European Journal of Molecular & Clinical Medicine
ISSN 2515-8260 Volume 07, Issue 01, 2020

ORAL NIFEDIPINE VERSUS ORAL LABETALOL IN THE TREATMENT OF PREGNANCY INDUCED HYPERTENSION

Dr. R.P.Patange[1], Dr. Archna V. Rokadhe[2], Ghori R. Shinde[3], Sanjay N. Jadhav[4], Dr. Ashitosh Bahulekar[5]

[1]*Department Obstetrics and Gynaecology of Krishna Institute of Medical Sciences Karad - 415110, Maharashtra*

[2]*Department Obstetrics and Gynaecology of Krishna Institute of Medical Sciences Karad - 415110, Maharashtra*

[3]*Department Obstetrics and Gynaecology of Krishna Institute of Medical Sciences Karad - 415110, Maharashtra*

[4]*Department Obstetrics and Gynaecology of Krishna Institute of Medical Sciences Karad - 415110, Maharashtra*

[5]*Department Obstetrics and Gynaecology of Krishna Institute of Medical Sciences Karad - 415110, Maharashtra*

Abstract: This study was undertaken to determine the effectiveness of two anti-hypertensive drugs: oral Nifedipine and oral Labetalol in cases of extreme preeclampsia in terms of their side effect profile, BP regulation, time taken to lower BP, and number of doses required. The objective of the study was to calculate the time required to reduce the blood pressure to the target level of 90 / 100 mmHg diastolic and less than 160mmHg systolic.In the labetalol group the mean SBP before treatment was 158mm of Hg which was reduced to 140 mm of Hg. The decline rate in the labetalol group was 11.77%. This study proved that labetalol reduces the BP more effectively than nifedipine and also has minimal side effects with less frequent dosing schedule as compared to nifedipine thus indicating that labetalol is better than nifedipine in lowering the BP in cases of preeclampsia.

Keywords: Labetalol, Nifedipine, Hypertension, Pregnancy, Preeclampsia

1. INTRODUCTION

Hypertensive conditions during are very common in pregnancy and along with hemorrhage and infection shape a dangerous triad [1]. Preeclampsia has been defined as hypertension plus significant proteinuria. With preeclampsia, which is characterized by a diverse set of multiorgan processes and variable appearance, early diagnosis and variable presentation [2]. Maternal complications of acute hypertension in pregnancy include eclampsia, cerebrovascular accident, abruption placenta, renal failure, hepatic dysfunction and HELLP syndrome. Such adverse conditions have been described in the SOGC, SOMANZ, JNC and ACOG guidelines as factors that may increase concern of preeclampsia in the absence of a proteinuria center on maternal end-organ impairment, maternal symptomatology, irregular maternal laboratory tests and fetal morbidity [3-6]. The fetus is also at risk of growth restriction, prematurity, asphyxia and intra uterine death due to placental abruption. Definitive management is termination of pregnancy which cannot be done due to pre maturity. It is therefore important to prolong the pregnancy till foetal survival is good.

Various anti-hypertensive drugs have been used to control blood pressure in cases of preeclampsia. These include methyldopa, nifedipine, labetalol and hydralazine. Many trials have been conducted so far to compare the efficacy of these drugs but each has its own risks and benefits and no single drug has been found to be superior than the other.

Nifedipine has been commonly used in India for the treatment of preeclampsia. It is a calcium channel blocker and it inhibits influx of calcium ions to vascular smooth muscles resulting in arterial vasodilatation. It is administered orally and has the advantage of being cost effective. It is however banned in countries like Australia because of sudden unpredictable fall of blood pressure and cardiac side effects. Labetalol, a beta blocker, has arteriolar vasodilating action that lowers blood pressure by lowering the peripheral resistance. It gives better control of blood pressure with very little side effects. It is now considered as a first line drug in the management of preeclampsia. Very few studies comparing the efficacy of Nifedipine and Labetalol have been done so far. As such drug of choice for management of preeclampsia has not been recognized. Hence there is need for comparison between the two drugs to know which one is superior.

2. AIM & OBJECTIVES

To compare the efficacy and safety of oral labetalol with oral nifedipine in the management of preeclampsia in relation to Control of blood pressure, time and number of doses required to lower the BP, adverse effects of drugs and maternal and perinatal outcome.

3. REVIEW OF LITERATURE

Since the period of Hippocrates Preeclampsia/eclampsia has been regarded as a scientific phenomenon. Zweifel first named the hypothesis disorder toxemia in 1916 [7]. Hypertensive disorders represent the most common medical complications of pregnancy. They are more common in primigravidae when compared to multiparas, elderly gravidae, multiple gestations, and with previous history of hypertensive disorders of pregnancy & family history. Early and regular antenatal care reduces the incidence of severe disease and its complications like eclampsia thus improving maternal and fetal outcome. The aim is to maintain BP within the target range, prevent convulsions, prevent maternal complications, ensure fetal well-being and to deliver the baby on the best day, in the best way and in the best place. Gestational hypertension/ mild preeclampsia can be managed conservatively until 37 weeks or until complications develop. In those who are managed conservatively, regular maternal fetal surveillance is essential to ensure fetal well- being. Usually indicated in women with eclampsia or to prevent convulsions in impending eclampsia or severe preeclampsia .There is no clear agreement regarding its role in mild preeclampsia. Magnesium sulphate is the drug of choice.

Labetalol, a selective α1 and a non selective β blocker decreases systemic vascular resistance, slows the heart rate, reducing myocardial oxygen demand. It doesn‘t reduce peripheral, renal, cerebral, coronary and utero placental blood flow [8].

If the drug is given intravenously, 20 mg initial dose, followed by 40-80 mg every 10 minutes, until the therapeutic response is achieved . It can also be given in IV drip, dissolving 250 mg in 250 ml of normal saline and giving 20 ml/min (20mg/ hour) and adjusting the rate up or down according to the patient‘s response. If given orally 75% of the drug is inactivated in the first liver pass. The initial dose is 100 mg twice daily. This dose may be increased according to the patient‘s response. The maximum dose is 2400mg/day. Labetalol is usually well tolerated. It reduces the blood pressure smoothly but rapidly without the associated tachycardia characteristic of nifedipine/ hydralazine [9].

4. METHODOLOGY

Randomized controlled trial study was performed with pregnant women with diastolic BP persistently 100mmHg or more than 100 mm of Hg and systolic BP >160mmHg. 50 in group A (patients receiving nifedipine) and 50 in group B (patients receiving labetalol). All pregnant patients admitted in KIMS for severe preeclampsia.

The study was conducted in the department of OBGY at Krishna Institute of Medical Sciences during the period from May 2014 to May 2016. Enrolled patients were randomized to receive either oral Nifedipine or oral Labetalol after taking informed consent. Randomization was done alternately. Once the patient was randomized to a group, a proforma regarding the basic details of the patient was entered. Patients randomized to oral Nifedipine received 10mg stat and BP was checked every 5 minutes till target blood pressure was reached. If there was no fall in BP after 15-20minutes, a second dose of 10 mg was given. Nifedipine was never given sublingually. The time required to reach the target BP and the number of doses required were noted. Patients randomized to oral Labetalol received 100 mg stat and BP was checked every 5 minutes till target blood pressure was reached. Additional 100mg dose was given if required. The time required to reach the target BP and the number of doses required were noted.

Patients belonging to both groups were observed in the hospital till spontaneous vaginal delivery occurred at term. If the gestational age was > 34 weeks with worsening of condition, termination of pregnancy was done. If gestational age was 28- 34 weeks, 2 doses of Betamethasone 12 mg, 24hours apart was given for fetal lung maturity. At term, pregnancy was terminated by either vaginal delivery or LSCS.

5. OBSERVATION AND RESULTS

Table 1: Distribution of cases according to gravid status

PARITY	NIFEDIPINE	LABETALOL
G1	25(50%)	33(66%)
G2	14(28%)	12(24%)
G3	10(20%)	2(4%)
>G3	1(2%)	3(6%)

Value of $\chi^2 = 7.591$, p= **0.0553, not significant**

As shown in table no. 1, in Nifedipine group 25(50%) patients were primigravida, 14(28%) patients were 2nd 32ravid, 10(20%) patients were 3rd 32ravid and 1(2%) patient was more than 3rd 32 ravid. In Labetalol group 33(66%) patients were primigravida, 12(24%) patients were 2nd 32ravid, 2(4%) patients were 3rd 32ravid and 3(6%) patients were more than 3rd 32 ravid. After applying Chi-square test there is no significant difference between gravid status and both the groups.

Table 2: Distribution of cases according to gestational age

Gestational Age (weeks)	NO.OF PATIENTS	
	NIFIDEPINE GROUP	**LABETALOL GROUP**
28-32	7 (14%)	14 (28%)
33-36	27 (34%)	25(50%)

>37	16 (32%)	11(22%)
MEAN	**34.23**	**33.51**

Value of $\chi^2 = 3.3362$, p= 0.188607, not significant

In the above table 2, 7 patients were in the gestational age group of 28-32 weeks, 27 were in the group of 33-36weeks and 16 were in the group of >37 weeks gestational age in the Nifedipine group. In the labetalol group, 14 patients were in the gestational age group of 28-32 weeks, 25 in the group of 33-36 weeks and 11 were in the group of >37 weeks gestational age.

Table 3: Distribution of cases according to BMI

BMI(kg/m^2)	**NO. OF PATIENTS**	
	NIFIDEPINE GROUP	**LABETALOL GROUP**
20-25	36 (72%)	28 (56%)
26-30	13 (26%)	20 (40%)
>30	1 (2%)	2 (4%)
MEAN	**25.52**	**25.82**

Value of $\chi^2 = 2.8182$, p= 0.244365, not significant

In the above table no. 3, 36 patients had BMI in the range of 20-25, 13 in the range of 26-30 and only 1 patient had BMI more than 30 in the nifedipine group. In the labetalol group, 28 patients had BMI in the range of 20-25, 20 in the range of 26-30 and only 2 had BMI more than 30.

Table 4: Statistical measures of Diastolic Blood Pressure Pre and Post medication

	Nifedipine			**Labetalol**		
Measures	DBP (PRE)	DBP (POST)	Decli Ne Rate	DBP (PRE)	DBP (POST)	Decline Rate
***Mean±Sd**	104.6±11.25	90.8±10.31	13.2 %	104±10.26	90±11.06	13.5%
Max	120	100		130	100	
Min	90	80		100	80	

In the above table no. 4, by applying Student‘s Paired _t‘ there is a significant decline rate in DBP in both the groups ($p<0.05$) But group Labetalol showed more decline rate as compared to group Nifedipine. In Nifedipine group the mean diastolic BP pre medication was 104.6 mm of Hg, which reduced to 90.8 mm of Hg. The decline rate was 13.2%. In Labetalol group the mean diastolic BP pre medication was 104 mm of Hg, which reduced to 90 mm of Hg. The decline rate was 13.5%.

Table 5: Complications due to Pregnancy Induced Hypertension

Complications	Nifedipine	Labetalol
Imminent Eclampsia	5(10%)	3(6%)
Hellp	4(8%)	3(6%)
Abruption	2(4%)	1(2%)
CVA	0(0%)	0(0%)
Renal Failure	2(4%)	1(2%)

As shown in table no. 5, in Nifedipine group 13 patients out of 50 had complications wherein 5(10%) patients had imminent eclampsia, 4(8%) patients had HELLP syndrome, 2(4%) patients had abruptio placenta, and 2(4%) patients had renal failure while none had CVA. In Labetalol group 8 patients out of 50 had complications wherein 3(6%) patients had imminent eclampsia,3(6%) patients had HELLP syndrome, 1(2%) patients had abruptio placenta, 1(2%) patient had Renal failure while none had CVA.

6. DISCUSSION

This controlled randomized analysis contrasts the effectiveness of two antihypertensive medications, oral nifedipine, and oral labetalol. In this study with 100 patients, 50 were randomized to the nifedipine group and 50 to the labetalol group. p value of Table 1 (distribution of cases according to gravid status) is p=0.055275. This result is not significant. This indicates that there is no significant difference between gravid status and both the groups. p value of Table 2 (distribution of cases according to gestational age) is p=0.188607. This result is also not significant indicating that both the groups were comparable in terms of gestational age. p value of Table 3 (distribution of cases according to BMI) is p=0.244365. This result is not significant indicating that both groups are comparable in terms of BMI. So, both groups were similar in terms of age, gravid status, gestational age and BMI. The present study reveals that oral labetalol reduces BP more effectively than oral nifedipine. Mean SBP before treatment in nifedipine group was 157.8 mmof Hg which was reduced to 141.2 mm of Hg. Maximum pre systolic BP was 180 mm of Hg and minimum was 130 mm of Hg, and following treatment the maximum measure was reduced to 160 mm of Hg and minimum to 120 mm of Hg. In the labetalol group the mean SBP before treatment was 158mmof Hg which was reduced to 140 mm of Hg. Maximum pre systolic BP was 200 mm of Hg and minimum was 130 mm of Hg, and following treatment the maximum measure was reduced to 160 mm of Hg and minimum to 130 mm of Hg.

7. CONCLUSION

In the present study, even though Nifedipine achieved the target blood pressure more rapidly and with fewer initial doses than Labetalol, it was found that overall labetalol was more effective in lowering the blood pressure compared to nifedipine. As far as the side effects were concerned, labetalol had very few side effects than nifedipine. Nifedipine has the disadvantage of having more side effects thus having an influence on patient compliance and patient satisfaction. Thus the present study concludes that labetalol seems to be a better alternative and is considered as a first line drug for the management of preeclampsia. In conditions where labetalol is contraindicated, nifedipine is used for lowering the BP.

8. REFERENCES

[1] Williams‘s obstetrics 23rd edition; 34th chapter - In pregnancy hypertension: 706 - 709.
[2] New York State Department of Health (NYSDOH). Hypertensive Disorders In Pregnancy; Guideline Summary. May 2013
[3] Society of Obstetricians and Gynaecologists of Canada (SOGC): Clinical Practice Guideline- Diagnosis, Evaluation and Management of the Hypertensive Disorders of Pregnancy. March 2008.
[4] Society of Obstetric Medicine of Australia and New Zealand (SOMANZ). Guidelines for the Management of Hypertensive Disorders of Pregnancy. 2008.
[5] National High Blood Pressure Education Program, National Heart, Lung and Blood Institute. The Seventh Report of the Joint National Committee on Prevention, Detection, Evaluation and Treatment of High Blood Pressure (JNC7). August 2004.
[6] American College of Obstetricians and Gynecologists (ACOG). Practice Bulletin-Diagnosis and Management of Preeclampsia and Eclampsia. January 2002.
[7] Zweifel P. Eklampsie. In Doderlein A(ed) Handbuch der Gerburtshilfe, 11, Wiesbadevi.Bergman, 1916; 672-676.
[8] Arulkumaran S S, Gita A, Penna L K. The management of labour 3rd ed.2011;463,471.
[9] Renu M. Ian Donald‘s Practical Obstetrics Problems 6th ed.2007;299.