Original Article

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Comparison of the Efficacy of Labetalol and Nifedipine in Preeclampsia: A Prospective Interventional Study

Obstetrics and Gynaecology Section

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ABSTRACT

Introduction: Hypertensive disorders of pregnancy constitute the most widely analysed conditions in pregnancy. Previously, methyldopa was the most commonly used drug, which nowadays has been largely replaced by T. labetalol and T. nifedipine due to the slower onset of action of methyldopa. Chronic hypertension is associated with more maternal and perinatal adverse events, so it is important to determine the optimal antihypertensive therapy.

Aim: To compare drug side effects, obstetric complications, and mode of delivery between Group A (T. labetalol administered) and Group B (T. nifedipine administered).

Materials and Methods: A prospective interventional study was conducted in the Department of Obstetrics and Gynaecology, Dhiraj Hospital and SBKS Medical Institute and Research Centre, Vadodara, Gujrat, India from December 2022 to May 2023 at Dhiraj Hospital, involving 200 pregnant women with hypertension or Blood Pressure (BP) readings ≥140 mmHg Systolic Blood Pressure (SBP) or ≥90 mmHg Diastolic Blood Pressure (DBP) after 20 weeks gestation. They were randomly divided into two groups: Group A (n=100) with T. labetalol administered and Group B (n=100) with T. nifedipine. The two groups were compared with variables like age, side effects of respective drugs, pregnancy complications, and outcomes, including vaginal or caesarean delivery. The Chi-square and t-test were used to compare variables between the two groups.

Results: The mean age in Group A was 25.52±4.10 years, and in Group B, it was 25.95±4.47 years. In Group A (T. labetalol), the majority of cases, i.e., 34 (34%), required a 200 mg dose, followed by 300 mg in 26 (26%) of cases. In Group B (T. nifedipine), the majority of cases, i.e., 48 (48%), required a 30 mg dose, followed by 20 mg in 28 (28%) and 40 mg in 24 (24%) of cases. In Group A (T. labetalol), 2 (1%) cases had Intrauterine Growth Restriction (IUGR), 4 (2%) had oligohydramnios, and 2 (1%) had Intrauterine Demise (IUD). In Group B (T. nifedipine), 6 (3%) cases had IUGR, 6 (3%) had oligohydramnios, and 0 (0%) mmHg had IUD. No significant difference was found between Group A and B (p=0.213). In Group A (T. labetalol), 76 (38%) cases had vaginal delivery, 14 (7%) had emergency caesarean sections, and 10 (5%) had elective caesarean sections. In Group B (T. nifedipine), 70 (35%) cases had vaginal delivery, 18 (9%) had emergency caesarean sections, and 12 (6%) had elective caesarean sections. No significant difference was found between groups A and B (p=0.628). Post-intervention SBP in Group A was 126.06±6.6 mmHg, and in Group B, it was 126.96±8.17 mmHg with no statistically significant difference (p=0.3925). Post-intervention DBP in Group A was 80.6±2.38 mmHg, and in Group B, it was 80.2±1.40 mmHg with no statistically significant difference (p=0.14).

Conclusion: Both T. labetalol and T. nifedipine were found to be equally effective. However, with respect to drug side effects and tolerability, T. labetalol was found to be significantly better compared to T. nifedipine.

Keywords: Caesarean section, Diastolic blood pressure, Systolic blood pressure

INTRODUCTION

Preeclampsia is hypertension with proteinuria that occurs after 20 weeks of gestation in women whose Blood Pressure (BP) was previously normal and returns to normal by 12 weeks of gestation [1]. High blood pressure disorders complicate about 5 to 10% of pregnancies, and the prevalence of preeclampsia is about 3.9% [2]. As it could be accompanied by bleeding and infection, it has a huge impact on maternal mortality. In developed countries, mortality due to hypertensive disorders in pregnancy is about 16% [3], while in India, it ranges between 15-18% [4].

About half of this mortality can be prevented. The prevalence of chronic hypertension in pregnancy is expected to increase with maternal age and the global obesity epidemic [5]. Chronic hypertension is associated with more maternal and perinatal adverse events, so it is important to determine the optimal antihypertensive therapy. Data supporting guidelines on the prescription of antihypertensive drugs for chronic hypertension in pregnancy are scarce. In India, methyldopa, labetalol, and nifedipine are the most commonly used antihypertensive drugs during pregnancy [5]. Previously, methyldopa was the most commonly used drug, which has nowadays been largely replaced by labetalol and nifedipine due to the slower onset of action of methyldopa. Both labetalol and nifedipine have a fast onset of action and effectively treat high blood pressure with minimal side effects for the mother and foetus [6]. Even though sufficient information on the efficacy of both drugs is available through previous studies, we conducted the present study with the aim to compare drug side effects, obstetric complications, and outcomes between Group A (labetalol administered) and Group B (nifedipine administered).

MATERIALS AND METHODS

A prospective interventional study was conducted in the Department of Obstetrics and Gynaecology, Dhiraj Hospital and SBKS Medical Institute and Research Centre, Vadodara, Gujrat, India, from December 2022 to May 2023. Prior to the study, permission was obtained from the Institutional Ethics Committee (SVIEC/ON/Medi/RP/Jan/24/29). Anonymity and confidentiality of the participants were maintained throughout the study. Participants had the right to opt out at any stage without providing a reason, without jeopardising their right to receive appropriate treatment and care.

A total of 200 antenatal women with preeclampsia, fulfilling inclusion and exclusion criteria, were enrolled, and consent was obtained from all.

Sample size calculation: The sample size was calculated using World Health Organisation (WHO) statistical software. The assumption for sample size estimation was based on the hypothesis test for the difference of two proportions (two-sided test). The estimated sample size was sufficient to detect a 20% difference between the two groups at a significance level of 5%, with a study power of 90%. The estimated sample size was 100 for each group.

Inclusion and Exclusion criteria: Two hundred antenatal women with preeclampsia (pregnant women with hypertension or BP readings ≥140 mmHg SBP or ≥/90 mmHg DBP after 20 weeks' gestation [7]) with a gestational age between 20 and 40 weeks, irrespective of parity and gravida, were enrolled. Women with eclampsia, chronic hypertension, and those with co-morbidities such as heart disease, diabetes mellitus, bronchial asthma, gestational diabetes mellitus, and renal disease were excluded.

Study Procedure

After conducting a detailed history and clinical examination, in addition to routine blood investigations, fundus examination of the eye, and ultrasound of the abdomen, the diagnosis of preeclampsia was established. Subsequently, all patients were admitted and commenced on antihypertensive treatment. A total of 200 enrolled patients were randomly assigned to two groups as follows:

- Group A (n=100): Women were treated with T. Labetalol.
- Group B (n=100): Women were treated with T. Nifedipine.

T. Labetalol was initiated at an initial dose of 100 mg. Blood pressure was measured every two hours, and the dose was increased by 100 mg every six hours until adequate control was achieved. On the following day, the total required dose was divided and given as a twice-daily dosage, which was continued from the 2nd day of treatment. T. Nifedipine was started at a dose of 10 mg, with blood pressure measured every two hours. The drug dose was increased by 10 mg every six hours until adequate control was achieved. The total dose was divided and administered as a thrice-daily dosage from the 2nd day, and this dose was continued thereafter. Serial monitoring of blood pressure was conducted four times a day, with the focus on maintaining normal systolic blood pressure.

In patients with a gestational age of less than 37 weeks, once adequate control was achieved and if the patient was compliant with follow-up, they were discharged. Patients were then followed-up in the antenatal Outpatient Department every week, and their blood pressure was monitored. Pregnancy was terminated at 37 weeks of gestation, and patients were discharged after the fifth day following delivery. Antihypertensive treatment was continued if the blood pressure was ≥150/100 mmHg until two weeks postpartum, after which it was tapered. Any side effects of the antihypertensive drugs and obstetric complications were noted. The final outcomes, including the mode of delivery, were recorded.

STATISTICAL ANALYSIS

The statistical analysis was performed using Statistical Packages for Social Sciences (SPSS) software, version 20.0. The data were expressed in the form of frequency with percentages n (%). The χ2-test was used to estimate categorical data and study the association between two variables, while the t-test was used for continuous variables. A p-value less than 0.05 was considered statistically significant.

RESULTS

As shown in [Table/Fig-1], the maximum cases of preeclampsia cases (102 or 51%) occurred in the age group of 21 to 25 years. The mean age in Group A was 25.52±4.10 years, and in Group B, it was 25.95±4.47 years. In Group A (T. Labetalol), the majority of 34 cases (34%) required a 200 mg dose, followed by 26 cases (26%) needing 300 mg, and 22 cases (22%) requiring 400 mg. In Group B (T. Nifedipine), the majority of cases (48% or 48%) required a 30 mg dose, followed by 28 cases (28%) needing 20 mg, and 24 cases (24%) requiring 40 mg [Table/Fig-2].

Age years	Group A n (%)	Group B n (%)	Total n (%)	Chi-square	p-value
≤20	8 (4%)	6 (3%)	14 (7%)	0.769	0.856 (NS)
21-25	52 (26%)	50 (25%)	102 (51%)		
26-30	24 (12%)	24 (12%)	48 (24%)		
>30	16 (8%)	20 (10%)	36 (18%)		
Total n (%)	100 (50%)	100 (50%)	200 (100%)	-	-

[Table/Fig-1]: Age distribution.
Chi-square test was used

Dose (mg)	Group A, n (%)	Dose (mg)	Group B, n (%)
200	34 (34%)	20	28 (28%)
300	26 (26%)	30	48 (48%)
400	22 (22%)	40	24 (24%)
500	14 (14%)	-	-
600	4 (4%)	-	-
Total n (%)	100 (100%)	-	100 (100%)

[Table/Fig-2]: Drug dosing distribution.

As shown in [Table/Fig-3], in Group A (T. Labetalol), no cases reported any side effects. However, in Group B (T. Nifedipine), 1 case (0.5%) experienced giddiness, 2 cases (1%) had palpitations, and 3 cases (1.5%) suffered from headaches. T. Labetalol exhibited better tolerability compared to T. Nifedipine.

Side-effects	Group A, n (%)	Group B, n (%)	Total n (%)
Giddiness	0 (0%)	1 (0.5%)	1 (0.5%)
Palpitation	0 (0%)	2 (1%)	2 (1%)
Headache	0 (0%)	3 (1.5%)	3 (1.5%)
None	100 (50%)	94 (47%)	194 (97%)
Total n (%)	100 (50%)	100 (50%)	200 (100%)

[Table/Fig-3]: Drug side-effects distribution.

According to [Table/Fig-4], in Group A (T. Labetalol), 2 cases (1%) had IUGR, 4 cases (2%) had oligohydramnios, 2 cases (1%) had IUD, and the remaining 92 cases (46%) had no complications. In Group B (T. Nifedipine), 6 cases (3%) had IUGR, 6 cases (3%) had Oligohydramnios, 0 cases had IUD, and the rest 88 cases (44%) had no complications.

Complication	Group A n (%)	Group B n (%)	Total n (%)	Chi-square	p-value
IUGR	2 (1%)	6 (3%)	8 (4%)	4.48	0.213 (NS)
Oligohydramnios	4 (2%)	6 (3%)	10 (5%)		
IUD	2 (1%)	0	2 (1%)		
None	92 (46%)	88 (44%)	180 (90%)		
Total n (%)	100 (50%)	100 (50%)	200 (100%)	-	-

[Table/Fig-4]: Obstetric complication.
Chi-square test was used

As shown in [Table/Fig-5], in Group A (T. Labetalol), 76 cases (38%) had vaginal delivery, 14 cases (7%) had an emergency caesarean section, and 10 cases (5%) had an elective caesarean section. In Group B (T. Nifedipine), 70 cases (35%) had a vaginal delivery, 18 cases (9%) had an emergency caesarean section, and 12 cases (6%) had an elective caesarean section. No significant difference was found between Group A and B (p=0.628).

Outcome	Group A n (%)	Group B n (%)	Total n (%)	Chi-square	p-value
Vaginal delivery	76 (38%)	70 (35%)	146 (73%)	0.928	0.628 (NS)
Emergency caesarean section	14 (7%)	18 (9%)	32 (16%)		
Elective caesarean section	10 (5%)	12 (6%)	22 (11%)		
Total n (%)	100 (50%)	100 (50%)	200 (100%)	-	-

[Table/Fig-5]: Final outcome.
Chi-square test was used

As displayed in [Table/Fig-6], among the vaginal deliveries, 8 cases (11%) in Group A and 10 cases (14%) in Group B had a normal labour. In total, 56 cases (73%) in Group A and 48 cases (68%) in Group B had a normal labour. Total 8 (11%) cases (11%) in Group A and 6 cases (9%) in Group B had a normal labour. Total 4 (5%) in Group A and 6 (9%) in Group B had a normal labour.

Mode	Group A n (%)	Group B n (%)	Total n (%)	Chi-square	p-value
Natural labour	8 (11%)	10 (14%)	18 (9%)	1.278	0.734 (NS)
Natural labour with episiotomy	56 (73%)	48 (68%)	104 (52%)		
Outlet forceps delivery	8 (11%)	6 (9%)	14 (7%)		
Vacuum delivery	4 (5%)	6 (9%)	10 (20%)		
Total n (%)	76 (100%)	70 (100%)	146 (100%)	-	-

[Table/Fig-6]: Mode of vaginal delivery.

As seen in [Table/Fig-7], the post-intervention SBP mean±SD in Group A was 126.06±6.6 mmHg, and in Group B was 126.96±8.17 mmHg, with no statistically significant difference (p=0.3925). The post-intervention DBP mean±SD in Group A was 80.6±2.38 mmHg and in Group B was 80.2±1.40 mmHg, with no statistically significant difference (p=0.14).

Parameters	Group A (Labetalol) Mean±SD	Group B (Nifedipine) Mean±SD	p-value
Pre intervention SBP (mmHg)	152.9±10.73	151.64±9.02	0.3698 (NS)
Post intervention SBP (mmHg)	126.06±6.6	126.96±8.17	0.3925 (NS)
Pre intervention DBP (mmHg)	89.1±8.88	87.6±8.42	0.22 (NS)
Post-intervention DBP (mmHg)	80.6±2.38	80.2±1.40	0.14 (NS)

[Table/Fig-7]: Pre and post intervention Blood Pressure (BP) readings.
t-test was used

DISCUSSION

In the present study, the maximum number of preeclampsia cases, i.e., 102 (51%), were from the age group 21 to 25 years. In a similar study by Deshmukh UB et al., (2021), the maximum number of patients in both groups (labetalol and nifedipine) belonged to the age group of 21-25 years [8]. Dalal N et al., (2019), in their study, found that the maximum number of patients in the Labetalol group, i.e., 36 (48%), and in the Nifedipine group, i.e., 38 (50.6%), belonged to the age group of 21-25 years [9]. Sarulatha D et al., (2020), in their study, found that the maximum number of patients in the Labetalol group, i.e., 35 (46.7%), and in the Nifedipine group, i.e., 42 (56%), belonged to the age group 20-25 years [10].

In the present study, in Group A (T. Labetalol), the majority of cases (34%) required a 200 mg dose, followed by 26% needing 300 mg and 22% requiring 400 mg. In Group B (T. Nifedipine), the majority of cases (48%) required a 30 mg dose, followed by 28% needing 20 mg and 24% requiring 40 mg. In a similar study by Deshmukh UB et al., (2021), Group A (labetalol) received a starting dose of 100 mg BD, which was increased to 200 mg TDS, whereas Group B (nifedipine) received a starting dose of 10 mg BD, which was increased to 20 mg TDS. Additional labetalol dose requirements were found in two women, and nifedipine in three women [8].

In the present study, in Group A (T. Labetalol), not a single case reported side effects, whereas in Group B (T. Nifedipine), 0.5% of cases reported giddiness, 1% had palpitations, and 1.5% experienced headaches. In a similar study by Deshmukh UB et al., (2021), they reported headaches, palpitations, and hypotension in the nifedipine group [8]. Patel AR et al., (2020) reported that three patients experienced giddiness, two had palpitations, and four had headaches after receiving tablet nifedipine, while two patients complained of palpitations after receiving the tablet labetalol [11].

In Group A (T. Labetalol), 38% of cases had vaginal delivery, 7% had an emergency caesarean section, and 5% had an elective caesarean section. In Group B (T. Nifedipine), 35% had vaginal delivery, 9% had an emergency caesarean section, and 6% had an elective caesarean section. In a similar study by Dalal N et al., (2019), in the nifedipine group, a higher number (56%) of women underwent LSCS, whereas in the labetalol group, the majority (74%) had undergone normal vaginal delivery out of a total of 150 cases, and this difference was found to be statistically significant ($p<0.05$) [9]. No significant difference was found in the spontaneous onset of labour amongst study groups. However, the incidence of induction of labour was slightly higher in the labetalol group (61.3%) compared to the nifedipine group (57.3%).

Sarulatha D and Menag M (2020) found the vaginal delivery rate in the Labetalol group to be 34.7% and the caesarean section rate as 65.3%, whereas in the Nifedipine group, the vaginal delivery rate was 45.3% and the caesarean section rate was 54.7% [10]. Patel AR et al., (2020) discovered that in Group A (labetalol), 20 patients were delivered by caesarean section, nine of whom were full-term and 11 were preterm. Total 40 patients were delivered by vaginal delivery, 38 of whom were full-term and two were preterm. In Group B (nifedipine), 23 patients were delivered by caesarean section, nine of whom were full-term and 14 were preterm. A total of 37 were delivered by vaginal delivery, 34 of whom were full-term and three were preterm. Giannubilo SR et al., (2012) found a higher rate of intrauterine growth restriction infants among women treated with labetalol compared with nifedipine (38.8% vs. 15.5%) [12].

In Group A (Labetalol), none of the patients developed any side effects, whereas in Group B (Nifedipine), 6 (6%) out of a total of 100 (100%) developed side effects. Among these, 1 (1%) had dizziness, 2 (2%) had palpitations, and 3 (3%) had headaches. This proves the better tolerability of Labetalol. Although nifedipine is known for a 25% reduction in SBP, DBP, and mean BP [13]. In opposition to present study results, Raheem IA et al., (2012) and Shi DD et al., in their studies found that Nifedipine reduces BP with fewer doses when compared with the Labetalol group [14,15]. Ultimately, the choice of drugs that will be used to control hypertension to some extent depends mainly on the clinician's experience and familiarity with the drug [16].

Limitation(s)

Small study group size and investigator bias were present as the total cases were randomly divided into two groups based on the investigator's choice.

CONCLUSION(S)

Both T. Labetalol and T. Nifedipine were found to be equally effective in achieving the desired decrease in blood pressure in preeclampsia. However, concerning drug side effects and tolerability, T. Labetalol was significantly better compared to T. Nifedipine. Also, the prevalence of obstetric complications was found less in the T. Labetalol group compared to the T. Nifedipine group. However, the results showed no statistically significant difference.

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