

Original Research Article

## **A Comparative study of IV Labetalol and IV Hydralazine on mean arterial blood pressure changes in pregnant women with hypertensive emergency**

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**Abstract:** The study was undertaken to compare lowering of blood pressure in pregnant women with hypertensive emergency by IV Labetalol and IV Hydralazine and to find out which drug produces better effect. This prospective type of interventional study was conducted in SMS Medical College, Jaipur among 226 women admitted with SBP  $\geq 160$  or DBP  $\geq 110$  mmHg or both. Women divided in 2 groups (113 each) divided randomly: Labetalol (Group-A), Hydralazine (Group-B). We measured the difference between pretreatment and after treatment mean arterial blood pressure. Pretreatment mean arterial blood pressure was  $127.40 \pm 40$  and  $126.61 \pm 6.475$  mmHg in labetalol and Hydralazine group respectively. After treatment mean arterial blood pressure was  $112.25 \pm 5.821$  and  $109.27 \pm 14.30$  mmHg in labetalol and Hydralazine group respectively. Mean arterial blood pressure change was  $15.14 \pm 8.02$  mmHg in labetalol group and  $17.34 \pm 13.42$  mmHg in hydralazine group. ( $p=0.136$ , Not significant). Labetalol and Hydralazine both drugs are first line drugs in severe hypertension in pregnancy as in our study both drugs control blood pressure in similar way.

**Keywords:** Hypertensive emergency, pregnancy, IV Labetalol, IV Hydralazine, MABP

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### **INTRODUCTION**

Hypertensive disorders of pregnancy are one of the most common medical complications of pregnancy and is a major cause of maternal, fetal and neonatal morbidity and mortality [1,2]. They complicate about 5-10% of all pregnancies [3]. "Hypertensive emergency is a condition of hypertension (systolic BP  $\geq 160$  mmHg or diastolic BP  $\geq 110$  mmHg or both) which is acute in onset, persistent for 15 minutes or more" [4]. The immediate goal of management of severe hypertension in pregnant women is predominantly related to maternal safety, such as the prevention of stroke, rather than the prevention of the long term sequelae of hypertension hence it is recommended treatment to lower systolic blood pressure below 160 mmHg and diastolic below 110 mmHg [5].

Intravenous Labetalol and Hydralazine are both considered first-line drugs for the management of acute, severe hypertension [6]. Hydralazine is a direct-acting smooth muscle relaxant used to treat

hypertension by acting as a vasodilator primarily in arteries and arterioles. Labetalol is alpha -1 selective, nonselective beta adrenergic blocker drug causes a decrease in systemic arterial blood pressure and systemic vascular resistance without a substantial reduction in resting heart rate, cardiac output, or stroke volume.

We compared both the drugs to find out the difference between controls of the blood pressure.

### **MATERIAL & METHODS**

This prospective type of interventional study was conducted from May 2014 to Nov 2015 on 226 women admitted with pregnancy more than 24 weeks with hypertensive emergency. We included single or multiple pregnancy with Systolic BP  $\geq 160$  mmHg or diastolic blood pressure  $\geq 110$  mmHg, or both and Gestational age  $>24$  weeks who had no contraindication to the use of Hydralazine or Labetalol and Haemodynamically stable. We excluded the women

who had Asthma, Idiopathic, Systemic lupus erythematosus & related disease, Thyrotoxicosis, Coronary artery disease, Aortic stenosis, mitral stenosis, corpulmonale. A written informed consent was taken. Cases were randomly divided in two groups of 113 each. Group-A: Labetalol group and Group-B: Hydralazine group.

The sample size was calculated as total 226 cases, 113 in each group (Hydralazine and Labetalol group) at 95% confidence interval and 80% power to verify the expected difference of 15% in proportion of persistent severe hypertension (25% and 10%) in Hydralazine and Labetalol group respectively observed in a pilot study conducted in 40 patients at Zenana Hospital, Jaipur.

Detailed history, proper general physical, systemic and per abdominal examination was done. Standard mercury sphygmomanometer with appropriately sized cuff was used. The first and fifth Korotkoff sounds were recorded for systolic and diastolic blood pressure respectively. The blood pressure was measured with patient in left lateral recumbent position with the patient's arm at the level of the heart for all measurements. Blood pressure was measured in both arms. Urine protein got done by dip stick method. Investigations CBC, LFT, RFT, serum electrolytes, serum LDH, peripheral blood film, BT, CT, PT, APTT, urine complete and microscopy got done. Management of severe preeclampsia was done as prevention of seizures and control of hypertension. All women already experienced eclamptic seizure or having any signs of impending eclampsia received magnesium sulphate according to Pritchard regime - as a 4 g intravenous loading dose over 10 minutes and 10 g intramuscularly (5g in each buttocks). Maintenance dose 5 g intramuscularly in alternate buttocks was administered every 4 hours until 24 hours after first dose or delivery whichever is later.

Antihypertensive Labetalol or Hydralazine was given. Reconstitution of IV Hydralazine was done by dissolve Hydralazine 20 mg powder with 2mL of Sodium Chloride 0.9% in vial then further diluted with 18 ml Sodium Chloride 0.9%. This equates to Hydralazine 1mg /ml.

Initially 5 mg of Hydralazine administered intravenously slowly over 2 minutes. If the desired BP was not obtained in the 20 minutes following the first dose we injected 10 mg of intravenous Hydralazine (equating to 10mL of the diluted solution) slowly over 2-4 minutes. If desired BP was not obtained within 20 minutes then third dose of 10 mg of IV Hydralazine (10 ml solution) given slowly in 2-4 minutes. If BP not controlled after giving 3 doses we used other hypertensive drug.

Inj. Labetalol 20 mg liquid solution (4 ml ampule) reconstituted with 16 ml of Sodium Chloride 0.9% to make 20 ml solution of 1 mg/ml. Initial dose administered IV Labetalol 20 mg with in 2 min. If after 15 min desired blood pressure was not obtained then we doubled the previous dose (40 mg). If no control of blood pressure in 15 minutes then next dose of 80 mg given. If desired BP was not achieved then we repeated it two more times in every 15 min. (up to a maximum of 300 mg). If still BP was not controlled then other antihypertensive treatment could be used.

We monitored BP, heart rate, maternal oxygen saturation level, and respiration. Blood pressure checked every 5 minutes for 15 minutes following initial administration then every 15 minutes for 1 hour. Then every 30 minutes thereafter until BP was remained stable and was within an acceptable range. Our protocol established that if the maximum dose was reached without an adequate control of the blood pressure (SBP <160 mmHg or DBP < 110 mmHg), a second antihypertensive was used.

We monitored the fetal heart rate continuously by electronic cardiotocography until BP remained stable (continuous CTG during administration and for 30 minutes after administration).

Statistical analysis was performed with the Microsoft Excel, SPSS, Trial version 20 for Windows statistical software package (SPSS inc., Chicago, IL, USA) and PRIMER. The data was analyzed by using both descriptive and inferential Statistics. The Categorical data were presented as numbers (percent) and were compared among groups using Chi square test. Groups were compared for demographic data were presented as mean and standard deviation and were compared using by students t-test. Probability p-value <0.05 was considered statistically significant.

## RESULTS

Patients in both groups were similar with respect to age, parity gestational age (Table-1). Baseline pretreatment MBP were similar, comparable, no significant difference was observed in both groups.

Pretreatment mean arterial blood pressure was 127.40±40 and 126.61±6.475 mmHg in labetalol and Hydralazine group respectively. After treatment mean arterial blood pressure was 112.25±5.821 and 109.27±14.30 mmHg in labetalol and Hydralazine group respectively. Mean arterial blood pressure change was 15.14 ± 8.02 mmHg in labetalol group and 17.34 ± 13.42 mmHg in hydralazine group. (p=0.136, Not significant). In the analysis of the primary outcome (antihypertensive efficacy), we did not find statistical difference in MABP between the Hydralazine and Labetalol groups but overall effect of both the drugs

was comparable as mean arterial blood pressure controlled in similar way (table 2).

**Table-1: General Characteristics of Studied Population**

Characteristics	Labetalol	Hydralazine	Total
Age (yrs)			
< 25	67 (59.29%)	66 (58.41%)	133 (58.85%)
> 25	46 (40.71%)	47 (41.59%)	93 (41.15%)
Parity			
Nulliparous	59 (52.21%)	66 (58.41%)	125 (55.31%)
Multiparous	54 (47.79%)	47 (41.59%)	101 (44.69%)
Gestational Age			
<37 weeks	73 (64.60%)	55 (48.67%)	128 (56.64%)
>37weeks	40 (36.40%)	58 (51.33%)	98 (43.36%)

**Table-2: Mean Arterial Blood Pressure Change (Primary Outcome)**

Group	Mean Arterial BP			p-value, LS
	Before	After	Mean Change	
Labetalol	127.40±8.382	112.25±5.521	15.14±8.02	0.136, NS
Hydralazine	126.61±6.475	109.27±14.30	17.34±13.42	

**DISCUSSION**

This randomized clinical trial using either Hydralazine or Labetalol demonstrated that both drugs were found effective and rapid antihypertensive agents in hypertensive emergencies as severe preeclampsia. This finding collaborate earlier studies including Cochrane review on the efficacy of either drugs in hypertensive crisis in pregnancy [7-9]. In our study group Most of the cases belonged to 21-25 years age group this finding is in contrary with previous studies Ramesh K et al, Lamminpää R *et al.*[10-11]. Majority of the patients in both the groups of our study were nulliparous. This supported the fact that Preeclampsia is more common among primigravida[12].No significant difference was observed between mean arterial blood pressure after giving drugs. No statistically significant difference was observed in mean arterial change of blood pressure and this result was similar with study of Delgado de Pasquale *et al.* [9].

In meta-analysis conducted by Duley *et al.* they found insufficient data for reliable conclusions about the comparative effects of these two antihypertensive agents[8].

**CONCLUSION**

The aim of antihypertensive therapy is to control the blood pressure. We studied Parentral Hydralazine and Labetalol and we found both the drugs control mean arterial blood pressure in similar way, no agent is clearly superior to other. To conclude, we can say that choice of antihypertensive should depend on the clinicians experience and familiarity with a particular drug. Also the availability and cost of the drug are important requirement for use of particular drug.

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