

SAFETY AND EFFICACY OF HYDERALZINE IN HYPERTENSIVE DISORDERS OF PREGNANCY

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ABSTRACT

Objectives: To find out safety and efficacy of IV bolus hydralazine in reducing blood pressure in severe hypertension during pregnancy.

Methodology: All pregnant patients with systolic blood pressure 160 or above and diastolic blood pressure 109 mmHg with eclampsia and hypertensive emergencies were included. The initial dose of hydralazine was 5 mg IV bolus then repeated 1mg at 20 minutes interval. Outcome measures to start treatment were, systolic and diastolic blood pressure, time required for achieving the desired BP level, total dose needed, side effects of drugs, maternal and fetal outcome in terms of safety and efficacy.

Results: One hundred and ten patients with eclampsia and hypertensive emergencies were included in the study. The mean + SD (range) of maternal age was 26.70 + 6.70(18 - 45 years). Blood pressure before starting therapy was systolic 165.5 + 16.65, and diastolic blood pressure was 115.45 + 8.25mmHg. After starting therapy, a significant difference ($P < 0.001$) was observed with fall in systolic blood pressure 131.2 + 9.49 and in diastolic blood pressure 93.68+6.30mmHg. In 94(85.5%) patients, IV bolus hydralazine took 60 minutes, however, in 3(2.7%) > 180 minutes time was required to control the blood pressure. Total dose of drug required was < 6 mg in 40(38.4%) patients, 6 to 14 mg in 44(40%) and in 17(15.5%) women 15 to 20 mg of dose was needed to control the blood pressure. Only 9(8.18%) needed dose between 21 to 30 mg IV bolus hydralazine.

Conclusion: Hydralazine is safe and effective in controlling the blood pressure in severe hypertension during pregnancy and after delivery.

KEY WORDS: Hydralazine, Severe hypertension, Morbidity.

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INTRODUCTION

Hypertension in pregnancy is a common cause of maternal and perinatal morbidity and mortality. Control of maternal blood pressure

and maintenance of placental blood flow are important objectives in the treatment. Antihypertensive treatment in pregnancy is necessary to protect the mother from dangers of severe hypertension. Cerebral hemorrhage is the most serious complication in cases of pre-eclampsia and eclampsia.¹

If drug therapy is deemed necessary, the use of oral antihypertensive with established fetal safety profiles (e.g. methyldopa, labetalol, hydralazine, long-acting nifedipine) is generally preferred. Drugs used in higher levels of blood

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pressure are parenteral hydralazine and labetalol.

Hydralazine, a potent arterial vasodilator, has long been the standard therapy for the management of hypertensive emergencies complicating pregnancy. Parenteral hydralazine may be used for the management of severe hypertension when blood pressure must be lowered immediately.

Hydralazine has been used effectively and generally is considered the parenteral hypotensive agent of choice for the management of hypertensive emergencies associated with pregnancy (e.g., preeclampsia, eclampsia). The usual initial adult IV dose of hydralazine hydrochloride is a bolus dose of 5–10 mg followed by IV doses of 5–10 mg (range: 5–20 mg) every 20–30 minutes as and when necessary to achieve an adequate reduction in blood pressure. It can be increased to 40mg per dose. Blood pressure should be closely monitored when parenteral hydralazine is employed.² The hypotensive effect begins within 5 to 20 minutes, maximum in 10 – 80 minutes and lasts for 2 – 6 hours. About 85 – 87% of hydralazine is bound to plasma protein. It is metabolized in GI mucosa and liver, and is rapidly excreted in urine as metabolized. It crosses the placenta and breast milk.³

The protocol using bolus injection of hydralazine, 5mg IV, and every 15 to 20 minutes until diastolic blood pressure is reduced to 100 mm Hg. The objective of this study was to see the safety and efficacy of intravenous Bolus Hydralazine in severe hypertension during pregnancy.

METHODOLOGY

This study was conducted at gynae department, Liaquat University Hospital, Hyderabad for a period of one year from June 2007 to May 2008. Total obstetrics admissions were 2742, out of them 110(4.0%) patients with eclampsia or hypertensive emergencies during antepartum, intrapartum, and postpartum periods were admitted through OPD and emergency department. Informed written consent was taken after detailed history, thorough examination and investigations. Patients irrespective of age and

parity at any gestational age with systolic blood pressure 160 or above, diastolic 109 or more mm Hg were included. Most patients also received magnesium sulphate prophylactically or to control seizures. Hypertensive emergency was defined as a sustained systolic blood pressure SBP of ≥ 170 mm Hg or DBP ≥ 115 mm Hg on repeated measurements at 15 minutes apart while the patient was in a lateral recumbent position. Dose of hydralazine was given by senior doctor as per protocol. Initial dose was 5 mg IV bolus state then 1mg at 20 minutes interval was given till the desired blood pressure was achieved.

Patient was monitored by recording blood pressure, heart rate for any side effects such as headache, nausea, vomiting and sudden hypotension. Fetal monitoring was done by clinical recording of fetal heart sounds and CTG. Outcome measures were systolic blood pressure and diastolic blood pressure at the start of treatment, time required to achieve the desired BP level, total dose needed side effects of drugs, maternal and fetal outcome. Information was recorded on structured proforma.

Drug usage: One ampoule of one ml contains 20 mg hydralazine, diluted in 3 ml of distilled water making one ml = 5mg. initiation of drug was done by giving 5mg IV bolus then 5 mg every 20 minutes. Total maximum dose given was upto 30 mg.

Data Analysis: The data was evaluated in statistical program SPSS version 16.0. Qualitative data are presented as n(%) and continuous variables are expressed as Mean + standard deviation and student *t* test was applied to compare the means (2 tailed) of systolic and diastolic blood pressure among the before and after therapy. *P* value < 0.05 was considered as statistically significant level.

RESULTS

During study period total obstetric admissions were 2742. One hundred and ten women presented with eclampsia or hypertensive emergencies. It was more prevalent in young reproductive age with mean age + SD (range) 26.70 + 6.70(18 – 45 years). Fifty three (41.8%) patients

Table-I: Demographic details of the patients (n = 110)

Parameters	n(%)
Age (in years) Mean + SD (Range)	26.70 + 6.70(18 - 45)
Gestation age(in weeks):	
26 - 35 weeks	53(4.18)
> 36 weeks	38(34.5)
Mode of Delivery:	
Spontaneous vaginal delivery	43(39.1)
Ventous	12(10.9)
Cesarean section	55(50.0)
Time required during therapy(in minutes):	
< 60	94(85.5)
61 - 180	13(11.8)
> 180	03(2.7)
Blood pressure before therapy:	
Systolic (Mean + SD, Range)	165.5+16.65 (140-240)
Diastolic (Mean + SD, Range)	115.45 + 8.25 (105 - 150)
Blood pressure after therapy:	
Systolic (Mean + SD, Range)	131.2+9.49 (110-160)
Diastolic (Mean + SD, Range)	93.68 + 6.30 (80 - 110)
Type of hypertension:	
Anterartum	83(75.5)
Intrapartum	08(7.3)
Postpartum	19(17.3)
Fetal outcome:	
Intrauterine death	13(11.8)
Alive	33(30.0)
Asphyxiated (APGOR 4-6 at 1 min)	64(58.2)

came between 26 to 35th week of gestation, 38(34.5%) presented at more than 36 week of gestation and 19(17.2%) with postpartum eclampsia so frequency of severe hypertension was more during antepartum and intrapartum period. Out of 110 women, 55(50.0%) women were delivered by cesarean section and normal vaginal delivery respectively. [Table-I]

Before starting therapy, the mean systolic + SD was 165.5 + 16.65 and diastolic was 115.45 +

8.25. After giving IV bolus hydralazine, mean + SD fall in systolic blood pressure was 131.2 + 9.49 and diastolic blood pressure 93.68 + 6.30 with highly significant difference ($P < 0.001$). [Table-II] Time required to control blood pressure was <60 minutes in 94(85.5%) & 13(11.8%) patients took 60 to 180 minutes to respond however, in 3(2.7%) patients > 180 minutes were required to achieve the desired level. [Table-I]

Forty (36.4%) patients < 6 mg dose of hydralazine was effective, in 44(40%) women 6 to 14 mg of drug needed to control the blood pressure. Only 9(8.18%) needed dose between 21 to 30 mg. No side effect was found with hydralazine except few patients complained of headache and no treatment failure was seen in patients during their antepartum period. However three patients of postpartum eclampsia did not respond to even maximum dose upto 30 mg therefore they were switched over to other therapy. [Table-III]

Regarding fetal outcome in our study 64(58.2%) babies were born with apgar score <6, 33(30%) babies were alive, only 13(11.8%) were delivered dead at our hospital as well as at home or local hospital. [Table-I]

DISCUSSION

Intravenous hydralazine is a drug of 1st choice and perhaps the most widely used agent for acute management of severe hypertension in pregnancy. Its advantages included lack of adverse affect on fetal circulation, long experience with the drug and convenient administration as oral, IV / IM.⁴ In a study by S. Paterson - Brown conducted at 3 UK teaching hospitals, seventy women received IV bolus hydralazine and reduction in mean arterial pressure was 12 mmHg after 1st bolus dose, it was controlled in 89% by bolus injection.²

Table-II: Efficacy of drug (n = 110)

Parameters	Before(n = 110)	After(n = 110)	P value
Blood Pressure:			
Systolic	165.5 + 16.65	131.2 + 9.49	< 0.001*
Diastolic	115.4 + 8.25	93.6 + 6.30	< 0.001*

Results are presented as Mean + Standard Deviation *P value is statistically high significant

Table-III: Total dose required (n = 110)

Dose (in Mg)	n(%)
< 6	40(36.4)
6 - 14	44(40.0)
15 - 20	17(15.5)
21 - 30	9(8.1)

Our study showed control of blood pressure in all 107(97.2%) women, similarly a study conducted by Mosammat Rasheed⁵ at Bangladesh observed that out of 77 patients 44(57.1%) received IV bolus hydralazine and there was no treatment failure.

In our study women were selected irrespective of age parity and type of eclampsia. Similar selection was done by Mosammat Rasheeda.⁵ Because of incidence of cardiovascular, cerebrovascular accidents, convulsions related to severe hypertension, quick fall in blood pressure is justified. In our study patients received IV bolus hydralazine, blood pressure reduced to required level less than 100 mmHg in less than 60 minutes in 94(85.5%) of women. It is similar to the time taken in a study of Mosammat Rasheeda in which 44(57.1%) women who received IV bolus, she achieved goal within 65.23 + 23.38 minutes. The doses we used were not high so our primary outcome was to control blood pressure as quickly by as possible. The maximum dose we used was upto 30mg, was effective from 5 to 20 mg in 91% of patients out of 110. Only nine women out of 110 needed dose between 20 to 30 mg. Similar results were found by Mabie WC who compared Labetalol with hydralazine in a ratio 2:1. In this study hydralazine lowered mean arterial blood pressure more than did Labetalol 33.3 + 13.2 versus 25.5 + 11.2 mmHg.⁶

A study done on 40 diagnosed cases of eclampsia at Lady Willington Hospital Lahore where they compared IV bolus with continuous drip of hydralazine. They observed that 60 - 70% less time was required and 37.5-50% less drug quantity was used in bolus IV hydralazine versus continuous infusion of hydralazine.⁷

CONCLUSION

Our study shows that IV bolus hydralazine can be used safely and effectively in patients

with severe hypertension during pregnancy and even after delivery. It is affordable, easily available so by using this drug we can reduce the morbidity and mortality related to severe hypertension with minimum side effects.

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