ACUTE MANAGEMENT OF HYPERTENSIVE EMERGENCIES IN PREGNANCY: ORAL NIFEDIPINE VERSUS INTRAVENTOUS LABETALOL

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ABSTRACT

Objective: To compare the outcome of oral Nifedipine & intravenous Labetalol in severe pregnancy induced hypertension in terms of time taken to achieve the target blood pressure.

Study Design: Randomized controlled trial.

Place and Duration of Study: Conducted at department of Obstetrics & Gynaecology, Combined Military Hospital Lahore, from Jan 2014 to Jun 2014.

Materials and Methods: After taking ethical approval, pregnant women at ≥28 weeks of gestation with sustained blood pressures of ≥160/110 mmHg were included in the study. Patients were randomly assigned into two groups to receive either oral Nifedipine or intravenous Labetalol. The data was collected and analyzed on SPSS version 20.

Results: In oral Nifedipine group 64% patients were between 18-30 years while 36% were between 31-35 years of age. In intravenous Labetalol group, 58% patients were between 18-30 years while 42% were between 31-35 years of age. Fifty two percent patients in oral Nifedipine group & 54% cases in intravenous labetalol were between 29-34 weeks of gestation while 48% patients in oral Nifedipine and 46% in intravenous labetalol group were between 35-40 weeks of gestation. Time taken to achieve the target blood pressure is 31.14 ± 3.14 minutes in Oral Nifedipine & 51.08+4.11 minutes in Intravenous Labetalol group. A p-value was 0.011671 which was significant.

Conclusion: Nifedipine is more effective in severe pregnancy induced hypertension to achieve the target blood pressure as compared to labetalol. It is more suitable in our setup as it is economical and easy to administer.

Keywords: Intravenous labetalol, Oral Nifedipine, Severe pregnancy induced hypertension.

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INTRODUCTION

Hypertension is the most common medical disorder, reported to complicate 10% of the pregnancies and remains a major cause of maternal, fetal and neonatal morbidity and mortality not only in less developed but also in the industrialized countries1. It can be either pre-existing hypertension that is present before or in the first twenty weeks of gestation or new onset hypertension that develops for the first time after 20 weeks of gestation, during labour or delivery2. Gestational hypertension is defined as systolic blood pressure ≥140 mmHg and/or diastolic blood pressure ≥90 mmHg in a previously normotensive pregnant woman who is ≥20 weeks of gestation and has no proteinuria or new signs of end-organ dysfunction. The blood pressure readings should be documented on at least two occasions at least four hours apart. It is considered severe when sustained elevations in systolic blood pressure ≥160 mmHg and/or diastolic blood pressure ≥110 mmHg are present for at least four hours. It is associated with increased adverse maternal and perinatal outcomes. These women are at an increased risk of fatal intracranial haemorrhage; hence they require an immediate and effective antihypertensive treatment to decrease the risk of maternal death3. National institute for health and clinical excellence guideline has recommended inpatient treatment of severe hypertension of pregnancy with labetalol (oral or parenteral), intravenous Hydralazine or oral Nifedipine as first line alternative antihypertensives4. Nifedipine acts primarily on vascular smooth muscle cells by inhibiting the influx of calcium in smooth muscle cells, Nifedipine prevents vasoconstriction5. The principal physiologic action of labetalol is to
competitively block both alpha and beta adrenergic receptors causing a decrease in systemic arterial blood pressure and systemic vascular resistance in patients with severe hypertension. In developed countries, hypertensive disorders of pregnancy were responsible for 16.1% (6.7-24.3%) of all maternal deaths. Although severe hypertension should be avoided, anti hypertensive treatment itself does not alter disease progression but it does potentially prevent cerebrovascular events. The purpose of the study was to find out which of the two drugs, is better in achieving the target blood pressure in short time.

**MATERIAL AND METHODS**

The study has conducted at department of Obstetrics & Gynaecology CMH Lahore, form Jan 2014 to June 2014. After taking ethical approval letter from the hospital ethical committee, pregnant women at ≥28 weeks of gestation with sustained blood pressures of ≥160/110 mmHg and having normal fetal cardiotocograph were included in the study. All patients with history of allergy to labetalol or Nifedipine, any fetal heart rhythm abnormality, non-pregnancy related hypertension or any other medical disorders were excluded from study. Moreover patients who received any anti-hypertensive treatment in the last 72 hours were also not included. After taking informed consent patients were randomly assigned to two groups using a table of random numbers to receive either oral Nifedipine or intravenous labetalol. Target blood pressure was defined as blood pressure of ≤150/100 mmHg as recommend in NICE Guidelines. Patients randomized to oral Nifedipine received 10mg initially with repeated doses of 20mg every 20 minutes for up to maximum of 5 doses or until target blood pressure was achieved. Patients randomized to intravenous labetalol received 20mg initially over 2 min, with repeat dosing at 20, 40 or 80 mg every 10 min until the target blood pressure of ≤150/100 mmHg is achieved or for a maximum of 300 mg has been administered. The dosing regimens for each study medication corresponded with regimens from previous clinical trials and the difference in dosing regimens had no effect on the results of the trial as both drugs had different mechanism of actions. Blood pressure was measured by mercury sphygmomanometer and continued every 15 minutes for at least 60 minutes or longer until target blood pressure was achieved. The fetus was monitored on a continuous basis during the course of treatment. After completion of the trial a questionnaire was completed by the doctor in charge regarding the outcome of the drug used. The main outcome measure was the time taken to achieve the target systolic blood pressure of ≤150 mmHg and diastolic blood pressure of ≤100 mmHg. All data was entered and analyzed by SPSS system 20. Qualitative variables like gender was expressed by frequency and percentages. Quantitative data like age and time taken to achieve target blood pressure was expressed using mean and standard deviation. T-test was used as a test of significance to compare the effect of both drugs. A *p*-value ≤0.05 was considered as significant.

**RESULTS**

A total of 100 cases (50 in each group) were enrolled in this study after fulfilling the inclusion/exclusion criteria to compare the outcome of oral Nifedipine and intravenous labetalol in severe pregnancy induced hypertension in terms of time taken to achieve the target blood pressure. The age distribution of the patients is shown in table-I. Comparison of outcome of oral Nifedipine and intravenous labetalol in severe pregnancy induced hypertension in terms of time taken to achieve the target blood pressure is shown in table-III. In our study, 64% (n=32) in oral Nifedipine and 58% (n=29) cases in intravenous labetalol were recorded between 18-30 years while 36% (n=18) in oral Nifedipine and 42% (n=21) in intravenous labetalol group were recorded between 31-35 years of age, mean ± SD was calculated as 27.48 ± 4.76 and 27.96 ± 4.79 years respectively while comparison of outcome of oral Nifedipine and intravenous labetalol in severe pregnancy induced hypertension in terms of time taken to
achieve the target blood pressure reveals that 31.14 ± 3.14 minutes in oral nifedipine and 51.08 ± 4.11 minutes in Intravenous Labetalol group was recorded. A p-value was calculated as 0.06671, which shows insignificant difference between the two groups.

**DISCUSSION**

Hypertension is the most frequently encountered medical disorder in obstetrics practice & remain a major cause of maternal, fetal & neonatal morbidity & mortality if neglected. Nifedipine is the most commonly used anti-hypertensive for blood pressure control in severe hypertension because of its easy availability, rapid onset of action, ease of oral administration and satisfactory reduction in blood pressure in our country. Intravenous labetalol is also recommended as one of the first line agents in the management of acute severe hypertensive disorder of pregnancy along with hydralazine. IV labetalol can also be given where control of blood pressure is required in labour prior to caesarean section or when the patient is in coma. The findings of the current study are consistent with a trial conducted by Raheem et al (2011) comparing oral Nifedipine and intravenous labetalol for acute blood pressure control in hypertensive emergencies of pregnancy the median time taken to achieve target blood pressure was 30 minutes (interquartile range, IQR 22.5-67.5 minutes) versus 45 minutes (IQR 30-60-minutes) for Nifedipine and labetalol respectively (p=0.59) and concluded that both drugs are similarly effective in controlling severe hypertension of pregnancy. Another study by Badal Dhali and co-workers\textsuperscript{10} compared the time taken to reach the therapeutic goal blood pressure after using intravenous labetalol & oral Nifedipine in severe pregnancy induced hypertension and recorded that patients received oral Nifedipine achieved the goal therapeutic blood pressure more rapidly in 28.2 ± 11.7 minutes as compared with 48.4 ± 23.5 minutes in those received intravenous labetalol (p=0.001) and concluded that oral Nifedipine & intra-venous labetalol regimens are effective in the management of severe hypertension in pregnancy. Our results are consistent with the above study, as the time duration to achieve the target blood pressure was comparatively lower in Nifedipine group and is statistically significant. Another randomized controlled trial by Vermillion ST and colleagues\textsuperscript{11}, where nifedipine

| Table-I: Age Distribution of the patients (n=100). |
| Age (in years) | Oral Nifedipine (n=50) | Intravenous Labetalol (n=50) |
| No. of patients | % | No. of patients | % |
| 18-30 | 32 | 64 | 29 | 58 |
| 31-35 | 18 | 36 | 21 | 42 |
| Total | 50 | 100 | 50 | 100 |
| Mean ± SD | 27.48 ± 4.76 | 27.96 ± 4.79 |

p=0.616, Not Significant

| Table-II: Gestational age of the patients (n=100). |
| Gestational Age (in weeks) | Oral Nifedipine (n=50) | Intravenous Labetalol (n=50) |
| No. of patients | % | No. of patients | % |
| 29-34 | 26 | 52 | 27 | 54 |
| 35-40 | 24 | 48 | 23 | 46 |
| Total | 50 | 100 | 50 | 100 |
| Mean ± SD | 34.46 ± 3.07 | 34.54 ± 3.05 |

p=0.896, Not Significant

| Table-III: (N=100). |
| Mean time taken | Oral Nifedipine (n=50) | Intravenous Labetalol (n=50) |
| 31.14 ± 3.14 | 51.08 ± 4.11 |

p=0.06671, Statistically significant
group had comparatively reduced duration of controlling of blood pressure than labetalol group. The Nifedipine in our setup is more suitable considering the fact that it is cheaper, easier to store, easier to administer as it is given orally, whereas IV labetalol is more expensive, needs to be stored at a lower temperature and needs slow IV administration.

CONCLUSION

We concluded after comparison of the outcome of oral nifedipine and intravenous labetalol in severe pregnancy induced hypertension in terms of time taken to achieve the target blood pressure that both drugs are effective but Nifedipine is quick in achieving the target blood pressure and is more suitable in our setup because its economical easily available and easy to administer.

CONFLICT OF INTEREST

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

REFERENCES


