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Management of Hypertensive Emergencies of Pregnancy by Hydralazine Bolus Injection vs Continuous Drip -- A Comparative Study

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Published: 09/12/2002

Abstract and Introduction

Abstract

This prospective study was conducted at Dhaka Medical College and Hospital, Bangladesh. The objective was to identify the time required to control high blood pressure levels in obstetric patients by injection of hydralazine in a bolus intravenous dose vs continuous drip. Seventy-seven patients with eclampsia and hypertensive emergencies comprised the target population. Patients were managed either by hydralazine drip in normal saline (existing official protocol, $n = 33$) or hydralazine bolus injection (as experiment, $n = 44$) until diastolic blood pressure fell to 90-95 mmHg. Results were compared. Student's *t*-test was done for statistical significance, and a *P* value of $< .05$ was considered as significant. The groups were similar with respect to maternal age and their mean systolic and diastolic blood pressure at the time of enrollment. Patients who received bolus injection required less time to achieve the therapeutic goal (65.23 +/- 23.38 minutes) than continuous drip (186.36 +/- 79.77 minutes; $P < .001$). The experimental group also required significantly lower doses (6.68 +/- 1.66 mg) in comparison to that required by control group (20.07 +/- 11.38 mg; $P < .001$). There was no overshoot hypotension in either group. The data suggest that hydralazine bolus dose is equally safe and more effective than continuous drip in the management of hypertensive emergencies in pregnancy.

Introduction

Control of maternal blood pressure and maintenance of placental blood flow are important objectives in the treatment of hypertensive disorders during pregnancy. Antihypertensive treatment in pregnancy is necessary to protect the mother from dangers of severe hypertension. Cerebral hemorrhage is the most serious complication for women with pre-eclampsia and eclampsia.^[1] There is no controversy about the use of antihypertensive therapy in eclampsia, as it reduces cerebral arterial vasospasm, which causes eclamptic seizures.^[2]

Hydralazine, a potent arterial vasodilator, has long been the standard therapy for the management of hypertensive emergencies complicating pregnancy. The exact mode of action for hydralazine is not fully understood, although endothelial mechanisms and medial smooth muscle hyperpolarization may be involved.^[3,4] In animal studies, the drug causes vasodilatation in both the maternal and fetal placental circulation.^[5] The management of severe hypertension in severe pre-eclampsia or eclampsia remains somewhat controversial. Findings of randomized trials have suggested that nifedipine and labetalol are superior or equivalent to hydralazine for severe hypertension in pregnancy.^[6,7] But researchers found neuromuscular blockade, potent hypotension, and cardiac toxicity when nifedipine was used with anticonvulsant magnesium sulphate.^[8-11] Labetalol is not available in Bangladesh. We use magnesium sulphate routinely for our eclamptic patients. Thus, for management of acute hypertensive crisis, hydralazine is the first-line treatment of choice. The guidelines prepared by the Eclampsia Working Group for Bangladesh propose that hydralazine be administered via intravenous continuous drip. But it takes a considerable time to achieve the therapeutic goal using this method of administration. Mabie and colleagues^[7] have followed a protocol using bolus injection of hydralazine, 5 mg IV, every 10 minutes until diastolic blood pressure (DBP) is reduced to below 100 mm Hg. In this study, we report our experience with hydralazine direct bolus injection for our eclamptic patients. Our aim was to compare the efficacy of continuous drip and bolus administration with regard to reduction of high blood pressure to a desired level within a short time.

Materials and Methods

This study was conducted at Dhaka Medical College Hospital between June 1999 and June 2000 in 77 patients with eclampsia (convulsions, edema, proteinuria) and severe hypertension. Patients were enrolled during antepartum, intrapartum, and postpartum periods. All patients were receiving magnesium sulphate for seizure prophylaxis at the time of enrollment. 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.

Enrolled patients were divided to receive either intravenous bolus hydralazine (experimental, group A, $n = 44$) or intravenous drip of hydralazine (existing official protocol, group B, $n = 33$). Bolus injection was given by consulting or senior doctors. Initially, a 5-mg bolus dose was administered, then 2 mg at 15-minute intervals until the desired reduction of blood pressure was achieved, ie, DBP 90-95 mm Hg (see footnote). Each patient in this group received a total of 11 mg (5 + 2 + 2 + 2 mg) in the first hour. In group B, intravenous drip, 20 mg in 200 cc normal saline, at a rate of 10 drops/minute was administered initially and then increased by 5 drops at 15-minute intervals until the therapeutic blood pressure goal was achieved (again, DBP 90-95 mmHg). Thus, the patients in group B received 1050 drops at the end of the first hour, which is equivalent to 70 mL of fluid (1 mL = 15 drops) containing 7 mg hydralazine. For both groups, blood pressure was recorded every 5 minutes in the first hour and then at 15-minute intervals until stable blood pressure was achieved. Maternal pulse and fetal heart rate in undelivered patients were also measured.

The primary outcome was the time required to achieve therapeutic blood pressure goal, ie, $< 160/100$ mm Hg (DBP 90-95 mm Hg). The study was approved by the institutional review board, which consisted of the head of the department and other professors of that department. Data were analyzed by calculating mean and standard deviation. A student's *t*-test was done for comparison of mean. A *P* value of $< .05$ was considered as significant.

Footnote

Although Mabie and colleagues^[7] used 5 mg at 10-minute intervals, we did not feel confident about giving 5 mg at 10-minute intervals. We used 5 mg stat and then a reduced dose. We are continuing to follow this protocol at our institution with success. In some cases when there is a delay in blood pressure reduction, we use 5 mg at 15-minute intervals, which is usually given by senior doctors.

Results

Seventy-seven patients were selected for the 2 treatment groups; 33 were recruited for hydralazine IV drip and 44 were recruited for direct injection of hydralazine. Although randomization was not done, the groups were similar with respect to maternal age, mean SBP and mean DBP (Table 1), parity, type of eclampsia, gestational age, and mode of delivery (Table 2) at the time of enrollment. This is because of the common patient profile of eclampsia at our institution: young, primiparous, lower social class, and no antenatal checkup.

Table 1. Table 1. Patient Profile

Patient Profile	Bolus injection $n = 44$ (mean SD)
Age (yrs)	24.09 +/- 4.93
SBP before Rx (mm Hg)	162.27 +/- 11.65
DBP before Rx (mm Hg)	122.95 +/- 6.85
Total dose (mg)	6.68 +/- 1.66
Time required (min)	65.23 +/- 23.38
SBP after Rx (mm Hg)	135 +/- 7.83
DBP after Rx (mm Hg)	92.72 +/- 2.49

DBP= diastolic blood pressure; NS= not significant; Rx= treatment; SBP= systolic blood pressure

Table 2. Table 2. Outcome of Pregnancy

Parameters	Number
Parity	
Nil	31
1-3	13
Type of eclampsia	
APE	35
PPE	9
Gestational age	
32-36	14
37-39	21
Mode of delivery	
Spontaneous vaginal delivery	7
Ventouse	1
Cesarean section	27
Fetal outcome	
Alive	35
Asphyxiated (APGOR 4-6 at 1 min)	6
Birth weight	
1.6 -2.4 kg	12
2.5 -2.8 kg	23
1st week death	2

APE= antepartum eclampsia; PPE= postpartum eclampsia

Patients who received direct hydralazine injection (group A) achieved the therapeutic blood pressure goal within 65.23 +/- 23.38 minutes (mean ± SD) as compared with 186.36 +/- 79.77 minutes in those who received hydralazine drip (group B) ($P < .001$). Group A also required significantly lower doses of hydralazine (6.68 +/- 1.66 mg) to reach the blood pressure goal in comparison to that required by group B (20.07 +/- 11.38 mg; $P < .001$). Both modalities were ultimately effective in reaching the therapeutic goal. The maximum time needed to reach the therapeutic goal was 300 minutes in group B and 95 minutes in group A. One patient in group B required crossover as blood pressure remained static (160/120 mm Hg) for 60 minutes of IV drip with increasing drop at 15-minute intervals. After treatment, the mean values of SBP and DBP were 135 +/- 7.83/ 92.72 +/- 2.49 mm Hg in group A vs 139.09 +/- 6.68/93.18 +/- 2.40 mm Hg in group B. Thus, hydralazine direct injection lowered blood pressure more effectively than drip.

The Figure depicts the average decrease in mean DBP over time for the 2 study methods. Group A had a quicker onset of action than group B. The drop in DBP was significantly greater in group A at 45, 60, and 90 minutes but greater in group B at 115, 130, and 210 minutes.

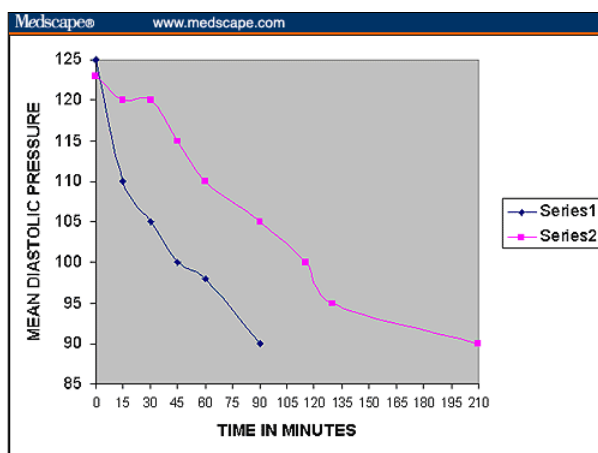


Figure 1. Average decrease in mean DBP

No failure of treatment and crossover was found in group A, but 1 patient in group B did not respond at all (blood pressure was constantly 160/120 mm Hg) to drip until she received 7 mg/hour in the first hour. Then, we crossed her over to bolus 5 mg IV stat. She did not require a further dose; at the end of 20 minutes, her blood pressure dropped to 140/90 mm Hg. Five patients in group B needed a second administration 6-9 hours after achieving therapeutic goal because of a subsequent rise of blood pressure. (This blood pressure increase occurred despite the administration of maintenance therapy with an oral antihypertensive). No such case was found in group A. There was no hypertensive crisis in either group. In group B, the maximum time required to achieve therapeutic goal was 5 hours. In this case, we did not cross over for quick response, as the patient was responding slowly from the beginning.

Twenty-seven percent of the group B patients responded to a low dose (7-10 mg) of hydralazine, 18.18% required 11-12 mg, and 54.54% required 17-37 mg. On the other hand, patients in group A required a very low dose to achieve therapeutic goal. Eighty-six percent required 5-7 mg, and 14% required 9-12 mg to control blood pressure. Antepartum and postpartum dose requirements did not differ with either group.

There were no adverse maternal effects in either group. No patient experienced overshoot hypotension. There was no difference in maternal pulse rate or fetal heart rate in undelivered patients.

Discussion

A number of parenteral drugs may be used for lowering blood pressure in hypertensive pregnant patients. Each has its own merits and demerits. Hydralazine is a well-accepted drug for management of hypertensive emergencies during pregnancy. Treatment reduces the likelihood of cerebral hemorrhage and left ventricular failure and may also be a contributing factor in seizure prevention.^[2] In this study, we administered hydralazine, 11 mg/hour (5 + 2 + 2 + 2 mg), at a bolus dose at 15-minute intervals (group A) and as continuous drip, 7 mg/hour in the first hour (and titrating upward in the second and subsequent hours as necessary) (group B). The onset of action of hydralazine is 10-20 minutes,^[12] so we chose an administration interval of 15 minutes for both groups. We found that bolus injection achieved the therapeutic blood pressure goal more rapidly and with smaller doses than continuous drip. Although we gave 11 mg/hr in the first hour, most of the patients (86%) required only 5-7 mg to achieve therapeutic blood pressure goal. On the other hand, in group B, the dose was titrated by increasing the drops every 15 minutes, and more than half of the patients (54%) required 17-37 mg drug to achieve the therapeutic goal.

The maximum time required to achieve therapeutic goal was significantly shorter in group A (1 hour and 35 minutes) than in group B (5 hours). Because the incidence of cardiovascular accident, cerebrovascular accident, and convulsion is related to severe hypertension, a quick reduction of blood pressure is justified. In this regard, type, dose, and mode of administration of drug are important factors to achieve the desired result. Hydralazine is a potent antihypertensive, and bolus injection reduces blood pressure more quickly than continuous drip. Mabie and colleagues^[7] used bolus injection to minimize the risk of reactive hypotension. They argued that with constant infusion, it is difficult to determine the cumulative dosage the patient has received. Although some investigators reported overshoot hypotension in the hydralazine group in their randomized trial,^[6,7] we found no overshoot hypotension in our study.

The most frequent side effects of hydralazine administration are decreased uteroplacental perfusion, headache, tachycardia, palpitation, and fluid retention.^[12] Reduced uteroplacental perfusion causes fetal distress,^[13] but it requires a daily dose of more than 200 mg and precipitous drop in the diastolic pressure -- usually below 80 mm Hg.^[12,13] The doses we used were not so high, so our observations were focused on the primary outcome of time to achieve hypertensive control and not on the prevalence of secondary outcomes such as maternal and fetal side effects. However, we recorded maternal pulse and clinical assessment of fetal heart rate. There were 8 cases of fetal distress (5 in group A and 3 in group B), in which fetal tachycardia was associated with deeply stained liquor. In all other patients, fetal heart rate was within the normal limit.

Mabie and colleagues^[7] used 5 mg hydralazine at 10-minute intervals, whereas we used 5 mg stat then 2 mg at 15-minute intervals. In 5 cases, we used 5 mg at 15-minute intervals, observed no complications, and achieved the desired result with 2 doses only (ie, within half an hour). Those 5 patients were not included in this study, but their outcomes suggest that repeated bolus dosing is safe and that the higher dose may yield better results.

This small study with convenient sampling suggests that bolus hydralazine is equally safe but more effective than continuous drip in reducing blood pressure. In addition, it requires a lower dose to reduce blood pressure to a desired level. A larger randomized trial may be warranted to confirm the results of this small study.

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Begum MR, Quadir E, Begum A, Akhter S, Rahman K. Management of Hypertensive Emergencies of Pregnancy by Hydralazine Bolus Injection vs Continuous Drip -- A Comparative Study. MedGenMed 4(4), 2002 [formerly published in Medscape Women's Health eJournal 7(5), 2002]. Available at: <http://www.medscape.com/viewarticle/440158>.

Medscape General Medicine. 2002;4(4) © 2002 Medscape
