EFFICACY OF HYDRALAZINE IN COMPARISON WITH LABETALOL FOR CONTROL OF SEVERE HYPERTENSION IN PATIENTS WITH ECLAMPSIA

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ABSTRACT

Objective: To compare the efficacy of intravenous hydralazine with intravenous labetalol for control of severe hypertension in eclamptic patients.

Study Design: Cross-sectional study.

Place and Duration of Study: Obstetrics and Gynecology unit "B", PGMI Lady Reading Hospital Peshawar, from Mar 2017 to Sep 2017.

Methodology: Total 206 patients were included in this comparative study. They were randomly divided into two groups; group A and group B, each group comprising of 103 patients. The group A was given 5mg hydralazine as an initial intravenous bolus. After 20 minutes blood pressure was measured and if systolic and diastolic blood pressures were found to be >160 mmHg and>110mmHg respectively, the same dose was repeated maximally 3 times. The group B received 20mg labetalol as an initial intravenous bolus, then after every 20 minutes followed by 80mg to a maximum of three doses if systolic and diastolic blood pressures persisted >160 mmHg and >110mmHg respectively.

Results: Mean age in group A was 27 ± 2.93 years whereas in group B mean age was 29 ± 3.18 years. Moreover, blood pressure was effectively lowered in 92% patients of group A and in 90% patients of group B. There was no statistically significant difference found between the efficacies of the two drugs.

Conclusion: It was found that efficacy of the two drugs is similar in lowering blood pressure in eclamptic patients.

Keywords: Eclampsia, Efficacy, Hydralazine, Hypertension, Labetalol.

INTRODUCTION

Eclampsia is the development of grand mal seizures with no previous neurological disease (epilepsy) accompanied by pre-eclampsia (blood pressure of >140/90 mmHg) and proteinuria >300mg in 24 hours, developing after 20 weeks of pregnancy and persist up to 6 weeks postpartum in previously normotensive patient. Disorders related with hypertension produce complications in 10 to 15% of all pregnancies[1]. It is considered as one of the major factors of maternal mortality and morbidity world wide[2]. One out of every ten pregnancies gets complicated by hypertension leading to 16% deaths in the developed and 10-15% deaths in the developing countries[3]. It is responsible for 17.4% (167/958) of all the direct maternal mortality in the Khyber Pukhtunkhwa province of Pakistan[4]. Hypertension in pregnancy increases the risk of HELLP syndrome (hemolysis, elevated liver enzymes, low platelet count), placental abruption, preterm delivery, caesarean delivery in mothers. In babies it may leads to perinatal death, still birth, neonatal death, small for gestational age and other serious neonatal morbidities but prompt recognition and treatment can reduce the risk of these complications[5,6].

Treatment of hypertension related with eclampsia remains a challenging task. Various studies are performed in this regard but still there is no definite consensus has been made regarding the effectiveness of a single best antihypertensive to attain short term success in controlling hypertensive crises, without affecting the maternal and fetal safety. Modern evidence indicated that if hypertension in pregnancy is not managed

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Received: 02 Oct 2019; revised received: 16 Jan 2020; accepted: 24 Jan 2020

properly, can lead to severe complications in both mother and fetus, therefore, it is important to adequately control hypertensive crises in our obstetric population. Hydralazine, a vasodilator, and labetalol, an adrenoceptor blocker, are two anti-hypertensive drugs most commonly used for the management of hypertensive crisis in pregnancy by intravenous route[7]. The drug of choice for the management of severe hypertension in pregnancy is intravenous hydralazine but it is associated with many side effects as compare to labetalol[8]. Some studies suggests that labetalol is more effective than hydralazine in lowering blood pressure in eclamptic patients while the other studies are in favour of hydralazine[8].

The present study was designed because of the controversy regarding the effectiveness of labetalol in lowering blood pressure in eclamptic patients, due to scarcity of local data on this topic and increasing load of eclamptic patients at our hospital. If labetalol is found to be more effective than hydralazine, then it may prove to be a very useful agent with less adverse effects for the management of hypertension in eclamptic patients. Moreover, it might be helpful for further researches.

METHODOLOGY

This cross-sectional study was performed in Obstetrics and Gynaecology unit 'B' of post-graduate Medical Institute (PGMI) Lady Reading Hospital, Peshawar after approval from the hospital ethics and research committee (No. Ob/Gyn-556). Total sample size calculated was 206, which is 103 in each group[7]. Patients with age 16-45 years, who have grand mal seizures with no previous neurological disease (epilepsy), blood pressure (BP)>140/90 mmHg, proteinuria >300 mg in 24 hours developing after 20 weeks of pregnancy and remained up to 6 weeks post-partum in previously normotensive patient were included in the study by systematic random sampling. Patients with seizures if found to have high blood pressure due to other reasons (pheochromocytoma, renal failure, hyperaldosteronism) were excluded from the study. Informed written consent was taken after explaining the procedure, effects and adverse effects of drugs. Patients who have contraindication for labetalol or hydralazine like patients with heart block, heart failure, arrhythmias or pacing device were excluded from the study. Detailed history was taken from each patient, period of gestation was calculated by 1st trimester scan. BP of the patients was checked with standard sphygmanometer in lying position (45°) at the level of the heart. An appropriate cuff size was used. Urine protein was checked by urine dipstick. The patients were then randomized into 2 groups, group A and group B by lottery method. The group A received 5mg hydralazine as an initial bolus by slow intravenous injection in not less than five minutes. After 20 minutes BP was measured and if systolic BP still continued to be >160 mmHg or diastolic BP>110 mmHg, the same dose with same protocol was repeated till the desired effect was attained. Three doses were maximally repeated. The group B received 20mg labetalol as the initial intravenous bolus in not less than 10 minutes followed by 80mg every 20 minutes to a maximum of three doses. Patient remained hospitalized during this time period to monitor the BP and to achieve target BP. All the patients obtained their prescribed medicine from local pharmacy with the same trade names to control bias. Patients in both group A & B were almost similar with respect to weight, age, culture, dietary habits and baseline systolic and diastolic BP. All the data was recorded on a pre-designed performa. Those patients whose BP was not controlled even with maximum doses of hydralazine and labetalol, the drug was discontinued, cardiologist opinion was sorted and were excluded from the study. The effect of age and body mass index (BMI) of patients on the effectiveness of hydralazine and labetalol was also determined in lowering blood pressure in patients with eclampsia.

Data Analysis

Analysis of data was done by using SPSS version 16. Quantitative variables like age, BMI, were described as mean and standard deviation

(SD). Categorical variables like efficacy was described in term of frequencies and percentages. Chi square test was applied to compare efficacy of drugs between the two study groups. A *p*-value less than or equal to 0.05 was considered significant. Efficacy was stratified among age and BMI to see effect modifiers. Post stratification Chi square test was also applied. All the results were presented in the form of tables and charts.

RESULTS

Out of 206 patients, the efficacy of hydralazine was found in 95% of patients while 93% of the patients were effectively treated with labetalol. The effectiveness of hydralazine and labetalol in relation to age and BMI was also determined.

Age distribution among two groups was analyzed as in group A mean age was 27 ± 2.93 while in group B it was 29 ± 3.18. Similarly mean BMI was 25 ± 3.36 in group A and 26 ± 3.81 in group B. Further subdivisions and details regarding age and BMI are shown in table-I. Regarding efficacy of the drugs, BP was found to be well controlled in both group Aand B with no statistically significant difference of *p*-value 0.621 (table-II). When further comparison of efficacy of hydralazine and labetalol was done on the basis of age and BMI, statistically insignificant difference was found (table-III).

Table-I: Age and BMI status of the patients (n=206).

		Group A (Hydralazine)	Group B (Labetalol)
Age	Mean ± SD	27 ± 2.93 yrs	29 ± 3.18 yrs
	15-25 years	43 (42%)	40 (39%)
	26-35 years	36 (35%)	37 (36%)
	36-45 years	24 (23%)	26 (25%)
BMI	Mean ± SD	25 ± 3.36	26 ± 3.81
	≤25	74 (72%)	77 (75%)
	>25	29 (28%)	26 (25%)

Table-II: Efficacy of hydralazine and labetalol (n=206).

Efficacy	Group A (hydralazine)	Group B (labetalol)	*p*-value
Effective	95 (92%)	93 (90%)	0.621
Not effective	8 (8%)	10 (10%)	
Total	103 (100%)	103 (100%)	

Table-III: Effect of age and BMI on efficacy of hydralazine and labetalol (n=206).

		Efficacy	Group A (Hydralazine)	Group B (Labetalol)	*p*-value (Chi-square test)
Age	15-25 years	Effective	40 (19.4%)	36 (17.47%)	0.620
		Not effective	3 (1.45%)	4 (1.94%)	
	26-35 years	Effective	33 (16%)	33 (16%)	0.719
		Not effective	3 (1.45%)	4 (1.94%)	
	36-45 years	Effective	22 (10.6%)	24 (11.6%)	0.933
		Not effective	2 (0.97%)	2 (0.97%)	
BMI	≤25	Effective	69 (33.50%)	71 (34.4%)	0.806
		Not effective	5 (2.42%)	6 (2.91%)	
	>25	Effective	26 (12.62%)	22 (10.67)	0.575
		Not effective	3 (1.45%)	4 (1.94%)	

DISCUSSION

Severe hypertension in pregnancy (systolic BP ≥160 mmHg &/or diastolic BP ≥ 110 mmHg) must be managed sensibly to prevent complications of mother and fetus. Severe pre-eclampsia, cerebrovascular accidents, hypertensive crisis and HELLP syndrome are the main causes of mortality[9]. The incidence is relatively more in developing countries due to malnutrition, hypoproteinemia and poor obstetric facilities. Generally, 10–15% of maternal deaths are directly linked with pre-eclampsia and eclampsia[10]. Hydralazine, the most frequently used agent, produces abrupt hypotension and tachycardia. Labetalol on the other hand because of combined alpha and beta receptor blocking effects lacks these adverse effects[11].

A study was performed in India to compare the effectiveness of hydrazaline and labetalol in pregnancy induced hypertension. A total of 226 patients were enrolled in the study; 113 in each group. When the two groups were compared, insignificant difference was found[12]. Another study was conducted by Nombur and his colleagues in Nigeria, results revealed no significant difference in the efficacy of hydralazine and labetalol treated groups[13]. A similar study was performed by Verma *et al*, they included 130 patients; 65 in each group. When the efficacy of hydralazine and labetalol was compared in terms of reducing blood pressure, results were found statistically insignificant[14]. Holbrook and his colleagues did systematic review done also shown insignificant difference in the efficacy of the two drugs[15]. Tabasi and his co-workers also performed the same study and found that hydralazine is 95% while labetalol is 96% effective in lowering blood pressure, showing insignificant difference[16]. Similar findings were observed by De Pasquale *et al*, Gaur *et al*, and Vigil-De Graciaet alin which no significant differences were observed between groups treated with hydralazine and labetalol[17-19].

Another study was done in Karachi to evaluate the efficacy of hydrazaline and labetalol in lowering blood pressure in pregnant ladies. A total of 78 patients were included in the study. Labetalol was found to be more effective than hydralazine with mean fall in blood pressure of 29.10 ± 7.21 mmHg and 25.05 ± 10.15 mmHg respectively[8].

The findings of the current study which showed no significant difference between the efficacy of hydralazine and labetalol in controlling blood pressure is in accordance with the results of most of the studies, while in contrast to a single study performed at Karachi, Pakistan.

CONCLUSION

Hydralazine and labetalol were found equally effective in lowering blood pressure in eclamptic patients.

CONFLICT OF INTEREST

This study has no conflict of interest to be declared by any author.

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