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ORIGINAL ARTICLE

Comparison between adverse effects of intravenous Inj Labetalol Vs Inj Hydralazine during treatment of Hypertension in Pregnancy

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ABSTRACT

Aim: To examine and compare side effects of intravenous Labetalol and Hydralazine in the treatment of Hypertension in pregnancy in developing countries like Pakistan.

Methodology: A six-month randomised controlled experiment was undertaken at the Lady Aitchison Hospital's, Department of Obstetrics and Gynaecology. In the study, 330 individuals with severe hypertension who were between the ages of 20 and 35 years old and had been pregnant for more than 20 weeks were included. Patients were split into two groups of equal size. Group A was administered a 20mg IV bolus of Labetalol while Group B was administered a 5-10mg IV bolus of Hydralazine. The patients were monitored during the administration period of 60 minutes and all this data was entered into a proforma.

Results: Females had an average age of 27.43±3.47 years and average gestational age in females was 28.98±4.49 weeks. The systolic blood pressure in all females was 109.43 ±16.93mmHg after 60 minutes of therapy, and mean diastolic blood pressure was 77.28±14.73mmHg. A total of 135(40.9%) women suffered from maternal hypotension [27(16.36%) with Labetalol vs 108(65.43%) with Hydralazine], and 55(16.68%) females exhibited abnormal fetal heart rate [1 (0.61%) with Labetalol and 54(32.72%) with Hydralazine]. Therefore, the Hydralazine adverse effect was statistically significant (p-value = 0.000).

Practical Implication: If the results of this study are applied in clinical practice in patients of pregnancy induced hypertension, female patients ca be prevented of side effects of hydralazine by using labetalol to treat hypertension in pregnancy, so it is very beneficial for patients.

Conclusion: The study concludes that use of Hydralazine in females with PIH should be discouraged, whereas the use of Labetalol should be encouraged in a developing country like Pakistan.

Keywords: Pregnancy Induced Hypertension (PIH),Gestational Hypertension(GH), hypotension, headache, abnormal fetal heart rate, palpitation, tachycardia, intravenous.

INTRODUCTION

According to current recommendations, Gestational hypertension (GH) is described as a pregnant woman's SBP of 140mmHg and DBP of 90 mmHg for whom the BP was common prior to pregnancy, whose pregnancy is equal to or longer than 20 weeks, and who is not excreting protein in the urine[1-3]. To diagnose GH, a patient's blood pressure should be monitored at least two times and with a 6-hour delay between each examination[4]. Severe GH is defined as a continuous rise in SBP of 160 and DBP of 110 for more than 6 hours

GH is one of the most common problems that pregnant women have, and it affects roughly 2-3 percent of pregnancies. Society of Obstetricians & Gynecologists of Canada (SOGC) evaluated GH guide-lines in 2008 and separated them into two types: already existing Hypertension and Hypertension developed in pregnancy[6].GH is a condition that develops in the second part of pregnancy (equivalent to or more than 20 weeks) without protein excretion in the urine, and whose blood pressure returns to normal once the baby is delivered. Preeclampsia affects around a third of pregnant women who attend the Gynae OPD with GH later. As a result, people with GH should be constantly examined for signs of pre-eclampsia[7]. Although the pathogen

In future, GH may be a precursor to long-term uncontrolled blood pressure[8].To obtain excellent control the objective of medical therapy is to achieve a DBP of < 100-105 mm Hg and an SBP < 160 mm Hg. In the event of women who already have high blood pressure and are experiencing problems with one or more essential organs, a blood pressure of (140/90)[9,10] is recommended. For many years, hydralazine was the usual therapy for gestational hypertension, but it had several adverse effects and appeared to increase pre-eclampsia[11,12]. Our goal was to determine the adverse effect of intravenous Labetalol & intravenous Hydralazine during the management of hypertension during pregnancy. As per previous studies, obstetricians mostly choose IV Hydralazine although; it has greater adverse effects than Labetalol. Because Labetalol has fewer adverse effects and takes effect rapidly, it should be first-line treatment for PIH patients. However, it is not commonly used in the underdeveloped countries like Pakistan due to conflicting results.

We aim to undertake this particular study to validate the pattern of adverse effects of Labetalol & Hydralazine. So that we can guide doctors towards effective therapy for the treatment of PIH in the future.

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MATERIALS & METHODS

This RCT had been going on for 6 months in the Department of Obstetrics & Gynecology, Lady Aitchison Hospital, Lahore, as per ethics committee approval. The sample size was estimated using a 95% power test, a 5% margin of error, and the predicted proportion of adverse effects, which would have been 2.5% in patients treated with intravenous Labetalol and 10% in patients treated with intravenous Hydralazine. A purposeful sampling strategy was used to enroll the patients after 20 weeks of pregnancy and a maternal heart rate of 60-100 beats per minute. Patients in age range of 20–35 years with more than 20 weeks of gestation and sustained severe hypertension (defined as systolic blood pressure more than 160 mmHg and diastolic blood pressure more than 110 mmHg) had their blood pressure measured on two occasions at least 6 hours apart during pregnancy. Patients with twin pregnancies, a past of heart rhythm abnormalities, a cardiac issue, asthma, hypersensitivity to Hydralazine or Labetalol, hypertension and use of any antihypertensive drugs prior to pregnancy, or who had taken medication for PIH, eclampsia, or pre-eclampsia in the last 72 hours were excluded from the study. Patient demographic information was documented, and informed permission was acquired. Using the lottery approach, patients were split into two groups (A:B). Those in A received an intravenous infusion of 20 mg of labetalol. Every 10 minutes, dose was raised by 40 and 80 milligrams, up to a maximum of 300 milligrams. Because blood pressure changes quickly, it was monitored with every 10 minutes of intervals. Following that, repeating dosages for 1 hour were given until blood pressure management was attained (target BP of

140/90). Patients in Group B received an intravenous hydralazine bolus of 5–10 mg depending upon the severity of their hypertension, which was repeated every 20 minutes up to an upper dosage of 30 mg (maximum 5 doses). Because the impact is gradual, blood pressure was measured every 15-20 minutes. After that, additional doses were given for 1 hour until control of blood pressure was achieved, and then treatment was stopped. We monitored the patients for 60 minutes for pharmacological adverse effects, including maternal hypotension, headache, palpitation, tachycardia, and aberrant foetal heart rate (defined as a fetal heart rate differing from 100-160 beats per minute within 60 minutes after drug administration). All this data was logged on a proforma. SPSS version 26 was used to enter and analyse the data. The mean and standard deviation of quantitative data, including age and gestational age, were computed. The frequency and proportion of qualitative characteristics such as maternal hypotension, various side effects, & abnormal foetal heart rate were calculated. The maternal hypotension, other adverse effects, and abnormal foetal heart rate in two groups were compared using Chi-square test. A p-value of less than 0.05 was considered significant for this study.

RESULTS

This study included 360 patients with an average age of 27.42 3.49 years. At time of presentation, average gestational age of females was 28.97 ± 4.48 weeks. Females had a mean SBP of 109.44 ± 16.92mmHg and a mean diastolic blood pressure of 77.28±14.73mmHg. Females in the IV Labetalol group had a mean SBP of 116.75 ± 12.75mmHg and a mean diastolic blood pressure of 86±10.13mmHg after the administration of the drug. IV Hydralazine group had a mean systolic blood pressure of 102.13±17.42mmHg and a mean DBP of 68.56 ± 13.45 mmHg after the administration of the drug. There were 135/360 (40.9%) women in this research who had maternal hypotension, with 27/165 (16.36%) belonging to the Labetalol group and 108/165 (65.45%) belong to Hydralazine group. Difference between two was statistically significant, with Hydralazine being related to higher maternal hypotension than Labetalol (p-value = 0.000). A total of 55/360 women (16.68%) developed abnormal fetal heart rate, with 1 (0.61%) belonging to the Labetalol group, whilst in the Hydralazine category, abnormal fetal heart rate accounted for 54 (32.72%) of the total. Difference between[two groups was very significant, with Hydralazine group being linked to more disturb fetal heart rate (FHR) than Labetalol (p-value = 0.000).22 (6.67%) women in this research experienced additional adverse effects, with 5 (3.03%) females in the Labetalol group and 17 (10.3%) in the Hydralazine group.

Table 1: Adverse effect between both groups

	Labetalol N=165	**Hydralazine N=165**	**p-value**
Age (Years)	27.73±3.70	27.12±3.25	
Gestational Age (wks)	28.92±4.49	29.02±4.48	0.835
SBP (mmHg)	116.76±12.75	102.12±17.45	0.001
DBP (mmHg)	86.00±10.14	68.58±13.42	0.001
Maternal hypotension	27(16.36%)	108(65.45%)	0.000
Abnormal FHR	1(0.61%)	54(32.72%)	0.000
Other side effects	5(3.03%)	17(10.3%)	0.008
Headache	2(1.21%)	16(9.69%)	0.001
Tachycardia	2(1.21%)	12(7.27%)	0.006
Palpitation	3(1.81%)	13(7.87%)	0.010

The difference between the two groups was substantial, with the Hydralazine group having greater adverse effects than the Labetalol group (p-value = 0.008). There were 18 (5.45%) women in this research who complained of headaches, with 2 (1.21%) in the Labetalol group and 16 (9.69%) in the Hydralazine group. The difference between the two groups was statistically significant, with Hydralazine being linked with a higher headache than Labetalol (p-value = 0.001). There were 14 (5.45%) women with tachycardia in this trial, with 2 (1.22%) belonging to the Labetalol group and 12 (7.28%) belonging to the Hydralazine group. Difference between two groups was statistically significant, with hydralazine causing more tachycardia than labetalol (p-value = 0.006). In this study, 16 (5.45%) of the women experienced palpitation, with 3(1.81%) belong to the Labetalol group and 13 (7.87%) belong to the Hydralazine group. Difference between the two group was substantial, with the Hydralazine group being linked to higher palpitation than the Labetalol group (p-value = 0.010).

DISCUSSION

GH is thought to be one of the most common medical conditions in pregnancy, affecting 10% of pregnancies and causing complications for roughly 240,000 expected women each year[13,14]. It's linked to a bad prognosis for both mom and fetus, and it has both long-term and short-term consequences. Drugs meant to lower blood pressure are widely used in GH, despite the lack of evidence of their advantages or drawbacks[15]. Many medicines are used for this purpose, and different recommendations recommend different drugs, amounts, and schedules, but nothing is known about their mechanism of action, dispersion, or effects on the mother and fetus. There have been a few RCTs that compared GH treatment medications to placebo. Because of the limited sample sizes, the statistical significance from these experiments is insufficient. They state that there is no additional advantage to pharmaceutical therapy and that there are no helpful or detrimental consequences during delivery. Furthermore, there are no statistics on prenatal anomalies, poor neonatal outcomes, or long-term baby prognosis. Due to regulatory and legal concerns, issues like these arose because of a lack of focus and assistance from the government and pharmaceutical companies in researching pregnant women. As a result, a substantial study in this sector is required to solve the pertinent challenges[16].

As a result, we registered 360 females with PIH, with an average age of 27.41±3.47 years. At the time of presentation, the average gestational age of females was 28.97±4.48 weeks. As per the studies, females and gestational age were virtually the same at the time of presentation with PIH [17,18].

After 60 minutes of the administration of labetolol and hydralazine, blood pressure of both groups was taken once again to record the difference in BP and other adverse effects between the two regimens. It was noticed that post-treatment mean SBP&DBP was 109.43/77.28±16.93/14.73 mmHg in IV Labetalol group, the mean SBP&DBP of females was 116.77/86±12.74/10.15mmHg in IV Hydralazine group, and mean SBP&DBP of mothers was 102.13/68.59±17.44/13.43mmHg. Difference between two groups was statistically significant, and it seemed that blood pressure was lower with Hydralazine as compared to Labetalol. Difference between two groups was considerable, and it appeared that hydralazine reduced blood pressure more than labetalol.

However, when it came to maternal hypotension, it was discovered that 135 women (40.9%) developed it, with 27(16.37%) in the Labetalol group and 108 (65.44%) in the Hydralazine group. Difference between two groups was extremely significant, with Hydralazine group being linked to higher maternal hypotension than Labetalol group (p-value = 0.000). According to our literature studies, hydralazine causes more hypotension than labetalol[19] as per meta-analysis (66.67% vs. 16.67%)[20]. However, our research has shown that Hydralazine is linked with higher maternal hypotension than Labetalol.In our study, greater FHR was found in 55 (16.67%) of the women, with 1 (0.62%) belonging to the Labetalol group and 54(32.73%) to the Hydralazine group. Although difference between two groups was large, the research found that greater FHR in both groups was relatively comparable (Hydralazine: 7.81% vs. Labetalol: 5.8%)[17]. Hydralazine was linked to a higher risk of adverse effects on fetal heart rate than other antihypertensives (11% (0–56%) vs. 0% (0–51%). This also supports the notion that Hydralazine should not be used to lower

blood pressure in those with PIH[20].Other adverse effects were seen in 22(6.67%) women, with 5 (3.03%) from the Labetalol group and 17 (10.3%) from the Hydralazine group. 14 (5.47%) women developed increased heart rate, out of which 2(1.22%) belonged to the Labetalol group, while 12(7.29%) from the Hydralazine group, and 16(5.43%) women developed palpitation, out of which 3(1.83%) belonged to the Labetalol group, while 13(7.89%) from the Hydralazine group, and 16(5.45%) women developed tachycardia. Other antihypertensives were linked to greater palpitations than hydralazine (18% vs 0%)[20]. Overall, the Hydralazine group had more maternal problems, but difference was not statistically significant. In our study and previous trials evaluating them in treatment of severe hypertension in pregnancy, they are associated with a significant prevalence of maternal problems. Although the medicine might be a factor, the most common cause is pregnancy-related hypertension[17,20,23]. Other negative effects include headache, palpitation (10% vs. 2.51%), &fetal heart rate abnormalities (33.33% vs. 0%)[17,20]. Despite the fact that there were no significant differences in maternal hypotension (Hydralazine 2% vs Labetalol 0%), headache (Hydralazine7% vs Labetalol 11%), palpitations (Hydralazine 10% vs Labetalol 2%), or maternal tachycardia (Hydralazine 6% vs Labetalol In both groups, fetal heart rate was quite similar (Hydralazine 7.81% vs Labetalol 5.81%)[17]. Some studies found no significant differences in prenatal or neonatal issues between the two groups[24].

CONCLUSION

In this study, the difference in adverse effects was significant, and it appeared that maternal hypotension, aberrant fetal heart rate, and other side effects such as headache, palpitation, and increased heart rate were greatly reduced when Labetalol was administered instead of Hydralazine. Because Labetalol has fewer adverse effects and is effective rapidly, it should be considered as a first-line treatment for women with PIH. Finally, Labetalol is a better medicine for managing PIH since it has a lower risk of problems and adverse effects.

Conflict of interest: Nil

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