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Oral Nifedipine and Intravenous Labetalol for Hypertensive Emergencies in Pregnancy: A Comparative Study

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Abstract: ***Background: Hypertensive emergency in pregnancy is defined as persistent acute - onset, severe hypertension (Systolic BP >160 mmHg or diastolic BP >110 mmHg or both) in the setting of preeclampsia or eclampsia. Objective: Compare safety and efficacy of oral nifedipine and intravenous labetalol for acute blood pressure control in hypertensive emergencies of pregnancy Study design: a randomised comparative hospital based study conducted in Department of Obstetrics and Gynaecology, SMS Medical College, Jaipur from April 2021 to Nov 2021. Sample: 80 women with hypertensive emergencies. Method: Divided into 2 groups of 40 each. Nifedipine grp received 10mg tab every 20 min till maximum of 5 doses and labetalol grp was given iv labetalol in escalating doses of 20, 40, 40, 80 and 80mg every 20 min till a target BP was achieved. Main outcome measures: Better treatment for Hypertensive emergencies of pregnancy. Results: In our study, mean time required to achieve target BP in nifedipine and labetalol group was 45+14.84 and 54+18.22 minutes (p value 0.018) respectively. Mean decrease in SBP after treatment was 59 ± 21.1 mmHg in Nifedipine group as compared to 42.25 ± 22.7 mmHg in Labetalol (p - value = 0.001). Also the mean decrease in DBP in nifedipine group was 37.5 ± 11.49 mmHg as compared to 27.75 ± 15.34 mmHg in labetalol group (p - value = 0.001). There were no significant differences between side effects and fetomaternal outcome. Conclusion: Oral Nifedipine controls hypertension more rapidly and with fewer doses and is as safe as iv Labetalol.***

Keywords: nifedipine, labetalol, hypertensive emergency

1. Introduction

Hypertensive disorders are one of the most common medical disorders complicating pregnancy.1 These complicate upto 10% of pregnancies worldwide constituting one of the greatest causes of maternal and perinatal mortality and morbidity worldwide.2The American College of Obstetricians and Gynaecologists (ACOG) describes a hypertensive emergency in pregnancy as acute - onset, severe hypertension persisting for 15 min or more in setting of preeclampsia or eclampsia.3 Severe hypertension in pregnancy is defined as a systolic blood pressure (SBP) more than or equal to 160 mmHg and/or a diastolic blood pressure (DBP) more than or equal to 110 mmHg.4

A hypertensive emergency requires hospitalization, immediate antihypertensive treatment to reduce maternal blood pressure without substantially decreasing placental perfusion and compromising the fetus, and delivery of the infant as soon as possible. The goal is to achieve a target BP of less than or equal to 150/100 mmHg in order to prevent repeated, prolonged exposure to severe systolic hypertension, with subsequent loss of cerebral vasculature auto regulation. Hence antihypertensive drugs which can be used for control of hypertensive emergencies of pregnancy are nifedipine, labetalol and hydralazine.

Labetalol is a combined α - and β - adrenergic blocker that acts by causing vasodilatation. It is a pregnancy category C drug. It can be used in drowsy and unconscious patients. Its side effects includes orthostatic hypotension (due to alpha blocker action), difficulty in sleeping, drowsiness, weakness, scalp tingling, drug eruption. Labetalol is contraindicated in asthma, congestive heart failure, any degree of heart block, bradycardia, hypotension or those in cardiogenic shock.5Nifedipine is a calcium channel blocker. Nifedipine effectively dilates the arterioles in preference to veins thus producing an effective vasodilatation without producing postural hypotension. It reduces the total peripheral resistance and thereby reduces the after load. It is a pregnancy category C drug and has the advantage of being cost effective, rapid onset of action, long duration of action, oral bioavailability, easier to store and infrequent side effects.6 Sublingual route is not recommended since it produces a rapid fall of the blood pressure. However it is known to cause reflex tachycardia and headache.2 Nifedipine doesn't adversely affect uterine or umbilical blood flow. In this study we have compared oral nifedipine and intravenous labetalol for blood pressure control in hypertensive emergencies in pregnancy.

2. Material and Methods

The study was conducted in Department of Obstetrics and Gynaecology, SMS Medical College, Jaipur from April

2021 to Nov 2021. It was a hospital based prospective randomised interventional comparative study conducted on 80 pregnant women with hypertensive emergency fulfilling inclusion criteria and exclusion criteria.

Inclusion criteria: Patients with singleton viable pregnancies with persistent systolic BP ≥160 mmHg or diastolic BP ≥110 mmHg or both

Exclusion criteria: Any medical disorders like cardiac disease, bronchial asthma, hematological disorder, diabetes mellitus, liver or renal disorders and thyrotoxicosis or any allergy or contraindications to Labetalol or Nifedipine.

After proper counselling regarding the purpose of study, a written and informed consent was taken following which 80 cases were randomly divided in two groups - Group - A (oral Nifedipine) and Group - B (iv labetalol) 40 in each group. Standard Mercury sphygmomanometer of appropriate sized cuff was used to measure BP with the patient in sitting or semi reclining position with back support. All basic investigations and sonography with doppler was done. Oral Nifedipine or iv Labetalol were given as: -

Oral Nifedipine (Group - A): Patients in this group were given 10 mg oral tablet initially, with repeated doses of 10 mg, every 20 minutes, for up to a maximum of 5 doses, or until the target BP was achieved whichever was earlier.

IV Labetalol (Group - B): Patients in this group, were given 20 mg intravenous labetalol initially followed by escalating doses of 40 mg, 80 mg, 80 mg, and then 80 mg, every 20 minutes, until the target BP was achieved, or for a maximum of five doses whichever was earlier.

Goal was to achieve a target BP of less than or equal to 150/100 mmHg. Any Side effects of drugs were noted in both the groups. Monitoring of fetal heart rate was done continuously by electronic cardiotocography until BP remained stable (continuous CTG monitoring). In case of non - reassuring maternal or fetal status the trial protocol was abandoned and appropriate measures were taken. Continuation or termination of pregnancy was decided according to gestational age, maternal and fetal condition. The time and dosages taken to control BP in each group. Finally data obtained was statistically analysed with suitable statistical software. The categorical data was presented as numbers (percent) and were compared among groups using chi - square test. Demographic data was presented as standard deviation compared between groups using students 't' test. P - value <0.05 was considered statistically significant.

3. Results

We randomised 80 pregnant women with hypertensive emergency (40 in each group) to receive oral Nifedipine in group A and iv Labetalol in group B.

Tables

Table 1: Clinical characteristics of women in both the study groups

	Group A	Group B	P value
Mean Age	26.4 ± 4.65	25.3 ± 5.03	0.772
Primi gravida	52.5%	60%	0.652
Mean gestational age	33.17 ± 3.9	34 ± 3.86	0.99
Mean SBP	187.2 ± 19.48	183.8 ± 20.96	0.442
Mean DBP	119.50 ± 11.31	114.8 ± 14.85	0.112

Table 2: Comparison of the primary outcome in both the study groups

	Group A	Group B	P value
Mean Doses	2.25 ± 0.74	2.7 ± 0.91	0.018 (Sig)
Mean Time	45.00 ± 14.84	54.00 ± 18.22	0.018 (Sig)
Mean Decrease in SBP	59 ± 21.1	42.25 ± 22.7	0.001 (HS)
Mean Decrease in DBP	37.5 ± 11.49	27.75 ± 15.34	0.001 (HS)

Table 3: Adverse effects of drugs in the study groups

Complications	Group - A		Group - B		p - value
	No.	%	No.	%	
Drowsiness	2	5.00	4	10.00	0.671 (NS)
Headache	2	5.00	4	10.00	0.671 (NS)
Nausea	2	5.00	2	5.00	0.99 (NS)
Postural Hypotension	1	2.50	0	0.00	
Decreased Urinary Ouput	0	0.00	0	0.00	
Hypersensitivity Reaction	0	0.00	0	0.00	

Table 4: Distribution of patients according to mode of delivery

Mode of Delivery	Group - A		Group - B	
	No.	%	No.	%
Pregnancy Continue	16	40.00	12	30.00
Vaginal delivery	14	35.00	16	40.00
LSCS	10	25.00	12	30.00
Total	40	100.00	40	100.00

p = 0.642 (NS)

Table 5: Fetal outcome in the study groups

Fetal Outcome		Group - A		Group - B		p - value
		No.	%	No.	%	
APGAR Score <7		7	17.50	10	25.00	0.585 (NS)
NICU Admission	Preterm	4	66.67	5	100.00	
	MAS	2	33.33	0	0.00	
	Total	6	15.00	5	12.50	0.99 (NS)
Perinatal Mortality		0	0.00	0	0.00	

In our study, the mean age in nifedipine group was 26.4 ± 4.65 years and in labetalol group was 25.3 ± 5.03 years. Most of the patients were primigravidas with 52.5% and 60% in nifedipine and labetalol group respectively. Also the mean gestational age in Group - A was 33.17 ± 3.9 weeks and in Group - B was 34 ± 3.86 weeks. Thus both the groups did not differ significantly in mean age, gravidity and gestational age. (Table 1)

The Mean Systolic BP in Group - A was 187.2 ± 19.48 mmHg and in Group - B was 183.8 ± 20.96 mmHg (p - value = 0.442) whereas the mean DBP in Group - A and Group - B was 119.5 ± 11.31 mmHg and 114.8 ± 14.85 mmHg respectively p - value = 0.112). There was no significant statistical difference in mean SBP and mean DBP in both the groups (Table 1)

In our study, it was found that Nifedipine required significantly fewer doses and less time to achieve target BP than Labetalol. The mean dose required in nifedipine group to achieve target BP was 2.25 ± 0.74 and in Labetalol group was 2.7 ± 0.91 which was found to be statistically significant (p - value = 0.018). The mean time required to achieve target BP in Nifedipine and Labetalol group was 45.00 ± 14.84 min and 54.00 ± 18.22 min respectively which was also found to be statistically significant (p - value = 0.018). Mean decrease in SBP after treatment was 59 ± 21.1 mmHg in Nifedipine group as compared to 42.25 ± 22.7 mmHg in Labetalol (p - value = 0.001). Also the mean decrease in DBP in nifedipine group was 37.5 ± 11.49 mmHg as compared to 27.75 ± 15.34 mmHg in labetalol group (p - value = 0.001). This difference in mean decrease in SBP and DBP was found to be statistically significant. Thus decrease in systolic BP and diastolic BP after treatment was more in nifedipine group as compared to labetalol group. (table 2)

Side effects of drugs on mother and fetus were transient and tolerable and were comparable in both the groups.5% cases in Group - A and 10% cases in Group - B complained of headache. Drowsiness was also seen in 5% and 10% cases in Group - A and Group - B respectively.5% cases in both groups complained of nausea. Postural hypotension was reported in 2.5% cases in Group - A. (table 3)

Regarding mode of delivery, vaginal and caesarean delivery rates were 35% and 25% in nifedipine group and 40% and 30% in labetalol group and there was no significant difference found between the groups (p - value = 0.642) (table 4).

There was no significant difference found in fetal outcome in both groups.17.5% and 25% babies in Group - A and Group - B respectively had APGAR score < 7 (p value 0.585) The number of NICU admission was 15% in Group - A as compared to 12.5% in Group - B (p value 0.99). The cause of NICU admissions were prematurity and meconium aspiration. There was no perinatal mortality reported in the study. (table 5)

4. Discussion

A hypertensive emergency of pregnancy is one of the life threatening complications encountered in obstetrics. Management of hypertension in pregnancy is a challenging task, because drastic reduction of BP leads to uteroplacental insufficiency & that may lead to intrauterine fetal death and continuation of pregnancy with severe hypertension leads to adverse feto - maternal outcome. While there are a wide variety of pharmaceutical agents available, the mechanism of action and contraindications of each must guide the choice of treatment for optimal care. Although both labetalol & nifedipine are better alternative to previously used hydralazine, our study showed nifedipine controls severe hypertension more rapidly and with fewer doses without significant overshoot hypotension & other maternal &fetal side effects.

In the present study the mean dose required in nifedipine group to achieve target BP was 2.25 ± 0.74 and in Labetalol group was 2.7 ± 0.91 which was found to be statistically significant (p - value = 0.018). The mean time required to achieve target BP in Nifedipine and Labetalol group was 45.00 ± 14.84 min and 54.00 ± 18.22 min respectively which was also found to be statistically significant (p - value = 0.018). Hence Nifedipine required significantly fewer doses and less time to achieve target BP as compared with IV Labetalol. These findings were similar to that found in a study conducted by Shekhar S et al (2013) [7] where the median time taken to achieve target blood pressure was 40 minutes (interquartile range, 20 - 60 minutes) compared with 60 minutes (interquartile range 40 - 85 minutes) for nifedipine and labetalol, respectively (p=.008). The median dose required was two (interquartile range 1 - 3) compared with three (interquartile range 2 - 4.25) for nifedipine and labetalol, respectively (p=.008).

In a study by Prof. S. Randhoni Devi et al (2017) [8], The mean time was 71.00 ± 66.60 minutes in labetalol group and 25.20 ± 14.03 minutes in the nifedipine group (p - value of < 0.01) and mean doses were 1.12 ±.32 in nifedipine group and 2.04 ± 1.37 in labetalol group (p - value <0.01). Gavit Y et al (2018) [9] also had similar findings in his study.

Side effects of drugs included nausea, postural hypotension, headache, drowsiness but the results were comparable in both the groups. Dhali B et al (2012) [10] and Shekhar S et al (2013) [7] also found the side effect profiles of both the drugs were similar.

In our study, 17.5% and 25% babies in Group - A and Group - B respectively had APGAR score < 7, the number of NICU admission was 15% in Group - A as compared to 12.5% in Group - B which was also not statistically significant. NICU admissions were due to prematurity and meconium aspiration syndrome. There was no perinatal mortality reported in the study. Prof. S. Randhoni Devi et al (2017) [8] also found insignificant variation in percentage of NICU admission in the both groups (labetalol group = 14% versus nifedipine group = 4%; p =.081).

5. Strength and Limitations

Strength of the study are firstly the participants were diverse in socioeconomic indicators thereby enhancing the generalisability of our findings. Secondly as this study relied on BP measurements hence the BP was recorded by trained professionals using a standard protocol. The limitations include firstly, the sample size of the study was small for the result to be significant enough to be applicable to the general population but it was big enough to be significant for the study population. Secondly, it was a randomised control study but not double blind so there is a chance of observer bias. Also the long term outcome was not observed. Hence to overcome these further multicentric studies should be undertaken to evaluate the applicability of our result to the entire region.

6. Conclusion

Our present study compared the efficacy and safety of oral Nifedipine and IV Labetalol in reaching the therapeutic goal. From the study, it is concluded that both oral Nifedipine and IV Labetalol are effective, safe and well tolerated, however,

oral Nifedipine may be preferable because it is less cumbersome with oral administration, flat dose schedule and controls hypertension more rapidly with fewer doses.

Disclosure of interest
None declared.

Details of ethical approval
This research article was ethically approved by institutional review board SMS medical college Jaipur

References

[1] Cunningham FG, Leveno KJ, Bloom SL, et al. Hypertensive disorders of pregnancy. Chapter in Cunningham, F Gary. III. Williams, Jeds, Williams Obstetrics, 25th edition; 34: 706709.
[2] American College of O, Gynecologists, Task Force on Hypertension in P. Hypertension in pregnancy. Report of the American College of Obstetricians and Gynecologists' Task Force on Hypertension in Pregnancy.
[3] Committee on Obstetric Practice. Committee Opinion no.514: emergent therapy for acute - onset, severe hypertension with preeclampsia or eclampsia. Obstet Gynecol.2011; 118: 1465–8.
[4] National Institute of Health and Clinical Excellence. Hypertension in Pregnancy. The management of hypertensive disorders during pregnancy. Clinical guidelines CG107 Issued: 2010.
[5] MacCarthy EP, Bloomfield SS. Labetalol: a review of its pharmacology, pharmacokinetics, clinical uses and adverse effects. Pharmacotherapy.1983; 3 (4): 193–219.
[6] Kumari VR, Saraswathi K, Srilaxmi A. Oral nifedipine versus intravenous labetalol for control of blood pressure in severe preeclampsia. J. Evolution Med Dent Sci.2016; 5 (20): 994 - 997, doi: 10.14260/jemds/2016/231
[7] Shekhar S, Sharma C, Thakur S, Verma S. Oral Nifedipine or Intravenous Labetalol for hypertensive emergency in pregnancy: a randomized controlled trial. Obstet Gynecol.2013; 122 (5): 1057 - 63.
[8] Prof. S. Randhoni Devi, Dr. R. K. Praneswori Devi, Dr. L. Ajit Kumar, Dr. Romita Devi, Dr. Sujit Das, Dr. Deepthambika and Dr. Abhipsa. Comparative Study Between Oral Nifedipine and Intravenous Labetalol in Management of Severe Pregnancy Induced Hypertension. European Journal of Pharmaceutical and Medical Research.2017; 4 (9): 291 - 296.
[9] Gavit Y, Sharma D, Dixit PV. A comparative study of oral nifedipine and intravenous labetalol in control of acute hypertension in severe pre - eclampsia and eclampsia. International Journal of Reproduction, Contraception, Obstetrics and Gynecology.2018 Feb; 7 (2): 719 - 724.
[10] Dhali B, Bhattacharya S, Ganguly R, Bandyopadhyay S, Mondal M, Dutta M. A randomized trial of intravenous labetalol and oral nifedipine in severe pregnancy - induced hypertension. Int J Reprod Contracept Obstet Gynecol.2012; 1: 42.