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COMPARATIVE EVALUATION OF ORAL NIFEDIPINE VERSUS INTRAVENOUS LABETALOL FOR ACUTE BLOOD PRESSURE CONTROL IN CASES OF SEVERE PREGNANCY INDUCED HYPERTENSION

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ABSTRACT

Hypertension is the most frequently encountered medical disorder in obstetrics practice & remain a major cause of maternal, fetal & neonatal morbidity & mortality **AIMS AND OBJECTIVES** To assess the effectiveness & safety of oral Nifedipine & intravenous Labetalol in terms of time , dose required to achieve target Blood pressure and side effects in severe PIH **METHODS** The study was a hospital based prospective randomized comparative study conducted in Obstetrics & Gynaecology department of Teerthanker Mahaveer Medical College & Research Centre, Moradabad, Uttar Pradesh , India .The study population comprised of pregnant women more than 20 weeks of gestation with blood pressure reading ≥160/110 mmHg who fulfilled the inclusion criteria **RESULTS** - In Nifedipine group majority of the patients took single dose to achieve the target BP (64.1%) while in Labetalol group 44.7% patients took two doses to achieve target blood pressure and the mean time required to reach target blood pressure was 28.72 ± 12.81 minutes in the Nifedipine group and 36.32±16.67 minutes in the Labetalol groups.**CONCLUSION** - Both the Labetalol & Nifedipine regimen are equally effective & well tolerated when used for the rapid control of blood pressure in severe hypertension in pregnancy with its minimal side effects and better tolerability without having severe adverse maternal and fetal effects. But Nifedipine may be preferable as in a limited resource setting, oral Nifedipine is cheap and easily available drug so it can be preferable in these settings.

KEYWORDS

Severe Pregnancy Induced Hypertension ,Labetalol , Nifedipine

INTRODUCTION

Hypertension is the most frequently encountered medical disorder in obstetrics practice & remain a major cause of maternal, fetal & neonatal morbidity & mortality not only in less developed but also in the industrialized countries.[1]The impact due to hypertensive disorders in pregnancy on maternal and neonatal mortality and morbidity is very high in India and other developing countries.[2,3]Hypertensive disorders of pregnancy accounts for 5% to 10% of all pregnancies, and together they are one member of the deadly triad - along with haemorrhage and infection.[4] According to World Health Organization at least a woman dies every seven minutes from complications of hypertensive disorders of pregnancy.[5] Prevalence of hypertensive disorders of pregnancy was 7.8% with preeclampsia in 5.4% of the study population in India.[6]

National institute for health and clinical excellence has defined severe hypertension in pregnancy as systolic blood pressure 160 mmHg or greater, diastolic blood pressure 110 mmHg or greater.[7]The spectrum of hypertensive diseases that can complicate pregnancy are broad ranging from gestational hypertension, preeclampsia, chronic hypertension and chronic hypertension with superimposed pre-eclampsia.[8]Preeclampsia, a multisystem disorder defined as hypertension of 140/90mmHg or more associated with significant proteinuria (≥30mg/dl in random urine samples or >300mg/24hrs urine or on dipstick 1+ or more proteinuria), usually develops after 20weeks of gestation.[8]Severe pre-eclampsia/eclampsia with blood pressure reading ≥160/110 mmHg is a disease of multiple organ system that is unique to pregnancy can cause maternal complications like Eclampsia, HELLP syndrome, acute renal failure, cerebrovascular accidents etc. It has effect on the fetus like fetal growth restriction, oligohydramnios, and fetal distress. As per NICE clinical guideline 107 - Hypertension in Pregnancy the first line antihypertensives which can be used in severe pregnancy induced Hypertension are Labetalol (Oral/intravenous), Hydralazine (intravenous) or Nifedipine (oral). Of those we had chosen i.v. Labetalol and oral Nifedipine for controlling the acute blood pressure in severe pregnancy induced hypertension.[9]

AIM

Comparative evaluation of oral Nifedipine versus intravenous (i.v.) Labetalol for acute blood presure (B.P.) control in cases of severe pregnancy induced hypertension (PIH).

OBJECTIVES

To assess the effectiveness & safety of oral Nifedipine & i.v. Labetalol in terms of time , dose required to achieve target B.P. and side effects in severe PIH

INCLUSION CRITERIA:1.Women with ≥ 20 weeks of period of gestation with blood pressure ≥160/110 mm of Hg.2.Maternal heart rate between 60-120 beats per minute.

EXCLUSION CRITERIA: History of Cardiac disease , Bronchial asthma , Allergy to Labetalol or Nifedipine , Severe hepatic & renal diseases , haematological disorders , Patients with essential hypertension , Eclampsia.

METHODOOGY: The study was a hospital based prospective randomized comparative study conducted in Obstetrics & Gynaecology department of Teerthanker Mahaveer Medical College & Research Centre , Moradabad, Uttar Pradesh , India , over a period from december 2017 to july 2019. It this study,80 pregnant women more than 20 weeks of gestation with severe pregnancy induced hypertension (according to ISSHP) – who required acute Blood pressure control were randomly divided into two groups of 40 each– Group L (Labetalol group)- i.v. labetalol 20 mg initially followed by accelerating doses of 40 mg, 80 mg & 80 mg (maximum of 4doses = 220mg) every 20 minute or until target blood pressure was achieved [16-19]; and Group N (Nifedipine group)- oral nifedipine 10 mg initially followed by 20 mg every 20 minutes for upto maximum of 5 doses(90 mg) or until target blood pressure was achieved. [16-19]

After informed consent had been obtained, a thorough history was taken. A detailed general, systemic and obstetric examination was carried out. Necessary laboratory investigations were done. Assessment of fetal wellbeing was carried out by clinical and ultrasonic evaluation. Patients were randomly allocated into two, 40

patients in each groups, Group L and Group N. Women were randomly assigned to be started either with i.v. labetalol or oral nifedipine until satisfactory BP control was achieved (≤150/100 mmHg).During the study period maternal blood pressures was recorded at every 20 minutes interval till achievement of target blood pressure (≤150/100 mmHg), then every 20 minutes for next 2 hours then every hourly till the BP was settled. In case of treatment failure (blood pressure not decreasing with maximum dose of either drug), drug regime was to be crossed over.

During the course of the study maternal and fetal heart rate was recorded every 20 minutes. Any side effects related to the drugs were recorded.

Outcomes were observed taking into account the following observations:

- Time taken to achieve target B.P. ≤ 150/100 mm Hg
- Total antihypertensive doses to achieve the target blood pressure ≤150/100 mm Hg
- Cross over to alternate anti-hypertensive to achieve acute control of Blood pressure
- Reported side effects like nausea, vomiting, dizziness, chest-pain, palpitation,headache etc.

DATA ENTRY AND STATISTICAL ANALYSIS:- Data were analyzed and statistically evaluated using SPSS-PC-20 version.

ETHICAL CONSIDERATIONS:-The protocol of the thesis was approved by the ethical & research committee of Teerthanker Mahaveer Medical College & Research Centre, Moradabad, Uttar Pradesh, India.

OBSERVATION AND RESULTS

The observations and results of the study are presented as below.

Table-1: Distribution of patients according to age between the groups

Age in years	Group N (n=40)		Group L (n=40)		p-value1
	No.	%	No.	%	
20-25	15	37.5	22	55.0	0.19
26-30	10	25.0	11	27.5	
31-35	14	35.0	7	17.5	
>35	1	2.5	0	0.0	
Mean±SD	28.30±4.53 years	26.25±4.48 years	0.05		

1Chi-square test

Table-2: Comparison of gravidity between the groups

Gravidity	Group N (n=40)		Group L (n=40)		p-value1
	No.	%	No.	%	
Primi	16	40.0	19	47.5	0.58
G2	10	25.0	10	25.0	
G3	7	17.5	8	20.0	
≥G4	7	17.5	3	7.5	

1Chi-square test was used

Table-3: Distribution of patients according to gestational age at time of presentation between the groups

Gestational age in weeks	Group N (n=40)		Group L (n=40)		p-value1
	No.	%	No.	%	
<28 weeks	1	2.5	1	2.5	0.25
28-34 weeks	11	27.5	15	37.5	
35-37 weeks	13	32.5	17	42.5	
>37 weeks	15	37.5	7	17.5	

1Chi-square test was used

Table-4: Comparison of presenting symptoms between the groups

Presenting symptoms#	Group N (n=40)		Group L (n=40)		p-value1
	No.	%	No.	%	
Headache	38	95.0	35	87.5	0.23
Epigastric pain	15	37.5	13	32.5	0.63
Vomiting	15	37.5	17	42.5	0.64
Blurring of vision	17	42.5	13	32.5	0.35

1Chi-square test, #Multiple response

Table-5: Comparison of biochemical parameters between the groups

Biochemical parameters	Group N (n=40)		Group L (n=40)		p-vlue1
	Mean	SD	Mean	SD	
Platelet count lkh/mm3	1.72	0.76	1.46	0.47	0.07
Uric acid	6.53	1.81	6.55	1.48	0.94
S. creatinine	0.76	0.22	1.80	4.59	0.18
B. urea	25.11	8.86	22.47	9.77	0.22
SGOT	37.66	25.68	50.45	31.58	0.06
SGPT	27.26	21.95	43.43	26.02	0.06
ALP	247.83	118.09	217.35	67.30	0.16
LDH	1199.25	1255.86	717.00	76.37	0.63

1Unpaired t-test

.

Table-6: Comparison of mean time to achieve target BP

Mean time to achieve target BP	Group N (n=39)		Group L (n=38)		P value
	Mean	SD	Mean	SD	
Mean time to achieve target BP (min)	28.72	12.81	36.32	16.67	0.02

Table-7: Comparison of mean total dose required to achieve target BP

Mean total dose required to achieve target BP	Group N (n=39)		Group L (n=38)		P value
	Mean	SD	Mean	SD	
Mean total dose required to achieve target BP	1.44	0.64	1.82	0.83	0.02

Table-8: Cross over treatment of drugs between the groups

Crossover treatment	Group N		Group L		p-value1
	No.	%	No.	%	
Yes	1	2.5	2	5.0	0.98
No	39	97.5	38	95.0	

In present study 1 patient in group N and 2 patients in group L required crossover treatment.

Table-9: Comparison of side effects between the groups

Side effects	Group L (n=40)		Group N (n=40)		P value
	No.	%	No.	%	
Postural hypotension	0	0.0	2	5.0	0.49
Drowsiness	11	27.5	3	7.5	0.03
Nausea	1	2.5	2	5.0	0.98
Palpitation	0	0.0	10	25.0	<0.001
Headache	5	12.5	7	17.5	0.53
Hypersensitivity	0	0.0	0	0.0	-

Constipation	0	0.0	0	0.0	-
Flushing (reddening of the skin)	0	0.0	3	7.5	0.24
Weakness	0	0.0	0	0.0	-
Dizziness	3	7.5	1	2.5	0.61
Cough	0	0.0	0	0.0	-
Shortness of breath	0	0.0	0	0.0	-
Edema	0	0.0	0	0.0	-
Heartburn	1	2.5	0	0.0	0.98
Muscle cramps	0	0.0	0	0.0	-
Blue lips and fingernails	0	0.0	0	0.0	-
Chest congestion	0	0.0	0	0.0	-
Pain or discomfort in the arms, jaw, back, or neck	0	0.0	0	0.0	-
Fever	0	0.0	0	0.0	-
Sweating	3	7.5	1	2.5	0.61
Decreased urine output	2	5.0	0	0.0	0.49

DISCUSSION

Hypertension in pregnancy, called a disease of degree is more of a sign than a disease by itself. All patients were comparable with respect to demographic parameters (age, gravida and gestational age), presenting symptoms and signs.

In the present study almost all the patients were aged between 19-35 yrs. The mean age in group N was 28.30±4.53 years and in group L was 26.25±4.48 years. In following studies conducted the maternal mean age in both the group in Shekhar S et al[11] was 25.9 years, Swapan D et al[12] was 25.4 years while in Raheem IA et al[13] was 31.4 years as the distribution of age was from 20 to 40 years.

In our study maximum patients of severe pregnancy induced hypertension were primigravida in both the groups, 47.5% in the Labetalol group & 40% in the Nifedipine group followed by second gravida. Similar to our study, Gavit Y et al[10]also found maximum patients of severe pre-eclampsia were primigravida and second gravida in both the groups. This states that high incidence of pre-eclampsia found in primigravida. In other studies,also maximum patients of severe pre-eclampsia were primigravida as in study by Raheem IA et al[13] 36 (72.0%) out of 50 patients were primigravida, in ShekharS et al[11] study 58 out of 60 patients were primigravida, while in Swapan D et al[12]49 out of 100 patients were primigravida.

In present study, gestational age at presentation in most of the patients were >37 weeks of gestational age in group Nifedipine, while in group L maximum patients were between 35-37 weeks of gestational age. The analysis derived states that severe incidence in this study was higher in beyond later weeks of gestation. Gavit Y et al[10] also reported that most patients with pre-eclampsia belonged to 38-39 weeks of gestational age 57.5% in the Labetalol group and 50% in the Nifedipine group, followed by 37-38 weeks. The result found in other studies was Raheem IA et al[13], Shekhar S et al[11], Swapan D et al[12]shows period of gestation in IV Labetalol and Oral Nifedipine are 36.3-38.6 and 35-38.6, 36-38 and 37-38, 38-40 and 38-40 weeks respectively.

In our study, most common symptom reported by patients was headache (95.0% in group N & 87.5% in group L). Other presenting symptoms were blurring of vision (42.5% in group N & 32.5% in group L), vomiting (37.5% in group N & 42.5% in group L) and epigastric pain (37.5% in group N & 32.5% in group L).These are the impending signs of sever preeclampsia as reported by Peres GM et al. (20)

In present study Urine albumin was checked for all study subjects. 1+ and 2+ were most common finding seen in pregnant women with high BP. In 11 (27.5%) subjects in group N and 10 (25.0%) subjects in group L 3+ or more protein was seen in urine. Similar to our study Dalal N et al[15] also reported 1+ and 2+ as most common finding in both groups. Different biochemical tests like platelet count, uric acid, S. creatinine, Blood urea, SGOT, SGPT, ALP etc were also performed in our study in all study subjects. Both the group were comparable in these findings. No significant difference was observed between both groups. In most of the patients platelet count was less than 1.5 lakh/μL. In the study of Vrunda et al, mentioned that severity of disease and thrombocytopenia closely correlated, which indicates that thrombocytopenia is directly proportional to the severity of toxemia of pregnancy.[18]

In our study, mean time required to reach target blood pressure i.e. <150/100, was 28.72 ± 12.81 minutes in the Nifedipine group and 36.32±16.67 minutes in the Labetalol groups. This comparison showed significant difference between the two groups with a 'P' value of 0.02. Finding of our study was also similar to study by Alam A et al[16] in which oral nifedipine achieved target BP (≤150/100 mmHg) more rapidly in 26.25±12.60 minutes (Mean±SD), in comparison to 32.62±12.19 minutes (Mean±SD) with IV labetalol, (p=0.024). Study conducted by Vermillion ST et al[14] also found that nifedipine took significantly less time (mean±SD, 25±13.6 minutes) in comparison to labetalol group (43.6±25.4 minutes; P = 0.002) in achieving the target BP. In another study by Gavit Y et al[10], mean time required to control BP was 43±14.71 minutes in IV Labetalol groups and 28±10.90 minutes in Oral Nifedipine group. Another study by Sivaranjani et al[19] reported that mean time mean time required to control BP was 50.40±10.98 minutes in IV Labetalol groups and 47.01±5.77 minutes in Oral Nifedipine group. The results of studies conducted mean time required for IV Labetalol and oral Nifedipine to achieve BP 140/90 mm Hg in severe pre-eclampsia in Raheem IA et al[13] was 45 and 30 minutes, Shekhar S et al [11] was 60 and 40 minutes, respectively. While in Swapan D et al[12]was 47.2±13.5 minutes and 45.6±14.5 minutes. In study by Dhali B et al [1], patients received oral nifedipine achieved the goal therapeutic blood pressure more rapidly in 28.2±11.7 minutes (mean±SD) as compared with 48.4±23.5 minutes in those received intravenous labetalol (p=0.001).

In the present study, mean number of doses required to achieve target BP in Group N it was 1.44±0.64 and in Group L was 1.82±0.83with p value 0.02, which was statistically significant. So, oral nifedipine took significantly less number of doses in achieving target BP in comparison to intravenous labetalol. Similar to our study, Alam A et al[16] also reported that Oral nifedipine group required less number of doses to achieve the targ7t BP in comparison to IV labetalol (1.75±0.840 vs. 2.18±0.83). Shekhar S et al[11], also noted that significantly less number of doses of nifedipine was required to achieve target blood pressure compared to labetalol. In study by Sivaranjani et al[19], mean number of doses required in i.v. labetolol group was 2.16 and in nifedipine group was 2.04.

In group Nifedipine, most common side effect observed in our study was palpitation in 25.0% cases followed by headache (17.5%), drowsiness (7.5%), flushing (7.5%), postural hypotension (5.0%)and sweating (2.5%) while in labetalol group drowsiness was most common side effect (27.5%) followed by headache (12.5%), dizziness (7.5%) sweating (7.5%) and decreased urinary output (5.0%). Adverse effects occurred during treatment in our study with antihypertensive agents, were transient and tolerable. There were no maternal and fetal adverse events, which resulted in need for discontinuation of medication in present study. In study by Alam A et al[16], palpitation was seen in 2.5% of subjects in nifedipine group while headache and dizziness was observed in both group.In contrast to our study, Gavit Y et al[10] reported 2.5% patients had headache in each group while in the IV Labetalol group, 2.5% of the patients had postural hypotension, 5% of had drowsiness and 17.5% had palpitations. Another study by Sivaranjani et al[19] also reported headache as a side effect of Labetalol group in 4% subjects while in the Nifedipine group 4% of the patients had postural hypotension, palpitations were present in 12% in labetalol group and 4% in nifedipine group.

In present study 1 patient in group N and 2 patients in group L required crossover treatment while in study by Alam A et al[16], both the drugs were successful in achieving the target blood pressure within the study period and so no patients required crossover treatment.Vermillion ST et al[14], and Gavit Y et al[10], in their studies reported 100% success rate to achieve the target blood pressure with both drugs. In study by Shekhar S et al[11], Failure to achieve target BP occurred in five women (16.6%) randomized to labetalol compared with one woman in the nifedipine group (3.3%) so crossover treatment was given in these cases. Raheem IA et al[13] reported very high failure rate (20%) with both drugs and requiring crossover treatment whereas in study by Swapan D et al[12], 12% and 14% of patients in the Labetalol and Nifedipine group respectively required crossover therapy. The

Cochrane review[21] on drugs for the treatment of very high blood pressure in pregnancy conclude that until & unless better evidence is available the choice of antihypertensive should depend on the clinician's experience & familiarity with a particular drug, and its adverse effects.

CONCLUSION

Hypertensive disorders of pregnancy is one of the most common causes of high maternal death in India and globally as well. Management of hypertension in pregnancy is a challenging task, because drastic reduction of BP leads to utero placental insufficiency & that may lead to intrauterine fetal death and continuation of pregnancy with severe hypertension leads to adverse feto-maternal outcome. Neither of the drugs was associated with any hazardous effect on mother and fetus.From the results of our study we can well conclude that both the Labetalol &Nifedipine regimen are equally effective & well tolerated when used for the rapid control of blood pressure in severe hypertension in pregnancy with its minimal side effects and better tolerability without having severe adverse maternal and fetal effects. But Nifedipine may be preferable as it is a simple, flat dose and is an oral regimen. Also, in a limited resource setting, oral Nifedipine is cheap and easily available drug so it can be preferable in these settings.

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REFERENCES

1. Dhali B, Bhattacharya S, Ganguly RP, Bandyopadhyay S, Mondal M, Dutta M et al. A randomized trial of intravenous labetalol and oral nifedipine in severe pregnancy induced hypertension. Int J Reprod Contracept Obstet Gynecol. 2012;1:42-6.
2. Ray JG, Vermeculen M, Burrows E, Burrows R. Use of antihypertensive medication in pregnancy and the risk of adverse perinatal outcomes: McMaster outcome study of hypertension in pregnancy 2 (MOS HIP 2). BMC Pregnancy Childbirth. 2001;1:6-14.
3. Nakhai-Pour HR, Rey E, Berard A. Antihypertensive medication use during pregnancy and the risk of major congenital malformation or small-for gestational-age newborns. Birth Defects Res B Dev Reprod Toxicol. 2010;89(2):147-54.
4. Martin JN, Owens My, Keiser SD. Standardized Mississipi protocol treatment of 190 patients with HELLP syndrome: slowing disease progression and preventing new major maternal morbidity. Hypertens Pregnancy. 2012;31(1):79.
5. Von Dadelszen P, Magee L. What matters in preeclampsia is the associated adverse outcomes: the view from Canada. Current opinion in obstetrics and gynecology. 2008;20(2):110-5.
6. Fisher S, Roberts JM. The placenta in normal pregnancy and preeclampsia. In Taylor RN, Roberts JM, Cunningham FG (eds): Chesley's Hypertensive Disorders in Pregnancy, 4th Ed. Amsterdam, Academic Press; 2015.
7. Lo JO, Mission JF, Caughey AB. Hypertensive disease of pregnancy and maternal mortality. Curr Opin Obstet Gynecol. 2013.
8. Cunningham FG, Leveno KJ, Bloom SL, Hauth JC, Rouse DJ, Spong CY. Pregnancy Hypertension. Text Book of Williams Obstetrics. 23rd Edition, New York, McGraw Hill, 2010, p. 706-757.
9. NICE clinical guideline 107 - Hypertension in pregnancy : the management of hypertensive disorders during pregnancy. Issued August 2010 last modified : January 2011.
10. 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. Int J Reprod Contracept Obstet Gynecol. 2018;7:719-24.
11. 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.
12. Swapan D, Swagata B, Prakash D, Biswajit M. Comparative study of intravenous Labetalol and oral Nifedipine for control of blood pressure in severe preeclampsia. IOSR J Dental Med Sci. 2015;14(10):22-7.
13. Raheem IA, Saaid R, Omar SZ, Tan PC. Oral nifedipine versus intravenous labetalol for acute blood pressure control in hypertensive emergencies of pregnancy: a randomised trial. BJOG. 2012;119:78–85.
14. 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 Obstet Gynecol. 1999 Oct;181(4):858-61.
15. Nilesh Dalal, Dr. Somen Bhattacharjee and Dr. Mansi Tiwari. A comparative study of oral labetalol versus oral nifedipine in hypertensive disorders of pregnancy. International Journal of Clinical Obstetrics and Gynaecology 2019; 3(3):132-6.
16. Alam A, Zakaria SMA. Oral nifedipine versus intravenous labetalol for acute blood pressure control in hypertensive emergencies of pregnancy: a randomized controlled trial. Int J Reprod Contracept Obstet Gynecol. 2019;8:1921-7.
17. Weiner CP. Preeclampsia-eclampsia syndrome and coagulation. Clin Perinatol. 1991 Dec;18(4):713-26. Review.
18. Vrunda JK, Saila S. Lowered platelet count. A prognostic index in pregnancy induced hypertension. J Obstet Gynaecol Ind. 2004;54(3):235-236.
19. Sivaranjani BSV, Aruna V. Comparison of Efficacy of Intravenous Labetalol versus Oral Nifedipinein Control of Acute Hypertension in Severe Pre-Eclampsia/ Eclampsia. IOSR Journal of Dental and Medical Sciences (IOSR-JDMS). Volume 15, Issue 12 Ver. X (December. 2016), PP 71-74.
20. Peres GM, Mariana M, Cairrão E. Pre-Eclampsia and Eclampsia: An Update on the Pharmacological Treatment Applied in Portugal. J Cardiovasc Dev Dis. 2018 Mar;5(1):3.
21. Duley L, Henderson-Smart DJ, Meher S. Drugs for treatment of very high blood pressure during pregnancy (review). The Cochrane Collaboration, 2013, Issue – 7.