Original Article

Role of Labetalol in Control of Severe Hypertension in Pregnancy

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Abstract

Objective: To determine the efficacy of Labetalol in the control of severe hypertension in pregnancy.

Study Design: Therapeutic Clinical Trial.

Setting: Gynae unit 1, Holy Family Hospital, Rawalpindi.

Study Duration: 1st April 2010-31st Dec 2010

Methodology: All the pregnant women with BP of ≥160/110 mm of Hg admitted in labour ward were included in the study. Those with bronchial asthma, cardiac failure, heart block, cardiogenic shock, severe bradycardia and hypersensitivity to the drug were excluded from study. Data was collected on a pre-designed proforma. Outcome measures were dose required to achieve the target BP, time taken to achieve the target BP(diastolic BP≤ 100mmHg), adverse reactions and feto-maternal outcome. Analysis of data was done on SPSS Version 16.

Results: Total patients included in the study were 71. Women between 21-30 years were 54 (76%) & 17 (24%) were between 31-40 years. Twenty seven (38%) were Primigravida, 38 (53%) were P1-P4 and 6 (9%) were P5 and above. Out of 71 patients, 10 (14%) presented with PIH, 18 (25%) with Preeclampsia, 39 (55%) with Eclampsia and 4 (06%) with Chronic HTN. Sixty four (90%) of patients presented in 3rd trimester. Range of BP at the time of presentation was from 160/110-250/140 mm of Hg. In 45 (64%) women BP was controlled with labetalol 20-100 mg, while 13 (18%) required >100-200mg and13 (18%) >200-300 mg of labetalol. Time taken to achieve the target BP was 1hour in 43 (60%) women, 2 hrs in 14 (20%), 3 hrs in 14 (20%). Thirty six (50%) women experienced no side effects and in the remaining 50% nausea and vomiting were the common side effects. None of our patients experienced arrhythmias. After the achievement of target BP, 2/3rd (n=52) were switched over to oral preparation of labetalol. Thirty two patients (45%) delivered vaginally and 39 patients (55%) delivered by caesarean section. Regarding the neonatal out-

come 59 (83%) delivered alive and 12 (17%) delivered dead babies. Out of the babies delivered alive, 19 (32%) were shifted to nursery, one baby expired and remaining, 18 were discharged. Majority of women were discharged in healthy state (n= 63) (89%), 08 (11%) were transferred to ICU/ medical unit, out of whom 2 expired later.

Conclusion: Labetalol is an effective drug in controlling severe HTN in pregnancy and is associated with mild side effects Foetomaternal outcome was good.

Key words: Labetalol, Hypertension, Eclampsia.

Introduction

Pregnancy induced hypertension complicates about 10% of pregnancies and pre-eclampsia affects 2-8% of pregnancies.[1] The incidence of eclampsia varies greatly between settings, being higher in developing countries where it affects between 1/100 to 1/1700 deliveries, whilst in industrialized countries it affects about 1/2000 deliveries.(1) Pre eclampsia and eclampsia increase maternal and perinatal morbidity and mortality. It is the 2nd major cause of maternal mortality in Pakistan. [2]

Recent National Institute of Health and Clinical Excellence(NICE) guidelines on Hypertension in Pregnancy which were revised in Jan 2011, recommended Labetalol as 1st line drug for treatment of hypertension in pregnancy.[3, 4]

Labetalol is a selective alpha(α)1 and non-selective beta adrenergic blocker used parenterally for immediate reduction in blood pressure in severe hypertension. The principal physiologic action of labetalol is to competitively block adrenergic stimulation of β-receptors within the myocardium (β1-receptors) and within both bronchial and vascular smooth muscle β2-receptors as well as α1 receptors within vascular smooth muscle. It causes decrease in systemic arterial blood pressure and systemic vascular resistance without a substantial reduction in resting heart rate, cardiac output and stroke volume. It can be given in oral form also. It is completely absorbed from gastrointestinal tract with peak plasma levels occurring 1-2 hrs after oral administration. Its metabolism is primarily hepatic. These metabolites are present in plasma and excreted in urine and via bile into feces. Its half life is 6-8 hrs.[5]

Stabilization of are hypertensive patient before planning delivery is the hallmark of management. The objective of our study is to determine the efficacy of labetalol in control of severe hypertension in a setting like ours, where every patient cannot be monitored electronically.

Methodology

The study was conducted at Holy Family Hospital Gynae Unit 1, for a period of 1 year from 1st January 2010 to 31th December 2010. Approval from recognised ethical committee taken before starting the study (document attached). Total number of deliveries in year 2010 was 8492. Patients who presented with hypertensive disorders were 508(6%). All the pregnant women with BP of ≥160/110 mm of Hg admitted in labour ward were

included in the study. Women with bronchial asthma, cardiac failure, heart block, cardiogenic shock, severe bradycardia and hypersensitivity to drug were excluded from the study.

Labetalol was administered intravenously via 2 regimens. During the treatment patient was kept in supine position because substantial fall in BP on standing was expected.

1 Repeated I/ V injections: 20 mg by slow I/V injection over 2 min. (Supine B.P was measured immediately before and at 5 and 10 mins after injection to evaluate response). Additional injection of 40mg or 80 mg was given at 10 min intervals until desired supine B.P was achieved or total of 300 mg labetalol HCL has been injected. (Max dose 300mg/24 hrs).[5]

2 Slow I/V infusion: Infusion was prepared by diluting the vial contents to commonly used I/V fluids (Ringer lactate, 5% Dextrose water, Normal Saline)

A: Method

Forty ml labetalol + 160 ml IV fluid. Resultant 200ml solution contains 200 mg of labetalol i.e. 1mg/ml. It was administered at a rate of 2ml/min to deliver 2mg/min.

B: Method

Forty ml labetalol +250 ml IV fluid, the resultant solution contained 2mg/3ml. It was administered at a rate of 3ml/min.[5]

The concerned patient was monitored by recording Pulse/BP every 5 mins during active treatment, 15 min for 1st hr, 30 min for next 5 hrs, hourly till 24 hrs. Our target was to achieve the diastolic BP≤100 mm of Hg within 1 hr. The patient was observed for any adverse reactions like postural hypotension, moderate hypotension, sweating, flushing, arrhythmias, dizziness, vertigo, nausea and vomiting.

For maintenance therapy the patient was switched over to Oral Labetalol 100mg b.d to a maximum dose of 2400mg / day. Our outcome measures were dose required to achieve the target BP, time taken to achieve the target BP, adverse reactions and feto-maternal outcome. Information was recorded on structured Performa. Data was analysed on SPSS version 16.

Results

Total patients included in the study were 71. Our study showed that hypertension in pregnancy is more prevalent in younger women. Two third (76%) of women were between 21-30 years & 17 (24%) were 31-40 years. Twenty seven (38%) were primigravida, 38(53%) were P1-P4 and 6 (9%) were P5 and above. Out of 71 patients >50% of patients presented with eclampsia and 25% with pre eclampsia, while PIH was present in 10 patients (Figure 1). Majority of the patients presented in 3rd trimester i.e. 64 (90%) where as 5 (7%) presented in 2nd trimester while rest 2 (3%) were in the postpartum period.

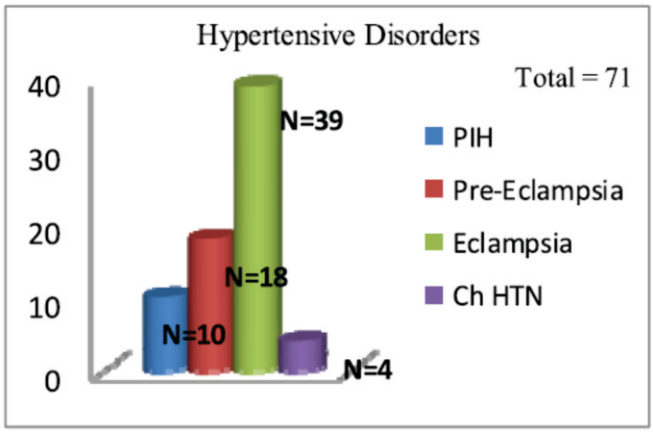

Figure 1. Frequency of Hypertensive disorders presenting in pregnancy.

Range of BP at the time of presentation was from 160/110-250/140 mm of Hg (Table 1). In 45 (64%) women BP was controlled with labetalol 20-100 mg, while 13 (18%) required between 100-200mg and13 (18%) between 200-300 mg. Time taken to achieve the target BP (diastolic BP≤100 mm of Hg) was 1hour in 43 (60%) women, 2 hrs in 14 (20%), 3 hrs in 14 (20%). Thirty six (50%) experienced no side effects and in remaining 50% nausea & vomiting were the major side effects (Figure 2). None of our patients experienced arrhythmias. After the achievement of target BP 2/3rd (n=52) were switched over to oral preparation of labetalol (100 mg b.d) and remaining 1/3rd (n=19) were given methyldopa (250 mg tds) and calcium channel blocker(Adalat Retard 20 mg b.d). Our 45% (32) patients delivered vaginally & 55% (39) had caesarean section. Regarding the neonatal outcome, 59 (83%) were delivered alive and 12 (17%) were received dead (no other cause was found except raised B.P). Out of 59, 19 (32%) were transferred to the nursery, where one baby expired and rest of 18 babies were discharged, Thus there were 12 intrauterine deaths and 1 early neonatal death (Figure 3). Majority of women n= 63 (89%) were discharged in healthy state, rest of 08 women (11%) were transferred to ICU/ medical unit, out of whom 2 expired later. We also compared the data of year 2009 and 2010 of our unit (Table II). Total no of Eclampsia received in 2009 were 28 while 39 in 2010. Maternal deaths due to Eclampsia and its complications were 4 in 2009 and 2 in 2010 (Table II). It means we were able to save 24 women in 2009 and 37 women in 2010 after the introduction of use of Labetalol. Labetalol (intravenous & oral) helped in rapid stabilization of mother and decreased the interval between initial presentation and delivery and saved the mother as well as foetus from complications associated with Eclampsia.

Table I. Range of blood pressure, dose of labetalol, and the time taken to achieve the target blood pressure

	Minimum	Maximum
BP at the time of presentation	130/110 mm of Hg	250/140 mm of Hg
Dosage required to achieve the target BP	20 mg	300 mg
Time taken to achieve the target BP	15min	3 hrs

Table II. Comparison of Maternal Mortality

	2009	2010
Total Eclampsia	28	39
Total Maternal Mortality	29	40
Maternal Mortality due to Eclampsia	4	2
Near Missed	25	38

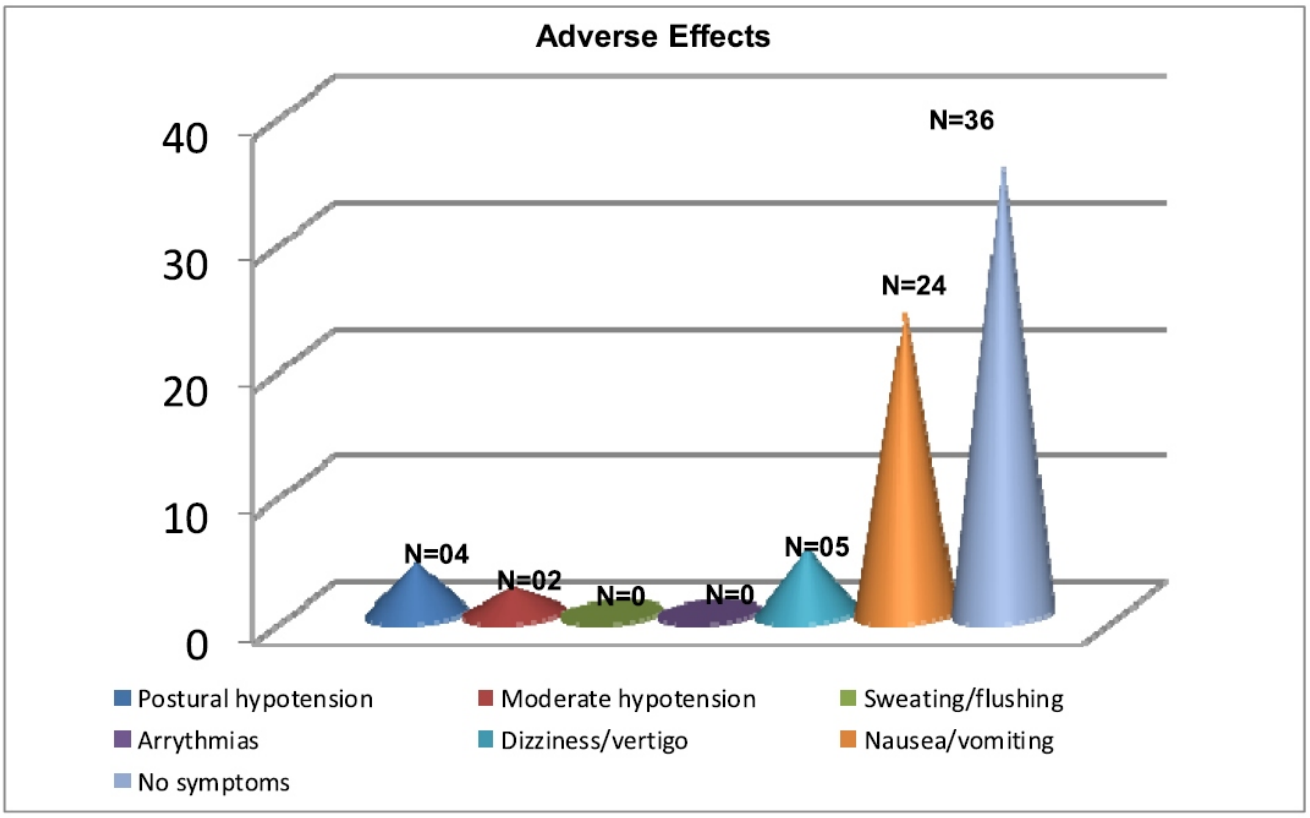

Figure 2. Adverse reactions seen with the use of Labetalol

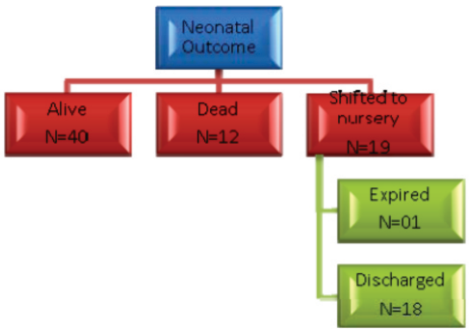

Figure 3. Neonatal Outcome in patients receiving Labetalol

Discussion

Hypertension in pregnancy is the common cause of maternal and perinatal morbidity and mortality. Control of BP 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 hemorrahge is the most serious complication in case of pre-eclampsia and eclampsia. [6]

Use of Intravenous labetalol to treat acute hypertension in pregnancy as a first line drug has been recommended and has a better safety profile.[4, 7]

Literature review has showed Labetalol to be a good alternative to hydralazine in control of severe hypertension in pregnancy.[8]

In our study we use repeated injections or slow I/V infusion of Labetalol to control the BP. Prichard BN in his study also proved that intravenous Labetalol is best given as a graded infusion or as

repeated small bolus injections to assure a smooth fall of BP.[9]

According to our study Labetalol is an effective hypotensive agent, as in all the patients we were able to control the BP but dosage and time duration was different. Our results are comparable with results of Mahmoud et al and Cruick Shank et al, in whose patients the BP control was achieved in 85%-88% patients. [10, 11]

Fifty percent of our patients did not experience any side effects. In remaining 50% nausea and vomiting were the major side effects. Another study published in the literature also showed that no serious side effects were observed with labetalol except slight breathlessness.[12, 13]

After controlling the BP 2/3rd of our patients were given oral Labetalol 100 mg in twice daily dosage. There are several studies in the literature showing that orally administered Labetalol in twice daily regimen is an effective antihypertensive drug. BP control is more frequently achieved in hypertensive pregnancies with Labetalol than with methyldopa as a first line treatment.[14]

Conclusion

Labetalol is an effective drug in controlling severe hypertension in pregnancy. It is associated with mild side effects and good feto-maternal outcome.

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