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RESEARCH ARTICLE

A comparative study of intravenous hydralazine versus labetalol in the management of severe hypertension in pregnancy

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ABSTRACT

Objective: The objective of this study is to compare the efficacy as well as safety profile of hydralazine and labetalol in severe hypertension of pregnancy. **Methodology:** Hundred (100) women with severe pregnancy induced hypertension were randomly allocated into two groups of 50 each. Study group was given intravenous hydralazine and control group was treated with labetalol. The efficacy of two drugs were noted in terms of time taken to achieve target blood pressure, number of doses required and number of patients developing severe persistent hypertension. **Results:** The average time taken to control blood pressure (BP) in hydralazine group was 32.66 ± 18.79 minutes and 30.70 ± 20.46 minutes in labetalol group and this was statistically significant ($p<0.001$).There was no statistical difference between the two drugs in terms of efficacy, perinatal outcome and adverse affect except headache which was significantly more in hydralazine group. **Conclusion:** Both hydralazine and labetalol can be used to treat hypertensive emergencies.

Keywords: Hydralazine, labetalol, severe hypertension in pregnancy, headache, sudden hypotension.

Hypertensive disorders of pregnancy are one of the most common medical complications. It affects 10-15% of all pregnancy and a major cause of maternal, fetal and neonatal morbidity and mortality.[1, 2] Around the world this group of disorders comprise one of the four leading causes of maternal death. According to National High Blood Pressure Education Programme (NHBPEP) working group and American college of obstetricians and gynaecologists (ACOG) hypertension in pregnancy is defined as diastolic blood pressure >90 mm of Hg or systolic blood pressure >140 mm of Hg after 20 wks of gestation in women with previously normal blood pressure.[3,4]

Pre-eclampsia is a syndrome which may also be associated with myriad signs and symptoms such as edema, visual disturbance, headache and epigastric pain. It is also associated with laboratory abnormalities like elevated liver enzymes and low platelet count

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(HELLP syndrome). There is a consensus that due to their risk the patient should be treated with anti hypertensive agent to achieve rapid control of hypertension.

Hydralazine and labetalol are two most commonly used antihypertensive agents used for hypertensive crisis. Hydralazine is a direct acting smooth muscle relaxant acting as a vasodilator primarily in arteries and arterioles. Labetalol is an α and non selective β blocker. It decreases blood pressure by decreasing systemic vascular resistance. The purpose of this study is to evaluate intravenous hydralazine versus intravenous labetalol regimens in terms of their speed, efficacy and tolerability in the acute control of blood pressure in severe hypertension of pregnancy.

Materials and method

A randomized controlled trial was conducted in the Department of Obstetrics and Gynaecology from February 2016 to December 2016 at PBM Hospital, Bikaner comparing hydralazine to labetalol in the management of severe hypertension. For the sample size calculation a rate of persistent severe hypertension of 3.8% in the hydralazine group and 13.5% in the labetalol group α error rate of 5% and a power of 80% calculated sample size was 100.

The pregnant women were randomized into two groups using computer generated table randomly either intravenous hydralazine or intravenous labetalol. In study population, women with >28 weeks pregnancy were taken and divided in two groups on basis of computer generated table. Proper informed written consent was obtained from both groups. Patients were eligible for inclusion if they were 18-35 years old, >28 weeks gestation, singleton pregnancy, hemodynamically stable and BP >160/110 mmHg. Patients with essential hypertension, cardiac disease, bronchial asthma, hematological disorder, sensitive to labetalol or hydralazine, thyrotoxicosis, liver disorders, multifetal gestations and hemodynamic instability were excluded.

Group A - treated with Hydralazine (50 cases); Group B - treated with Labetalol (50 cases).

Patients randomized to the hydralazine group were administered 5mg of intravenous hydralazine. Blood pressure was checked every 15 minutes. The dose was repeated every 15 minutes until the target blood pressure that is SBP <160mmHg and DBP <110 mmHg was achieved. The dose was limited to maximum of 4 doses. Patients in the control group were administered with 20 mg (4 ml) of labetalol. Blood pressure was measured every 15 minutes. The second dose of 40 mg (80 ml) labetalol was given if the target BP was not achieved within 15 minutes. If blood pressure was not controlled another 80 mg was infused, this was repeated at 15 minutes interval for maximum total dose of 220 mg. Inj. labetalol was infused at a slow rate over 2-5 minutes. The time required for BP control to target value was noted. The number of doses required to achieve target BP was noted. Adverse effects like maternal hypotension, tachycardia, and nausea were noted. Data obtained was analysed statistically. Chi square test, student t-test and fischer exact test were used to analyse the data. Probability value <0.05 were considered significant. Quantitative variables have been indicated in mean ± SD.

Results

A total of 100 women meeting the inclusion criteria were included in the study. The baseline variables were similar in both arms of study (table 1). In the study group the mean time required to achieve target BP was 32.66 ± 18.79 minutes while in the control group it was 30.70 ± 20.46 minutes. This difference was found to be significant due to faster onset of action of labetalol.

Table 1: Baseline variables of patients

Variables	Group A	Group B
Age in years	24.8 ± 3.80	24.64 ± 3.79
Gestational age in weeks	35.96 ± 1.92	35.66 ± 1.73
Booking status (Booked) in %	68	44
Gravidity (Gravida 1) in %	64	56

Table 2: Baseline variables, dose and time required to achieve target BP

Variables	Group A	Group B	P value
Initial systolic BP (mm Hg)	168.12 ± 12.06	168.88 ± 12.33	0.378
Initial diastolic BP(mm Hg)	110.60 ± 6.80	112.68 ± 10.12	0.214
Final systolic BP(mm Hg)	146.16 ± 9.27	146.52 ± 10.12	0.327
Final diastolic BP(mm Hg)	92.6 ± 5.01	94.96 ± 9.96	0.011
Duration needed to control BP in minutes	32.6 ± 8.79	30.70 ± 20.46	< 0.001
Doses given to control BP	1.7 ± 0.64	1.80 ± 0.81	0.865

In the hydralazine group 24 patients and 21 patients in labetalol group achieved target blood pressure after single dose. In both groups 19 patients achieved target BP after 2 doses and this difference was not significant. Thus there was no difference between the two drugs with respect to the number of doses required to achieve the target blood pressure. There were 2 treatment failures in hydralazine and 3 in labetalol group (table 2).

Table 3: Distribution of cases according to Maternal and Fetal outcome

Variables	Group A Number	Group B Number
Maternal complications		
Headache	7	1
Nausea	1	2
Vomiting	0	2
Eclampsia	1	0
Modes of delivery		
Vaginal delivery	40	41
LSCS	10	9
Fetal outcome		
NICU admission	34	33
VLBW (1.0-1.5Kg)	3	2
LBW (1.6-2.5Kg)	18	13
Normal BW (2.6-3.9Kg)	29	35

The perinatal outcome in two groups were analysed on the basis of live or still birth, NICU admission and birth weight. The difference was not statistically significant.

The adverse effects of the two drugs are comparable and there was no statistical difference between the two drugs. Headache was significantly more in hydralazine group (table 3).

Discussion

This study demonstrates that both the drugs remain as effective antihypertensive agents in hypertensive emergencies as severe preeclampsia. This finding correlate earlier studies including cochrane review on the efficacy of both drugs in hypertensive crisis in pregnancy [5-7].

The average time taken to achieve desired BP control in hydralazine group was 32.66 ± 18.79 minutes and 30.70 ± 20.46 minutes in labetalol group and this was statistically significant (p <0.001). This was contrary to other studies where time taken to achieve desired BP control was similar for both groups. This may be due to faster onset of action of labetalol compared to hydralazine. In the present study target BP was achieved after single dose in 24 (48%) patients in hydralazine group and 21 (42%) in the labetalol group. In both groups 19 patients achieved target BP after 2 doses and this difference was not significant. This finding perhaps forms the basis of accepting the null hypothesis in this study that demonstrated no superiority of one over the other in achieving fast blood pressure control. In our study it was seen that 2 patients in hydralazine group and 3 patients in labetalol group has severe persistent hypertension (p value=0.646) which was statistically insignificant. There were no significant adverse events attributed to either drugs in terms of adverse effects like maternal tachycardia (0:1), nausea (1:2), vomiting (0:2).There was no maternal hypotension in both groups. Similar safety profile and findings were seen in studies of Pasquale[8] and Nombur[9]. However headache was significantly more frequent in patients given hydralazine as compared to labetalol group [7 (14%) patients in hydralazine group had headache compared to 1 (2%) patients in labetalol group]. This difference was statistically significant. This may be due to dilatation of capacitance vessels in the cerebral circulation resulting in severe headache.

There was no significant difference in fetal outcome in both groups where 47 (94%) patient in hydralazine

and 49 (98%) patients in labetalol group had live fetal outcome (p value=0.307) further collaborating the finding of non superiority of these drugs over one another. The patients who did not have live fetal outcome were the patients who had documented IUD before commencement of treatment in hydralazine and labetalol groups. These deaths were more likely to be the complication from uteroplacental insufficiency or abruption placentae than from the effect of either hydralazine or labetalol group. Sixty eight percent (68%) babies in hydralazine group required NICU admission and 66% babies in labetalol group required the same. These were mainly pre term or LBW or were kept in observation for few hours. This was non significant similar to the findings of Nombur [9] and Deka Nabanita [10]. The recorded VLBW and LBW were not statistically different between both groups. In a meta analysis conducted by Duley et al [6] they found insufficient data for reliable conclusions about the comparative effects of these two antihypertensive drugs. They concluded that until better evidence is available, the choice of antihypertensive should depend on what is known about adverse drug effects and how familiar the clinician is with a particular drug. Our findings in this study may add to the existing knowledge on this subject matter. However larger trials of community based study on severe hypertension in pregnancy are needed to confirm these findings.

Conclusion

Thus labetalol and hydralazine were found to be equally effective in terms of number of doses required to achieve the target blood pressure. Mean time duration to achieve the target blood pressure was slightly lower for labetalol than hydralazine due to faster onset of action of labetalol. Apart from headache there was no significant difference between the two drugs in terms of adverse effects like maternal tachycardia, nausea, vomiting. Headache was significantly more in hydralazine group compared to labetalol. The two drugs were similar when perinatal outcome, NICU admission were compared.

To conclude, choice of antihypertensive should depend on the clinicians experience, familiarity, drug availability and cost of the drugs. This study has shown that hydralazine and labetalol fulfill the criteria required for an antihypertensive drug to treat severe hypertension in pregnancy with adequate efficacy and safety.

Conflict of interest: None. **Disclaimer:** Nil.

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