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***Original Research Article***

# THE PREVALENCE OF EFFECTIVENESS OF BOLUS DOSE OF I/V HYDRALAZINE VERSUS I/V LABETALOL FOR THE EARLIER CONTROL OF BLOOD PRESSURE IN SEVERE PREECLAMPTIC PATIENT: A COMPARATIVE STUDY

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**Abstract:** *Topre-eclampsia efficacy of hydralazine and labetalol for the management of blood pressure in patients with severe pre-eclampsia to improve maternal and fetal outcomes. 6 months from March 2022 to September 2022 in the Department of obstetrics and gynecology, Liaquat University Hospital, Hyderabad and Razia Iqbal Hospital Multan, a Cross-sectional study was carried out. The study was conducted on 57 women diagnosed with severe preeclampsia. The subjects were divided into two groups. Group A was administrated I/V hydralazine bolus doses of 5 mg over 2 minutes with an interval of 20 minutes. Group B was administered I/V labetalol bolus doses of 20mg over 2 minutes at an interval of 10 minutes. The average age of the patients was 25.58±3.89 years. The efficacy of bolus dose of hydralazine (82.1%) and labetalol (75.9%) was statistically insignificant (p=0.56). The average time was 52 minutes the total hydralazine was 12.25 mg, in the case of the labetalol group the average time was 18.62 minutes, and the total dose was 68.28 mg. Both hydralazine and labetalol have similar efficacy as antihypertensive medications and can be used to treat hypertensive disorders in pregnant women.*

**Keywords:** Preeclampsia, Hydralazine, Labetalol, Blood pressure

## Introduction

Severe preeclampsia is defined as high blood pressure I.e. up to 160/110mmHg associated with proteinuria and persistent central nervous system symptoms like disrupted mental state, blurred vision, visual impairment, headache or persistent epigastric pain (Fox et al., 2019). Almost 5-8% of women report an incidence of preeclampsia in their pregnancies (Filipek and Jurewicz, 2018). Severe pre-eclampsia accounts for 10-15% of maternal deaths worldwide (Rana et al., 2019). There are various clinical presentations of eclampsia affecting almost every organ of the body including headache, tinnitus, visual disturbances, brisk tendon reflexes, oliguria, epigastric pain, vaginal bleeding and dyspnea caused by cerebral edema, acute renal failure, subcapsular hepatic hematoma, placental abruption and cardiac failure (Snydal, 2014). There are various treatment options available for severe pre-eclampsia including oral and parental drugs. Hydralazine (Apresoline) is one of the parenteral drugs which is used to treat hypertension. It acts as a smooth muscle relaxant and vasodilator primarily in arteries and arterioles, thus decreasing blood pressure (Syed et al., 2020). It is administered as 5-10mg I/V and can be repeated every 20 minutes up to a maximum of 30mg (Verma et al., 2018).

Labetalol is another parenteral drug with a mixed alpha/Beta antagonist. It decreases blood pressure by blocking α1 adrenoceptors in peripheral vessels and performs intrinsic activity at β1 adrenoceptors, thereby lowering blood pressure and reducing heart rate (Pandey, 2018). Labetalol is administered as an I/V bolus at a dose of 20mg, with repeat doses (40,80,80 and 80mg) every 10 minutes up to a maximum of 300mg (Cox et al., 2019). A study assessing the efficacy of hydralazine and labetalol to treat severe preeclampsia in pregnant patients was 3.8% and 13.8% respectively (Magee et al., 2011). Severe preeclampsia is associated with significant for maternal morbidity and mortality and requires prompt management to avoid this morbidity. This study aims to compare the efficacy of hydralazine

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and labetalol for the management of blood pressure in patients with severe preeclampsia to improve maternal and fetal outcomes.

**Methodology**

A comparative retrospective study was conducted in the Department of Obstetrics and Gynecology, Liaquat University Hospital, Hyderabad and Razia Iqbal Hospital Multan from March 2022 to September 2022. A total of 57 women within the age range of 18 to 35 years old diagnosed with severe preeclampsia were included in the study by non-probability consecutive sampling. The sample size was calculated by using the raosoft software for sample size calculation keeping a 95% confidential interval and a 5% margin of error. All patients signed written consent to become a part of the study. Pregnant women who had any other associated co-morbidity along with severe preeclampsia like diabetes mellitus, preexisting renal disease, chronic hypertension etc. were excluded from the study. The study design was approved by the Ethical Committee of the Hospital.

The patients who passed the inclusion criteria were consecutively divided into two groups A (28 patients) and B (29 patients). I/V bolus doses of 5mg hydralazine were administered to Group A over 2 minutes after 20 minutes difference each. Blood pressure and pulse were monitored after every 10 minutes. If the systolic blood pressure was 160 mm Hg and diastolic blood pressure was 110 mm Hg after 20 minutes difference, the second dose was administered. If 20 minutes after the second dose, SBP was equal to higher than 160 mm Hg and DBP was equal to or higher than 110 mm Hg, the next dose was administered. If the blood pressure threshold kept increasing after the third dose, a 4th dose was administered. A maximum of 20mg was administered in 4 bolus doses of 5mg each.

Similarly, I/V 20 mg bolus doses of Labetalol were administered over 2 minutes with 10 minutes difference between each. Blood pressure and pulse were monitored after 10 minutes. If the systolic blood pressure reached 160 mm Hg and diastolic blood pressure was at 110 mm Hg after 10 minutes intervals, the second dose of 40 mg was administered. The third dose of 80 mg was administered if SBP was equal to or higher than 160 mm Hg and DBP was equal to or higher than 110 mm Hg after 10 minutes intervals. If the blood pressure thresholds kept increasing after the third dose, the fourth and fifth dose of 80mg was administered. A maximum of five doses of a total of 300 mg were administered. All the data were analyzed by SPSS version 16. Mean and standard deviation was used to represent quantitative variables. The Chi-square test was used to compare the results in both groups. A p-value less than 0.05 was considered statistically significant.

**Results**

A total of 57 women with severe preeclampsia were selected for the study and were divided into Groups A and B. Group A was administered four I/V bolus doses of 5mg hydralazine and group B was administered five I/V 20 mg bolus doses of Labetalol. The average age of the patients was 25.58±3.89 years. The age distribution in both groups is shown in Table I. The results and effectiveness of bolus doses in both groups for respective drugs are shown in Table II. 23 patients (82.1%) in the hydralazine group showed a positive response to the drug. Similarly, 22 patients (75.9%) in the labetalol group showed effective results. The effectiveness of bolus dose of hydralazine and labetalol was statistically not significant (82.1% vs. 75.9% p=0.56). The mean time taken and total dose to control blood pressure was 41.42±15.32 minutes and 10.36±3.82 mg in a bolus dose of hydralazine while the mean time taken and the total dose in labetalol group was 18.62±6.39 minutes and 68.28±4.45mg as shown in Table II.

Stratification analysis was performed with respect to age groups and parity but no significant difference between groups was observed after stratification of age and parity as shown in Table III, IV, V and VI respectively.

**Table I: Mean Age of The Patients with Respect to Groups**

| **Statistics** | | **Group A n=28** | **Group B n=29** |
|---|---|---|---|
| **Mean ± SD** | | 24.18±3.0 | 26.63±4.21 |
| **95% Confidence Interval for Mean** | **Lower Bound** | 23.01 | 25.33 |
| | **Upper Bound** | 25.34 | 28.53 |
| **Median (IQR)** | | 25(5) | 26(5) |

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**Table II: Compare the Bolus Doses of Hydralazine and Labetalol for The Control of Blood Pressure in Severe Pre Eclamptic-Patient**

| Variable | Group A (n=28) | Group B= 29 | P-value |
|---|---|---|---|
| **Effectiveness** | | | |
| **Yes [Systolic BP <150mmHg and dystolic BP < 110 mmHg]** | 23 (82.1%) | 22 (75.9%) | 0.56 |
| **No [Systolic BP >150mmHg and dystolic BP >110 mmHg]** | 5 (17.9%) | 7 (24.1%) | |
| **Time taken to control blood pressure (Minutes)** | 41.42±15.32 | 18.62±6.39 | - |
| **Total Dose Needed (mg)** | 10.36±3.82 | 68.28±4.45 | - |

*Chi-Square test applied*

**Table III: Compare the Effectiveness of Bolus Dose of Hydralazine and Labetalol for The Control of Blood Pressure in Severe Pre Eclamptic Patient For ≤25 Years Of Age**

| Effectiveness | Group A n=20 | Group B n=11 | P-Value |
|---|---|---|---|
| **Yes [Systolic BP <150mmHg and dystolic BP < 110 mmHg]** | 17(85%) | 6(54.5%) | 0.095 |
| **No [Systolic BP >150mmHg and dystolic BP >110 mmHg]** | 3(15%) | 5(45.5%) | |
| *Fisher exact test applied* | | | |

**Table IV: Compare the Effectiveness of Bolus Dose of Hydralazine and Labetalol for The Control of Blood Pressure in Severe Pre Eclamptic-Patient For >25 Years Of Age**

| Effectiveness | Group A n=8 | Group B n=18 | P-Value |
|---|---|---|---|
| **Yes [Systolic BP <150mmHg and diastolic BP < 110 mmHg]** | 6(75%) | 16(88.9%) | 0.56 |
| **No [Systolic BP >150mmHg and dystolic BP >110 mmHg]** | 2(25%) | 2(11.1%) | |
| *Fisher exact test applied* | | | |

**Table V: Compare the Effectiveness of Bolus Dose of Hydralazine And Labetalol For The Control Of Blood Pressure In Severe Pre Eclamptic Patient For Primipara**

| Effectiveness | Group A n=12 | Group B n=10 | P-Value |
|---|---|---|---|
| **Yes [Systolic BP <150mmHg and diastolic BP < 110 mmHg]** | 11(91.7%) | 7(70%) | 0.29 |
| **No [Systolic BP >150mmHg and dystolic BP >110 mmHg]** | 1(8.3%) | 3(30%) | |
| *Fisher exact test applied* | | | |

**Table VI: Compare the Effectiveness of Bolus Dose of Hydralazine and Labetalol for The Control Of Blood Pressure In Severe Pre Eclamptic Patient For Multipara**

| Effectiveness | Group A n=16 | Group B n=19 | P-Value |
|---|---|---|---|
| **Yes [Systolic BP <150mmHg and dystolic BP < 110 mmHg]** | 12(75%) | 15(78.9%) | 0.99 |
| **No [Systolic BP >150mmHg and dystolic BP >110 mmHg]** | 4(25%) | 4(21.1%) | |
| *Fisher exact test applied* | | | |

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## Discussion

Preeclampsia is one of the most frequent disorders reported by pregnant women. Preeclampsia and eclampsia both pose a great risk of mortality and morbidity to the mother and child during pregnancy worldwide (Macedo et al., 2020). National High
Blood Pressure Education Program recommends the use of severe hypertension I.e SBP $\geq$ 150 mmHg or DBP $\geq$ 110 mmHg for treatment of preeclampsia during pregnancy (Program, 2000). Various oral and parenteral drugs are administered for lowering blood pressure. Hydralazine is one of these drugs that acts as a vasodilator and when administered intravenously, successfully helps in treating hypertension in pregnant women (GUL et al., 2019). However, it results in side effects such as headache, emesis and nausea. Labetalol, a beta-blocker, is also administered intravenously as a first-line treatment in preeclamptic patients (Rose and Jeyarani, 2019). It has lesser side effects on the mother, however, some studies have associated it with neonatal bradycardia (Vigil-De Gracia et al., 2006).
In the present study, 57 preeclamptic women were selected for treatment with hydralazine or labetalol. Most of the women were multigravida. Research about the incidence of nulliparity shows that preeclampsia is a very frequent condition in first-time mothers (Kumari et al., 2020). The women in our study were aged 18 to 35 years with an average age of 25.58±3.89 years.
Patients were divided into two groups: A and B. Group A was administered four I/V bolus doses of 5mg hydralazine and group B was administered five I/V 20 mg bolus doses of Labetalol. The efficacy of both drugs did not differ significantly (p=0.56). A total of 12.25mg of hydralazine was effective in lowering blood pressure in 52 minutes. While 68.28mg of labetalol took a mean time of 18.62 minutes to treat the preeclampsia. Similar results were reported by other related studies (Wu et al., 2022). The efficacy and safety of these both drugs have been proved by research and comply with the findings of our study (NAZ and JAWAD).
A study by Purvi et al (Patel et al., 2018), reported that hydralazine and labetalol were both equally effective in managing severe hypertension in pregnant women. However, labetalol worked faster than hydralazine in achieving the target blood pressure. Labetalol achieved a lower blood pressure threshold in 81.5% of patients, while hydralazine achieved the desired result in 69.5% of patients.
In another study conducted by Paulino et al. (Vigil-De Gracia et al., 2007) it was reported that the difference in efficacy and safety of hydralazine and labetalol in the treatment of preeclampsia in pregnant women was not significant. However, labetalol caused fewer maternal adverse effects than hydralazine with caused tachycardia and palpitations in some cases. But both groups were safe to use for treating hypertension in pregnant patients.
Our study has some limitations. Our study had a limited sample size. In addition, the age range of patients was 18 to 35 years due to which the effects of hydralazine and labetalol in women older than 35 years were not studied.

## Conclusion

Both hydralazine and labetalol have similar efficacy as antihypertensive medications and can be used to treat hypertensive disorders in pregnant women.

## Conflict of interest

The authors declared absence of conflict of interest.

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