Original Article

The Efficacy of Hydralazine and Nifedipine in the Management of Severe Pre-Eclampsia

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Abstract

Objective: To compare the efficacy of Hydralazine with Nifedipine in women with severe pre-eclampsia.
Design: It is quasi experimental study.
Place and Duration of Study: Lady Aitcheson Hospital (public sector hospital affiliated with King Edward Medical University, Lahore) from April 2012 to September 2012.
Subject and Methods: Sixty pregnant women with severe pre-eclampsia were included in the study. They were divided in two groups A and B by using random number table.
Results: In group A and group B, mean age was 25.9 ± 4.1 and 28.0 ± 4.6 respectively. Mean gestational age of group A was 36.7 ± 3.0 and group B was 36.7 ± 3.2 respectively. Mean diastolic blood pressure of group A and group B was observed 116.0 ± 7.2 and 116.6 ± 5.1 respectively. The mean time in minutes to achieve effective blood pressure control in group A was 68.33 ± 15.16 and group B was 110.17 ± 43.69 ($P \leq 0.001$). Sudden fall of blood pressure was observed in two patients (6.7%) of group A and five patients (16.7%) of group B ($P = 0.22$).
Conclusion: The study concluded that intra venous Hydralazine is a useful antihypertensive agent comparable to Nifedipine but with fewer side effects.

Key Words: Proteinuria, Severe Hypertension, Pre-eclampsia, Hydralazine, Nifedipine.

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Introduction

Hypertension in pregnancy is defined as diastolic blood pressure of at least 90 mm of Hg or systolic pressure of 140 mm of Hg (Diastolic blood pressure is the pressure at which phase 5 Korotokoff sound disappears) and is recorded on two occasions 06 hours apart.[1]

Severe hypertension during pregnancy remains a common and potentially devastating complication.[2] Hypertensive disorders are responsible for approximately 15% of maternal mortality. Gestational hypertension includes a spectrum of disorders including transient hypertension, pre-eclampsia and eclampsia.[3]

Pre-eclampsia affects 5 to 10% of pregnancies and

is a major cause of maternal and fetal morbidity and mortality in developing countries.[4]

It has been estimated by the World Health Organization (WHO) that worldwide about 60,000 women die due to pre-eclampsia. PIH occurs in around 16 – 24% of first pregnancies and 12 – 15% of subsequent pregnancies.[5] Pre-eclampsia is defined as the hypertension developing after 20 weeks of gestation period, during labor puerperium, in previously normotensive women. There needs to be one measurement of diastolic blood pressure of 110 mm of Hg or more on two occasions and consecutive measurements of diastolic blood pressure of 90 mm of Hg or greater, four hours or more apart at rest after 20 weeks of gestation to qualify for the definition.[6]

Pre-eclampsia carries increased risk of morbidity to mother and fetus. It may lead to eclampsia where seizures develop in association with a high risk of fetal and maternal mortality. Detection of disease in early stage and appropriate treatment can improve outcome of both mother and fetus.[7] Early and appropriate use of antihypertensive drugs will reduce the risk for pregnant women and their fetuses.[8]

The aim of antihypertensive management in pregnancy is to produce optimal decrease in blood pressure within an acceptable time period; with minimum risks to mother and fetus. Three short acting antihypertensive agents, Hydralazine, Labetalol and Nifedipine (sublingual or orally administered) are commonly used to control acute, very high blood pressure in hypertensive pregnant women who may require emergency Caesarian Section and often receive Magnesium Sulphate.[9]

For many years, Hydralazine has been the recommended antihypertensive of first choice for severe hypertension in pregnancy.[10]

Nifedipine is a calcium channel blocker and studies of calcium channel blockers in pregnancy have proven their safety.[11]

Materials and Methods

This is the study conducted in the Department of Obstetrics and Gynaecology, unit IV, Government Lady Aitcheson Hospital, Lahore. The same was started in April 2012 and completed in September 2012. Sixty pregnant patients with severe pre-eclampsia were included in it. The patients were divided in two groups A and B, using a random number table. Sampling technique adopted was convenience non probability sampling. All patients were beyond 20 weeks of gestation (either from LMP or scan) and were severely pre-eclamptic with diastolic blood pressure ≥ 110 mm of Hg on admission. Cardiac patients were excluded from the study. The study was approved by the Hospital Ethical Committee. Informed consent was obtained from each of the patients. Study subjects were randomly allocated to two groups. Group A of 30 patients were treated with intravenous Hydralazine and Group B of 30 patients were given Nifedipine orally.

Basic demographic information was obtained including age, parity, gestational age, previous history of current pregnancy and booking status. Blood pressure was taken by standard Mercury Sphygmomanometer and Krotocoff K^5 was considered for diastolic blood pressure. Proteinuria of mother was checked and cardiotocography (CTG) of fetus done. Blood pressure was monitored every 15 minutes. The dose of drug needed for effective control was recorded. Time needed to achieve effective BP control i.e. systolic BP > 20% and diastolic >10% of reduction in baseline readings were noted. Mean of urinary output was recorded. Any adverse effect of drug on mother and fetus were noted.

Patients were followed for 24 hours after starting medication. Relevant data was recorded and collected through specially designed Performa. After collection of data, statistical analysis was performed on SPSS-12 version. The comparison of numerical data was tested for significance by "t" test. Any side effects to mother (headache, sudden fall of BP, tachycardia etc) and to fetus (distress, poor APGAR etc) were compared and tested for significance by chi-square test. P value of equal to or less than 0.05 was considered significant.

Results

In group – A, 5mg I/V Hydralazine was given as bolus dose and it was repeated at 20 – 30 minutes interval according to blood pressure. In group-B, 10 mg Nifedipine was given orally and was repeated after 30 minutes time according to blood pressure.

Distribution of cases by measurement of blood pressure at admission showed mean systolic blood pressure in group – A and group – B as 177.8 ± 9.9 and 173.8 ± 14.3 respectively. Mean diastolic blood pressure of group – A and group – B were observed 116.0 ± 7.2 and 116.0 ± 5.1 respectively (Table 1).

Mean time in minutes to achieve effective blood pressure in group-A was 68.33 ± 15.16 and in group –

B was 110.17 ± 43.69 (P > 0.0001) (Table 2).

Adverse effects of drugs were noted in both groups. 22 patients (73.3%) of group – A and 25 patients (83.3%) of group-B showed certain adverse effects as a whole (P = 0.34). Maternal tachycardia was observed in 17 patients (56.7%) of group – A and 14 patients (46.7%) of group-B (P=0.43) (Table 3).

Nausea / Vomiting was observed in only 1 patient (3.3%) in group – A and 3 patients (10%) of group – B (P = 0.30) (Table 4). Sudden fall of blood pressure was observed in 2 patients (6.7%) of group – A and 5 patients (16.7%) of group – B (P = 0.22) (Table 5). Cardiotocography (CTG) was done before and after administration of drugs and only 1 patient (3.7%) developed abnormality of trace in group – A and 1 patient (3.6%) in group – B (P = 0.97). Three cases in group – A and two cases in group – B were intrauterine deaths at the time of admission (Table 6).

In case of delivery, APGAR score was noted at 5 minutes interval in all delivered cases and 1 baby (4.0%) in group – A and two babies (7.4%) in group – B had APGAR score less than 6 (P = 0.59) (Table7).

Three cases in group – A were having dead fetuses at the time of admission and two cases were managed conservatively after controlling blood pressure and did not deliver. Two cases in group-B had intrauterine deaths and one case did not respond to oral Nifedipine and drug was changed, so APGAR score was not included (Table 7).

Discussion

Hypertensive disorders complicate 12 – 22% of all pregnancies and one of the leading causes of maternal and fetal morbidity and mortality. In minority of cases, it is associated with proteinuria and this indicates a multisystem disease, also known as pre-eclampsia which is related to serious consequences if not diagnosed in time and managed properly. To decrease the adverse outcome, associated with this multi – organ disease, an improved community health education, prenatal care and obstetrical facilities are vital, hence to save the mothers and the babies.

Table 1: Distribution of cases by blood pressure.

Blood Pressure (MmHg)	Group – A (Hydralazine) N = 30		Group – B (Nifedipine) N = 30		P value
	Mean	S.D	Mean	S.D	
Systolic blood pressure	177.8	9.9	173.8	14.3	0.21
Diastolic blood pressure	116.0	7.2	116.6	5.1	0.68

Key: SD: Standard deviation

Table 2: Distribution of cases by time (minutes) needed to achieve effective blood pressure.

Group	Mean	S.D	P value
Hydralazine (Group – A)	68.33	15.16	P < 0.001
Nifedipine (Group – B)	110.17	43.69	

Key: SD: Standard deviation

Table 3:
Distribution of cases by maternal tachycardia.

Tachycardia	Group – A (Hydralazine) n = 30		Group – B (Nifedipine) n = 30	
	Number	Percentage	Number	Percentage
Yes	17	56.7	14	46.7
No	13	43.3	16	53.3
Total	30	100.00	30	100.0
Chi square	0.60			
P value	0.43			

Table 4:
Distribution of cases by nausea / vomiting.

Nausea / Vomiting	Group – A (Hydralazine) n = 30		Group – B (Nifedipine) n = 30	
	Number	Percentage	Number	Percentage
Yes	01	3.3	03	10.0
No	29	96.7	27	90.0
Total	30	100	30	100.0
Chi square	1.07			
P value	0.30			

Table 5:
Distribution of cases by sudden fall of blood pressure.

Sudden Fall of Blood Pressure	Group – A (Hydralazine) n = 30		Group – B (Nifedipine) n = 30	
	Number	Percentage	Number	Percentage
Yes	02	6.7	05	16.7
No	28	93.3	25	83.3
Total	30	100.0	30	100.0
Chi square	1.45			
P value	0.22			

Table 6: Distribution of cases by abnormal cardiotocography.

Abnormal Cardiotoco-graphy	Group-A (Hydralazine) n = 27		Group – B (Nifedipine) n = 28	
	Number	Percentage	Number	Percentage
Yes	01	03.7	01	03.6
No	26	96.3	27	96.4
Total	27	100.0	28	100.0
Chi square	0.001			
P value	0.97			

Note:
3 cases in group-A were of intrauterine death at the time of admission
2 cases in group-B were of intrauterine death at the time of admission

Table 7:
Distribution of cases by APGAR Score at 5 minutes.

APGAR Score at 1 min	Group – A (Hydralazine) n = 25		Group – B (Nifedipine) n = 27	
	Number	Percentage	Number	Percentage
Yes	01	04.0	02	07.4
No	24	96.0	25	92.6
Total	25	100.0	27	100.0
Chi square	0.28			
P value	0.59			

Note:
3 cases in group-A was intrauterine deaths at admission and 2 cases were managed conservatively and did not deliver.
2 cases were intrauterine deaths at admission and in one case, patient did not respond to oral Nifedipine and drug was changed, so APGAR score not included.

Cases which require protocol determined management are often defined as those with severe hypertension (greater than 160/110 mm of Hg) or hypertension with additional complications such as headache, visual disturbance and epigastric pain etc.

This study aimed to compare the efficacy of Hydralazine with Nifedipine in women with severe pre-eclampsia. It was also desired to compare maternal adverse effects (like headache, tachycardia, acute hypotension and nausea or vomiting) and fetal side effects (like variations in fetal heart rate and cardiotocography trace) of Hydralazine and Nifedipine. The goal of therapy is to find the drug which is effective with minimum side effects.

Hydralazine can be used safely as a first line treatment in acute emergencies. In this study we chose sixty pre-eclamptic patients at random and found that approximately half of them were parlous women (twenty nine were primigravida and thirty one were multigravida). Our observation was comparable to a study conducted by Brown on 825 women with pre-eclampsia, where he found that approximately two fifths of women were parlous.[15]

In a study, Duley et al analyzed that women who do not receive prenatal care are seven times more likely to die from complications related to pre-eclampsia and eclampsia than women who receive some level of prenatal care.[2]

In order to evaluate critically, the effect of Hydralazine, this study included women with severe pre-eclampsia and I/V bolus doses were given according to blood pressure and effective reduction in both systolic and diastolic blood pressure were achieved.

Nifedipine is extensively used calcium channel blocker in pregnancy, but in view of its limited safety data, it is recommended as an alternative to more established treatments only if these are ineffective.

Lew and Klonis in 2005 also found desirable efficacy of Hydralazine dealing with patients of eclampsia and pre-eclampsia in emergency department at Maroondah Hospital, Australia. Hydralazine is the initial intravenous agent of choice in Australia.[17]

Aali and Nejad carried out a study in 2002 and they concluded that effective control of blood pressure was achieved in both treatment arms while treating 126 pre-eclamptic patients who were randomized to receive either Nifedipine or intravenous Hydralazine. In neither of two groups any serious side effects both in mother or fetus were noted.[16]

Similarly, this study reflects that patients in both groups showed blood pressure control but control was achieved quite earlier in patients who were given I/V Hydralazine boluses. On other side, adverse effects were only minor in both groups.

In current study, it has been shown that maternal side effects were there but no effect on fetal cardiotocography has been found with Hydralazine, which is similar to the results of a study carried out by Magee et al.[9]

Meta – analysis of randomized controlled trials by Magee et al (2003) comparing Hydralazine against other short acting antihypertensive for severe hypertension in pregnancy showed that Hydralazine was associated with a trend towards more severe hypertension than Nifedipine. Hydralazine was associated with more maternal side effects and less neonatal bradycardia. But the study concluded that results were not enough to guide clinical practice and adequately powered clinical trials are needed.[9]

Kumar et al studied the effects of Nifedipine used sublingually in women with pregnancy induced hypertension and found Nifedipine is effective in attenuating the hypertensive response to laryngoscopy and intobation but not the tachycardia response in patients scheduled for caesarean section under general anesthesia.

Present study clearly showed that Hydralazine and Nifedipine both are effective drugs to be used in controlling blood pressure in severe pre-eclampsia but Hydralazine is a better choice to achieve effective control in relatively shorter time with minimal side effects. In managing hypertensive emergencies, intravenous (IV) administration is safer than oral administration because it is easier to combat inadvertent hypotension by stopping an IV injection than it is to stop intestinal absorption of an orally administered drug.

Conclusion

The study concluded that Hydralazine is a useful antihypertensive agent comparable to Nifedipine but with fewer side effects.

Hydralazine, short acting anti-hypertensive drug, when used as intravenous boluses, is a good drug to control blood pressure in a relatively shorter time and with minimal side effects on mother and fetus than patients treated with Nifedipine.

On the basis of this study, intravenous Hydralazine appears to be a safe, well tolerated and promising drug to achieve effective blood pressure control.

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