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Research Paper

Intra-Venous Labetalol in The Management of Severe Pregnancy-Induced Hypertension

Medical Science

KEYWORDS : Pregnancy-induced hypertension, Intra venous labetalol

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ABSTRACT

Objective: To study the maternal and fetal outcome in patients with severe pregnancy-induced hypertension treated with intra-venous labetalol.

Methods: A prospective hospital based study was conducted in the Department of Obstetrics & Gynecology, Maharaja Agrasen Medical College, Agroha, Hisar from January 2013 to August 2013.Twenty five patients with severe pregnancy induced hypertension received intravenous labetalol in sequentially escalating dosages every 15 minutes (10mg, 20 mg, 40 mg, 80mg and maximum 220 mg). Target was to achieve systolic blood pressure of <155 mm Hg and diastolic blood pressure of <105 mm Hg. Age, gravid Status, gestational Age, efficacy of the drug to achieve target blood pressure, time taken to Control Blood Pressure, drug dosage required, systolic and diastolic blood pressures during first hour, side effects, maternal and Perinatal outcomes were studied.

Results: The pretreatment mean systolic and diastolic blood pressure were 185.4 ± 13.5 mmHg and 120.3 ± 4.6 mm Hg respectively. Target blood pressure was achieved in 19(76%) patients. The mean time taken to control blood pressure in the study group was 57.63± 14.37 minutes. The mean number of drug dosages required were 3.84±0.95. The mean apgar score at 5 minute was 8.29±1.3 and the side effects were tolerable.

Conclusion: Intra-venous labetalol is an effective first line anti-hypertensive drug for acute control of blood pressure in the management of severe pregnancy induced hypertension. The maternal and fetal outcome is good with minimal side effects.

Introduction

Globally hypertensive disorders of pregnancy complicate approximately 5–10 % of pregnancies[1]. Incidence of hypertensive disorders in India is found to be 10.08 %[2]. Approximately 72,000 pregnant women die every year because of eclampsia and severe preeclampsia. That amounts to nearly 200 women every day. Preeclampsia–eclampsia ranks second only to hemorrhage as a specific, direct cause of maternal death. The risk that a woman in a developing country will die of preeclampsia or eclampsia is about 300 times that of a woman in a developed country[3].

The benefits of acute pharmacological control of severe hypertension prior to and/or post delivery are generally accepted. The American College of Obstetricians and Gynecologists (ACOG) recently convened a task force on hypertension in pregnancy which have provided an up to date statement with recommendations on treatment of hypertension in pregnancy[4]. It has recommended antihypertensive therapy for women with preeclampsia and sustained SBP ≥ 160 mmHg or DBP ≥ 110 mmHg.

For emergency treatment in preeclampsia, IV hydralazine, labetalol and oral nifedipine can be used [5]. Labetalol is a non-selective β-blocking agent with vascular α-$_1$-receptor blocking capabilities [6]. Labetalol is used frequently for the treatment of severe acute hypertension during pregnancy. This study aims to assess the role of intra-venous labetalol in the management of severe pregnancy-induced hypertension.

Material and methods:

A prospective hospital based study was conducted in the Department of Obstetrics & Gynecology, Maharaja Agrasen Medical College, Agroha, Hisar from January 2013 to August 2013.

Ethical committee approval was obtained. Written informed consent was obtained from all the patients.

Inclusion Criteria: Antenatal women with singleton pregnancy with ≥160 mm Hg systolic and ≥110 mm Hg diastolic blood pressure, proteinuria 2+ dipstick in midstream urine sample, and after 32 weeks of pregnancy till term, admitted to the institute on IPD basis.

Exclusion Criteria: Women with bronchial asthma, bradycardia and cardiac failure (contra-indications of labetalol therapy) were excluded.

Intravenous labetalol was administered 10 mg slowly which was doubled every 15 minutes till a maximum dose of 220 mg was given or blood pressure was controlled. Target was to achieve systolic blood pressure of <155 mm Hg and diastolic blood pressure of <105 mm Hg. If the target blood pressure was not achieved with the maximum dose of intravenous labetalol, second line antihypertensive drug was started.

Methods:

All patients were subjected to detailed history, general physical examination and systemic examination after taking informed consent. The following baseline parameters were evaluated:

Clinical:

- Blood pressure was obtained with a mercury sphygmomanometer, taking the fifth Korotkoff sound for the diastolic blood pressure. The measurement of blood pressure was continued every 15 minutes for at least 60 minutes or longer until target blood pressure <155/105 mmHg was achieved (both targets had to be fulfilled).
- Partogram
- Ocular fundus examination.

II. Biochemical:

- Hemogram
- Urine albumin by dipstick method
- Random blood sugar
- Serum creatinine and serum uric acid
- Platelet count
- Liver Function Tests
- Total Serum Proteins

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III. Nonstress test

Outcomes studied were:

- Control of Blood Pressure: Number of patients in which blood pressure control was achieved, time taken to control blood pressure, drug dosage required for blood pressure control
- Mode of labour
- Induction –delivery interval
- Mode of delivery
- Incidence of maternal morbidity and mortality
- Apgar score of the new born.
- Incidence of perinatal morbidity and mortality.
- Side effects of the drugs in the mother as well as the neonate.

Statististical Analysis:

In our study the data have been expressed as mean ± standard deviation or percentage.

The mean $(\overline{X})$ of the data is calculated as :

$$\text{Mean } (\overline{X}) = \frac{X_1 + X_2 + X_3 ..... + X_n}{n}$$

The standard deviation (S) is calculated using formula:

$$S \sqrt{\frac{1}{n-1} \sum (x - \bar{x})^2}$$

S = standard deviation

n = number of patients

X = values of data

$\overline{X}$ = arithmetic mean of the values

$$X^2 = \sum \frac{(O-E)^2}{E} \quad \text{Where}$$

O = Observed frequency

E = Expected frequency

Results

A total of 25 antenatal women with severe preeclampsia and eclampsia participated in the study. 17 patients had severe pre-eclampsia, 4 ante-partum eclampsia and 4 intra-partum eclampsia. Table 1 shows the baseline characteristics of the study group. The pretreatment mean systolic and diastolic blood pressure were 185.4 ± 13.5 mmHg and 120.3 ± 4.6 mm Hg respectively.

Table 2 shows the outcomes of the study. Target blood pressure of <155/105 mm Hg was achieved in 19(76%) patients. Out of the 6 patients in which blood pressure could not be controlled with intravenous labetalol, 5 patients responded to nifedipine. Persistently high blood pressure (B.P.>160/110 mmHg for >12 hours despite adding second line antihypertensive was seen in 1 case. The mean time taken to control blood pressure in the study group was 57.63± 14.37 minutes. The mean number of drug dosages required were 3.84±0.95.

The mean systolic blood pressure readings 15 min, 30 min, 45 min and 60 min after treatment were 178.1 ± 12.1, 170.7 ± 12.8, 164.2 ± 12.0 and 157.0± 12.2 mm Hg respectively. The corresponding mean diastolic blood pressure readings were 115.3 ± 3.8, 110.8 ± 3.1,106.6 ± 4.3 and 101.2±7.8 mm Hg respectively (Table 3).

In the study group, 4 patients had bishop score <6 and 21 patients had bishop score ≥6 (Table 1). Out of 25 patients, 6(24%) were induced while 19(76%) had spontaneous labour. The mean induction delivery interval was12 ± 4 hours. 15(60%) patients delivered vaginally, 9(36%) underwent lower segment caesarean section and 1(4%) forceps delivery (Table 2).

In the present study, abruptio and magnesium toxicity were observed in one (4 %) case each. Two(8%) patients had postpartum haemorrhage. One(4%) patient had convulsions. Two(8%) patients developed pulmonary edema and 2(8%) maternal mortalities were recorded. Two patients (8%) complained of vomiting in this group (Table 4) and sudden fall in blood pressure was seen in one (4%) patient (Table 2).

In the present study, mean apgar score at 5 min was 8.3 ± 1.3. Hypoglycemia was observed in one neonate. Hypoglycemia was transient and clinically insignificant. Hyperbilirubinemia and respiratory distress syndrome were observed in two cases each while one case each had meconium aspiration syndrome and peripheral circulatory failure. There were four NICU admissions and one neonatal mortality (Table 5).

Discussion

Preeclampsia and eclampsia are a major cause of maternal and perinatal morbidity and mortality. A recent Confidential Enquiry into Maternal and Child Health (CEMACH) report has attributed the occurrence of fatal intracranial haemorrhages to inadequate treatment of severe systolic hypertension (≥160 mmHg) in women with pre-eclampsia can lead to intracranial haemorrhages , and recommends urgent and effective antihypertensive treatment for such cases[7]. Recent guidance from the National Institute for Health and Clinical Excellence, UK, recommends inpatient treatment of severe hypertension of pregnancy with labetalol (oral or intravenous), intravenous hydralazine or oral nifedipine as first-line alternative antihypertensives within the critical care setting[8].

The present study shows that intravenous labetalol regimen is effective in controlling severe hypertension in pregnancy, with the target blood pressure achieved in 76% of cases within five doses or within 75 minutes of commencing treatment. Our study is in agreement with recent guidelines and expert opinion that intravenous labetalol is a suitable first-line antihypertensive for hypertensive emergencies of pregnancy[8,9,10].

In a study conducted by Das S et al[11], the mean systolic BP was 186.2 ± 12 mm Hg and the mean diastolic BP was 118.11 ± 8 mm Hg. The mean time required to achieve target BP of 150/90 mm Hg was 47.2 ± 13.5 mins. Total antihypertensive dose required to achieve target blood pressure was 96 ±37.8mg. In the present study, the pretreatment mean systolic and diastolic blood pressure were 185.4 ± 13.5 mmHg and 120.3 ± 4.6 mm Hg respectively.

The mean time taken to achieve target blood pressure <155/105 mm Hg was 57.63± 14.37 minutes. In the present study, a lower starting dose of intra venous labetalol was used which might be responsible for longer time taken to control blood pressure.

Raheem I et al[12] conducted a double-blind randomised trial to compare oral nifedipine with intravenous labetalol in their rapidity to control hypertensive emergencies of pregnancy. In the labetalol arm, 25 pregnant women with severe gestational hypertension ≥160/110, received intravenous labetalol injection (in an escalating dose regimen of 20, 40, 80, 80 and 80 mg) every 15 minutes until the target blood pressure of ≤150/100 mmHg was achieved. Median systolic blood pressure was 170(165-180)mmHg and median diastolic blood pressure was 108(100-112)mm Hg. Target blood pressure was achieved in 80% of patients which is comparable with our study. Mean time taken to control

blood pressure was 54 ± 42 minutes. Total antihypertensive drug doses required to achieve target blood pressure levels were 3.75 ± 1.5 compared to 3.84±0.95 in the present study.

The aim of antihypertensive drugs is not to achieve a normotensive state as a sudden fall in blood pressure can lead to ischemic damage. Sibai has suggested to keep systolic blood pressure between 140 and 155 mmHg and diastolic blood pressure between 90 and 105 mmHg in severe pre-eclampsia[10]. The present study aimed to achieve systolic blood pressure <155mm Hg and diastolic blood pressure <105 mm Hg.

Labetalol has been claimed to be superior to hydralazine when given intravenously in that it produces a smooth progressive fall in blood pressure without episodes of hypotension or side effects such as tachycardia and palpitations[13]. In the present study, blood pressure was smooth in all patients except one. Sudden fall in blood pressure was reported in one patient. Her baseline blood pressure was 170/136 mmHg and it fell to 110/80 mmHg on receiving 10mg of iv labetalol. It was readily controlled by elevating the foot end and bolus intravenous fluids. Patient did not have any clinical or electrocardiographic evidence of myocardial ischemia. No neurological complication was seen.

2 patients (8%) complained of vomiting in the study group. Wall Manning and Simpson[14] also reported 10% incidence of gastrointestinal symptoms.

Our study is in agreement with Michael CA[15] , who reported that labetalol did not cause significant side effects in pregnant patients, postural hypotension occurred in four patients, scalp tingling in two, and lethargy, headache, and generalized rash in one patient. It was not necessary to discontinue the drug because of side effects.

Redman et al [16] reported that the most common side effect with labetalol has been the acute onset of tremulousness or shakiness which must be distinguished from impending eclampsia. In our study this side effect was not observed.

In the present study, mean apgar score at 5 minute was 8.29±1.3. In the study by Das S et al, 90% neonates had a five minute apgar score of >7 compared to 84% in our study. Out of 50 neonates, one case of hyperbilirubinemia , ten cases of IUGR and one perinatal death were reported by them. Out of 25 live births in the present study, 6 IUGR, 2 hyperbilirubinemia, 2 respiratory distress syndrome, one peripheral circulatory failure and one meconium aspiration syndrome were reported. There were 4 NICU admissions and one neonatal mortality. The higher rate of neonatal complications in our study could be due to lower gestation age (mean 35.5 ± 3.5 weeks) compared to that in Das S et al (≥36 weeks)[11].

In the present study, no case of neonatal bradycardia was reported while one neonate had hypoglycemia which was transient. Our study is in agreement with Macpherson et al who reported that labetalol does not cause clinically important sympathetic blockade in the mature newborn infant[17].

Conclusion

Intra-venous labetalol is an effective first line anti-hypertensive drug for acute control of blood pressure in the management of severe pregnancy induced hypertension. The maternal and fetal outcome is good with minimal side effects.

Table 1: Baseline characteristics of the study group

Characteristics	n=25
Age(years)	23.1 ± 3.8
Gravidity	1.8±1.04
Gestation age(weeks)	35.5 ± 3.5
Systolic blood pressure(mm Hg)	185.2 ± 21.0
Diastolic blood pressure(mm Hg)	120.4 ± 8.3
Magnesium sulphate	25
Bishop score <6 ≥6	 4 21

Table 2. Maternal outcomes of intravenous labetalol

	N=25	%
Number of patients in whom target blood pressure was achieved	19	76
Time (minutes) taken to achieve blood pressure ≤150/100 mmHg	78.42±51.29	
Total antihypertensive doses to achieve blood pressure ≤150/100 mmHg	3.84±0.95	
Mode of labour Spontaneous Induced	 19 6	 76 24
Induction delivery interval (hrs)	12±4.0	
Mode of delivery Caesarean Vaginal delivery Forceps delivery	 9 15 1	 36 60 4
Side effects Vomiting Sudden fall in B.P.	 2 1	 8 4

Table 3: Pre –treatment and post treatment blood pressures in the study group

	Pretreatment B.P.	B.P. 15 min after treatment	B.P. 30 min after treatment	B.P. 45 min after treatment	B.P. 60 min after treatment
Systolic B.P.	185.4±13.5	178.1 ± 12.1	170.7 ± 12.8	164.2 ± 12.0	157.0± 12.2
Diastolic B.P.	120.3 ± 4.6	115.3 ± 3.8	110.8 ± 3.1	106.6 ± 4.3	101.2± 7.8

Table 4: Maternal complications

Maternal complications	n = 25 No.	%
Abruptio	1	4
PPH	1	4
Shock	1	4
Pulmonary Edema	2	8
MgSO4 Toxicity	1	4
Convulsions	1	4
Persistently High B.P.	1	4
Expired	2	8

Table 5: Perinatal outcome

Perinatal outcome	N=25	%
Apgar score	8.3±1.3	
Hypoglycemia	1	4
Hyperbilirubinemia	2	8
Meconium aspiration syndrome	1	4
Respiratory distress syndrome	2	8

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NICU admissions	4	8
Neonatal mortality	1	4

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