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A Randomized Trial Of Intravenous Labetalol Versus Oral Nifedipine In Acute Blood Pressure Control In Hypertensive Emergencies Of Pregnancy.

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ABSTRACT

Hypertensive disorders of pregnancy accounts for 5% to 10% of all pregnancies, and together they are one member of the deadly triad - along with hemorrhage and infection. According to World Health Organization at least a woman dies every seven minutes from complications of hypertensive disorders of pregnancy. Prevalence of hypertensive disorders of pregnancy was 7.8% with preeclampsia in 5.4% of the study population in India. To compare safety and efficacy of intravenous labetalol with oral nifedipine to control blood pressure in hypertensive emergencies of pregnancy. 106 consecutive patients were randomized to receive either intravenous labetalol in escalating doses of 20 mg, 40 mg, 80 mg, 80 mg, and 80 mg along with placebo tablets or nifedipine 10 mg tablet orally along with placebo saline injections every 15 minutes up to five doses. The treatment is crossed over to the other group if reduction in both systolic and diastolic blood pressure $\leq 150/100$ mm Hg does not occur. The median time taken to attain target blood pressure was 45 minutes and 30 minutes in labetalol and nifedipine groups, respectively ($P = 0.17$). Median number of doses required was three and two to achieve blood pressure control in labetalol and nifedipine groups, respectively ($P = 0.23$). Cross over treatment was required in 9.40% in labetalol group and 11.30% in nifedipine group ($P = 0.75$). Side effects profile between the two drugs were also similar ($P = 0.06$). Intravenous labetalol and oral nifedipine are equally efficacious in controlling hypertensive emergencies of pregnancy.

Keywords: Preeclampsia, eclampsia, labetalol, nifedipine, sustained severe hypertension

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INTRODUCTION

Hypertension in pregnancy, called a disease of degree is more of a sign than a disease by itself. With various advancements in the pathophysiology and various insights into the prevention of this disease, effective and timely control of hypertension is still the most imperative step in the management [1]. Concerns akin to maternal morbidity, mortality and fetal and neonatal outcomes imply the impact of the disease in the obstetric population. The recent management option explores the various modalities in prediction and prevention of hypertension in pregnancy. However, the only effective therapy is the delivery of the fetus and placenta [2]. The ancillary therapy is principally symptomatic and not directed at the fundamental cause. Effective pharmacologic therapy modifies the course of the disease. The effective use of anti-hypertensive therapy should be based on well-designed controlled clinical trials and the experience of the clinician with the drugs. Hypertensive disorders complicate 5-10% of all pregnancies worldwide [3]. In India, pregnancy induced hypertension, along with sepsis and hemorrhages, contributes to 80% of the maternal mortality. Dangerous hypertension is a harbinger of cerebrovascular accidents, eclampsia, hypertensive encephalopathy and other end organ damage with a poor perinatal outcome. In order to mitigate the morbidity and the mortality, numerous antihypertensive agents are being used to control blood pressure in severe preeclampsia. Numerous reports signify that reducing severe hypertension reduces maternal death [4]. Antihypertensive drug in pregnancy should effectively reduce the blood pressure of the mother, should not cause acute hypotension, should not have any deleterious effects on the fetus in utero, and should not have any adverse interaction with other drugs including those commonly used in pregnancy and in labour [5]. The use of the drug should modify the course of the disease and it should prevent the development of complications. Hydralazine, diuretics and alpha methyl dopa are not recommended for use in severe hypertension as first line drugs due to adverse maternal, fetal outcomes and late onset of action of the latter. Labetalol was studied for its use in treatment of hypertensive urgencies in the general population. The smooth onset of action with minimal change in cardiac output and heart rate makes it a unique drug in the management of hypertensive emergency in pregnancy [6]. Nifedipine has been evaluated for its immediate onset of action and ease of administration and no reported adverse effects on the mother or the fetus and on the course of labour [7,8]. This study ventures to compare the pharmacodynamics of intravenous labetalol and oral nifedipine in patients with severe hypertension and to compare the maternal and fetal outcomes and adverse effects of both the drugs.

MATERIALS AND METHODS

This Prospective study was carried out on pregnant women admitted in the labor ward in the Department of Obstetrics and Gynecology, Sri Venkateshwara Medical College Hospital & Research Institute, Chennai-600 067 between September 2022-september 2023. One hundred and six consecutive patients satisfied the inclusion criteria and were recruited in the present study.

Inclusion Criteria

Age - 18 to 35 years, All pregnant women of 20 weeks gestation or more; excluding parity and booking status, Singleton pregnancy, Sustained severe hypertension: Systolic blood pressure ≥ 160 mm Hg; diastolic blood pressure ≥ 110 mm Hg; or a mean arterial pressure of > 125 mmHg, lasting for 15 minutes or more in the past 4 hours on at least 2 occasions. Severe pre-eclampsia according to the consensus by the national high blood pressure education program, NHBPEP 2000.

Exclusion Criteria

Eclampsia; HELLP syndrome, Bronchial asthma, Cardiac failure, Cardiac rhythm abnormalities, Chronic hypertension, Co-existent diseases like diabetes mellitus, rheumatic heart disease, congenital heart disease, renal or hepatic disorders, Multiple pregnancy, Exposure to either drugs prior to the study.

A thorough history was elicited from the patients regarding age, parity, socio economic status, booking history, history suggestive of imminent symptoms. Their past history regarding bronchial asthma, cardiac diseases, prior drug intake for hypertension and other medical disorders were also obtained. A meticulous general examination and obstetric examination were carried out. On general examination, patients' level of consciousness, degree of anemia, edema, jaundice, pulse rate, respiratory

rate and temperature were ascertained. Blood pressure measurement was done with the mercury sphygmomanometer with the patient lying at an angle of 45 degrees. The mercury manometer placed at the level of patients' heart. The measurements were taken in the right arm. The fifth Korotkoff, K5 sound was taken for diastolic blood pressure cut off. When K5 was not heard, muffling of the sound, K4 was considered. Systemic examination and obstetric examination were carried out. Fetal wellbeing was ascertained with the use of cardiotocograph before and after the usage of anti-hypertensive agents and other drugs. After explaining the condition of the patient and getting prior informed consent, the pregnant women were randomized with computer generated numbers into two groups to receive either oral nifedipine or intermittent intravenous labetalol injections. **Group A:** Fifty three patients were selected consecutively according to random numbers to receive the package containing intravenous labetalol injection in escalating doses of 20 mg, 40 mg, 80 mg, 80 mg, 80 mg and a placebo tablet for every fifteen minutes until the target blood pressure of $\leq 150 / \leq 100$ mm Hg was achieved. **Group B:** Fifty-three patients were randomized to receive the package containing nifedipine 10 mg tablet orally and intravenous placebo saline injections of 4 ml, 8ml, 16 ml, 16 ml, 16 ml up to five doses, every fifteen minutes till the target blood pressure of $\leq 150 / \leq 100$ mm Hg was achieved. The drug regime was crossed over to the other group if the initial regime was found unsuccessful after five cycles and blood pressure monitoring done. Patient was made to rest in bed in left lateral position. Blood pressure was noted every 15 minutes. Once the blood pressure was $<150 / 100$ mm Hg, no further trial medication was given until two consecutive readings were $> 160/ 110$ mm Hg. After successful control of blood pressure, further antihypertensive therapy was started two hours after the last trial medication. A careful obstetric examination was carried out. Bishop's score was calculated. Fetal status is ascertained by cardiotocograph. Delivery of the fetus and placenta was expedited according to individual condition of the patients. Induction of labour was done with intra-cervical PGE₂ gel instillation. Acceleration of labour was done with intravenous oxytocin infusion. Caesarean section was done for obstetric, fetal indications and failed inductions. Maternal side effect profile was recorded. Neonatal monitoring included number of admissions in the neonatal intensive care unit, occurrences of hypotension and hypoglycaemia. During the course of trial, maternal heart rate and fetal heart rate was monitored every 15 minutes. The trial was abandoned when there was non-reassuring fetal status and if maternal complications like hypotension, chest pain occurred.

Statistical analysis

All the data were entered consecutively in a predefined data information sheet and analysis was done using SPSS 20 software. Differences in categorical and continuous data were assessed using the Chi square test and Student 't' test, respectively. The tests were two sided. The statistical test is considered significant if the calculated p value is less than 0.05.

RESULTS

Table 1: Age Distribution

| S. NO. | AGE | GROUP A LABETALOL (n=53) | | GROUP B NIFEDIPINE (n=53) | | TOTAL (n=106) |
|------------------------------|----------------|---|--------|------------------------------|-------|----------------|
| | | NUMBER | % | NUMBER | % | |
| 1. | ≤ 20 YEARS | 10 | 18.90% | 13 | 24.5% | 23 (21.70%) |
| 2. | 21 to 29 YEARS | 34 | 64.10% | 32 | 60.4% | 66 (62.30%) |
| 3. | ≥ 30 YEARS | 9 | 17% | 8 | 15.1% | 17 (16%) |
| MEAN (S.D.) | | 24.89 (4.25) | | 24.81 (4.22) | | |
| STATISTICAL INFERENCE | | T = 0.092 Degree of freedom = 104 P = 0.927 | | | | |

There is no significant difference in ages of the recruited patients in both the groups. The mean age in labetalol and nifedipine groups was 24.89 and 24.81 years respectively. The majority of the patients had an age belonging to the category of 21 to 29 years. 18.90 % and 24.50% from group A and group B respectively had ages 20 years and below.

Table 2: Parity

| S.NO. | PARITY | GROUP A LABETALOL (n=53) | | GROUP B NIFEDIPINE (n=53) | | TOTAL (n=106) |
|------------------------------|--------|--|--------|------------------------------|--------|---------------|
| | | NUMBER | % | NUMBER | % | |
| 1. | PRIMI | 40 | 75.47% | 27 | 50.94% | 67 (63.20%) |
| 2. | G2 | 7 | 13.20% | 13 | 24.53% | 20 (18.90%) |
| 3. | G3 | 3 | 5.66% | 9 | 16.98% | 12 (11.30%) |
| 4. | G4 | 3 | 5.66% | 4 | 7.55% | 7 (6.60%) |
| STATISTICAL INFERENCE | | $\chi^2=7.465$, Degree of freedom = 3 P= 0.058 > 0.05 | | | | |

Parity was comparable in group A and group B. There is no significant difference in the parity of both the groups. Majority of the patients constituting 75.47% of group A and 50.94% of group B were primigravida. 63.20% enrolled in the study were primigravida. There is a higher incidence of preeclampsia in the first pregnancy.

Table 3: Body Mass Index

| S.NO | BMI | GROUP A LABETALOL (n=53) | | GROUP B NIFEDIPINE (n=53) | | TOTAL (n=106) |
|------------------------------|----------------------------------|--|--------|------------------------------|--------|----------------|
| | | NUMBER | % | NUMBER | % | |
| 1. | 25 to 29.99 kg/m ² | 20 | 37.70% | 20 | 37.70% | 40 (37.70%) |
| 2. | ≥ 30 kg/m ² | 33 | 62.30% | 33 | 62.30% | 66 (62.30%) |
| MEAN (S.D.) | | 30.93 (2.33) | | 30.90 (2.18) | | |
| STATISTICAL INFERENCE | | $\chi^2=1.000$, Degree of freedom = 1, 1.000 > 0.05 | | | | |

Most of the patients namely 66, constituting 63.30% had a body mass index exceeding 30 belonging to the category obesity. There is no significant difference in the body mass index between the two groups.

Table 4: Systolic Blood Pressure

| S.NO. | SYSTOLIC BLOOD PRESSURE | GROUP A LABETALOL (n=53) | | GROUP B NIFEDIPINE (n=53) | | TOTAL (n=106) |
|------------------------------|-------------------------|--|--------|------------------------------|--------|------------------|
| | | NUMBER | % | NUMBER | % | |
| 1. | 160 to 169 mm Hg | 23 | 43.40% | 19 | 35.80% | 42 (39.6%) |
| 2. | 170 to 179 mm Hg | 17 | 32.10% | 28 | 52.80% | 45 (42.5%) |
| 3. | ≥ 180 mm Hg | 13 | 24.50% | 6 | 11.20% | 19 (17.9%) |
| MEAN (S.D.) | | 171 (9) | | 170 (8) | | |
| STATISTICAL INFERENCE | | T= 0.477 Degree of freedom = 104 0.635 > 0.05 Not Significant | | | | |

The baseline systolic blood pressure of the patients recruited in both the groups did not differ significantly. The mean systolic blood pressure in intravenous labetalol group was 171 mm Hg whereas it was 170 mm Hg in oral nifedipine group. 43.40% of patients in group A had a blood pressure range of 160 to 169 mm Hg. 52.80% of patients in nifedipine group had a blood pressure range of 170 to 179 mm Hg.

Table 5: Diastolic Blood Pressure

| S. NO. | DIASTOLIC BLOOD PRESSURE | GROUP A LABETALOL (n=53) | | GROUP B NIFEDIPINE (n=53) | | TOTAL (n=106) |
|------------------------------|--------------------------|--|--------|---------------------------|--------|---------------|
| | | NUMBER | % | NUMBER | % | |
| 1. | < 110 mm Hg | 13 | 24.50% | 15 | 28.30% | 28(26.40%) |
| 2. | ≥ 110 mm Hg | 40 | 75.50% | 38 | 71.70% | 78(73.60%) |
| MEAN (S.D.) | | 112(7) | | 111(8) | | |
| STATISTICAL INFERENCE | | T= 0.160 Degree of freedom = 104 0.873 > 0.05 Not Significant | | | | |

The baseline diastolic blood pressure did not vary significantly in the groups. The mean of the baseline diastolic blood pressure were 112 mm Hg and 111 mm Hg in the groups A and B, respectively. 75.50% and 71.70% in groups A and B had diastolic blood pressure more than 110 mm Hg.

Table 6: Heart Rate

| S. NO. | HEART RATE | GROUP A LABETALOL (n=53) | | GROUP B NIFEDIPINE (n=53) | | TOTAL (n=106) |
|------------------------------|----------------------|---|--------|---------------------------|--------|---------------|
| | | NUMBER | % | NUMBER | % | |
| 1. | ≤ 90 per minute | 39 | 73.60% | 44 | 83% | 83(78.30%) |
| 2. | 91 to 100 per minute | 12 | 22.60% | 8 | 15.10% | 20(18.90%) |
| 3. | ≥ 101 per minute | 2 | 3.80% | 1 | 1.90% | 3(2.80%) |
| STATISTICAL INFERENCE | | $\chi^2 = 1.435$ Degree of freedom = 2 0.488 > 0.05 | | | | |

There was no significant difference in the baseline heart rate between the groups. Majority of the patients in group A (73.60%) and group B (83%) had heart rate less than 90 per minute during the commencement of the study.

Table 7: Degree Of Proteinuria

| S.NO. | PROTEINURIA | GROUP A LABETALOL (n=53) | | GROUP B NIFEDIPINE (n=53) | | TOTAL (n=106) |
|-------|-------------|--------------------------|--------|---------------------------|--------|---------------|
| | | NUMBER | % | NUMBER | % | |
| 1. | 1+ | 21 | 39.62% | 23 | 43.40% | 44(41.50%) |
| 2. | 2+ | 13 | 24.53% | 13 | 24.53% | 26(24.50%) |
| 3. | 3+ | 19 | 35.85% | 17 | 32.08% | 36(34%) |

Degree of proteinuria by dipstick estimation did not differ significantly in the groups A and B.

Table 8: Time Taken To Achieve Target Blood Pressure

| S.NO. | TIME TAKEN | GROUP A LABETALOL (n=53) | | GROUP B NIFEDIPINE (n=53) | |
|-------|--------------|--------------------------|--------|---------------------------|--------|
| | | NUMBER | % | NUMBER | % |
| 1. | 15 minutes | 4 | 7.55% | 1 | 1.89% |
| 2. | 30 minutes | 8 | 15.09% | 18 | 33.96% |
| 3. | 45 minutes | 20 | 37.74% | 12 | 22.64% |
| 4. | 60 minutes | 13 | 24.53% | 9 | 16.98% |
| 5. | 75 minutes | 3 | 5.66% | 7 | 13.21% |
| 6. | ≥ 90 minutes | 5 | 9.43% | 6 | 11.32% |

In group A, 20 patients, constituting 37.7% of the recruited reached the target blood pressure of less than 150/ 100 mm Hg in 45 minutes. 18 patients, constituting 34% of group B achieved the target blood pressure range by 30 minutes. The median time taken in group A is 45 minutes and that of group B

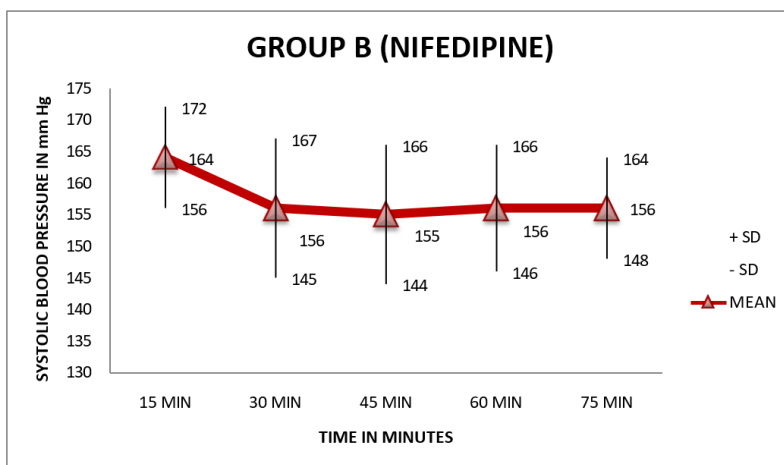
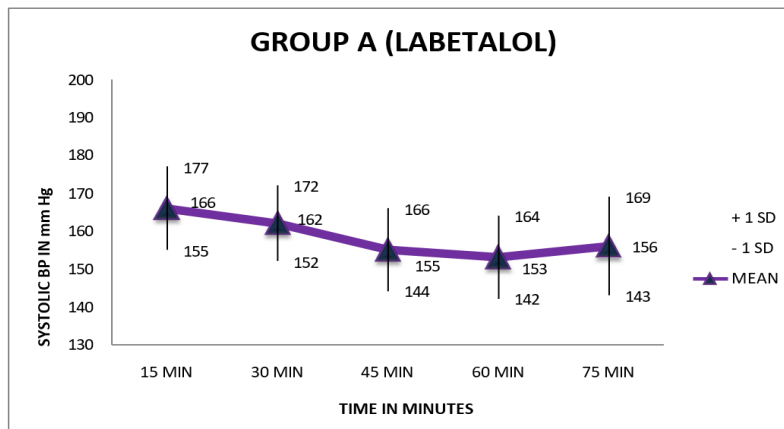
is 30 minutes. Overall, there is no statistically significant change regarding the time taken to achieve the target blood pressure.

Table 9: Number Of Doses Required To Achieve Target Blood Pressure

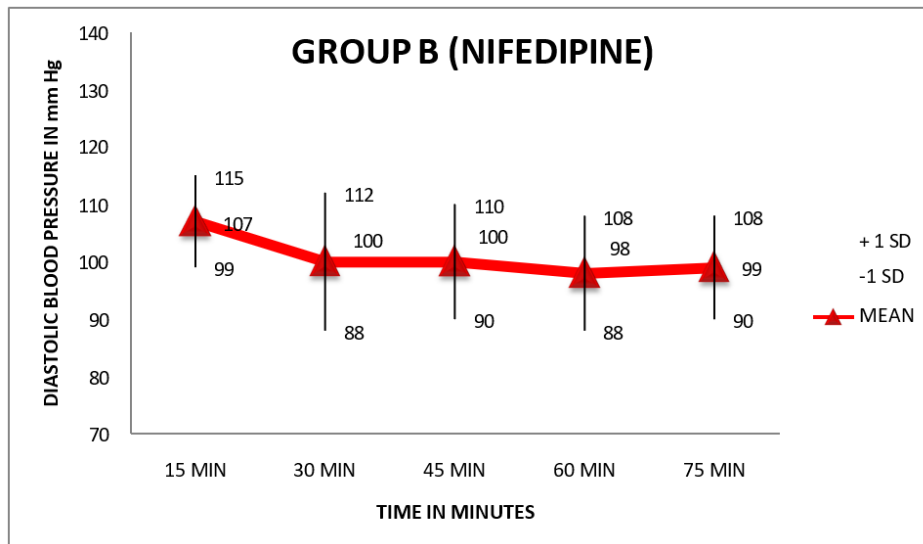
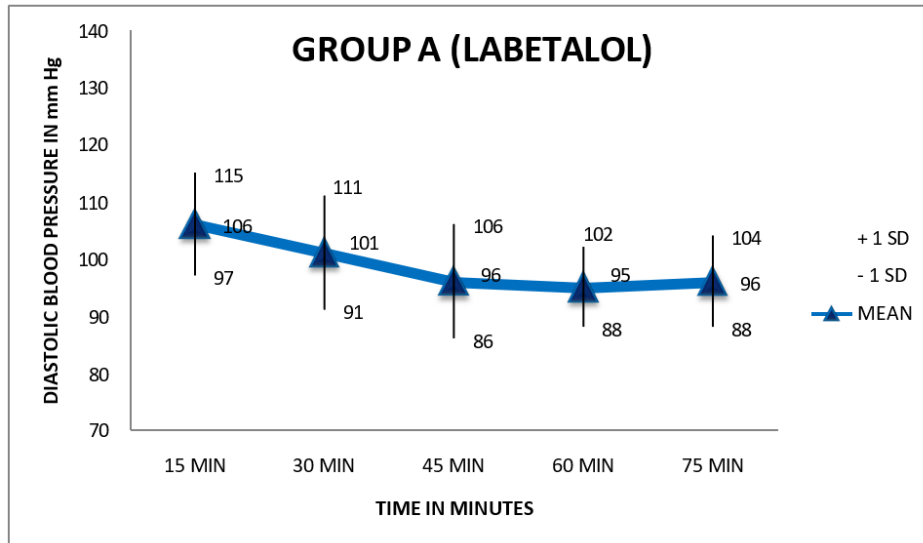
| S. NO. | NUMBER OF DOSES | GROUP A LABETALOL (n=53) | | GROUP B NIFEDIPINE (n=53) | | TOTAL (n=106) |
|--------|-----------------|--------------------------|-------|---------------------------|-------|---------------|
| | | NUMBER | % | NUMBER | % | |
| 1. | 1 | 4 | 7.5% | 1 | 1.9% | 5 (4.72%) |
| 2. | 2 | 7 | 13.2% | 18 | 34% | 25 (23.58%) |
| 3. | 3 | 19 | 35.8% | 14 | 26.4% | 33 (31.13%) |
| 4. | 4 | 11 | 20.8% | 9 | 17% | 20 (18.87%) |
| 5. | 5 | 7 | 13.2% | 5 | 9.4% | 12 (11.32%) |
| 6. | 6 | 2 | 3.8% | 2 | 3.8% | 4 (3.77%) |
| 7. | 7 | 3 | 5.7% | 4 | 7.5% | 7 (6.60%) |

Excluding 5 patients in group A and 6 patients in group B, who required cross over treatment and achieved control of blood pressure at 105 minutes each, the rest of the patients (31.10%) reached target blood pressure of < 150/ 100 mm Hg after three doses of antihypertensive. 35.80% of patients enrolled in group A reached the target blood pressure on administration of three consecutive doses of antihypertensive, while 34% of that in group B achieved target blood pressure in two doses of the drug administered. But the difference is not statistically significant.

Graph 1: Systolic Blood Pressure After Anti-Hypertensive Treatment



Graph 2: Diastolic Blood Pressure After Anti-Hypertensive Treatment



The fall in diastolic blood pressure was comparable in both the groups. The labetalol group has a greater mean fall of diastolic blood pressure at 45 minutes. The mean fall was greatest at 30 minutes for the nifedipine group. On comparison of both the groups, the rate of fall of diastolic blood pressure was not found to be statistically significant.

Table 10: Treatment Cross Over

| S. NO. | CROSS OVER | GROUP A LABETALOL (n=53) | | GROUP B NIFEDIPINE (n=53) | | TOTAL (n=106) |
|------------------------------|------------|--|--------|---------------------------|--------|---------------|
| | | NUMBER | % | NUMBER | % | |
| 1. | No | 48 | 90.60% | 47 | 88.70% | 95(89.60%) |
| 2. | Yes | 5 | 9.40% | 6 | 11.30% | 11(10.40%) |
| STATISTICAL INFERENCE | | $\chi^2 = 0.101$ Degree of freedom = 1 $0.750 > 0.05$ Not Significant | | | | |

Five patients (9%) out of 53 in group A and six patients (11%) in group B required cross over treatment to the alternate group. All the eleven patients from both the groups achieved control of blood pressure within 105 minutes of the commencement of the study.

Table 11: Induction

| S.NO. | INDUCTION | GROUP A LABETALOL (n=53) | | GROUP B NIFEDIPINE (n=53) | | TOTAL (n=106) |
|------------------------------|-------------------------------|---|--------|------------------------------|--------|------------------|
| | | NUMBER | % | NUMBER | % | |
| 1. | No induction | 6 | 11.30% | 3 | 5.70% | 9(8.50%) |
| 2. | Induction with cerviprime gel | 47 | 88.70% | 50 | 94.30% | 97(91.50%) |
| STATISTICAL INFERENCE | | $\chi^2=1.093$ Degree of freedom = 1 $0.296 > 0.05$ Not Significant | | | | |

Delivery of the baby was expedited after control of blood pressure. Induction with cerviprime gel was done to 88.70% and 94.93% of patients in group A and B after stabilizing the blood pressure.

Table 12: Induction Delivery Interval

| S. NO. | INDUCTION DELIVERY INTERVAL | GROUP A LABETALOL (n=53) | | GROUP B NIFEDIPINE (n=53) | |
|------------------------------|-----------------------------|---|--------|------------------------------|--------|
| | | NUMBER | % | NUMBER | % |
| 1. | Less than 12 hrs | 37 | 69.80% | 34 | 64.20% |
| 2. | More than 12 hrs | 16 | 30.20% | 19 | 35.80% |
| MEAN (S.D.) | | 13 (11) | | 13(11) | |
| STATISTICAL INFERENCE | | $T = -0.274$ Degree of freedom = 104 $0.785 > 0.05$ Not Significant | | | |

91.20% of the recruited patients were induced. 64.20% of the patients delivered within 12 hours of admission. There was no statistically significant variation in the groups A and B.

Table 13: Adverse Effects

| S.NO. | ADVERSE DRUG REACTIONS | GROUP A LABETALOL (n=53) | | GROUP B NIFEDIPINE (n=53) | | TOTAL (n=106) |
|------------------------------|----------------------------|--|-------|------------------------------|-------|------------------|
| | | NUMBER | % | NUMBER | % | |
| 1. | No notable adverse effects | 35 | 66% | 34 | 64.2% | 69 (65.1%) |
| 2. | Dizziness | 8 | 15.1% | 3 | 5.7% | 11 (10.4%) |
| 3. | Head ache | 3 | 5.7% | 6 | 11.3% | 9 (8.5%) |
| 4. | Palpitation | 0 | 0% | 4 | 7.5% | 4 (3.8%) |
| 5. | Nausea | 3 | 5.7% | 6 | 11.3% | 9 (8.5%) |
| 6. | Tremor | 2 | 3.8% | 0 | 0% | 2 (1.9%) |
| 7. | Pain at injection site | 2 | 3.8% | 0 | 0% | 2 (1.9%) |
| STATISTICAL INFERENCE | | $\chi^2 = 12.287$ Degree of freedom = 6 $0.056 > 0.05$ Not Significant | | | | |

No notable adverse effects were reported in the majority of the recruited patients. In group A, the common adverse effects were dizziness (15.10%) and head ache and nausea (5.7%). There were no instances of palpitations in group A. The common adverse effect of patients recruited in group B was head ache (11.3%). Similar number also complained of nausea in group B. 7.5% and 5.7% of patients in group B complained of palpitations and dizziness respectively. Overall, there was no significant difference in adverse effects in both the groups.

DISCUSSION

Hypertensive emergency in pregnancy is associated with a considerable morbidity and mortality in both maternal and neonatal populations. The primary aim is to reduce the dangerously elevated blood pressure and ameliorate the severity of the disease. In the present study, intravenous labetalol was compared with oral nifedipine in terms of efficacy and safety. The maternal and fetal outcome measures and side effect profiles of the drugs were also studied [9]. The patients enrolled in both the groups were comparable in terms of age, parity, booking status, gestational age at admission and body mass index. The mean age of the patients enrolled in the study was 24.89 years and 24.81 years in labetalol and nifedipine groups respectively. In the present study 40.57% patients presented in the gestational age of 34 to 36 weeks. Early onset disease at gestational age of less than 24 weeks was seen in 2.83% of the enrolled patients. The progressive risk of preeclampsia in obese is elucidated in the study by Sibai and colleagues. The risk is said to be increased by 13.3% in women with body mass index more than 35 kg/m². 62.30% of the patients enrolled in the labetalol and nifedipine groups fell under the category of obesity [10]. All the patients enrolled in the study were homogenous in terms of proteinuria. 39.62% of patients in labetalol group and 43.40% of the patients in nifedipine group had 1+ proteinuria on urine dipstick estimation which approximates to 30 mg/dl of proteinuria. 34% of the enrolled patients had 3+ proteinuria which amounts to 1 to 2 g/day of proteinuria [11]. A prospective study based on the finding through radiological investigative modalities such as single photon emission and cerebral computerized tomographic scan (SPECT) and transcranial Doppler findings in patients with eclampsia. 75% of the patients had perfusion defects in the watershed area in the parieto-occipital lobe arising out of cerebral vasospasm. The loss of cerebral autoregulation at elevated blood pressures, more particularly at a systolic blood pressure of more than 160 mm Hg, was theorized by Schwartz and co-workers in 2000. The mean systolic blood pressure of the patients enrolled in the labetalol and nifedipine groups in the present study was 171 mm Hg and 170 mm Hg, respectively. The mean diastolic blood pressure was 112 and 111 mm Hg in labetalol and nifedipine groups, respectively [12]. According to the Cochrane database on review of drugs, the utility of the antihypertensive drug should be based on the experience of the clinician with respect to its utility and adverse effects. In the present study, out of the 53 patients enrolled in labetalol group, 20 patients, constituting 37.74% of the study population achieved the target blood pressure of $\leq 150/100$ mm Hg in 45 minutes of commencement of the treatment, requiring three incremental doses of intravenous labetalol. The total dose administered was in labetalol group was 140 mg. In the nifedipine group, 33.96% of the enrolled patients required two doses of oral nifedipine constituting a dose of 20 mg of the drug. However, on statistical analysis, there was no significant difference in the time taken for both the drugs to act for reduction in systolic blood pressure. On the whole, except for the 11 patients who required cross over treatment, all the patients constituting 89.60% attained blood pressure control at 75 minutes [13]. On statistical analysis of the trend in reduction of the systolic blood pressure with respect to time, the difference of reduction in blood pressure was found to be significant at 30 minutes cut off. Oral nifedipine was found to be associated with a greater reduction in systolic blood pressure with respect to time. Similar trend was not seen in the case of reduction in diastolic blood pressure. Both the drugs were comparable in their reduction in diastolic blood pressure in the present study [14]. Eleven patients, five in labetalol group and six in nifedipine group, comprising 10.40% of the enrolled in the study, required cross over treatment. The number of doses of the other respective drugs after the crossover was similar in both the groups [15]. The above-mentioned patients achieved blood pressure control at 105 minutes after the commencement of the study. None of the enrolled patients developed hypotension during the study. The lowest blood pressure recorded during the study was 130/80 mm Hg. All the patients enrolled in the study received prophylactic magnesium sulphate therapy. None of the patients developed eclampsia in ante partum or post-partum periods [16]. Once the blood pressure was controlled, 97% of the enrolled patients in the present study were induced with cerviprime gel to expedite delivery. In patients with gestational age less than 34 weeks, steroids were administered after the control of blood pressure to accelerate the lung maturity. Fetal monitoring was done with non-stress test before and after administration of anti-hypertensive drugs and after induction of the patients. There was no cardiotocographic abnormality associated with the use of both the drugs [17]. Among the patients enrolled, 69.80% delivered vaginally and 30.20% delivered by caesarean section. 49.20% of the babies delivered had their birth weights ranging from 2 to 2.4 kg. In patients with early onset disease and those associated with intrauterine growth restriction, the birth weight was less than 1.9 kg which made 15.10% of the enrolled patients. There was no significant difference in birth weight in both the groups. 13.20% of new born from labetalol group and 20.80% of new born from nifedipine group were admitted for intensive care. The causes of admission were extreme prematurity and respiratory distress syndrome [18]. The outcome was similar in both the groups. None of the newborn had neonatal

hypoglycaemia or hypotension after birth. Out of 17% of the newborn admitted for intensive care, 7.50% of newborn from labetalol group and 13.20% of newborn from nifedipine group died due to extreme prematurity. Majority of the patients enrolled in the study did not report any notable adverse effects. The most commonly reported adverse effect in labetalol group was dizziness and that in nifedipine group was head ache and nausea [19]. None of the patients in the labetalol group had palpitations, though 7.5% of patients in the nifedipine group had complained of the same. 3.8% of the patients enrolled in the labetalol group had complained of tremor and pain at the injection site. On the whole, there was no statistically significant difference in adverse effects between both the groups [20].

CONCLUSION

Management of severe preeclampsia is in the control of blood pressure, prevention of complications, fetal surveillance and expedition of delivery if indicated. In the present study, the trend in reduction of blood pressure in patients with sustained severe hypertension with the use of intravenous labetalol and nifedipine was compared. From the present study, both the drugs were found to be safe and effective in the reduction of blood pressure. None of the drugs were associated with any detrimental maternal or fetal outcomes with respect to the anti-hypertensive usage. The tolerance of the patients towards both the drugs was similar. Intravenous labetalol provided a smooth and steady reduction in blood pressure. The use of nifedipine may be recommended in low resource settings since it has an oral regimen and dosage is simple when compared to incremental intravenous dosing of labetalol. In conclusion, both intravenous labetalol and oral nifedipine are equally efficacious and can be used as first line drugs for the use in acute blood pressure control of hypertensive emergency of pregnancy.

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