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A comparative study of oral labetalol versus oral nifedipine in hypertensive disorders of pregnancy

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Abstract
Introduction: In developed countries, 16 percent of maternal deaths were attributed to hypertensive disorders. Of hypertensive disorders, the preeclampsia syndrome is the most dangerous.
Material and Methods: The Present study was conducted in Department of Obstetrics & Gynecology M.Y.H, Indore from Sept 2015 to Sept 2017.A total number of 150 patients were randomly allocated into Group A Labetalol and Group B Nifedipine, Then the effects were compared.
Results: In the current study, the control of B.P. was better with nifedipine than with labetalol. Preterm labor was less with nifedipine which may be due to tocolytic effect of nifedipine but overall perinatal outcome was good in both the groups. Nifedipine gave better results in cases of hypertensive emergency. Both drugs had minimal side effects and drug compliance was better.
Conclusion: Nifedipine is as safe and effective as labetalol for the management of hypertensive disorders as well as in hypertensive emergency during pregnancy.

Keywords: Hypertension, labetalol, Nifedipine, B.P.

1. Introduction
Hypertensive disorders complicate 5 to 10 percent of all pregnancies that contributes greatly to maternal morbidity and mortality. Of these disorders, the preeclampsia syndrome, either alone or superimposed on chronic hypertension, is the most dangerous [1]. The World Health Organization (WHO) systematically reviews maternal mortality worldwide, and in developed countries, 16 percent of maternal deaths were reported to be due to hypertensive disorders [2]

2. Objectives
The present study was carried out with the following aims and objectives:
- To know the incidence & demographic aspects of hypertensive disorders in pregnancy.
- Comparison of efficacy of Labetalol and Nifedipine in controlling blood pressure in patients with PIH.
- To compare the effect of these drugs on proteinuria.
- To study the outcome of normal labor vs Cesarean section in patients on these drugs.
- To assess the perinatal outcome.

3. Materials and Methods
3.1 Study type: Comparative Randomized Prospective Study

3.2 Place of study: Department of Obstetrics & Gynecology M.Y.H, Indore (M.P.)

3.3 Duration of study: Sept 2015 to Sept 2017

3.4 Number of patients included: 150

3.5 Inclusion Criteria
1) All patients with hypertension whose two blood pressure recordings are $\geq$ 140/90 mm Hg more than 6 hours apart.
2) Patients with gestational age from 20 weeks of pregnancy till term.
3) Patients who give consent.

3.6 Exclusion Criteria

1) Multifetal pregnancy, eclampsia, and women with preexisting or concurrent medical disorders like diabetes mellitus, cardiac diseases, renal disease, thyrotoxicosis, hemophilia and chronic hypertension.
2) Patients who have IUD at presentation.
3) Patients those who do not give consent

3.7 Methodology

A total number of 150 patients were studied and 75 patients were randomly allocated into Group A Labetalol and Group B Nifedipine. Then the effects of labetalol and nifedipine were compared. Labetalol was started at an initial dose of 100 mg BD and the dose was increased as required. Maximum dose of 200 mg TDS was given. Nifedipine was started with an initial dose of 10 mg BD and the dose was increased up to 20 mg TDS. Patients were monitored daily for blood pressure, urine albumin using urine reagent strips.

4. Results

Table 1: Distribution of cases according to Age group

Age	Group A Labetalol		Group B Nifedipine	
	No.	%	No.	%
Upto 20 years	17	22.6%	15	20%
21-25 years	36	48%	38	50.6%
26-30 years	15	20%	16	21.4%
>30 years	7	9.4%	6	8%
Total	75	100.00	75	100.00
Mean ± SD	23.91 ± 3.74		23.68 ± 4.32	
't' value	0.732, df=148			
P value	0.465, Not significant			

Table 1 showing maximum number of patients in Labetalol and Nifedipine belonged to age group 21-25 years. The difference was found to be statistically not significant (P>0.05), showing that age was comparable between the two groups.

Table 2: Distribution of cases according to Gravidity

Gravidity	Labetalol Group		Nifedipine Group	
	No.	%	No.	%
1	35	46.6%	42	56%
2	20	26.6%	12	16%
3	13	17.33%	10	13.3%
4	5	6.66%	8	10.6%
5	2	2.6%	2	2.6%
6	0	0.00	1	1.3%
Total	75	100.00	75	100.00

Table 2 showing majority of patients were primigravida comprising 46.6% in Labetalol group and 56% in Nifedipine group. There was no statistically significant association seen between the gravidity and the groups.

Table 3: Distribution of cases according to Residence

Residence	Labetalol Group		Nifedipine Group	
	No.	%	No.	%
Rural	39	52%	38	51%
Urban	36	48%	37	48%

Table 3 showing majority of women belong to the rural areas in both the groups under study, showing that the distribution of women in both the groups in relation to residence is comparable.

Table 4: Distribution of cases according to literacy

Education status	Labetalol Group		Nifedipine Group	
	No.	%	No.	%
Illiterate	44	58%	43	57%
Literate	31	42%	32	43%

Table 4 showing most of the women in both the groups are illiterate. It may be a coincidental finding as the rural women are more in study group. There was statistically no significant difference seen in the groups with respect to education status (P>0.05).

Table 5: Distribution of cases according to gestational age on admission

Gestational Age	Labetalol Group		Nifedipine Group	
	No.	%	No.	%
20-24 weeks	0	0.00%	0	0.00%
24-27 weeks	2	0.02%	3	0.04%
27-31 weeks	7	0.09%	6	0.08%
31-34 weeks	14	18.6%	11	14.6%
34-37 weeks	25	33.3%	29	38.6%
37-40 weeks	27	36%	26	34.6%
Total	75	100%	75	100%

Table 5 showing the maximum no. of patients in both the groups entered the trial between the gestational age of 34-40 weeks of pregnancy.

Table 6: Comparison of mean SBP, DBP and MAP between the two groups before admission and after treatment

		Labetalol Group [Mean ± SD]	Nifedipine Group [Mean ± SD]	't' value	P value
SBP	On admission	154.27 ± 9.89	153.68 ± 9.93	0.36, df=148	0.718, NS
	After treatment	127.50 ± 20.3	121.30 ± 10.9	2.31, df=148	0.023*
DBP	On admission	113.50 ± 20.9	111.20 ± 8.05	0.88, df=148	0.382, NS
	After treatment	89.07 ± 6.40	84.40 ± 5.26	4.88, df=148	0.000*
MAP	On admission	127.1 ± 14.8	125.36 ± 6.05	0.92, df=148	0.358, NS
	After treatment	101.87 ± 8.30	96.71 ± 5.49	4.49, df=148	0.000*

Table 6 shows comparison of mean SBP, DBP and MAP between the two groups on admission and after treatment. All the parameters were comparable on admission (P>0.05). The mean SBP, DBP and MAP were significantly lower after the

treatment in comparison to on admission values in both the groups. (P<0.05). Amonth the two groups, nifedipine caused a much larger decrease in MAP as compared to labetalol although both drugs caused significant decrease in mean arterial pressure

Table 7: Albumin Levels in patients prior to starting treatment

Albumin	Labetalol Group		Nifedipine Group	
	No.	%	No.	%
+1	50	67%	53	70%
+2	24	32%	22	30%
+3	01	1%	0	0
Total	75	100.00	75	100.00

Table 7 shows that the distribution of women in both the groups is independent of the albumin level. (statististically insignificant).

Table 8: Albumin levels in patients after treatment

Albumin	Labetalol Group		Nifedipine Group	
	No.	%	No.	%
Nil	40	53.3%	54	72%
1+	35	46.7%	21	28%
Total	75	100.00	75	100.00

There was significant decrease in proteinuria reported, in Nifedipine group than Labetalol group (P<0.05).

Table 9: Distribution of cases according to Maternal Complications

Complications	Labetalol Group		Nifedipine Group	
	No.	%	No.	%
Severe hypertensive Episodes	3	4%	0	0.00
Placental abruption	0	0.00	1	1.33%
Eclampsia	2	2.66%	0	0.00
Maternal death	0	0.00	0	0.00
Severe hypotension	0	0.00	0	0.00

Incidence of severe hypertensive episodes were maximum in labetalol group. Incidence of placental abruption was nil in labetalol group. Incidence of eclampsia was nil in nifedipine group as compared to 2 cases in labetalol groups.

Table 10: Distribution of cases according to mode of delivery

Mode of Delivery	Labetalol Group		Nifedipine Group	
	No.	%	No.	%
Normal vaginal delivery	55	74%	42	56%
LSCS	20	26%	33	44%
Total	75	100.00	75	100.00

Table 10 shows the comparison of mode of delivery in relation to the groups. In nifedipine group, higher number of women underwent LSCS while in the labetalol group majority of the women had undergone normal vaginal delivery. The difference was found to be statistically significant (P<0.05). No significant difference statistically in terms of spontaneous onset of labor in the study groups. The incidence of induction of labor was slightly more in labetalol group as compared to nifedipine group.

Table 11: Distribution of cases according to fetal outcome

Fetal Outcome	Labetalol Group		Nifedipine Group	
	No.	%	No.	%
Preterm	23	30%	20	27%
Term	52	70%	55	73%
Total	75	100.00	75	100.00

No statistically significant difference in comparing fetal outcomes in the two groups. (p>0.05) The present study showed a lower incidence of preterm labor in Nifedipine group as compared to Labetalol group.

Table 12: Distribution of cases according to Birth weight

Fetal Outcome (Birth Weight)	Labetalol Group		Nifedipine Group	
	No.	%	No.	%
< 2.5 kg	30	40%	27	36%
≥ 2.5 kg	45	60%	48	64%
Total	75	100.00	75	100.00

No statistically significant result on comparing birth weight ≥ 2.5 kg in this study group. (p>0.05).

Table 13: Distribution of cases according to Neonatal outcome

Neonatal Outcome	Labetalol Group		Nifedipine Group	
	No.	%	No.	%
RDS	1	1.33%	4	5.33%
Jaundice	2	2.66%	2	2.66%
Hypoglycemia	0	0.00	1	1.33%
SGA	1	1.33%	1	1.33%
Still birth	3	4%	6	8%

There was no significant difference in both the groups in terms of perinatal morbidity (p>0.05). However need for NICU admissions was seen more in nifedipine.

5. Discussion

The maximum number of patients in labetatol and nifedipine group belonged to the age group 21-25 years and were primigravida. Shekhar *et al.* (2013) [3] and Hangarga US *et al.* (2016) [4] in a large well tolerated study had compared the two drugs and maximum subjects belonged to primigravida group and belonged to 20-25 years age group. Most of the women in both the groups are illiterate. Most of the patients between the gestational age of 34 to 40 weeks. Hangarga US *et al.* (2016) [4] conducted a similar study in which maximum patients belonged to gestational age of 35-40 wks. In our study we compared the fall in systolic and diastolic blood pressures in both the study groups. We also compared the Mean Arterial Pressure between both the groups. The fall in systolic and diastolic blood pressures in these groups showed significant difference.

In LABETALOL GROUP, The fall in MEAN SBP in this group was 26.8 mm Hg (154.27 ± 9.89 to 127.47 ± 20.27) and The fall in MEAN DBP in this group was 24.43 mm Hg. (113.50 ± 20.9 to 89.07 ± 6.40) which was statistically significant. Michael *et al.* (1982) [5] and Stott *et al.* (2016) [6] conducted a studies on women with severe hypertension complicating pregnancy with oral labetalol and found that effective control of blood pressure was achieved in maximum patients.

In nifedipine group THE fall in MEAN SBP in this group was 32.35 mm Hg(153.68 ± 9.93 to 121.33 ± 10.9). and The fall in MEAN DBP in this group was 26.8 mm Hg (111.20 ± 8.05 to 84.40 ± 5.26) which was statistically significant. Scardo *et al.* (1996) [7] evaluated the effects of oral nifedipine in preeclamptic patients and concluded that oral nifedipine was an effective antihypertensive agent with a steady decrease in MAP and systemic vascular resistance.

On comparing the SBP/DBP between both the groups, the fall in mean SBP and DBP was observed more in nifedipine group (SBP=32.35 & DBP=26.8 mm Hg) as compared to labetalol group (SBP=26.8 & DBP=24.43 mm Hg). S. Elatrous *et al.* (2002) [8] conducted a randomized prospective study to assess

the efficacy and safety of nicardipine in comparison to labetalol in the initial management of severe hypertension in pregnancy. Overall nicardipine caused a significantly greater decrease in systolic and diastolic BP. Dhali B *et al.* (2012) [9] randomized hundred patients into two groups, labetalol group & nifedipine group. Patients who received oral nifedipine achieved the goal therapeutic blood pressure more rapidly as compared with intravenous labetalol (p=0.001). The nifedipine group also required significantly fewer doses to reach the goal blood pressure. Shekhar *et al.* (2013) [3] conducted a randomized, double-blind, controlled trial for acute lowering of BP during hypertensive emergencies of pregnancy using labetalol and nifedipine. The patient comparison of the nifedipine and labetalol groups showed that both systolic BP and diastolic BP decreased significantly more rapidly in the nifedipine group. Shekhar S. *et al.* (2015) [10] did RCT to determine the efficacy and safety of oral nifedipine for treatment of severe hypertension of pregnancy compared with intravenous labetalol. Pts with BP >160/110 mm Hg were included. The study concluded that oral nifedipine was associated with less risk of persistent hypertension. Webster *et al.* (2017) [11] carried out a RCT enrolling pregnant women with chronic hypertension to compare treatment efficacy of labetalol and nifedipine. He observed that nifedipine use, was associated with a 7.4-mm Hg reduction (−14.4 to −0.4 mm Hg) in central aortic pressure, measured by pulse wave analysis. Jorge Duro-Gomez *et al.* (2017) [12] did an observational retrospective cohort study, included all pregnant women diagnosed with pre-eclampsia & were treated with oral nifedipine or oral labetalol. The mean reduction of BP was 31.19/15.67mmHg for the Nifedipine group and 30.1/11mmHg for the Labetalol group which was consistent with the findings in the current study. Raheem *et al.* (2011) [13] conducted a double-blind randomized trial and found that the fall in MAP in labetalol group was 25.23 mm Hg.(127.1 to 101.87) The fall in MAP in Nifedipine group was 28.65 mm Hg.(125.36 to 96.71) The statistical analysis showed significant result, hence proving Nifedipine to be a better drug for decreasing hypertension in pre-eclampsia patients. In another study, Scardo *et al.* (1999) [14] compared the hemodynamic effects of orally administered nifedipine and intravenously administered labetalol in preeclamptic hypertensive emergencies. The mean arterial pressure was significantly affected in both groups (nifedipine, P =.001; labetalol, P =.004). He observed that although the antihypertensive efficacy of both the drugs were comparable, nifedipine significantly increases cardiac index and decreases systemic vascular resistance whereas labetalol may not do so. 3 patients (4%) in our study who belonged to labetalol group failed to achieve fall in blood pressure and hence were being added with nifedipine. The combination therapy was effective and the Blood pressure was well controlled with both drugs. Stott *et al.* [6] (2016) conducted an observational study to evaluate the therapeutic response of oral labetalol in treatment of antenatal hypertension and to develop a prediction model to anticipate the response to labetalol monotherapy in women with hypertension and found that 26% failed to achieve control with labetalol alone. A randomized, double-blind, trial conducted was by Ohman *et al.* [15] (1985). After monotherapy with nifedipine for 6 weeks the supine BP was reduced by 18/13 mmHg, with labetalol the corresponding figure was 26/15 mmHg. The combined therapy induced a larger fall in BP, by 36/22 mmHg. Though here labetalol had a better antihypertensive action than nifedipine, but the combined therapy had a better effect then individual drug used alone. Shekhar *et al.* (2013) [3] conducted a randomized, double-blind, controlled trial for acute lowering of BP during hypertensive emergencies of pregnancy using labetalol and nifedipine. Failure to achieve target BP occurred in five women (16.6%) randomized to labetalol compared with one woman in the nifedipine group (3.3%). In the present study there is significant increase in cases reporting urine albumin nil after drug therapy with nifedipine than labetalol. The present study shows a slightly higher induction rate in labetalol group (61.3%) as compared to nifedipine group (57.3%). Shekhar *et al.* (2013) [3] conducted a similar study between labetalol and nifedipine and found that induction of labor was more in labetalol group which is comparable to current study. The rate of cesarean section for uncontrolled PIH was less in labetalol group compared with Nifedipine group.

The rate of cesarean section for uncontrolled PIH was less in labetalol group compared with Nifedipine group.

Observer	LSCS rate	
	Labetalol	**Nifedipine**
Raheem *et al*. (2011) [13]	52%	64%
Shekhar S *et al*. (2016) [10]	No difference	No difference
Hangarga US *et al*. (2016) [4]	42%	50%
Thakur *et al*. (2017) [16]	LESS	MORE
Jorge Duro-Gomez *et al*. (2017) [12]	75%	70%
Present study	26%	44%

The results in the current study are comparable to be study done by Raheem *et al.*, Hangarga US *et al.*, Thakur *et al.* stating that LSCS rate was higher in nifedipine group as compared to labetalol group. In the present study, the birth weight of the babies delivered to mothers of these groups were compared and gave insignificant result regarding each other. Also there was no congenital anomaly reported in the trial. The present study showed slightly lower incidence of preterm labor in Nifedipine group, however it was statistically insignificant. Giannubilo *et al.* [17] (2012) conducted a retrospective study in hypertensive patients treated during pregnancy with nifedipine or labetalol by monitoring maternal and fetal outcomes and found that there was a higher rate of intrauterine growth restriction infants among women treated with labetalol compared with those treated with nifedipine (38.8 vs. 15.5 %; $p < 0.05$). Present study showed insignificant difference in perinatal death. Nifedipine group had 6 cases of still birth whereas labetalol group had 3 perinatal deaths. All the babies who succumbed to death were extremely LBW with baby weight less than 1.5 kg. The perinatal morbidity include respiratory distress syndrome, jaundice and hypoglycemia were of insignificant difference in each group. Hangarga US *et al.* (2016) [4] compared the two drugs and found that the rate of still birth was 16% in nifedipine group, whereas only 4% in labetalol group. These findings were comparable to the current study.

The study of incidence of various maternal complications faced in this study are:

1. Incidence of severe hypertensive episode was 4% with labetalol whereas nil in nifedipine. In 3 cases, with labetalol, BP was controlled when combination of nifedipine was given along with labetalol.
2. Incidence of placental abruption was nil in labetalol and minimal (1.33%) in nifedipine.
3. Incidence of eclampsia was higher in labetalol and nil in nifedipine group.
4. No case of maternal death was reported.

In the comparative study of Labetalol and Nifedipine by Dhali B *et al.* (2012) [9], there was a little bit higher occurrence of eclampsia in labetalol group as compared to nifedipine group.

6. Conclusion

The present study was a prospective randomized trial in which labetalol and nifedipine were given to patients with hypertensive disorders of pregnancy. The control of blood pressure was better with nifedipine than with labetalol. Preterm labor was less with nifedipine which may be due to tocolytic effect of nifedipine. It was also observed that Nifedipine gave better results in cases of hypertensive emergency. Both labetalol and nifedipine had minimal side effects and drug compliance was better. Cost effectiveness was better with nifedipine. Thus, Nifedipine is as safe and effective as labetalol for the management of hypertensive disorders as well as in hypertensive emergency during pregnancy.

7. References

1. Martin JN Jr, Owens My, Keiser SD, *et al.* Standardized Mississippi protocol treatment of 190 patients with HELLP syndrome: slowing disease progression and preventing new major maternal morbidity. Hypertension Pregnancy. 2012; 31(1):79.
2. Khan KS, Wojdyla D, Say L, *et al.* WHO analysis of causes of maternal death: a systematic review. Lancet. 2006; 367:1066.
3. Shekhar S, Sharma C, Thakur S, Verma S. Oral Nifedipine or Intravenous Labetalol for hypertensive emergency in pregnancy: a randomized controlled trial. Obstetrics & Gynecology. 2013; 122(5):1057-63.
4. Hangarga US, Rita D, Harshitha K. Comparative study of labetalol and nifedipine in management of hypertensive disorders in pregnancy. Int J Reprod Contracept Obstet Gynecol. 2017; 6:194-7.
5. Michael CA. The evaluation of labetalol in the treatment of hypertension complicating pregnancy. British journal of clinical pharmacology. 1982; 1:13(S1).
6. Stott D, Bolten M, Salman M, Paraschiv D, Douiri A, Kametas NA. A prediction model for the response to oral labetalol for the treatment of antenatal hypertension. Journal of human hypertension, 2016.
7. Scardo JA, Vermillion ST, Hogg BB, Newman RB. Hemodynamic effects of oral nifedipine in preeclamptic hypertensive emergencies. American journal of obstetrics and gynecology. 1996; 175(2):336-40.
8. Elatrous S, Nouira S, Besbes LO, Marghli S, Boussarssar M, Sakkouhi M, *et al*. Short-term treatment of severe hypertension of pregnancy: prospective comparison of nicardipine and labetalol. Intensive care medicine. 2002; 28(9):1281-6.
9. 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.
10. Shekhar S, Gupta N, Kirubakaran R, Pareek P. Oral nifedipine versus intravenous labetalol for severe hypertension during pregnancy: asystematic review and meta-analysis. BJOG: An International Journal of Obstetrics & Gynecology. 2016; 123(1):40-7.
11. Webster LM, Myers JE, Nelson-Piercy C, Harding K, Cruickshank JK, Watt-Coote I, *et al*. Labetalol Versus Nifedipine as Antihypertensive Treatment for Chronic Hypertension in Pregnancy: A Randomized Controlled Trial. Hypertension, 2017, hypertensionaha-117.
12. Duro-Gómez J, Rodríguez-Marín AB, Giménez de Azcárete M, Duro-Gómez L, Hernández-Angeles C, Arjona-Berral JE, *et al*. A trial of oral nifedipine and oral labetalol in preeclampsia hypertensive emergency treatment. Journal of Obstetrics and Gynaecology. 2017; 19:1-3.
13. Raheem I, Saaid R, Omar S, Tan P. Oral nifedipine versus intravenous labetalol for acute blood pressure control in hypertensive emergencies of pregnancy: A randomised trial. BJOG. 2012; 119:78-85.
14. Scardo JA, Vermillion ST, Newman RB, Chauhan SP, Hogg BB. A randomized, double-blind, hemodynamic evaluation of nifedipine and labetalol in preeclamptic hypertensive emergencies. American journal of obstetrics and gynecology. 1999; 181(4):862-6.
15. Öhman KP, Weiner L, Von Schenck H, Karlberg BE. Antihypertensive and metabolic effects of nifedipine and labetalol alone and in combination in primary hypertension. European journal of clinical pharmacology. 1985; 29(2):149-54.
16. Thakur V, Thakur A, Saroshe S. Comparison of effect of nifedipine, labetalol and methyldopa in treatment of hypertension in pregnancy in a tertiary care government hospital. International Journal of Reproduction, Contraception, Obstetrics and Gynecology. 2016; 5(1):17-22.
17. Giannubilo SR, Bezzeccheri V, Cecchi S, Landi B, Battistoni GI, Vitali P, *et al*. Nifedipine versus labetalol in the treatment of hypertensive disorders of pregnancy. Archives of gynecology and obstetrics. 2012; 286(3):637-42.