were given Pritchard regimen. Decision to continue with conservative management of pregnancy or to deliver & mode of delivery was made depending on maternal & fetal indications. Then patients were followed until delivery & the various modes of delivery were noted. The indications for induction of labor if done were noted.

Results

A comparative study consisting of 30 pregnant women with severe hypertension treated with labetolol and 30 pregnant women with severe hypertension treated with nifedipine is undertaken to study the efficacy and safety of the drugs.

Table 1: Age distribution of patients studied

Age in years	Labetolol		Nifedipine	
	No	%	No	%
<20	4	13.3	12	40.0
21-25	20	66.7	12	40.0
26-30	3	10.0	5	16.7
31-35	3	10.0	0	0.0
36-40	0	0.0	1	3.3
Total	30	100.0	30	100.0
Mean ±SD	24.20±3.98		23.30±4.26	

Samples are age matched with P=0.401 shows age distribution of patients of both the groups.

All the patients were in age group 19-40 years. 66.71% of patients were between 21-25 years in labetolol group. 40% of patients in nifedipine group were between 21-25 years in. Youngest was 18 year in both the groups. Eldest was 40 year in nifedipine group. Mean age was similar in both the groups.

Table 2:Parity distribution of patients studied

Parity	Labetolol		Nifedipine	
	No	%	No	%
Primi	21	70.0	18	60.0
Multi	9	30.0	12	40.0
Total	30	100.0	30	100.0

Parity distribution is statistically similar in two groups with P=0.417

shows parity distribution of patients studied in each group with a range of primigravida to multigravida. As seen in the graph, gravida distribution shows maximum patients of severe hypertension were primigravida in both the groups, 70% in labetolol group and 60% in nifedipine group.

Table 3: Gestational age in weeks

Gestational age in weeks	Labetolol		Nifedipine	
	No	%	No	%
28-32	6	20.0	3	10.0
33-36	10	33.3	6	20.0
37 & above	14	46.7	21	70.0
Total	30	100.0	30	100.0

Distribution of gestational age is statistically similar in two groups with P=0.230

shows the gestational age at presentation in each group. Larger group of patients with severe hypertension belonged to 37 weeks and above, 46.7% in labetolol group and 70% in nifedipine group.

Table 4: Number of Patients had Eclampsia

Eclampsia	Labetolol		Nifedipine	
	No	%	No	%
Absent	26	86.7	30	100.0
Present	4	13.3	0	0.0
Total	30	100.0	30	100.0

shows number of patients had eclampsia at the time of starting treatment in both the groups. 13.3% of patients in labetolol group had eclampsia, but none of the patients in nifedipine group had eclampsia.

Table 5: Comparison of Treatment Failures

Treatment failure	Labetolol	Nifedipine
No failure	25(83.3%)	30(100.0)
Failure	5(16.7%)	0
Total	30(100.0%)	30(100.0%)

number of patients who did not respond to treatment and needed cross over treatment with another drug in both the groups. Total 16.7% of patients had treatment failure and needed another drug to control BP in labetolol group and none of the patients in nifedipine group needed another drug.

Table 6: Birth weight distribution

Birth weight (kg)	Labetolol (n=25)		Nifedipine (n=30)	
	No	%	No	%
1-1.5kg	2	8.0	0	0.0
1.6-2.0 kg	4	16.0	4	13.3
2.1-2.5kg	5	20.0	7	23.3
>2.5 kg	14	56.0	19	63.3

Distribution of Birth weight is statistically similar in two groups with P=0.532

shows the comparison of birth weight (kg) between two groups of patients studied. The mean birth weight was similar in both the groups. Maximum number of newborns were weighing > 2.5 Kg in both the groups

Table 7: Mode of delivery

Mode of delivery	Labetolol (n=25)		Nifedipine (n=30)	
	No	%	No	%
Vaginal delivery	17	68.0	14	46.7
Caesarean delivery	8	32.0	16	53.3

Distribution of Mode of delivery is statistically similar in two groups with P=0.112

comparison of mode of deliveries in between two groups studied. In labetolol groups 68% had vaginal deliveries and 32% had caesarean deliveries. In nifedipine group 46% was vaginal deliveries and 53% cesarean deliveries.

Statistical Methods: Descriptive and inferential statistical analysis has been carried out in the present study. Results on continuous measurements are presented on Mean SD (Min-Max) and results on categorical measurements are presented in Number (%). Significance is assessed at 5 % level of significance. The following assumptions on data is made, Assumptions: 1. Dependent variables should be normally distributed, 2. Samples drawn from the population should be random, Cases of the samples should be independent.

Discussion

Reduction of BP is an important strategy in the management of severe hypertension during pregnancy in the prevention of both maternal and fetal adverse events. Recommended drugs for the treatment of hypertensive crisis are IV hydralazine, IV labetolol and oral nifedipine. [6] The use of these drugs have been studied in a number of randomized control trials to evaluate the efficacy and safety. In the present study comparison between the anti-hypertensives labetolol and nifedipine in terms of efficacy and safety were assessed. [7]

All the patients studied were aged between 19 to 40 years. In labetolol group 66.7% patients were between 21-25 years and in nifedipine 40% of the patients were between 21-25 years. Youngest was 18-year-old in both the groups, eldest was 40 year old in nifedipine group. [8]

Mean Age Distribution

	Present Study		Bhadal Dhali et al., 2012[44]		Vermillan et al., 1999[45]	
	Labetolol	Nifedipine	Labetolol	Nifedipine	Labetolol	Nifedipine
Maternal mean age in years	24.20 ± 3.98	23.30 ± 4.26	24.30 ± 1.20	23.70 ± 1.40	27.0 ± 6.40	27.20 ± 7.30

Mean age in both the groups were similar. 24.2 ± 3.90 in labetolol and 23.3 ± 4.2 in nifedipine group. Comparable with vermillion et al., 1999 and Bhadal Dhali et al., 2012 studies where there is 24.30 ± 1.2 in labetolol group and 23.7 ± 1.4 in nifedipine group. [9] In Vermillan study mean age in labetolol group 27.0 ± 6.4 and nifedipine 27.2 ± 7.3. [10]

Parity distribution shows maximum patients of severe hypertension are primi gravidas.70% in labetolol group and 60% in nifedipine group. Our study is comparable to Bhadal Dhali study where maximum number was primigravida in both the groups, 82% in labetolol group and 80% in nifedipine group. Lakshmi Dasari et al., study also showed maximum patients were primigravidas. [11]

Gestational age in weeks

	Present Study		Vermillan et al.,		i Dasari et al., 2012	
	Labetolol	Nifedipine	Labetolol	Nifedipine	Labetolol	Nifedipine
Gestation (weeks)	33.8	34.2	33.6 ±6.0	34.3 ± 5.1	35.1	35.5

Mean gestational age is almost similar in both the groups. 33.8 in labetolol groups and 34.2 in nifedipine group. This was comparable to both Vermillan et al., and Lakshmi Dasari et al., studies. In Vermillan et al., study labetolol group shows 33.6 ± 6.0 in labetolol group. In 34.3 ±5.1 in nifedipine group and Lakshmi Dasari study, labetolol group shows 35.1 and nifedipine group 35.5.

Mode of Delivery

Doses	Present Study		IA Raheem et al., 2011	
	Labetolol	Nifedipine	Labetolol	Nifedipine
Vaginal Deliveries	17 (68.0%)	14 (46.7%)	12 (48.0%)	9 (36.0%)
Caesarean	8 (32.0%)	16 (53.0%)	13 (5.2%)	16 (64.0%)

There was little difference in the mode of deliveries in labetolol and nifedipine groups. Vaginal deliveries were 68% in labetolol group and 46.7% in nifedipine group whereas ceasarean section rate was 32% in labetolol group and 53% in nifedipine group. Increased ceasarean section rate in nifedipine group may be because of its tocolytic effect. Our study was comparable with IA Raheem study.

Perinatal Outcome.[12,13]

Perinatal outcome	**Present Study**		Lakshmi and Dasari et al. 2012	
	Labetolol	**Nifedipine**	Labetolol	Nifedipine
Preterm	12 (40%)	13 (43.3%)	10	12
IUGR	5 (16.7%)	3 (10.0%)	8	7
IUD	3 (10.0)	3 (10.0)	1	0
Still Birth	0 (0.0)	1 (3.3%)	6	8

No significant difference was found in the perinatal outcome in both the groups in regarding preterm deliveries, IUGR and intra uterine death of the fetus. Intrauterine death probably because of extremely preterm delivery (28 to 29 weeks) and very low birth weight < 1000 grams. It was almost comparable to Lakshmi and Dasari et.al study. [14,15]

Conclusion

Hypertensive disorders of pregnancy are one of the major causes of maternal and fetal morbidity and mortality. It forms a member of the deadly triad, along with hemorrhage and infection. Yet as long as its etiopathogenesis is unclear prophylaxis will be uncertain. Though the prevention is difficult, maternal and fetal morbidity and mortality can be reduced to a greater extent by early recognition and timely management. Reduction of BP is an important strategy in the management of severe hypertension for the prevention of both maternal and fetal adverse effects. Recommended drugs to manage hypertensive crisis are hydralazine, labetolol and nifedipine.

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