International Journal of Multidisciplinary Research and Development
Online ISSN: 2349-4182 Print ISSN: 2349-5979
www.allsubjectjournal.com
Volume 2; Issue 11; November 2015; Page No. 550-553

Role of oral nifedipine in severe hypertension in pregnancy in comparison with intravenous labetalol in terms of drug efficacy

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Abstract

Objective: To compare oral nifedipine with intravenous labetalol in rapidity of control of blood pressure in severe hypertension in pregnancy in terms of drug efficacy.

Study Design: A randomized clinical trial conducted at Department of Obstetrics and Gynaecology, King George hospital, Visakhapatnam.

Methods and Material: All antenatal mothers above 22 weeks period of gestation diagnosed as severe hypertension i.e. blood pressure > 160/110 mmHg are taken into the study. A total of 40 patients are randomly divided into two groups. Group-A received oral nifedipine 10mg tablets initially followed by 20mg (10, 20, 20, 20, 20mg) upto five doses every 20 minutes or until the target blood pressure of 150/100 mm of hg was achieved. Group-B received intravenous labetalol 20mg initially followed by 40mg in escalating doses (20, 40, 80, 80, 80mg) upto five doses every 15 minutes or until the target blood pressure was achieved. Crossover treatment was effected if initial treatment regimen was unsuccessful.

Result: The median time taken to achieve the target blood pressure was 30 minutes for oral nifedipine and40 minutes for intravenous labetalol. No crossover treatment was required in either group.

Conclusion: Both oral nifedipine and intravenous labetalol are similarly effective in control of severe hypertension in pregnancy.

Keywords: hypertension, labetalol, Nifedipine, efficacy.

1. Introduction

Hypertension complicates 5-10% of pregnancies (3). Hypertension is the most frequently encountered medical disorders of obstetrics and remain major cause of maternal , fetal and neonatal morbidity & mortality not only in less developed but also in industrialized countries. According to WHO systemic review on maternal mortality worldwide, hypertension remains a leading cause of direct maternal mortality.

Hypertension in pregnancy is defined as {as per National High Blood Pressure Education Program Working group (NHBPEP) and the American College of Obstetrician and Gynaecologists (ACOG) [1-3].1,2,3)}

1. Systolic blood pressure greater than or equal to 140mm hg and/or
2. Diastolic blood pressure greater than or equal to 90mm hg.

Hypertensive disorders of pregnancy are classified as [2-4]

1. Gestational hypertension: defined as new onset hypertension presenting after 20 weeks, during labour, or in first 24 hour postpartum without significant proteinuria, in previously normotensive non protein uric women.
2. Preeclampsia: defined as new onset hypertension presenting after 20 weeks with significant proteinuria greater than 0.3g/L in a 24 hour urine collection or 1+ by quantitative urine examination.
3. Eclampsia: defined as convulsive condition associated with preeclampsia.
4. Chronic hypertension: hypertension that is present at the booking visit or before 20 weeks or if the women is already on antihypertensive medication when referred to maternity services. It may be essential or secondary.
5. Preeclampsia with superimposed chronic hypertension: diagnosed when one or more features of pre-eclampsia (e.g. elevated liver enzymes, low platelets, proteinuria) develop for first time during pregnancy after 20 weeks, in a women with pre-existing chronic hypertension.

According to NICE guidelines, for the purpose of management, hypertension is further divided as per severity into

1. Mild
2. Moderate
3. Severe

Table 1

	Mild	Moderate	Severe
Systolic BP(mmHg)	140-149	150-159	≥160
Diastolic BP(mmHg)	90-99	100-109	≥110

Classification of antihypertensive in pregnancy [2, 7]

1. Beta Blockers: They act by competing with endogenous catecholamines for the beta adrenergic receptors. Beta blockers are ideal for the majority of patients with chronic hypertension and pregnancy.

Propranolol is an effective drug for the treatment of chronic hypertension.

Atenolol is selective beta-1 adrenergic blocking agent, but it has been associated with fetal growth restriction and is not used often during pregnancy.
Labetalol is a selective α1 and nonselective β blocker. Due to its low rate of adverse effects and good efficacy, labetalol is a good option for first line treatment of chronic hypertension.

2. Calcium Channel Blockers: Nifedipine
Nifedipine is a calcium channel blocker that impedes the influx of calcium into vascular smooth muscle cells, causing vascular relaxation and decreasing PVR.

3. Centrally Acting Adrenergic Agonist: Methyldopa
Methyldopa induces synthesis of alpha-methyl norepinephrine which stimulates alpha receptors and decreases sympathetic outflow from central nervous system. The most common side effect is postural hypotension, excessive sedation, depression.

4. Peripheral Vasodilator: Hydralazine
It is vasodilator which acts directly on the smooth muscle fibers of arterial circulation. The main obstetric use is to rapidly lower blood pressure in patients with severe pre-eclampsia and hypertensive crisis.
Royal College of Obstetrician and Gynaecologist (RCOG) [14] in their green top guidelines recommend the following drugs for rapid lowering of blood pressure in severe hypertension
1. Labetalol
2. Nifedipine
3. Hydralazine

Labetalol
Labetalol[9] is a competitive antagonist at both alpha and beta adrenergic receptor site. It is non-selective for β1 and β2 receptors but selective for α receptors. It is absorbed orally and extensively metabolized in liver and excreted by conjugation with glucoronic acid. Half-life is 2.5-8 hours. Side effects are gastrointestinal disturbances, dryness of mouth, fluid retention. Contraindicated in COPD, bronchial asthma, severe cardiac failure, cardiogenic shock, severe bradycardia, first degree heart block.

Dosage: It can be given by intravenous infusion- continuous or intermittent or oral tablets.
For intermittent dosing, 20 mg should be given intravenous bolus initially over a 2-minute period. Additional doses of 40-80mg may be given at 20-minute intervals. It is recommended not to exceed 220mg per treatment cycle. The maximum effect of IV labetalol is usually reached 5-minute after injection.

Nifedipine
Nifedipine [10-13] belongs to dihydropyridine calcium channel blocker of L-type voltage sensitive calcium channel. It acts by decreasing PVR. It is rapidly absorbed after oral administration and reaches peak level 30-minutes after ingestion. Metabolized in plasma and kidney. Half-life is 2-5 hours. Side effects are palpitation, headache, flushing, ankle edema, hypotension. The risk of neuromuscular blockade with concomitant use of magnesium sulphate.
Dosage. The NHBPEP Working group (2000) and RCOG (2006) recommend a 10 mg initially oral dose to be repeated after 30 minutes if necessary [3, 4].

Hydralazine
Hydralazine acts directly on arteriolar smooth muscle to reduce PVR. It is administered in intravenous boluses, starting at 5mg and increasing every 20minutes up to 20mg. The most frequent side effect is decreased utero placental insufficiency and hyper dynamic circulation. Hydralazine causes more maternal tachycardia and palpitations. For this reason a meta-analysis of randomized clinical trials using hydralazine for treatment of severe hypertension in pregnancy concluded that the evidence does not support the use of this agent when compared to labetalol and Nifedipine(2).
Among commonly used drugs in severe hypertension in pregnancy, both Nifedipine and labetalol have demonstrated comparable efficacy in various randomized trials [19].So the present study was done to compare efficacy of oral nifedipine and intravenous labetalol in severe hypertension in pregnancy [5, 6].

Methods and Materials
The present study is a randomized clinical trial conducted at Department of Obstetrics & Gynaecology, King George Hospital, Visakhapatnam attending labour room with >22 weeks period of gestation with severe hypertension in pregnancy (blood pressure ≥160/110 mm of hg) for a period of 6 months i.e. January 2015 to June 2015. Excluded were hypertension diagnosed before 20 weeks period of gestation / chronic hypertension / any systemic diseases causing hypertension / bronchial asthma / known heart disease. A total of 40 patients were randomly allocated in each group of 20.
In group-A, all the patients received nifedipine tablets orally 10mg initially, with repeated doses of 20mg every 20 minutes upto a maximum of five doses or until the target blood pressure of blood pressure <150/100mm of hg was achieved. In group-B, all the patients received intravenous labetalol 20mg initially followed by escalating doses of 40mg, 80mg then 80mg every 15minutes upto a maximum of five doses or until target blood pressure was achieved. It was decided, if the target blood pressure was not achieved after five doses, cross over treatment was done. However in our study, no case required any cross over treatment.
The primary outcome is to measure the time required to achieve the target blood pressure of <150/100mm of hg. The secondary outcome is to measure the maternal side-effects like headache, palpitations, chest pain, dizziness, nausea & vomiting and fetal heart rate changes.

Results

Table 2: Total number of patients studied (N=40)

Group-A (Oral nifedipine)	Group-B (Intravenous labetalol)
Target blood pressure was achieved after 1st dose(n=8) 40% 2nd dose(n=10) 50% 3rd dose(n=2) 10% 4th dose(n=0) 0% 5th dose(n=0) 0%	Target blood pressure was achieved after 1st dose(n=6) 30% 2nd dose(n=10) 50% 3rd dose(n=4) 20% 4th dose(n=0) 0% 5th dose(n=0) 0%
The median time required to reach the target blood pressure was 30 minutes.	The median time required to reach the target blood pressure was 40 minutes.

Table 3: Comparison of maternal side effects:

Group-A (nifedipine)	Group-B (Labetalol)
Headache n=4	Headache n=0
Dizziness n=5	Dizziness n=0
Palpitations n=1	Palpitations n=0
Chest pain n=0	Chest pain n=0
Nausea & vomiting n=0	Nausea& vomiting n=0

Table 4: Comparison of fetal effects:

Group-A (nifedipine)	Group-B (Labetalol)
No fetal heart rate changes.	No fetal heart rate changes.

Discussion

The Cochrane review on drugs for treatment of very high blood pressure in pregnancy concluded that until better evidence is available, the choice of antihypertensive should depend on the clinician′s experience and familiarity with a particular drug and on what is known about adverse effects. Our data indicate that both oral nifedipine and intravenous labetalol are effective in controlling severe hypertension in pregnancy. Both regimens are rapidly effective, with the target blood pressure achieved in 100% of cases within five doses or within 60 minutes of commencing treatment. Our data supports the recent guidelines aged expert opinion that oral nifedipine and intravenous labetalol are suitable first-line antihypertensive for hypertensive emergencies of pregnancy.

We set a target blood pressure of ≤150/100 mmHg for our patients, with the dosing regimen to be stopped once the goal is achieved. This target blood pressure is in keeping with Sibai′s suggestion to keep systolic blood pressure between 140 and 155 mmHg and diastolic blood pressure between 90 and 105 mmHg in severe pre-eclampsia[15]. Our target blood pressure is also consistent with the Cochrane review [16, 17] on antihypertensive drugs in pregnancy, which concluded that it remains unclear whether antihypertensive drug therapy for mild to moderate hypertension is worthwhile, as our target blood pressure ≤150/100 mmHg is well within the definition of moderate hypertension.

Table 5: Comparison of nifedipine and labetalol in various studies in terms of efficacy.

	Labetalol	Nifedipine
B.N.C. Pritchards	Equally efficacious	Equally efficacious
Sibai study	Efficacious	Efficacious
E.M. Symmonds & G.D. Lamming	Lowers BP satisfactorily	Efficacious
Present study	Efficacious	Efficacious

Conclusion

The present study is a randomized clinical trial conducted at King George Hospital. Several therapeutic regimens have been used for control of hypertension in pregnancy, but selection of an appropriate drug is difficult because no proper data is available on relative effectiveness and safety of various antihypertensive both on mother and fetus.

1. In the present study, efficacy of oral nifedipine and intravenous labetalol were compared. Both were found to be equally efficacious in rapidity of controlling blood pressure in severe hypertension in pregnancy.
2. Nifedipine resulted in complications like headache, dizziness, palpitations, but labetalol did not resulted in any complications.
3. Both the drugs were found to be safe for the fetus.
4. Both intravenous labetalol and oral nifedipine are efficacious in the control of hypertension. Selection of drug is to be individualized as per requirement.

References

1. James DK. High risk pregnancy, 3rd edition 772, 773, 777, 781.
2. Fernando arias, Shirish and Daftary, Amarnath Gbhide practical guide to high risk pregnancy, 3rd edition 414, 419, 421, 424.
3. GARY Cunninham F, Md Kenneth Leveno J, Steven Bloom L. Williams Obstetrics, 23RD edition, 706, 708, 707, 725.
4. Burrow, Duffy, Copel- medical complications during pregnancy, 6th edition, chapter-3 43, 44, 45.
5. American medical journals of obstetrics & gynaecology, Comparison of oral nifedipine and labetalol in hypertension. 8(4), 858-861.
6. American medical journal, Hemodynmic evaluation of nifedipine and labetalol in pre-eclampsia. 18(4), 862-866.
7. Basic and clinical pharmacology, 9th edition. Betram G. Katzung. Anti hypertensive agents, 165-176.
8. Text book of obstetrics including perinatology & contraception, 7th edition 219, 220, 221, 227, 239. Etiology, pathophysiology, management of PIH & chronic hypertension.
9. Journal of clinical pharmacology, Effectiveness of labetalol as an antihypertensive. 33(10), 979-988.
10. Lurie S, Fenakel K, Friedman A. Effect of nifedipine on fetal heart rate in the treatment of severe pregnancy induced hypertension. Am J Perinatol. 1990; 7:285-6.
11. Scardo JA, Vermillion ST, Hogg B, Newman RB. Hemodynamic effects of oral nifedipine in pre-eclamptic hypertensive emergencies in pregnancy. Am J Obstet Gynecol. 1996; 175:336-8.
12. Seabe SJ, Moodley J, Becker P. Nifedipine in acute hypertensive emergencies in pregnancy. S Afr Med J 1989; 76:248-50.
13. Walters N, Redman W. Treatment of severe pregnancy associated with hypertension with calcium antagonist nifedipine. Br J Obstet Gynecol 1987; 91:330-4.
14. The Royal College of Obstetrics and Gynaecology, United Kingdom. Green Top Guideline No. 10 (A). The management of severe pre-eclampsia/eclampsia, March, 2006. Accessible online www.rcog.org.uk/files/rcog-corp/uploaded-files/GT10aManagementpreeclampsia2006.pdf.
15. Sibai BM. Diagnosis and management of gestational hypertension and preeclampsia. Obstet Gynecol 2003; 1-2:181-92.
16. Duley L, Henderson-Smart DJ, Meher S. Drugs for treatment of very high blood pressure during pregnancy. Cochrane Database Sys Rev 2006; 3:CD001449.
17. Abalos E, Duley L, Steyn DW, Henderson-Smart DJ. Antihypertensive drug therapy for mild to moderate hypertension during pregnancy. Cochrane Database SYS rev 2007; 1:CD00252.

18. 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.or.uk/CG107. Last accessed 26 December, 2010.
19. Vermillion ST, Scardo JA, Newman RB, Chauhan SP. A randomized/double-blind trial of oral nifedipine and intravenous labetalol in hypertensive emergencies of pregnancy. Am J Obbstet Gynecol 1999; 181:862-6.