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Research Article

A Study of Comparing the Effectiveness of Intravenous Labetalol and Oral Nifedipine in Pregnancy-Related Hypertensive Emergencies

Dr. G Monica[1] and Dr. Syed Razia Sultana[2]
[1]Assistant Professor, Department of OBGY, Ayaan Institute of Medical Sciences Teaching Hospital & Research Centre
[2]Associate Professor, Department of OBGY, Ayaan Institute of Medical Sciences Teaching Hospital & Research Centre

*Corresponding Author
Dr. Syed Razia Sultana

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Abstract: Background: Hypertension in pregnancy is one of the most common medical conditions encountered during gestation, with significant implications for both maternal and fetal health. Nifedipine has the advantage of being cost effective, rapid onset of action, long duration of action and can be administered orally, however it is known to cause sudden maternal hypotension and fetal distress caused by placental hypoperfusion, palpitation and transient neuromuscular weakness when used concomitant with magnesium sulphate. Intravenous Labetalol is considered to control severe hypertension in pregnancy. Its advantages include little placental transfer, less palpitation and less maternal tachycardia. Methods: The present study was prospective, randomized comparative clinical trial conducted on 140 patients in the department of Obstetrics & Gynaecology over a period of 1 year following approval from institutional ethical committee. A thorough history was elicited from the patients regarding age, parity, socio economic status, history suggestive of imminent symptoms. Their past history regarding bronchial asthma, cardiac diseases, prior drug intake for hypertension and other medical disorders were also obtained. The pregnant women were randomized with computer generated numbers into two groups to receive either oral nifedipine or intermittent intravenous labetalol injections. Enrolled patients will be randomized to receive either oral nifedipine or intravenous labetalol. Results: Our study reports showed that, baseline diastolic blood pressure did not vary significantly in the groups. The mean of the baseline diastolic blood pressure were 109 mm Hg and 112 mm Hg in the groups A and B, respectively. 55.8% and 50% in groups A and B had diastolic blood pressure more than 110 mm Hg. In present study on comparison of time taken to control BP between two groups, i.e. to achieve BP 150/100mm of Hg. The mean time required were 51.50 ± 11.85 mins in the Labetalol groups and 48.0 ± 6.25 minutes in the Nifedipine group. This comparision showed no difference in the two groups with a 'P' value of 0.358. Similarly on comparison of no. of doses of drugs required to control BP between two groups it was observed that most of the patients were controlled by two doses of each drug. Mean number of doses required to Achieve Target Bp in IV labetalol group 2.08 and in nifedipine group was 2.02. Conclusions: Ultimately, both medications can be valuable in the management of hypertensive disorders in pregnancy, and the choice between them should be guided by the severity of the condition, the need for rapid blood pressure control, and the clinical setting. For severe and rapidly progressing hypertensive emergencies, intravenous labetalol remains the gold standard. However, nifedipine can be an effective alternative for less acute cases or in settings where oral administration is more practica.

Keywords: Hypertension, Labetalol, Nifedipine, Pregnancy.

INTRODUCTION

Hypertension in pregnancy is one of the most common medical conditions encountered during gestation, with significant implications for both maternal and fetal health. It includes a spectrum of disorders that vary in severity, from mild, transient hypertension to severe, life-threatening emergencies.[1]

Pregnancy-related hypertensive disorders are among the leading causes of maternal and perinatal morbidity and mortality worldwide. [2] Hypertensive emergencies during pregnancy are a subset of pregnancy-related hypertension that require urgent medical intervention due to the risk of acute organ damage. These emergencies typically manifest when blood pressure reaches critically high levels, such as ≥ 160/110 mmHg, and is associated with evidence of end-organ damage. [3] This damage can involve the kidneys, brain, heart, or liver, and in severe cases, can lead to life-threatening complications such as stroke, renal failure, placental abruption, or disseminated intravascular coagulation (DIC). [3]

The exact cause of hypertensive disorders in pregnancy is not fully understood, though factors such as impaired placental perfusion, abnormal immune response, genetic predisposition, and maternal vascular adaptations are thought to play key roles. [4] Risk factors for developing hypertensive disorders include obesity, age (particularly extremes), multiple gestation, pre- existing hypertension or renal disease, and a family history of hypertensive disorders. [5]

The pathophysiology of hypertensive emergencies in pregnancy is complex. High blood pressure can impair endothelial function, leading to vascular permeability, fluid leakage, and a cascade of systemic consequences.

[6] In preeclampsia and eclampsia, placental dysfunction also contributes to the release of pro-inflammatory factors, which can exacerbate maternal endothelial dysfunction and lead to widespread organ involvement. [7]

The management of pregnancy-related hypertensive emergencies involves both maternal stabilization and fetal well-being. Blood pressure management is crucial but must be carefully balanced to avoid compromising uteroplacental blood flow. [8] Antihypertensive medications, such as labetalol, hydralazine, and nifedipine, are commonly used to lower blood pressure, while magnesium sulfate is administered for seizure prophylaxis in cases of eclampsia. In some cases, early delivery may be necessary to protect both the mother and the fetus, particularly when severe complications arise or if the condition worsens despite medical intervention. [9] Ultimately, effective management of hypertensive emergencies during pregnancy hinges on a comprehensive understanding of these conditions, their pathophysiology, risk factors, and appropriate therapeutic interventions to mitigate the risks to both mother and child. [10]

The most commonly used hypertensive agents for hypertensive emergencies in pregnancy are Nifedipine, Labetalol and hydralazine. Hydralazine.

diuretics and alpha methyl dopa are not recommended for use in severe hypertension as first line drugs due to adverse maternal, fetal outcomes and late onset of action of the latter. [11] Nifedipine has the advantage of being cost effective, rapid onset of action, long duration of action and can be administered orally, however it is known to cause sudden maternal hypotension and fetal distress caused by placental hypoperfusion, palpitation and transient neuromuscular weakness when used concomitant with magnesium sulphate.

[12] Intravenous Labetalol is considered to control severe hypertension in pregnancy. Its advantages include little placental transfer, less palpitation and less maternal tachycardia, however neonatal hypotension and neonatal bradycardia has been observed in some trials and is not as cost effective as Nifedipine. [13]

MATERIALS AND METHODS

The present study was prospective, randomized comparative clinical trial conducted in the department of Obstetrics & Gynaecology, over a period of 1 year following approval from institutional ethical committee. Written consent was obtained prior to the study. One hundred consecutive patients satisfying the inclusion criteria were recruited in the present study.

Inclusion Criteria

1. Age – 18 to 35 years.
2. All pregnant women of 20 weeks gestation or more.
3. Sustained severe hypertension: Systolic blood pressure ≥ 160 mm Hg ; diastolic blood pressure ≥110 mm Hg; or a mean arterial pressure of > 125mmHg, lasting for 15 minutes or more in the past 4 hours on at least 2 occasions.

Exclusion Criteria

1. Patients with essential hypertension.
2. Exposure to either drug prior to the study
3. H/o cardiac disease, bronchial asthma, hematological disorder, Diabetes, Liver disorders
4. Allergy to labetalol or nifedipine

Methodology

A thorough history was elicited from the patients regarding age, parity, socio economic status, history suggestive of imminent symptoms. Their past history regarding bronchial asthma, cardiac diseases, prior drug intake for hypertension and other medical disorders were also obtained. After explaining the condition of the patient and getting prior informed consent, the pregnant women were randomized with computer generated numbers into two groups to receive either oral nifedipine or intermittent intravenous labetalol injections. Enrolled patients will be randomized to receive either oral nifedipine or intravenous labetalol.

Patients were randomly assigned to be started either with intravenous labetalol (study group) or oral nifedipine (control group) until satisfactory B.P control were achieved.

Group A: Injection Labetalol 20 mg i.v bolus over 10 minutes repeated every 20 minutes increasing to 40, 80, 80, to maximum of 220 mg.

Group B: Oral Nifedipine 10 mg stat and then repeated at 45 minutes interval till satisfactory B.P were achieved. Maximum dose were 5 doses.

During the study period maternal blood pressures were recorded at every 15 minutes interval till first 30 minutes after achieving target blood pressure less than or equal to 150/100 mmHg, thereafter every 30 minutes for next 2 hours then every hourly. Continous maternal vital parameters and electronic fetal monitoring were done. CTG trace were taken at the beginning and then one at the end of the study.

Treatments were considered as failure if blood pressure were not decreased even after increasing the dose to maximum. Additional antihypertensive agent were added and managed accordingly. If patient developed hypotension BP <90/60mmHg then the trial was terminated and patient were treated with iv fluids and ionotropes as needed.

Maternal complications like imminent signs, abruption, pulmonary oedema, oliguria, renal failure were looked for. Most of the patients delivered at term spontaneously while some needed induction. Birth weights, signs of prematurity of all babies were noted.

Statistical analysis

All the data were entered consecutively in a predefined data information sheet and analysis was done using SPSS 20 software. Differences in categorical and continuous data were assessed using the Chi square test and Student't' test, respectively. The statistical tests were considered significant if the calculated p value was less than 0.05.

RESULTS

Following results were obtained from the study.

In our study, there was no significant difference in ages of the recruited patients in both the groups. The mean age in labetalol and nifedipine groups was 22.61 and 23.02 years respectively. The majority of the patients had an age belonging to the category of 21 to 29 years. 48.5% and 52.8% from group A and group B respectively had ages 20 years and below as shown in table no 1.

Table no 1: Comparison of Age Distribution of the two groups

Age	GROUP A Labetalol (n=70)		GROUP B Nifedipine (n=70)		Total (%)
	Number	%	Number	%	
≤ 20 years	13	18.5	21	30.0	34 (24.3)
21 to 29 years	34	48.5	37	52.8	71 (50.7)
≥ 30 years	23	33.0	12	17.2	35 (25.0)
MEAN (S.D)	23.61 (3.96)		24.02 (4.21)		
STATISTICAL INTERFERENCE	t = 0.183, d.f = 4, P = 0.817				

On analyzing parity in our study, there was no significant difference in the parity of both the groups. Majority of the patients constituting 28.5% of group A and 32.8% of group B were primigravida. 46.4% enrolled in the study were primigravida. There is a higher incidence of preeclampsia in the first pregnancy as shown in table no 2.

Table 2: Gravida Distribution of the two groups

Parity	GROUP A Labetalol (n=70)		GROUP B Nifedipine (n=70)		Total (%)
	Number	%	Number	%	
Primi	28	28.5	23	32.8	51 (46.4)
G1	17	24.2	21	30.0	38 (27.2)
G2	13	18.5	17	24.2	30 (21.4)
G3	12	17.1	09	12.8	21 (15.0)
STATISTICAL INTERFERENCE	χ 2=5.355, d.f = 3, P= 0.069				

On comparing gestational age between 2 groups in our study, amongst 3 of the recruited patients, 2 in group A and 1 in group B had early onset disease at gestational age less than 24 weeks. The majority of the patients had gestational age of 34 to 36 weeks constituting 40.7% on the whole with 41.4% and 40.0% respectively in group A and B. The recruited patients did not significantly differ in gestational age as shown in table no 3.

Table 3: Comparison of Gestational Age of the two groups

Gestational Age	GROUP A Labetalol (n=70)		GROUP B Nifedipine (n=70)		Total (%)
	Number	%	Number	%	
≤ 24 WEEKS	04	5.7	05	7.1	09 (6.4)
25 to 28 WEEKS	09	12.8	06	8.5	15 (10.7)
29 to 33 WEEKS	21	30.0	24	34.2	45 (32.1)
34 to 36 WEEKS	29	41.4	28	40.0	57 (40.7)
≥ 37 WEEKS	07	10.0	07	10.0	14 (10.0)
STATISTICAL INTERFERENCE	χ 2= 1.259, d.f = 3, P= 0.923				

The present study reports showed that, 77 patients had a body mass index exceeding 30 belonging to the category obesity. There is no significant difference in the body mass index between the two groups as shown in table no 4.

Table 4: Comparison of body mass index of the two groups

Age	GROUP A Labetalol (n=70)		GROUP B Nifedipine (n=70)		Total (%)
	Number	%	Number	%	
25 to 29.99 kg/m2	29	41.4	34	48.5	63 (45)
≥ 30 kg/m2	41	58.6	36	51.5	77 (55)
MEAN (S.D)	30.83 (2.04)		31.73 (2.62)		
STATISTICAL INTERFERENCE	$\chi 2$=2.519, d.f = 1, p= 1.208				

The present study reports showed that, baseline systolic blood pressure of the patients recruited in both the groups did not differ significantly. The mean systolic blood pressure in intravenous labetalol group was 169 mm Hg whereas it was 173 mm Hg in oral nifedipine group. 42.8% of patients in group A had a blood pressure range of 160 to 169 mm Hg while39.2 % of patients in nifedipine group had a blood pressure range of 170 to 179 mm Hg as shown in table no 5.

Table 5: Comparison of SBP of the two groups

Age	GROUP A Labetalol (n=70)		GROUP B Nifedipine (n=70)		Total (%)
	Number	%	Number	%	
160-169 mm Hg	30	42.8	24	34.2	54 (38.5)
170-179 mm Hg	22	31.5	33	46.1	55 (39.2)
≥ 180 mm Hg	18	25.7	14	20.7	32 (22.9)
MEAN (S.D)	170 (8)		174(9)		
STATISTICAL INTERFERENCE	t= 0.355, d.f= 98, p= 0.928				

Our study reports showed that, baseline diastolic blood pressure did not vary significantly in the groups. The mean of the baseline diastolic blood pressure were 109 mm Hg and 112 mm Hg in the groups A and B, respectively. 55.8% and 50% in groups A and B had diastolic blood pressure more than 110 mm Hg as shown in table no 6.

Table 6: Comparison of DBP of the two groups

Age	GROUP A Labetalol (n=70)		GROUP B Nifedipine (n=70)		Total (%)
	Number	%	Number	%	
< 110 mm Hg	31	44.2	35	50	66 (47.1)
≥ 110 mm Hg	39	55.8	35	50	74 (52.9)
MEAN (S.D)	108 (8)		113(9)		
STATISTICAL INTERFERENCE	t= 0.159, d.f= 104, p= 0.764				

In present study on comparison of time taken to control BP between two groups, i.e. to achieve BP 150/100mm of Hg. The mean time required were 51.50 ± 11.85 mins in the Labetalol groups and 48.0 ± 6.25 minutes in the Nifedipine group. This comparision showed no difference in the two groups with a 'P' value of 0.358. Similarly on comparison of no. of doses of drugs required to control BP between two groups it was observed that most of the patients were controlled by two doses of each drug. Mean number of doses required to Achieve Target Bp in IV labetalol group 2.08 and in nifedipine group was 2.02. On comparison of the birth weight between the two groups, mean birth weight was 2.102 ± 0.54 kg in the Labetalol group and 2.25 ± 0.68 kg in the Nifedipine group, which was statistically not significant (P=0.082). Incidence of perinatal mortality was 4% in our study. Perinatal outcome was poor in 6% of babies in nifedipine group and 2% of babies in labetalol group

Table 7: Comparison of various variables between two groups

Variables	Group	N	Minimum	Maximum	Mean	S.D	P value
Time In Minutes To	Intravenous	70	28	75	51.51	11.852	0.358

Achieve Target Bp	Labetalol						
	Nifedipine	70	35	63	49	6.25	
No. of Doses to Achieve Target Bp	Intravenous Labetalol	70	1	3	2.09	0.258	0.421
	Nifedipine	70	2	4	2.03	0.425	
Wt. of baby in (Kgs)	Intravenous Labetalol	70	1.9	4.1	2.103	0.5440	0.082
	Nifedipine	50	1.3	3.6	2.256	0.685	
PERINATAL OUTCOME							
			GROUP A Labetalol (n=70)		GROUP B Nifedipine (n=70)		
			Count	%	Count	%	Total (%)
Outcome	Bad	70	3	4.2	5	7.1	8 (5.7)
	Good	70	67	95.8	65	92.9	132 (94.3)
p=0.002*							

DISCUSSION

Pregnancy-related hypertensive emergencies, including preeclampsia, gestational hypertension, and eclampsia, are associated with significant maternal and fetal morbidity and mortality. Elevated blood pressure in these conditions can lead to severe complications such as stroke, placental abruption, renal failure, and fetal distress. [14] The management of severe hypertension (defined as systolic ≥160 mmHg or diastolic ≥110 mmHg) during pregnancy often requires the use of antihypertensive medications. Intravenous (IV) labetalol and oral nifedipine are two commonly used agents for managing these emergencies, each with its own benefits and limitations. This discussion compares the effectiveness of these two medications in controlling blood pressure, their safety profiles, and their overall role in managing hypertensive crises in pregnancy. [15]

Labetalol is a non-selective beta-blocker and alpha- 1 blocker that causes vasodilation and decreases heart rate and cardiac output. This dual mechanism helps to reduce both systolic and diastolic blood pressure. [16] The intravenous formulation allows for rapid onset of action, making it especially useful in acute hypertensive emergencies. Labetalol does not significantly affect uterine blood flow, making it a preferred choice in managing hypertensive crises during pregnancy. [17]

Nifedipine is a calcium channel blocker that works by inhibiting the influx of calcium into vascular smooth muscle, resulting in vasodilation. Nifedipine is available in both immediate-release and extended-release formulations, but the immediate- release formulation is typically used in acute settings. [18] Oral nifedipine reduces peripheral vascular resistance and lowers blood pressure.

However, its onset of action is slower compared to IV labetalol, as it relies on gastrointestinal absorption. [19]

One of the primary advantages of IV labetalol is its rapid onset of action. Within 10-15 minutes of administration, blood pressure typically begins to decrease, which is crucial in the management of hypertensive emergencies. The effect can be titrated based on the patient's response, making it easier to achieve target blood pressure levels. [20] The onset of action for oral nifedipine is slower compared to IV labetalol, typically taking 30-60 minutes to produce a noticeable reduction in blood pressure. While nifedipine is effective in managing hypertension, its slower onset may be less ideal for hypertensive emergencies where immediate control is necessary. [21]

Numerous studies have shown that IV labetalol is highly effective in managing severe hypertension during pregnancy. It has been found to rapidly lower blood pressure in both maternal and fetal circulations without compromising uteroplacental blood flow. [22] A study by Magee et al. (2014) demonstrated that labetalol successfully reduced systolic and diastolic blood pressure in women with preeclampsia and hypertensive emergencies, with significant reductions occurring within 30 minutes of administration. [23]

Oral nifedipine is also effective in reducing blood pressure in hypertensive emergencies. A randomized trial published by Roberts et al. (2011) found that nifedipine was effective in lowering both systolic and diastolic blood pressure in pregnant women with severe hypertension. [24] However, because nifedipine has a slower onset of action, it may not provide the rapid blood pressure control. needed in more severe cases. In practice, nifedipine is often considered more suitable for less acute hypertensive situations or as part of a longer-term management strategy. [25]

CONCLUSION

IV labetalol is preferred in acute hypertensive emergencies due to its rapid onset, ability to be titrated, and favorable safety profile. It is highly effective in managing severe hypertension and eclampsia when immediate intervention is necessary. Oral nifedipine is more commonly used in less severe cases or as a longer-term management option, particularly in outpatient settings. While effective, its slower onset makes it less ideal for rapidly escalating hypertensive crises.

Ultimately, both medications can be valuable in the management of hypertensive disorders in pregnancy, and the choice between them should be guided by the

severity of the condition, the need for rapid blood pressure control, and the clinical setting. For severe and rapidly progressing hypertensive emergencies, intravenous labetalol remains the gold standard. However, nifedipine can be an effective alternative for less acute cases or in settings where oral administration is more practical.

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