ORIGINAL RESEARCH PAPER

Volume-7 | Issue-3 | March-2018 | PRINT ISSN No 2277 - 8179

INTERNATIONAL JOURNAL OF SCIENTIFIC RESEARCH

COMPARATIVE EVALUATION OF ORAL NIFEDIPINE VERSUS INTRAVENOUS LABETALOL FOR ACUTE BLOOD PRESSURE CONTROL IN SEVERE PRE-ECLAMPSIA.

Gynaecology

Sandhya Deora* MD *Corresponding Author

Reena Pal MD

ABSTRACT

Objective: To compare oral nifedipine versus intravenous labetalol for acute blood pressure control in severe pre-eclampsia.
Design: Randomised prospective comparative study.
Setting: Government Doon Medical College, Dehradun.
Method: 100 pregnant women with severe hypertension (≥160/110 mm Hg) who required immediate BP control were randomised to receive either intravenous labetalol or oral nifedipine.
Main Outcome Measure: Time taken to achieve a blood pressure of ≤150/100 mm Hg.
Results: The mean time taken to achieve target BP with labetalol was 30.6±11.53 minutes (mean ± SD) as compared with 27.4±11.25 minutes in those who received nifedipine (p=0.0483).
Conclusion: Both oral nifedipine and intravenous labetalol are equally efficacious in acute control of BP, however, oral nifedipine may be preferred due to ease of administration, flat dosing regimen, wide availability and low cost.

KEYWORDS

Severe pre-eclampsia, labetalol, nifedipine, outcome.

INTRODUCTION

Hypertension complicates about 6-8% of all pregnancies. The widely accepted classification presently is International Society for the Study of Hypertension in Pregnancy (ISSHP) (Brown et al., 2001)[1]. According to this classification there are four categories

(1) Pre-eclampsia
(2) Chronic hypertension – essential or secondary
(3) Pre-eclampsia superimposed on chronic hypertension and
(4) Gestational/pregnancy induced hypertension.

Pre-eclampsia as per ISSHP[2] classification is defined as new onset hypertension of more than 140/90 mm of Hg after 20 weeks gestation, proteinuria more than 300mg/day or a spot urine protein/creatinine ratio ≥ 30 mg protein/mmol creatinine.

Severe pre-eclampsia/eclampsia with blood pressure readings > 160/110 mmHg is associated with increased risks of complications like hypertensive encephalopathy, intra-cranial hemorrhage and increased fetal morbidity and mortality. The reduction of BP to levels below 150/100 mmHg is necessary to reduce complications. The first line anti-hypertensive medications recommended for acute control of BP in severe pre-eclampsia are intravenous hydralazine, oral or intravenous labetalol and oral nifedipine[5].

Nifedipine is used in hypertension because of its easy availability, rapid onset of action, ease of oral administration and satisfactory reduction of blood pressure.

Intravenous labetalol[3] is also recommended as one of the first line agents in the management of acute severe hypertensive disorder of pregnancy. Intravenous labetalol can also be given where control of blood pressure is required in labor prior to cesarean section or when patient is in coma.

Labetalol though effective in controlling acute hypertension is expensive and requires iv administration. Nifedipine on the other hand is cost-effective, orally administered and has proved efficacious in BP control. Hence we sought to evaluate oral nifedipine versus intravenous labetalol regimens in their speed, efficacy and tolerability in the acute control of severe hypertension in pregnancy.

AIMS AND OBJECTIVES

OBJECTIVE

To assess the efficacy of intermittent intravenous labetelol versus oral nifedipine capsules in controlling BP in cases of severe pre-eclampsia with BP ≥160/110 mm of Hg.

PRIMARY OUTCOME

Time taken to achieve blood pressure ≤ 150/100 mm of Hg.

SECONDARY OUTCOME

- Total anti-hypertensive doses to achieve blood pressure ≤150/100 mmHg
- Crossover to alternative antihypertensive.
- Management at the end of trial—expedited delivery / unexpedited delivery / expectant management.
- Mode of delivery – cesarean / vaginal
- Occurrence of Atonic PPH
- Neonatal outcome—
- Apgar score
- NICU admission
- Reported side effects—nausea, vomiting, dizziness, palpitations, headache, chest pain or others.

METHODS AND MATERIALS

The study group consisted of 100 women in late pregnancy with severe hypertension, (according to International Society for the Study of Hypertension in Pregnancy (ISSHP)[2]) who required acute blood pressure control.

STUDY DESIGN: A randomized prospective comparative clinical study in a tertiary care teaching hospital.

PLACE OF STUDY: Department of Obstetrics and Gynecology, **Govt Doon Medical College**, Dehradun.

Duration of study: 1st July 2016 to 31st Dec 2016

Antihypertensive drugs used in the study:
Injection labetalol 20 mg
Capsule nifedipine 10 mg

All the women were inpatients. Each participant's details along with their hospital registration number was recorded and entered into the proforma designed for the study.

Each subject was informed about the nature of the study and informed and written consent was taken.

Detailed history including obstetric and menstrual history with special attention to hemorrhagic disorders, thromboembolic episodes, epilepsy, hepatic or renal disorders and drug intake was taken. Complete clinical examination including the systemic and obstetrical examination was done.

INCLUSION CRITERIA

- Women with ≥ 24 weeks of gestation with blood pressure 160/110 mmHg or more

- Maternal heart rate between 60 and 120 beats per minute

EXCLUSION CRITERIA
- H/o cardiac disease
- H/o bronchial asthma
- H/o hematological disorder
- H/o allergy to labetalol or nifedipine
- Diabetes
- Pre-existing liver and kidney disease
- Maternal heart rate <60 or >120 bpm

Randomization and Group allocation
After thorough history taking and complete examination, women were randomly allocated into two groups by lottery system.

Regimen A: Women randomized to intravenous labetalol, received 20 mg initially, followed by escalating doses of 40mg, 80 mg, and then 80mg every 20 min until the therapeutic goal BP systolic ≤150 mmHg and diastolic ≤100 mm of Hg was achieved, or for a maximum of five doses (300 mg).

Regimen B: Women randomized to oral nifedipine received 10 mg initially, followed by 20 mg every 20 minutes for up to a maximum of 5 doses (90 mg) or until the goal BP was achieved.

All investigations including routine and pertaining to pre-eclampsia were done. Participants were rested in bed in semi-recumbent position. BP was obtained with a mercury sphygmomanometer, taking the disappearance of korotkoff V sound for the diastolic blood pressure. The measurement of BP was continued every 20 minutes for at least 60 minutes or longer until the target BP was achieved. Once the BP was ≤150/100 mmHg, no further study medication was given.

During the course of treatment with study drugs, the fetal heart rate along with maternal pulse and BP was monitored. Primary and secondary outcomes were recorded.

OBSERVATION AND RESULTS
TABLE 1: SOCIO-DEMOGRAPHIC CHARACTERISTICS

Characteristic	Labetalol (n=50)	Nifedipine (n=50)
Age(in years)	25.43	25.22
Parity(%) • Nullipara • Multipara	22 28	24 26
Mean Gestational Age(weeks)	37.36	37.50
MgSO4 administered (%)	6	4
IUD at the time of presentation (%)	3	4

TABLE 2: Outcomes of randomised study of oral nifedipine vs intravenous labetalol for acute blood pressure control in hypertensive crisis in pregnancy

	Randomised to labetalol (n=50)	Randomised to nifedipine (n=50)	P value
Primary outcome			
Time (minutes) taken to achieve target BP ≤150/100mmHg	30.6±11.53	27.4±11.25	0.05
Secondary outcomes			
Total antihypertensive doses to achieve target BP	1.53 (1-3)	1.37 (1-3)	0.06
Cross over to alternative antihypertensive	00	00	
Management			
-Expedited	28	23	
-Unexpedited	20	25	
-Conservative	2	2	
Mode of Delivery			
-Cesarean	17	16	
-Vaginal	31	32	
Apgar Score at 5 min			
-≥7	38	43	
-<7	10	5	
NICU admission	10	5	
PPH	5	6	
Sudden hypotension	0	1	
Reported side effects			
-Nausea	3	1	
-Vomiting	4	1	
-Dizziness	2	3	
-Headache	2	4	
-Palpitations	2	3	
-Chest pain	0	1	
-Shortness of breath	0	1	

DISCUSSION
MEAN TIME TO ACHIEVE TARGET BP (IN MINUTES)

TABLE 3.

	LABETALOL	NIFEDIPINE
Vermillion et al(1999)[6]	43.6	25
Raheem et al(2011)[7]	45	30
Dhali et al(2012)[8]	48	28.2
Shekhar et al(2013)[9]	60	40
Lakshmi et al(2013)[10]	Less	More
Present study	30.6	27.4

In the study by Vermillion et al(1999)[6], target systolic BP was higher but the diastolic BP similar to the present study (160/100 mmHg versus 150/100 mmHg) indicating more difficult to achieve target BP in our study. All the patients in our study were undelivered at the time of enrolment, whereas Vermillion included postpartum subjects. This is an important difference as almost two-thirds of our patients had their delivery expedited very shortly after achieving blood pressure control. In study by Lakshmi et al (2013)[10], they concluded that intravenous labetalol is more effective in reducing systolic BP, diastolic BP and MAP to target ends with lower number of doses. This difference in results may be due to the fact, that in their study oral nifedpine was given 10 mg followed by 10 mg every 30 minutes compared to our study where 10 mg dose of oral nifedipine was followed by 20 mg for four more doses and time interval between two doses was 20 minutes.

In the present study, 67% of the women in nifedipine group achieved target BP in single dose and 29% in two doses, whereas, 51% of the women in labetalol group achieved target BP in single dose and 45% in two doses. This is comparable to the study by Shekhar et al (2013)[9], where the mean dose to achieve target BP were 2 and 3 in case of nifedipine and labetalol respectively.

Target BP was achieved within five doses in both the groups with no failure and hence, no crossover treatment was required in the present study. This is comparable to the studies of Vermillion et al (1999)[6] and Dhali et al (2012)[8] who reported 100% success rate in achieving the target BP with both drugs.

The NICU admission rate in labetalol group (20%) and nifedipine group (10%) was comparable. The results of fetal outcome in terms of NICU admission were comparable to the study of Vermillion et al(1999)[6], Raheem et al(2011)[7], Dhali et al(2012)[8] and Shekhar et al(2013)[9]. In our study, the side effect profiles of both the drugs were same and this is consistent with the observations of previous studies. We did not witness any serious adverse maternal or neonatal effects attributable to either of the study medications per se. Minor side effects were infrequent and comparable among both the groups.

CONCLUSION
We concluded that both oral nifedpine and iv labetalol are equally efficacious in acute control of BP and side effects in both the groups were comparable. However, oral nifedipine may be preferred due to ease of administration, flat dosing regimen, wide availability and low cost.

REFERENCES

1. Brown, M.A., Lindheimer, M.D., de Swiet, M., Van Assche, A. and Moutquine, J.M. (2001). The classification and diagnosis of hypertensive disorders of pregnancy. Hypertens Preg, 20:9-14.
2. International Society for the Study of Hypertension in Pregnancy : www.isshp.org. : The definition of preeclampsia , severe and early onset preeclampsia.
3. Burnton, L.L., Lazo, J.S., and Parker, K.L. [Eds] (2006). Goodman and Gilman's The Pharmacological Basis of Therapeutics. 11thed. New Delhi: McGraw-Hill Companies, Inc.

4. National Institute of Health and Clinical Excellence. Hypertension in Pregnancy, The management of hypertensive disorders during pregnancy. Clinical guidelines CG107 Issued: August 2010. Accessible on http://guidance.nice.org.uk/CG107. Last accessed 26 December 2010.
5. Magee LA, Cham C, Waterman EJ, Ohlsson A, von Dadelszen P. Hydralazine for treatment of severe hypertension in pregnancy: meta-analysis. BMJ 2003;327:955–60.
6. Vermillion ST, Scardo JA, Newman RB, et al: A randomized, double-blind trial of oral nifedipine and intravenous labetalol in hypertensive emergencies of pregnancy. Am J Obstet Gynecol 1999; 181:858–861
7. Raheem IA, Saaid R, Omar S Z. Oral nifedipine versus intravenous labetalol for acute blood pressure control in hypertensive emergencies of pregnancy: a randomized trial: BJOG 2011; DOI: 10.1111/j.1471-0528.2011.03151.x(E pub ahead of print)
8. Dhali B, Bhattacharya S, Ganguly RP, Bandyopadhyay S, Mondal M, Dutta M, et al. A randomized trial of intravenous labetalol & oral nifedipine in severe pregnancy induced hypertension. Int J Reprod Contracept Obstet Gynecol 2012;1:42-6.
9. Shekhar S ; Hypertensive emergency: Nifedipine vs labetalol : VOL. 122, NO. 5, NOVEMBER 2013
10. Lakshmi B.S and Dasari P : Oral nifedipine versus intravenous labetalol in hypertensive urgencies and emergencies of pregnancy: a randomized clinical trial. Obstetric medicine, 02/06/13.