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TO COMPARE THE EFFECT OF HYDRALAZINE AND LABETALOL IN LOWERING SEVERE HYPERTENSION IN PREGNANCY

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ABSTRACT

OBJECTIVE:- To compare the efficacy of intravenous labetalol and intravenous hydralazine in lowering severe hypertension in patients of preeclampsia and pregnancy induced hypertension.

STUDY DESIGN:- Retrospective randomized clinical study

PLACE AND DURATION OF STUDY:- Nishtar hospital, Bakhtawar Amin hospital and CMH hospital Multan from November, 2019 to august, 2020.

METHODOLOGY:- Seventy eight patients admitted in the Obstetrics and Gynaecology department having preeclampsia or severe hypertension fulfilling the inclusion criteria, were enrolled in the study. The detailed data regarding maternal parameters was taken. The readings of systolic, diastolic and mean arterial pressure were taken before and after treatment. The mean fall in mean arterial pressure and time taken from for this was recorded. Data was analysed by using SPSS version 20. **RESULTS**:- The mean age of patients in hydralazine group(Group A) was 25.4 years while that of labetalol group (Group B) was 25.6 years. The average gestational age of Group A and B patients were 34 and 33 weeks respectively. The mean fall in mean arterial pressure with hydralazine group was 25.31± 4.3 while it was 28.69 ± 4.01with labetalol group with p value <0.001. The time required by Group A and B to achieve the target blood pressure was 25.56 ± 6.7and 22.41 ± 4.23 minutes respectively with p value <0.014. **CONCLUSION**:- Our study favors the use of intravenous labetalol in preeclampsia and severe hypertension in pregnancy as it lowers mean arterial pressure more as compared to intravenous hydralazine.

KEYWORDS:- Hydralazine, Labetalol, Mean Arterial Pressure, Pre-Eclampsia

INTRODUCTION

Hypertensive disorders during pregnancy are very prevalent and are leading cause of maternal mortality and morbidity in developed and under developed countries [1]. The prevalence of hypertensive disorders during pregnancy is up-to 10% worldwide [2]. Women of low socio-economic status are suffering more [3]. Severe hypertension is a serious multisystem disorder and if not treated properly and promptly, it can lead to various other

problems like placental abruption, eclampsia, HELLP syndrome and maternal or fetal demise [4].

the only effective way to treat pre-eclampsia (PE) is to deliver the baby but prompt treatment of hypertension and stabilization of the patient is very important to prevent further complications [5]. Recent guidelines from the National Institute of Health and Clinical Excellence, UK, recommend the use of intravenous (I/V) hydralazine, intravenous labetalol and oral nifedipine as first line drugs [6].

Hydralazine has been used as a first line drug to treat severe PE for a long time in Pakistan. Hydralazine is an anti-hypertensive drug and classified as potent vasodilator. It dilates the vessels with the help of endothelial nitric oxide[7]. The marked fall in B.P by hydralazine lead to reflex tachycardia which is a common adverse effect of it. This reflex tachycardia can lead to angina and myocardial infarction in prone patients. Labetalol is a non-selective α and β blocker and classified as sympatholytic antihypertensive [7]. As it lowers B.P, it also suppresses reflex tachycardia which is a common problem with hydralazine. In the meanwhile fetal bradycardia is a problem of concern with labetalol.

Pakistan has high burden of PIH and PE. Pre eclampsia leading to eclampsia is a very common cause of death in Pakistan and it accounts for one third maternal deaths [8]. There are no proper guidelines in our country to manage this treatable disease. The rationale of our study was to compare the effect of intravenous (I/V) hydralazine and Labetalol in PE and sever PIH in terms of reduction in mean arterial pressure as well as rapidity of lowering blood pressure. Our aim was to identify a drug that will be suggested to give better results in treating severe PE as well as a good choice to prevent various feto-maternal complications in this regard.

METHODOLOGY

This retrospective comparative study was conducted in Pharmacology department, Nishtar Medical University (NMU), Multan. The data was obtained from Obstetric and Gynaecology departments of Nishtar Medical University (NMU), Bakhtawar Amin Hospital and CMH Institute of Medical Sciences (CIMS), Multan from November, 2019 to August, 2020. To compare blood pressure lowering effects of hydralazine and labetalol, two groups were made. The patients who received hydralazine were enrolled in Group A and the patients who received labetalol were enrolled in Group B. The sample size was calculated as 78 and 39 females were enrolled in each group. The permission was taken from the Head of the departments and from the Head of the institutes and hospitals.

The inclusion criteria was made first which was women at gestational age of 26 -37 weeks, with systolic blood pressure (SBP) >160mmHg and diastolic blood pressure (DBP) > 110 mmHg along with alive fetus. Pregnant ladies with comorbidities, severe bradycardia and with dead fetus were not included in the study.

Total 78 patients who were admitted in the Obstetric and Gynaecology departments of NMU, Bakhtawar Amin Hospital and CIMS, Multan and fulfilled the inclusion criteria were enrolled in the study with prior permission from the chairperson of the departments. The complete data of the enrolled patients were entered on a preformed Performa. The detailed history, examination, investigations and treatment was studied from the recorded file of each patient and relevant information was taken.

The treatment protocol which was followed by the consultants and paramedical staff was up to the mark. The hydralazine group (Group A) received 5mg I/V slow bolus of hydralazine which was repeated every 20 minutes until the desired blood pressure was achieved or four doses were achieved whatever came first.

The labetalol group (Group B) was injected 20 mg slow bolus of labetalol initially. If it was not effective then 40 mg labetalol was given after 20 minutes and then 80 mg until the desired blood pressure was recorded or four doses were given. The initial reading of blood pressure of each patient was recorded on a predesigned Performa. We noted the final reading of blood pressure of each patient after treatment as well as the time taken by each drug to control the blood pressure. The initial and final mean arterial pressure was then calculated from the recorded data.

The data was then entered on excel sheets and analyzed by using SPSS version 20. To summarize the age, parity and gestational weeks, frequencies and percentages were used. Mean ± standard deviation was calculated for the numerical variables like age, gestational age, SBP, DBP, MAP and time. Group A and B were then stratified on the base of age, parity and gestational age to observe the effects of these parameters on outcome. Independent t- test was used to compare the results of two groups like fall in mean arterial pressure and time required to achieve the target blood pressure.

RESULTS

The results of maternal parameters like age, parity and gestational age are presented in table no I, II and III. The mean age of patients of hydralazine group was 25.4 years while that of labetalol group was 26.6 years. The mean parity of females in group A was 2 and mean parity of labetalol group females was 1.7. Mean gestational age of the patients in hydralazine group was 34 weeks while that of group B was 33 weeks.

Table I. Age distribution

Age of patients (years)	**Hydralazine group (Group A) n=39 %**	**Labetalol group (Group B) n=39 %**	**Total n=78 %**
15-25 years	16 41	12 31	28 36
26-35 years	20 51.3	25 64	45 58
>35 years	03 7.6	02 5	05 6
Mean age	25.4 years	26.6 years	

Table No. II Parity status

Parity	**Hydralazine group (Group A) n=39 %**	**Labetalol group (Group B) n=39 %**	**Total n=78 %**
< 3	30 77	32 82	62 79.4
≥ 3	09 23	07 18	16 20.5
Mean parity	2	1.7	

Table No. III Gestational age

Gestational age	**Hydralazine group (Group A) n=39 %**	**Labetalol group (Group B) n=39 %**	**Total n=78 %**
< 30 weeks	12 31	12 31	24 31
≥ 30 weeks	27 69	27 69	54 69
Mean gestational age	34 weeks	33 weeks	

The mean SBP of Group A patients at the time of admission was 174.2 ± 10.3 while the patients in Group B was 179.4 ± 13.1 mmHg. The mean DBP of Group A and B was 118.72 ± 5.6 and 118.82 ± 4.5 mmHg respectively. The mean arterial pressure calculated for hydralazine and labetalol group was 137.21 ± 6.2 and 138.6 ± 7.3 mmHg respectively. After treatment, the mean SBP of Group A and B was 141.4 ± 7.8 and 140.2 ± 8.4mmHg.

The mean DBP after treatment was 94.5 ± 5 and 91.3 ± 6 mmHg for hydralazine and labetalol group respectively. Hence the MAP of Group A was 107.5 ± 3.56 and Group B was 106.3 ± 4.52 mmHg. These results are shown in table no IV and V.

The mean of fall in MAP was 25.31 ±4.3 mmHg for Group A that was hydralazine treated group while the mean of fall in MAP was 28.69 ± 4.01 mmHg for Group B which was treated with labetalol. These mean values of two groups were compared by applying independent t test using SPSS version 20 and the p value calculated was 0.001 which indicates a statistically significant difference between the means of two groups. These results are expressed ion table no. VI.

48 out of 78 patients required the second dose of drug. Single dose of hydralazine was able to reduce blood pressure in 16 patients while single dose of labetalol achieves desired fall in MAP in 22 patients. The average time taken by the hydralazine to reduce the blood pressure and achieve the target levels was 25.56 ± 6.7 minutes. The mean time taken by the labetalol to attain target blood pressure was 22.41 ± 4.23 minutes. The mean time taken by the two groups was statistically analysed by using independent t test and the p value obtained was 0.015 which was statistically significant. These results are shown in table no. VI.

Table no. IV SBP, DBP and MAP at Presentation (n=78)

Groups	SBP	DBP	MAP
Hydralazine group (Group A) n=39	174.2 ± 10.3	118.72 ± 5.6	137.21 ± 6.2
Labetalol group (Group B) n=39	179.4 ± 13.1	118.82 ± 4.5	138.6 ± 7.3

Table no. V SBP, DBP and MAP after treatment (n=78)

Groups	**SBP**	**DBP**	**MAP**
Hydralazine group (Group A) n=39	141.4 ± 7.8	94.5 ± 5	107.5 ± 3.56
Labetalol group (Group B) n=39	140.2 ± 8.4	91.3 ± 6	106.3 ± 4.52

Table no. VI Fall in mean arterial pressure and time required to achieve target levels

Parameters	**Group A (Hydralazine group)**	**Group B (Labetalol group)**	**P value**
Fall in MAP(Mean ± SD)	25.31 ± 4.3	28.69 ± 4.01	0.001
Time to achieve target levels (Mean ± SD)	25.56 ± 6.7minutes	22.41 ± 4.23 minutes	0.015

DISCUSSION

Hypertension in pregnancy is a serious problem and the gravity of condition is raised if pre-eclampsia is there. Pre-eclampsia and severe hypertension can lead to various maternal

complications, as well as responsible for poor fetal growth and development. Hypertensive disorders of pregnancy are a leading cause of maternal morbidity and mortality worldwide. The risk of maternal death due to PE and severe hypertension is much more in developing countries like Pakistan as compared to developed countries [9].

The well-timed and accurate management of PE and severe hypertension is very important as these disorders can cause maternal end-organs damage like cerebral stroke. Threshold blood pressure at which treatment should be initiated is important. Mostly clinicians and researchers agree that treatment should start at B.P ≥ 150-160/100 mmHg [10]. Meanwhile rapid and marked reduction in blood pressure should be avoided as it can lead to poor placental perfusion and fetal compromise.

A randomized control trial done by Purvi Patel et al., in 2018 showed similar results as ours [11]. She compared the efficacy and safety of I/V hydralazine and labetalol ion severe hypertension in pregnancy. They found that I/V labetalol lowered MAP more rapidly as compared to I/V hydralazine which are similar to our findings.

Our results are consistent with the findings of Pattraporn et al., in 2020 who showed that labetalol is more effective in pre-eclampsia as compared to hydralazine [12]. A similar study conducted by Khan et al., showed results comparable to our findings[13]. They observed that mean fall in MAP was more with I/V labetalol as compared to I/V hydralazine and the time taken by the labetalol was less to achieve the target blood pressure.

Hydralazine has been used as a first line drug from many years especially in Pakistan to treat pre-eclampsia and severe hypertension. Many studies in this regard reported equal efficacy of hydralazine and labetalol supporting null hypothesis. Some studies favor hydralazine while some studies quote labetalol as superior drug. Hydralazine is associated with multiple adverse effects like headache, nausea and palpitations [14]. Intravenous labetalol is also used in Pakistan to treat severe pregnancy induced hypertension (PIH) and PE with diverse adverse effects of concern. Both drugs have their prones and cones that should be kept in mind while deciding the use of any drug.

CONCLUSION

In our randomized clinical trial done on pregnant ladies with pre-eclampsia and severe hypertension, labetalol proved superior to hydralazine in terms of more reduction of mean arterial pressure and rapidly achieving the target levels. Administration of drug in critical situations like hypertensive emergencies needs careful and wise judgement. Our study favors the use of labetalol in PE and severe hypertension in pregnancy but the final decision should be by the clinician present at that time keeping in mind all the good and bad points about the drug.

CONFLICT OF INTEREST:- There is no conflict of interest.

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Authors contribution:-

Bushra shaheen: Designed the study, approved the final manuscript.
Noaman ishaq: Data analysis and article writing
Saba batool: Reference writing and data collection
Moniba irum: Literature review and data collection
Abduljabbar: Initial writing of manuscript
Mehreen akhtar: Data entry and maintenance