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Original Article

COMPARATIVE STUDY OF LABETALOL AND NIFEDIPINE IN MANAGEMENT OF HYPERTENSIVE DISORDERS OF PREGNANCY

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ABSTRACT

Objective: The purpose of the study was to evaluate and compare effectiveness and safety of nifedipine and labetalol monotherapy in patients with hypertensive disorders of pregnancy.

M**ethods:** 100 antenatal patients were selected. Detailed obstetric history was taken and, clinical examination done and the blood pressure was checked and means arterial pressure was calculated as follows (SBP+2DBP)/3. Brachial artery blood pressure was checked with the patient in lateral recumbent position using calibrated mercury sphygmomanometer and appropriate cuff size. Korotkoff V was used to determine diastolic blood pressure. The blood pressure was monitored at 0, 6, 12, 24, 48, 72 h. The initial dosage of an antihypertensive drug and maximum dosage of the antihypertensive drug was observed.

Results: In the present study, it was noted that the change in mean arterial pressure from the time of admission to 72 h were noted in the two groups which received nifedipine (132.34 vs 96.74) and labetalol (132.07 vs 93.51). There was a significant fall in the mean arterial pressure at 6 h in nifedipine group which showed statistical difference. At 48 h and 72 h fall in MAP was noted in labetalol group, which is statistically significant. The study showed that there was a sudden fall in the mean arterial pressure in nifedipine group, but labetalol had smooth and persistent fall in mean arterial pressure. It was observed in the study that fetal outcome in terms of live births (96% vs 84%) was higher in labetalol group and need for NICU admission and preterm births (18% vs 10%) was more in nifedipine group.

Conclusion: The present study has shown that labetalol has got better and sustained control of hypertension in pregnancy.

Keywords: Nifedipine, Labetalol, Hypertension, Fetal outcome, Pregnancy

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INTRODUCTION

The World Health Organization (WHO) systematically reviews maternal mortality worldwide, and in developed countries, 16% of maternal deaths were reported to be due to hypertensive disorders. This proportion is greater than three other leading causes that include hemorrhage-13%, abortion-8 %, and sepsis–2% [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. The hypertensive disorders of pregnancy constitute the most widely studied, discussed and analyzed condition, because of the fact that they adversely affect both the mother and fetus [2]. They predispose to progression to severe forms of pre-eclampsia, eclampsia, HELLP syndrome, abruption placenta, haemorrhage, disseminated intravascular coagulation, acute renal failure and death, acute or chronic uteroplacental insufficiency resulting in ante or intrapartum anoxia that may lead to, intrauterine growth restriction, both asymmetrical as well as symmetrical thereby, compromising the intellectual abilities of the child in future, especially in symmetrical intra uterine growth restriction (IUGR); and preterm delivery and even fetal death [3]. A recent analysis of women who were recruited for the Royal College of General Practitioners oral contraception study showed that women with a history of hypertension in pregnancy have a significantly increased risk of hypertension, myocardial infarction, and ischemic heart disease later in life [4]. The studies have shown that early detection and treatment of hypertension in pregnancy and with timely management will effectively prevent most of the complications that may arise due to improper management. Various antihypertensive agents have been used in the management of hypertension in pregnancy. Worldwide there is acceptance among obstetricians that anti-hypertensive therapy has a role in the management of mild forms of hypertension, especially when it occurs in later weeks of pregnancy. When moderate to severe hypertension occurs with proteinuria, complications rate tend to increase. A wide variety of drugs have been advocated, and each group has different potential side-effects and adverse effects. Among commonly used drugs for pregnancy-induced hypertension (PIH), Hydralazine was temporarily withdrawn from the market in the early 1990s [5]. Three antihypertensive drugs like, nifedipine, methyldopa and labetalol, have been demonstrated to be safe for use in the pregnant women and are commonly used for the management of various hypertensive disorders during pregnancy [6]. Methyldopa may take a few days for onset of hypotensive effect, and so rapid dosage changes in the first 2 to 3 d should not be undertaken. Recently mostly used drugs suggested from literature include nifedipineand labetalol hydrochloride. Both nifedipineand labetalol have demonstrated comparable efficacy and a lower risk of overshoot hypotension and fetal distress when compared with hydralazine in randomized clinical trials [7]. The main objectives of the study were to compare the efficacy, safety, maternal and perinatal outcome of labetalol and nifedipine in hypertensive disorders of pregnancy. To evaluate and compare efficacy of antihypertensive agents in hypertensive disorders of pregnancy and to study and compare maternal outcome based on development of maternal complications in the treatment groups.

MATERIALS AND METHODS

Study design

A prospective comparative clinical study in a Tertiary Care Teaching Hospital.

Place of study

Navodaya Medical College, Hospital and Research Centre, Raichur.

Period of study

One year from January 2014 to December 2014.

Sample size

100 patients with 50 assigned to each group. The study group consists of 100 pregnant women attending ante-natal clinic with inclusion criteria below.

Inclusion criteria

All pregnant patients with systolic blood pressure of more than 140 mm of Hg diastolic blood pressure of more than 90 mm of Hg on two occasions four hours apart after 20 w of gestation along with/without protienuria admitted in the hospital during the study period.

Exclusion criteria

Patients with severe PIH with imminent eclampsia**,** heart diseases including IHD, haematological disorders, liver diseases and broncial asthama.

Antihypertensive drugs used in the study

Labetalol Tablets: Lobet-100 mg, (Samarth Pharma Pvt Ltd), Gravidol-100 mg, (Mercury Laboratory Pvt Ltd) and Nifedipine Capsules: Depin-10 mg, (Zydus Cadila).

Method of collection of data

100 antenatal patients were selected and 50 assigned to each group using a random number table. Detailed obstetric history was taken and, clinical examination done and the blood pressure was checked and means arterial pressure was calculated as follows (sbp+2dbp)/3. Investigations such as complete blood counts, coagulation profile, urine routine, 24hour urine protein, renal function tests, liver function tests, fundoscopy, non-stress test, obstetric scan and Doppler if indicated. The patients in group a received NIFEDIPINE 10-60 mg per day Group B received the drug LABETALOL 100-200 mg Bd. Brachial artery blood pressure was checked with the patient in lateral recumbent position using calibrated mercury sphygmomanometer and appropriate cuff size. Korotkoff V was used to determine diastolic blood pressure. The blood pressure was monitored at 0, 6, 12, 24, 48, 72 h. The initial dosage of antihypertensive drug and maximum dosage of the antihypertensive drug was observed, side effects if any associated with drug intake was noted. The maternal and fetal outcomes were noted. The maternal outcomes, including complications of preeclampsia and mode of delivery, the fetal outcomes like pre-maturity, still birth or neonatal death and need for NICU admission, were analyzed.

Statistical analysis

Observations were analyzed by applying SPSS 19.0 version and results were expressed in terms of mean and SD. Students paired t test was performed to find out the mean difference in each treatment group for pre and post-comparison. Unpaired T-test was performed in order to find out the mean difference between variables of two different treatment groups.

RESULTS

The study comprises of 100 ante natal cases with hypertensive disorders, selected as per the criteria. They were assorted in to two groups of 50 each for nifedipine and labetalol. Table 1 shows age wise distribution of cases. Mean age in Group A is 23.74 and in Group B is 23.76. Primigravida were associated with hypertensive disorders commonly in both the groups (table 2). Table 3 showed the distribution of patients according to booking status and the results revealed 82% in group A and 86 % in Group B are booked cases. 18% in Group A and 14% in Group B are unbooked cases. Table 4 showed that 31(62%) cases in group A and in group B 38(76%) cases are between 30-35 w of gestation. The mean gestational age in Group A is 36.18 w and in Group B is 36.52 w. Table 5 showed 24(48%) cases in group A and in group B 20(40%) cases had albuminuria indicating a percentage of cases with pre-eclampsia. Table 6 showed mean arterial pressure (MAP) at o hrs is 132.34 and after treatment in group A is 96.72 and in group B mean arterial pressure at 0 h is 132.07 and after treatment, it is 93.51. There is significant reduction in mean arterial pressure by 6 h in group a, which is statistically significant. Whereas at 24 h and 48 h the fall in MAP in group B is statistically significant. At 48 h the fall in MAP in group b to absolutely normal levels is statistically significant. Table 7 showed maximum dosage of drug used in group A is 30 mg in 38% cases and in group b 300 mg in 8% cases. Table 8 showed in group A 84% patients didn't have side effects; headache was the most common side effect in this group and was observed in 16% of patients. In group B 90% of the patients in this group didn't have any side effects, 10%had postural hypotension. In the group a 50% had vaginal delivery either spontaneous or induced and 50% had caesarian delivery. In group B 58%had vaginal delivery and 42% had caesarian delivery (table 9). Table 10 showed the mean birth wt in kgs in group A is 2.49 and group B is 2.57. Table 11 showed the increased preterm delivery in group a (18%), group b shows (10%) preterm delivery. Table 12 showed 84% live birth in group A and 96% live birth in group B. The mean duration of prolongation of pregnancy in Group A is 14.58 and Group B is 11.76 (table 13).

Table 1: Age-wise distribution of cases

Age group	Nifedipine		Labetol	
	Frequency	Percent	Frequency	Percent
20-25	41	82	39	78
25-30	8	16	8	16
>30	1	2	3	6
Total	50	100	50	100

Table 2: Distribution of patients according to gravida

Parity	Nifedipine		Labetol	
	Frequency	Percent	Frequency	Percent
Primi	24	48	30	60
G 2	16	32	9	18
G 3	7	14	5	10
G 4	1	2	4	8
G 5	2	4	1	2
G 7	0	0	1	2
Total	50	100	50	100

Table 3: Distribution of patients according to booking status

Type of cases	Nifedipine		Labetol	
	Frequency	Percent	Frequency	Percent
Booked	39	78	24	48
Unbooked	11	22	26	52
Total	50	100	50	100

Table 4: Gestational age-wise distribution of cases

Gestational weeks	Nifedipine		Labetol	
	Frequency	Percent	Frequency	Percent
20-25	1	2.0	0	0
25-30	5	10.0	4	8.0
30-35	10	20.0	6	12.0
35-40	31	62.0	38	76.0
>40	3	6.0	2	4.0
Total	50	100.0	50	100.0

Table 5: Distribution according to presence of albumin in urine

Urine albumin	A		B	
	Frequency	Percent	Frequency	Percent
Present	24	48.0	20	40.0
Absent	26	52.0	30	60.0
Total	50	100.0	50	100.0

Table 6: Mean arterial pressure before and after treatment

Time	Group	N	Mean	SD	T	df	p	Inference
0h	Nifedipine	50	132.34	5.11	.273	98	.786	Not
	Labetol	50	132.07	4.48			(>0.05)	significant
6h	Nifedipine	50	118.59	6.59	-4.679	98	.0001	Highly
	Labetol	50	123.89	4.56			(<0.001)	significant
12h	Nifedipine	50	113.30	6.82	-.277	98	.782	Not
	Labetol	50	113.62	4.88			(>0.05)	significant
24h	Nifedipine	50	108.61	5.90	.502	98	.040	Significant
	Labetol	50	107.02	4.11			(<0.05)	
48h	Nifedipine	50	102.84	5.25	1.984	98	.043	
	Labetol	50	100.93	4.32			(<0.05)	Significant
72h	Nifedipine	50	96.72	3.46	3.795	98	.0001	Highly
	Labetol	50	93.51	4.88			(<0.001)	significant

Table 7: Distribution of cases according to maximum dose of drug given

Nifedipine			Labetol		
Dose (mg)	Frequency	Percent	Dose (mg)	Frequency	Percent
10	0	0	100	0	0
20	12	24	200	46	92
30	38	76	300	4	8
Total	50	100		50	100

Table 8: Distribution according to side effects

Side effects	Nifedipine		Labetol	
	Frequency	Percent	Frequency	Percent
No	42	84	45	90
Headache	8	16	0	0
Giddiness	0	0	5	10
Total	50	100	50	100

Table 9: Distribution according to mode of delivery

Delivery mode	Nifedipine		Labetol	
	Frequency	Percent	Frequency	Percent
LSCS	25	50	21	42
Spontaneous	25	50	29	58
Total	50	100	50	100

Table 10: Birth weight in kgs

Variable	N	Mean	SD	Std. error	Range	Minimum	Maximum
Nifedipine	50	2.49	.32	.04	1.50	1.50	3.00
Labetol	50	2.57	.56	.08	2.50	1.40	3.90

Table 11: Gestational age at delivery

Pregnancy	Nifedipine		Labetol	
	Number	Percent	Number	Percent
Term	41	82	45	90
Preterm	9	18	5	10
Total	50	100	50	100

Table 12: Neonatal outcome

Outcome of pregnancy	Nifedipine		Labetol	
	Frequency	Percent	Frequency	Percent
Alive	42	84	48	96
Dead	8	16	2	4
Total	50	100	50	100

Table 13: According to prolongation of pregnancy

Prolongation of pregnancy	Group	N	Mean	Std. deviation	t	df		Inference
Days of prolongation of pregnancy	Nifedipine	50	14.58	20.89	.84	98	0.4 (>0.05)	Not significant
	Labetol	50	11.76	11.37				

DISCUSSION

This prospective study was undertaken among 100 antenatal women who have come to Department of Obstetrics and Gynaecology, Navodaya Medical College Hospital and Research Centre, Raichur between Jan 2014 and Dec 2014. Present study showed more number of patients at age group of 20-25 compared to other 2 studies, as the present study comprises large group of patients from rural set up (table 14). The present study showed majority of the women to be primigravidae which is comparable with other studies (table 15). The fall in blood pressure with labetalol is comparable to other studies (table 16). The fall in blood pressure with labetalol is comparable to other studies (table 17). Fall in MAP with nifedipine treatment is comparable to studies of Hangarga *et al.* [8] and Deshmukh *et al.* [9] Present study showed better control of MAP as compared to other studies. The present study had showed the adverse effects of 16% in Group A and 10% in Group B, which is comparable to the other studies by Hangarga *et al.* [8]. In a study done by Patel *et al.* [10] showed that the commonest adverse effects noted were occipital headache (3-9%), postural hypotension (3-8%), tachycardia (4-11%), and depression (2-7%). Tachycardia (11%) and occipital headache (9%) were more common with nifedipine compared to methyldopa and labetalol groups [10]. In the study it was observed that of the 100 patients 54% of the patients had vaginal delivery and 46% underwent caesarian section. Caesarian section (50% vs 42%) was higher in nifedipine group. The most common indication for caesarian section was fetal distress [11]. It was observed in the study that fetal outcome in terms of live births (96% vs 84%) was higher in labetalol group and need for NICU admission and preterm births (18% vs 10%) was more in nifedipine group. In similar study done by Donel *et al.* [12] concluded that both nifedipine and labetalol were effective in controlling mild to moderate hypertension in pregnancy, but after treatment, mean arterial pressure was well controlled with labetalol compared to nifedipine.

Table 14: Incidence of hypertension according to age of patients

Study	Age group	Incidence
Hangarga *et al.* [8]	21-25	47.36%
Deshmukh *et al.* [9]	21-25	47%
Present study	20-25	80%

Table 15: Gravida and para status

Study	Nifedipine	Labetalol
Hangarga *et al.* [8]	Primigravida (54%)	Primigravida (52%)
Deshmukh *et al.* [9]	Primigravida (59.41)	Primigravida (53.13)
Present study	Primigravida (48%)	Primigravida (62%)

Table 16: Blood pressure in mm Hg before and after treatment with nifedipine

Study	Pre-treatment	Post-treatment
Patel *et al.* [10]	180/120	120/80
Mac Donald *et al.* [11]	195/127	154/100
Deshmukh *et al.* [9]	170/110	130/80
Present study	170/110	130/80

Table 17: Blood pressure before and after treatment with labetalol

Study	Pre-treatment	Post-treatment
Patel *et al.* [10]	180/120	140/80
Mac Donald *et al.* [11]	198/128	163/100
Deshmukh *et al.* [9]	172/110	144/94
Present study	170/110	120/80

CONCLUSION

The present study has shown that labetalol has got better and sustained control of hypertension in pregnancy. Headache was the commonest side effect in nifedipine; postural hypotension was commonest in labetalol. Nifedipine required repeated administration for control of hypertension than labetalol. The present study indicates labetalol to be a better anti-hypertensive in terms of control of hypertension, mode of vaginal delivery, fetal outcome; however still large group studies may be required to confirm the findings of present study.

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AUTHORS CONTRIBUTIONS

All the authors have contributed equally

CONFLICTS OF INTERESTS

Declared none

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