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Nifedipine or Labetalol: Hypertension Management during Pregnancy

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Authors' contributions

This work was carried out in collaboration among all authors. All authors read and approved the final manuscript.

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ABSTRACT

Introduction: Hypertension complicates 10% of pregnancies causing significant morbidity and mortality worldwide. It is considered severe hypertension if Systolic >160 and Diastolic >110 lasting more than 15 minutes. It is an Obstetric emergency and needs prompt appropriate treatment.
Methods: A quasi-experimental study was conducted at Tehsil Headquarter Hospital. One hundred fifty patients were included in the study divided into two groups: Nifedipine group (n:75) getting oral Nifedipine and Labetalol group (n:75) getting IV Labetalol.
Results: This study shows that goal therapeutic blood pressure was reached earlier in patients receiving oral Nifedipine 28.2 ± 11.7minutes as compared with those receiving intravenous Labetalol 48.4 +- 23.5minutes.

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Fewer doses were required for the nifedipine group in contrast to the IV labetalol group Failure of treatment was higher among the IV labetalol group.
Conclusion: Oral nifedipine is as productive and safe as compared to Iv labetalol and is more convenient in Low resource settings.

Keywords: Oral nifedipine; Labetalol; Hypertension; pregnancy.

1. INTRODUCTION

Hypertension is the most common medical problem encountered during pregnancy which complicates one in ten pregnancies causing significant maternal, fetal and perinatal morbidity and mortality worldwide [1]. WHO estimated that hypertension is associated with 30% of all maternal deaths and 22% of all perinatal deaths [2,3]. Worldwide approximately 50,000 women will die each year from hypertensive disorders of pregnancy [3].

The term hypertension in pregnancy describes a broad spectrum of disorders, including mild hypertension to severe hypertension with organ failure. However, National High Blood pressure education program [4] has classified Hypertensive disorders in pregnancy into 4 categories: Chronic Hypertension, Preeclampsia-Eclampsia, Preeclampsia superimposed on Chronic Hypertension & Gestational Hypertension (also called Pregnancy Induced Hypertension).

According to ACOG Guidelines, [5] it is considered Severe hypertension if Blood pressure is systolic of 160 mm HG or higher, or diastolic of 110 mm HG or higher that lasts more than 15 minutes in both pregnant and postpartum women with preeclampsia or eclampsia is a hypertensive emergency. It is a significant predictor of cerebral hemorrhage and can lead to maternal death if not treated quickly and appropriately. This directs to swift but safe and controlled blood pressure lowering with Anti-hypertensive medication to avoid any serious medical complication.

The decision of drug selection is influenced by the clinician's experience with the drug, convenience of usage, medication cost, and the known adverse effects [6]. Due to insufficient data, there is no reliable evidence that one drug is preferable over others. Currently, trials have been done to compare nifedipine and Labetalol's efficacy and side effects in control of severe hypertension during pregnancy [7]. The results have very positively shown that Nifedipine is as productive as Labetolol in managing hypertensive crisis, which not only safely controls blood pressure but reaches therapeutic goals more rapidly, with lesser doses and fewer side effects [6,7].

In developing countries where the numbers of hospitals are too less, pregnant women go to the nearest small health units where they have their antenatal visits. Facilities at those health units are minimal, so when a pregnant patient is diagnosed with severe hypertension, it takes approximately half an hour to reach a hospital. Hence, the initial management is done at a basic unit to save women's lives in that critical time frame.

The objective of our study was to assess the efficacy, tolerability and comparison of oral Nifedipine and intravenous Labetalol in a hypertensive crisis of pregnancy.

2. MATERIALS AND METHODS

We performed a Quasi-experimental study at Tehsil Headquarters Hospital between the year 2017 to 2020.

A total of 150 pregnant participants were identified from the starting date to the end date. All these participants fulfilled the inclusion and exclusion criteria and were included in the study after informed consent. Non- probability convenient sampling and participants who did the sampling were equally divided into two groups.

The first group was called the Nifedipine group (n:75) who received oral Nifedipine where as the second group was called the Labetalol group (n:75) who received intravenous Labetalol.

2.1 Patients were Included in the Study According to the Following Inclusion Criteria

Pregnant patients age (18-35 years) Gestational age of 34 weeks or above using (LMP, USG EDD), patients having Blood pressure of more than 160mm of Hg systolic and 105mm or more

diastolic, having proteinuria of plus 1 or more on the dip stick & Patients both booked as well as non-booked were included in the study.

2.2 Exclusion Criteria

Patients with a history of exposure to either study medication in the last 24 hours, cardiac disease, hepatic or renal impairment, secondary hypertension, Gestational Diabetes Mellitus, lupus erythematous, and deranged NST were excluded.

2.3 Data Collection

Detailed history through general physical and obstetric examination was carried out. Baseline Vitals, including blood pressure, pulse, respiratory rate, pulse oximetry, and obstetric examination, including Urine dipstick and CTG was noted. All selected participants had intermittent blood pressure, pulse rate, and fetal heart rate monitoring every 10-15 minutes for the first three hours till the blood pressure was controlled.

The blood pressure was measured with the help of a mercury sphygmomanometer, and korotcoft V was taken as standard. Highly trained staff was used to measure BP, and it was measured thrice to rule out any false-positive or false-negative results. Detail regarding CBC, Urine R/E, LFT, Coagulation profile, and urinary protein was noted. Information collected was filled in performa

2.4 Treatment Protocol

Tab Nifedipine 05 mg was given orally & Inj Labetalol 20 mg was given intravenously as the initial dose, with repeated doses of 10 mg for Nifedipine and Labetalol 40 mg. The dose was repeated three times after 20 minutes each till a maximum dose of 40 mg for the Nifedipine group and 140 mg for the Labetalol group was reached or treatment failure was considered if blood pressure was not controlled.
The patient was kept under observation in the hospital for intermittent BP monitoring and possible side effects

2.5 Data Analysis

Data was analyzed on SSPS version 22. For the mean difference of pre and post-treatment blood pressure, no doses, no side effects, time to control blood pressure was analyzed by t-test. For the proportion of failed induction and hypertensive crises, chi-square was used. P-value of less than 0.05 was considered was significant Data was collected and analyzed with SPSS version 24.
The objective of the study:

To determine the efficacy of "oral Nifedipine" versus "Labetalol" drug among hypertensive pregnant participants.

3. RESULTS

This study shows that the goal therapeutic blood pressure was achieved more rapidly in Patients receiving Oral Nifedipine 28.2 ± 11.7minutes (mean ±SD) as compared with those receiving intravenous Labetalol 48.4 +- 23.5minutes ($p>0.05$) . The Nifedipine group also requires fewer doses (2.2 +- 0.5) in comparison with intravenous Labetalol group (3.2 +- 0.5) ($p<0.05$). The comparison of blood pressure control in Nifedipine group vs Labetalol group is described in Table 1.

The failure rate of treatment was higher among the IV Labetalol group, 11%, than the Oral Nifedipine group that was only 5% as explained in Table 2.

The comparison of dosage also significantly tells that lesser doses were required for the Oral Nifedipine group as described in Table 3.

Results 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 ($P >0.05$) as described in Table 4. Repeated measures analysis of variance indicated that in the first hour both systolic ($F = 87.6$, $P < 0.001$) and diastolic ($F = 55.8$, $P < 0.001$) blood pressure significantly decreased, but there was no difference between the Nifedipine and Labetalol groups for both systolic ($F = 0.12$, $P > 0.05$) and diastolic ($F = 0.92$, $P > 0.05$) blood pressure trends over time which is described in Table 5.

Crossover treatment was required in 20% of women from each group.

4. DISCUSSION

This study was conducted to find whether nifedipine was an effective and safe anti-hypertensive alternative to Labetalol in women

with severe preeclampsia. The study was conducted in a low-resource setting, where midwives and staff nurses managed the patient. It was not always possible to maintain an intravenous line immediately, so an effective oral anti-hypertensive in emergencies was needed. Till now, the choice of drugs that can be used to control severe hypertension depends on the clinician's experience and familiarity with the drug [8]. Our data indicate that both oral Nifedipine and Intravenous Labetalol are effective in controlling blood pressure in case of severe preeclampsia.

Both regimes are rapidly effective, with target blood achieved in 91% and 85% of cases with nifedipine and Labetalol, respectively, but fewer doses were needed in the case of the Nifedipine group (2.2 versus 3.2). There was no significant side effect except that 34%of patients in Nifedipine and 40% of Labetalol had hypertensive crises even after treatment later referred to tertiary care. Our data is in support of recent guidelines and expert opinion regarding the safety and suitability of oral nifedipine and intravenous Labetalol as first-line anti-hypertensive for severe preeclampsia.

Nifedipine has been used for the reduction of blood pressure in severe preeclampsia. A calcium channel blocker causes peripheral vasodilation. Extensive reviews on its pharmacokinetics and pharmacodynamics indicate that Nifedipine is associated with a 25% reduction in systolic, diastolic, and mean blood pressures [9] . In our study, the Oral Nifedipine took the lesser time (28.2±11.7 versus 48.4±11.7 mins) and fewer doses (2.2± 0.5 versus 3.2±0.5) to control the blood pressure when compared with injection Labetalol. These results are also supported by Raheem et al. [10], Dhannanjaya et al. [11], Vermillion et al. [12] and Dhali B et al. [8] in their studies where both Nifedipine and Labetalol are effective in the management of preeclampsia, but Nifedipine reduces the blood pressure in shorter duration of time and with fewer doses when compared with Labetalol group.

Table 1. Blood Pressure Control with Nifedipine Vs Labetalol

BP control	Nifedipine group N%	Labetalol group N%	Total N %	P value
Well controlled	69 (91.4)	64 (85.7)	133 (88.5)	0.452
Not Controlled	6(8.6)	11 (14.4)	17 (11.4)	

Table 2. Failed Treatment of Nifedipine Vs Labetalol

	Nifedipine group N%	Labetalol group N%	Total N %	P value
Failed Treatment	4 (5.1)	9 (11.4)	6 (8.4)	0.24

Table 3. Doses Required of Nifedipine Vs Labetalol for Hypertension Management

	Nifedipine group N%	Labetalol group N%	Total N %	P value
1st dose	17(22.8)	13(17.5)	30(20)	
2nd dose	28(37.1)	19(25.7)	47(31.4)	0.03
3rd dose	21(28.5)	28(37.1)	49(32.8)	
4th dose	9(11.4)	15(20)	24(15.7)	
Mean (SD)	2.3(1.01)	2.7(1.11)		

Table 4. Time to Control Blood Pressure in Minutes

	Nifedipine group N%	Labetalol group N%	Total N %	P value
20	17(22.8)	15(20)	32(21.4)	0.2
40	43(57.1)	34(45)	77(51.4)	
60	6(8.5)	15(20)	21(14.2)	
80	2(2.8)	2(2.8)	4(2.8)	
Mean	28.2	48.4		

Table 5. Hypertension Crisis Caused by Nifedipine Vs Labetalol

	Nifedipine group N%	Labetalol group N%	Total N %	P value
Hypertensive crises	24(31.4)	30 (40)	54(35.7)	0.036

The treatment regime used by Vermillion et al. for both the Nifedipine and the Labetalol are of higher dose that is 10mg for Nifedipine initially followed by 20 mg of further four doses of nifedipine i.e and 40mg,80mg,80mg,80mg for labetalol. Raheem et al. [10], Dhannanjaya et al. [11] used flat 10 mg of Nifedipine with the same doses for Labetalol.

We used 05 mg dose for Nifedipine and a 20 mg initial dose for Labetalol followed by three doses 20 minutes apart. The rationale behind selecting lower doses was that no study yet had compared the lowest blood pressure with higher doses. Few cases of myocardial infarction were reported in the literature due to rapid hypotension, which could be easily missed in a low resource center like ours. Though our study is comparable to the above studies in the form of control of blood.

Pressure and doses needed to achieve, but no study had compared the failure of treatment or hypertensive crises (raised blood pressure with 3 hours of control), which in our study was done to decide timely referral. There are 2 patients (5.1%) in the nifedipine group and four patients (11.4%) in the Labetalol group in whom blood pressure was not lowered even after four doses and treatment was deemed as failed.

11patient (31.4%) who took nifedipine had hypertensive crises compared with the Labetalol group in which 14(40%).

More than half of 56.6% of the women were primary gravidas in our study, and only 15% of patients were booked. This status (85% non-booked) of these patients suggests a need for better antenatal services to ensure prevention rather than cure preeclampsia.

CONCLUSIONS

Hypertension in pregnancy is a life-threatening complication. Therefore it is the demand of time for large trials to compare the efficacy of Oral Nifedipine and Intravenous Labetalol for treatment of severe hypertension during pregnancy.

Oral Nifedipine achieved the target blood pressure goal more rapidlyand with fewer doses than Labetalol. Nifedipine is administered orally, more economical, more accessible storage. Unlike Labetalol that is given intravenously, which is comparatively expensive. So more patient compliance with Oral Nifedipine is there , especially in a rural setting where well-trained staff is not present. Nifedipine is as productive and safe as Labetalol and may be advantageous in low-resource settings.

DISCLAIMER

The products used for this research are commonly and predominantly use products in our area of research and country. There is absolutely no conflict of interest between the authors and producers of the products because we do not intend to use these products as an avenue for any litigation but for the advancement of knowledge. Also, the research was not funded by the producing company rather it was funded by personal efforts of the authors.

CONSENT

They were written as well as oral consent was taken from all the participants.

ETHICAL APPROVAL

It is not applicable.

COMPETING INTERESTS

Authors have declared that no competing interests exist.

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