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Effect of Labetalol as an Antihypertensive Agent in Pre-Eclampsia

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Abstract

Background: Labetalol is an anti-hypertensive agent with alpha adrenergic and non-selective beta-adrenergic receptor blocking actions. It is recognized as first choice of antihypertensive agent in pre-eclampsia.

Material and Methods: A prospective longitudinal study of 200 cases of moderate to severe pregnancy induced hypertension treated with Labetalol was conducted over a period of two years to find out maternal and perinatal outcome.

Results: Labetalol therapy was effective in sixty four percent cases and pregnancy was continued for average of 16 days. Forty eight percent cases were delivered by caesarean section. One hundred and sixty four (82%) babies were live born. Four babies had intrauterine death (2%), thirty-two (16%) babies had fresh stillbirths and fourteen babies had early neonatal deaths.

Conclusion: The effective control of blood pressure with the use of Labetalol was observed in sixty four percent cases of moderate to severe pregnancy induced hypertension.

Keywords: Labetalol; Pre-eclampsia; Placental insufficiency

Introduction

Pre-eclampsia is a common hypertensive disorder of pregnancy and is an important cause of maternal and perinatal mortality and morbidity. It complicates around 5% to 15% of pregnancies and accounts for approximately a quarter of all antenatal admissions [1-3]. There is evidence that such pregnancies are commonly associated with reduced utero-placental blood flow. A number of antihypertensive medications are in use for control of blood pressure, but not all have proven to be safe during pregnancy. Labetalol is an adrenergic receptor-blocking agent that has both selective alpha-adrenergic and non-selective beta-adrenergic receptor blocking actions [4]. It is an oral and intravenous antihypertensive agent. Present study was conducted at tertiary care teaching hospital in view of the advantages of Labetalol, in regard to its availability for oral as well as intravenous route, effectiveness, minimal side effects and beneficial effect on utero-placental blood flow [5].

Material and Methods

A prospective longitudinal study was carried out in a 1,275 bedded tertiary care teaching hospital located in rural area of central India for a period of two years (October 2017 to September 2019). Two hundred pregnant women, who were admitted with moderate (150/100 mmHg to 159/109 mmHg) to severe (160/110 mmHg) pregnancy induced hypertension in third trimester of pregnancy were included in the study [6]. Women with serious complications of PIH like eclampsia, HELLP syndrome, Hepatic and renal failure, women already taking antihypertensive agents other than Labetalol, women having contraindications for the use of Labetalol, women with intrauterine fetal death were excluded from the study. Women were given complete bed rest. Blood pressure were recorded every four hourly. Complete history was obtained. Clinical examination was performed. Important hematological, urine, serological and radiological investigations were carried out for the purpose of diagnosis and for knowing the severity of the disease. Necessary investigations like obstetric ultrasound, color Doppler study to know status of placental perfusion, non-stress test, and fetal biophysical profile were carried to assess the fetal wellbeing. After confirming the diagnosis of moderate to severe PIH, antihypertensive treatment in the form of either intravenous or oral Labetalol was started as per the guidelines. Treatment with intravenous Labetalol was started in severe hypertension, in the dose of 20 mg i.v. over 2 min, blood pressure was monitored after 10 min, if there was no control of blood pressure, then 40 mg i.v. was repeated, followed by 80 mg i.v.

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Depending on the response of blood pressure, total of 140 mg i.v. Labetalol was used. The starting dose of oral Labetalol was 100 mg twice a day and was increased to maximum of 800 mg per day [7-9]; this was increased at half weekly intervals until control of blood pressure was achieved. Reduction in blood pressure below 140/90 mmHg was labeled as satisfactory controlled of blood pressure Women, who responded to initial oral or intravenous Labetalol, were allowed to continue with the pregnancy. The pregnancy was terminated in women, whose blood pressure continued to remain high. Cases were strictly monitored for the evidence of side effect of Labetalol. Patient's condition was monitored, counseling was done and written and informed consent was obtained.

All Labetalol responders were monitored on regular basis for control of blood pressure and for development of any maternal and fetal complications. Cases were kept in the high dependency unit till delivery. Time of delivery and mode of delivery was individualized. All newborn babies were managed by neonatologist. Low birth weight babies, IUGR babies and babies suffering from other complications were managed in neonatal intensive care unit. Women were discharged from the hospital after satisfactory control of blood pressure.

Results

Majority of the women were primigravida (67%) and un-booked (86%). The average gestational age at initial presentation was around 33 weeks. All women were treated either with intravenous or oral Labetalol in divided doses.

Out of total 200 cases of moderate to severe pre-eclampsia, 72 cases (36%) did not respond adequately to intravenous Labetalol therapy. The mean systolic blood pressure in this group after intravenous Labetalol was 171 ± 4 mmHg and mean diastolic pressure was 112 ± 2 mmHg. In view of the risk of serious maternal complications, decision of termination of pregnancy taken. Remaining 128 cases (64%) responded with satisfactory control of blood pressure. The average dose of oral Labetalol required to control blood pressure was 600 to 800 mg/day in divided doses. Pregnancy could be continued for average of 16 days. Rate of caesarean section was 48%. The indications for caesarean section were eminent eclampsia, failure of induction, fetal growth restriction, reduced placental function, intra-partum fetal distress, deteriorating renal and hepatic parameters, non-reassuring non-stress test, reduced fetal movements or demand by patient for caesarean section.

Six women developed accidental hemorrhages, three women developed features of HELLP syndrome, and two women had eclampsia following delivery or caesarean section. There was intrauterine fetal death, while on treatment in four cases. There was no maternal mortality in the present study.

One hundred and sixty-four (82%) babies were live born. Four babies had intrauterine death (2%), thirty-two (16%) babies had fresh stillbirths and fourteen babies had early neonatal deaths. The causes of stillbirths were severe birth asphyxia, extreme prematurity, severe placental insufficiency, and very low birth weight baby and meconium aspiration syndrome. All 32 stillbirths were seen in pregnancy of less than 34 weeks duration. The average gestational age in these babies was 32.5 weeks and average birth weight was 1,150 grams. Out of 164 live born babies, 72 babies were low birth weight, majority of these babies required admission in intensive neonatal care unit for varied duration. Causes of neonatal deaths were respiratory distress syndrome, severe birth asphyxia, meconium aspiration syndrome, neonatal sepsis etc. Overall perinatal mortality was 25%.

Discussion

A prospective longitudinal study was carried out to find out the effect of Labetalol on moderate to severe hypertension in 200 pregnant women in third trimester. Out of 200 cases, 72 women (36%) did not respond to intravenous Labetalol which was administered in incremental doses up to 180 mg. There was no satisfactory control in terms of reduction in blood pressure, thus the pregnancy was terminated in these cases in maternal interest. Remaining 128 cases (64%) were shifted to oral therapy after satisfactory control of blood pressure. The control of blood pressure occurred in 55% cases within 48 h of starting of Labetalol therapy [7], observed satisfactory control of blood pressure in 45 of the 51 treated women (88%) within 24 h. Several workers, Lardoux group and C. A Michael reported satisfactory control of blood pressure within 24 h in 82% to 92% of their cases respectively Michael C [8,9]. A, in his study of 25 cases of use of Labetalol in cases of severe hypertension in pregnancy reported effective reduction in blood pressure in 88% cases [9]. In their randomized controlled study reported satisfactory control of blood pressure in 45 of their 51 cases (88%), treated on Labetalol. The effect was short-lived and required dose escalation after 3.5 days in the majority of cases [7].

Conclusion

Development of hypertension during pregnancy is one of the serious complications. The maternal and perinatal outcome depends upon severity of hypertension, period of gestation and treatment received by women. Injection Labetalol by intravenous route and subsequently by oral route showed satisfactory control of blood pressure in 64% cases. The adverse perinatal outcome was mainly related to extreme prematurity, low birth weight, and utero-placental insufficiency due to moderate to severe PIH.

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