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Original Research Article

A comparative study of hydralazine versus labetalol in the management of pregnancy induced hypertension (PIH).

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Abstract: The objective of this study is to compare the efficacy as well as safety profile of Hydralazine and Labetalol in severe pregnancy induced hypertension. 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 the 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. The adverse effects of the two drugs and the perinatal outcome were also noted. There were no statistical difference between the two drugs in terms of efficacy, perinatal outcome and adverse effects except headache which was significantly more in hydralazine group. Both hydralazine and labetalol can be used to treat hypertensive emergencies and there is no significant difference between the two drugs.
Keywords: Pregnancy induced hypertension, hypertensive crisis, pre-eclampsia, labetalol, and hydralazine

INTRODUCTION

Hypertensive disorders complicate 5 to 10 percent of all pregnancies, and together they are one member of the deadly triad –along with haemorrhage and infections- that contributes to maternal mortality and morbidity [1]. Preeclampsia affects 5 to 8 percent of all pregnancies [2].

The complications of uncontrolled high blood pressure during pregnancy affect multiple organ systems and can be detrimental to both mother and fetus. Severe hypertension is associated with complications like hypertensive encephalopathy, eclampsia, intracranial haemorrhage, pulmonary edema. It can cause intrauterine growth restriction, preterm delivery and stillbirth in the fetus. Lowering of blood pressure to safe levels can prevent these complications. An ideal antihypertensive is the one which lowers blood pressure promptly but not abruptly without causing significant effect on the fetus.

Hydralazine and labetalol are two most commonly used antihypertensive agents used for hypertensive crisis. 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.

MATERIAL AND METHOD

A randomized controlled trial was conducted in the Department of Obstetrics and Gynaecology from July 2015 to June 2016 at Gauhati Medical College and Hospital comparing hydralazine to labetalol in the management of severe hypertension. 100 women with severe pregnancy induced hypertension with gestational age more than 28 weeks gestation were in included in the study.

Inclusion criteria: Patients with systolic blood pressure>=160mmHg and/or diastolic blood pressure>=110mmHg with pregnancy greater 28 weeks gestation.

Exclusion criteria: Patients with asthma, heart disease, allergic to hydralazine or labetalol, liver disease, diabetes, heart rate <60beats/min or >120beats/min.

All the patients included in the study were randomly divided into two groups.

Group A-treated with hydralazine (50cases) and

Group B-treated with labetalol (50cases).

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 systolic blood pressure<160mmHg and diastolic blood pressure <110mmHg was achieved. The dose was limited to maximum of 5 doses. Patients in the control group were administered with 20mg (4ml) of Labetalol. Blood pressure was measured every 15 minutes. The second dose of 40mg (80ml) labetalol was given if the target blood pressure was not achieved within 15 minutes. If blood pressure was not controlled another of 80 mg (16ml) was infused. This was repeated at 15 minutes interval for two more times till a maximum total dose of 300mg was administered (total 5 doses). Inj labetalol was always infused at a slow rate over 2-5 minutes.

The time required for blood pressure to reach the target value was noted. The number of doses required to achieve the target value was noted. The blood pressure was measured every 15 minutes for 2 hours. Adverse effects like maternal hypotension, tachycardia, nausea, abruptio placentae were noted if any were noted. The patients were followed up and complications arising as a result of severe hypertension were noted.

Data obtained was analysed statistically. Chi-square test, student t-test and Fisher exact test were used to analyse the data. Probability values less than 0.05 were considered significant. Quantitative variables have been indicated in mean + SD.

RESULTS AND OBSERVATIONS

A total of 100 women meeting the inclusion criteria were included in the study. The baseline variables were similar women in both arm of the study (Table 1).

Table 1: showing baseline variables

Parameter	Hydralazine Mean(SD)	Labetalol Mean(SD)	P value
Age	24.38 (5.49)	25.42 (5.21)	
Initial SBP	177.2 (13.7)	178 (18.7)	0.407
Initial DBP	117.4 (9.2)	115.4 (7.34)	0.116

In the study group, the mean time required to achieve target blood pressure was 31.6 + 18.30 minutes while in the control group it was 30.64 + 18.75 minutes (p=.401383). There is no significant difference between the two groups in terms of time taken to achieve the blood pressure.

Table 2: Showing time required in minutes to achieve target BP

Group	Mean	SD	P Value
Hydralazine (Group A)	31.6	18.30	P = .401383
Labetalol (Group B)	30.64	18.75	

In the hydralazine group 24 patients achieved target blood pressure after single dose, 2-3 doses were required in 15 patients and 4-5 doses were required in 9 patients. In labetalol group 25 patient's required single dose, 14 and 8 patients required 2-3 and 4-5 doses respectively. P value was calculated to be 0.91976 which is not statistically 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 failure in hydralazine group and 3 in labetalol group.

Table-3: Showing no. of doses required to achieve target BP

No. of doses	Hydralazine	Labetalol
1	24	25
2 to 3	15	14
4 to 5	9	8
Total	48	47
Chi Square	0.1032	
P value	0.94970	

Severe persistent hypertension was seen in 2 patients (4%) in the hydralazine group and 3 patients (6%) in the labetalol group. P = 0.646355 which is not statistically significant. Thus there is no difference between the two drugs. Combinations were used in these patients to control the blood pressure.

Table-4: Showing no. of patients having severe persistent hypertension

Severe persistent hypertension	Hydralazine		Labetalol	
	Number	Percentage	Number	Percentage
Yes	2	4	3	6
No	48	96	47	94
Chi square	0.2105			
P value	0.6463			

The perinatal outcome in the two groups were analysed on the basis of stillbirth ,fetal distress and NICU admission were similar in both the groups and no statistical difference was found between the two groups.

Table-5: Showing perinatal outcome

	Hydralazine		Labetalol		
	No. of cases	**%**	**No. of cases**	**%**	**P value**
Fresh stillbirth	2	4	3	6	0.6
Fetal distress	8	16	9	18	0.79
Admission to NICU	9	18	8	16	0.79

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-6: Showing adverse effects

	Hydralazine	Labetalol	P value
Maternal tachycardia	3	0	0.07864
Headache	13	2	0.002
Nausea/Vomiting	2	3	0.64
Abruptio placentae	4	3	0.6951

DISCUSSION

Thus from our study it was seen that both the drugs remains as effective antihypertensive agents in such hypertensive emergencies as severe preeclampsia.

This finding collaborates with earlier studies including Cochrane review on the efficacy of either drug in hypertensive crisis in pregnancy [5-7]. In the study group, the mean time required to achieve the target blood pressure was 31.6 + 18.30 minutes while in the control group it was 30 + 18.7 minutes. (P = .0401383). The time taken to achieve the target blood pressure was similar in both the groups. In the present study target blood pressure was achieved after single dose in 24 patients (48%) in the study group and 25 patients (50%) in the control group. 15 patients in the study group and 14 patients in the control group achieved target blood pressure after 2-3 doses while 4-5 doses were required in 9 patients in the study group and 8 patients in the control group. (P= 0.94970) which was insignificant. In our study it was seen that 2 patients (4%) in hydralazine group and 3 patients (6%) in labetalol group had severe persistent hypertension (p=.646355) which was statistically insignificant. There was no maternal hypotension in both groups. The absence of maternal hypotension and the relative success and safety profile observed in this study has earlier been reported by other workers using the same agents [5, 7]. Those who had fresh stillbirth in Hydralazine or Labetalol group were patients managed for abruptio placentae. These deaths were more likely to be the complication from the abruptio placentae than from the effect of either Hydralazine or Labetalol administration. This is because 3 and 2 of the stillbirths occurred before commencement of treatment in hydralazine and labetalol groups respectively. There were no significant differences in the fetal outcome in both the groups, further collaborating the finding of non-superiority of these drugs over one another. Headache was significantly more frequent in patients given hydralazine compared to labetalol. This correlates with the study of Lahaga Isaac Nombur *et al.;* [7] Vigil-De Gracia *et al.;* reported a rather higher frequency of maternal tachycardia and palpitations with the use of the hydralazine compared to the use of labetalol, but no statistically significant difference in frequency of headache among their study groups [4]. Other

researchers had reported similar adverse maternal side effects with either Hydralazine or Labetalol [6, 7].

In a meta-analysis conducted by Duley *et al.;* they found insufficient data for reliable conclusions about the comparative effects of these two antihypertensive agents [3] 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 have added to the existing knowledge on the subject matter.

SUMMARY AND CONCLUSION

Thus the two drugs labetalol and hydralazine were found to be equally effective in terms of time taken to achieve target blood pressure, no of doses required to achieve the target blood pressure. The number of patients having severe persistent hypertension was comparable in both groups. 2 patients in hydralazine group and 3 patients in labetalol group had severe persistent hypertension respectively. Apart from headache there was no significant difference between the two drugs in terms of adverse effects like maternal tachycardia, nausea/vomiting, abruptio placentae. Headache was seen significantly more in hydralazine group (26%) compared to labetalol (4%). There was no incidence of maternal hypotension in both the groups. The two drugs were similar when perinatal outcome like fresh stillbirth, fetal distress, NICU admission were compared. Apgar score at 1 minute and 5 minute was also comparable between the two groups.

It was seen that both Hydralazine and labetalol can be used as antihypertensive agents for controlling severe hypertension in pregnancy. The efficacy of the two drugs is comparable. Both the drugs can reduce blood pressure within a short period. There was no difference between the two drugs as far as maternal and fetal outcome was concerned. No serious side effects were noticed in both the groups, further supporting their utility in controlling hypertensive emergencies. Hence, the choice depends on availability, cost and individual choice of the physician.

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