Original Research Article

A Study of IV Labetalol Versus Oral Nifedipine in Severe Hypertension in Pregnancy (A prospective randomized comparative study)

Kirandeep Kaur[1], Gurdip Kaur[2], Parneet Kaur[2], Preet Kanwal Sibia[2], Satinder Pal Kaur[3]

[1]Junior Resident, [2]Professor, [3]Assosiate Professor

Department of Obstetrics and Gynaecology, Government Medical College, Patiala Punjab, India

Corresponding Author:

Dr Satinder Pal Kaur

House No 389, Phase - 1, Urban Estate Patiala 147001

Email: saka0275@gmail.com Mob: 9876122178

Abstract

Introduction:

Hypertensive disorders are most common medical complication of pregnancy with incidence ranging 2-8% of all pregnancies and are important cause of maternal and perinatal morbidity and mortality.

Aims & Objectives:

To compare the efficacy of intravenous labetalol and oral nifedipine in acute blood pressure control in severe hypertension in pregnancy.

Material & Methods:

A randomized controlled study was conducted in the Department of Obstetrics and Gynaecology, Govt. Medical College and Rajendra Hospital, Patiala. Total 100 subjects with gestation ≥ 28 weeks with blood pressure ≥ 160/110 mm of Hg were included in study and randomized equally in two groups. Group A received intravenous labetalol in escalating doses of 20 mg, 40 mg, 80 mg and 80 mg every 15 minutes and Group B received oral nifedipine in doses of 10 mg, 20 mg and 20 mg every 20 minutes until blood pressure of ≤150/100 mm of Hg was achieved. Cross over treatment was administered if the initial treatment failed. The time required achieve target blood pressure and adverse effects were noted. The statistical value of significance was taken as $p<0.05$.

Results:

The time required to achieve target blood pressure in Group A (Labetalol) was 30.00±13.89 minutes and in Group B (nifedipine) was 34.00±14.14 minutes with p value 0.512. The adverse effects noted with both the drugs were very few and of minor degree with no statistical difference.

Conclusion:

We concluded, Intravenous labetalol and oral nifedipine are equally effective in the control of severe hypertension in pregnancy.

Keywords:

hypertension in pregnancy, intravenous labetolol, oral nifedipine

Introduction:

Hypertensive disorders are most common medical complications of pregnancy with incidence ranges 2-8% of all pregnancies. In India 12% and in Asia 9% maternal mortality is contributed by hypertensive disorders. According to WHO estimate approximately 45000 women die each year from hypertensive disorders worldwide.[1] Incidence of preeclampsia in nulliparous women is found to be 3-

10% and in multiparous 1.4-4% in several worldwide studies reviewed by Staff and co-workers.[2]

According to American College of Obstetricians and Gynecologists (ACOG) hypertension in pregnancy is defined as systolic blood pressure of 140 mm Hg or higher and diastolic blood pressure of 90 mm Hg or higher after 20 weeks of gestation with previous normal BP [3]. Hypertension during pregnancy can be categorized as:

(1) preeclampsia-eclampsia, (2) chronic hypertension (of any cause),

(3) chronic hypertension with superimposed preeclampsia, and (4) gestational hypertension.

Severe hypertension i.e., blood pressure ≥160/110 mm of Hg is associated with risk of severe maternal and fetal complications like placental abruption, pulmonary edema, intracranial hemorrhage, eclampsia, end organ damage and poor perinatal outcome. The reduction of systolic blood pressure to 140-155 mm of Hg and diastolic blood pressure to 90-100 mm of Hg is required to reduce these complications.

Most commonly used drugs in severe hypertension during pregnancy are nifedipine, labetalol and hydralazine. Nifedipine is calcium channel blocker. It is commonly used antihypertensive in pregnancy because of being cost effective, rapid onset and long duration of action. Labetalol is non selective beta blocker and postsynaptic alpha-adrenergic blocker. Intravenous labetalol is used in severe hypertension of pregnancy to induce controlled rapid decrease in blood pressure. Hydralazine when used intravenously for control of severe hypertension in pregnancy, is associated with significant maternal hypotension, placental abruption, maternal oliguria and adverse effect on fetal heart rate.[4] A metanalysis of randomized clinical trials using hydralazine for treatment of severe hypertension in pregnancy concluded that the evidence does not support the use of these agents as first line drug when compared with labetalol and nifedipine.[5]

Thus, the study was conducted to compare oral nifedipine and intravenous labetalol in severe hypertension in pregnancy in terms of their rapidity to achieve target blood pressure, safety profile and fetomaternal outcomes.

Aims And Objectives

1. To compare the efficacy of intravenous labetalol and oral nifedipinein their rapidity and number of doses required to achieve blood pressure of ≤150/100mmHg in severe hypertension in pregnancy.
2. To study the safety profile of two drugs by observing side effects.
3. To evaluate fetomaternal outcomes in severe hypertension in pregnancy.

Material And Methods

This prospective, comparative and interventional study was conducted in the Department of Obstetrics and Gynecology, Govt. Medical College and Rajendra Hospital, Patiala during the period 2018-2019 after getting ethical clearance from the institutional ethical committee. 100 cases presenting with severe hypertension after 28 weeks of pregnancy were admitted and after taking informed and written consent, included in the study. Subjects were randomly allocated in two groups by using simple randomization method (lottery method). Each group included 50 subjects. Group A subjects received intravenous labetalol and Group B subjects received oral nifedipine.

Inclusion Criteria

(1) Pregnant subjects with severe hypertension having systolic blood pressure ≥160 mm Hg and diastolic blood pressure ≥110 mm Hg
(2) Period of gestation >28 weeks
(3) Proteinuria >300 mg/24 hrs urine or 1+ or greater in random urine dipstick.

Exclusion Criteria

Patients with:

(i) Known heart disease
(ii) Bronchial asthma
(iii) Chronic obstructive pulmonary disease
(iv) Patient with bradycardia (PR <60 bpm)
(v) Patients with allergic diathesis
(vi) Eclampsia

Method

Particulars of the subjects and history was recorded as per proforma. Period of gestation ascertained by date of last menstrual period and/or earliest ultrasound. General physical, systemic and obstetrical examination was done followed by routine and specific investigations. Vitals were recorded every 15 minutes till the control of blood pressure. Thereafter half hourly for 2 hours, then hourly for another 4 hours and then every 4 hourly.

Group A - Subjects received labetalol intravenously slowly in doses of 20mg, 40mg, 80mg and 80mg every 15 minutes with proper BP monitoring up to maximum of 220mg and end point was therapeutic goal of reducing BP ≤150/100mmHg or reaching the maximum dose. If BP still remained high alternative treatment was given.

Group B - Oral nifedipine was given in doses of 10mg, 20mg and 20mg every 20 minutes with proper BP monitoring and end point was therapeutic goal of reducing BP ≤150/100mmHg. If BP still remained high alternative treatment was given.

The various side effects of drugs like dizziness, palpitation, nausea, flushing, hypotension, excessive sweating was noted. After the successful control of blood pressure further antihypertensive therapy started after two hours of the last trial medication.

Primary outcome measure was assessed in terms of time taken to achieve target systolic blood pressure of ≤ 150 mm Hg and diastolic blood pressure of ≤100 mm Hg in both groups. Both had to be achieved.

Secondary outcome measures included adverse drug effects and fetomaternal outcomes. Maternal outcomes evaluated in the form of period of gestation at the time of delivery and mode of delivery. Fetal outcomes evaluated in the form of baby weight, Apgar scores and need for neonatal intensive care unit. Management was planned according to clinical condition and viability of fetus.

The data obtained was analyzed statistically using IBM SPSS version 22 software. Numerical data analysed by student t - test and categorical data analysed by Chi-square test or Fischer exact test. The statistical test is considered significant when calculated p value is less than 0.05 and considered highly significant when p value less than 0.001.

Results

The baseline characteristics like maternal age, parity, booked/unbooked status, gestational age and systolic and diastolic blood pressure at beginning of study were comparable in both groups (Table 1).

Table 1: Comparison of baseline characteristics of subjects in study groups

Characteristic	Group A (Labetalol) n = 50	Group B (Nifedipine) n = 50	p value
Age (in years) Mean ± SD	26.28 ± 4.74	26.26 ± 4.17	0.982
Booking status (%) Booked Unbooked	12 88	12 88	0.086
Gestational age (in weeks) Mean ± SD	36.19 ± 2.47	36.55 ±3.07	0.519
Primigravida (%)	62	44	0.109
Systolic BP (mm of Hg) Mean ± SD	166.12 ± 12.24	164.36 ± 9.33	0.421
Diastolic BP (mm of Hg) Mean ± SD	114.96 ± 8.76	112.12 ± 7.84	0.091

Table 2: Time taken to achieve target blood pressure

Time Taken	Group A (Labetalol) n = 50	Group B (Nifedipine) n = 50
Mean±SD	30.00±13.89 minutes	34.00±14.14 minutes
Median	30.00 minutes	40.00 minutes
Range	15-60 minutes	20-60 minutes
t-test	1.427	
p value	0.512(NS)	

Table 3: Target blood pressure achieved within 1 hour

Target blood pressure (in mm of Hg)	Group A (Labetalol) n = 50		Group B (Nifedipine) n = 50		x^2	p value
	No of subjects	%age	No of subjects	%age		
Systolic (≤150)	49	98	47	94	0.02	0.901(NS)
Diastolic (≤100)	48	96	46	92	0.02	0.899(NS)

The other outcomes measured were adverse effects of these drugs, cross over treatment required, mode of delivery, birth weight of new born, Apgar score and NICU admissions (Table 4). The most common side effects seen with labetalol were dizziness (10%) and excessive sweating (4%) and with nifedipine, palpitation (8%), nausea and flushing (4% each)

Table 4: Secondary outcomes measured in study groups

Outcome measured	Group A (Labetalol) n = 50	Group B (Nifedipine) n = 50	p value
Adverse effects (%) No notable adverse effect Adverse effect noted	 80 20	 78 22	0.378
Cross over (%) Required Not required	 4 96	 8 92	0.399
Mode of delivery (%) Vaginal Cesarean section	 62 38	 66 34	0.677

Birth weight (in Kg) Mean ± SD	2.10 ± 0.64	2.26 ± 0.73	0.282
Apgar score at 5 min <9 9	25 75	26 74	0.170
NICU admission Required Not required	21.15 78.85	26 74	0.084

Discussion

The mean age of subjects enrolled in this study was 26.28±4.74 years in labetalol group (Group A) and 26.26±4.17 years in nifedipine group (Group B). In a study conducted by Singh D et al [6] in 2013 the mean age of subjects in labetalol group was 25.3±3.96 years and in nifedipine group was 25.87±3.85 years.

In present study mean gestational age in labetalol group (Group A) was 36.19±2.47 weeks and in nifedipine group (Group B) was 36.55±3.07 weeks. In a study conducted by Shekhar S et al [7] mean gestational age was 36.1±3.2 weeks and 37.3±2.12 weeks in labetalol group and nifedipine group respectively. In present study with regard to gravida distribution maximum subjects were primigravida in both groups i.e., 62% in labetalol group (Group A) and 44% in nifedipine group (Group B) showing primiparity as a risk factor for pre-eclampsia. Similar observation was reported by Duckitt K et al [8] in their study.

Table 5: Comparison of mean baseline systolic and diastolic blood pressure

Author and year of study	Labetalol (Group A)		Nifedipine (Group B)	
	Systolic BP (in mm of Hg)	Diastolic BP (in mm of Hg)	Systolic BP (in mm of Hg)	Diastolic BP (in mm of Hg)
Dhali B et al [9] (2012)	163.2±1.5	110.7±1.4	163.5±1.8	111.2±1.8
Shekhar S et al [7] (2013)	168±13.8	110.±7.5	165±6.7	108±5.9
Kumari V R et al [1] (2014)	172.2±8.6	115.2±2.6	170.6±6.4	114.8±2.5
Gavit Y et al [10] (2016)	176.05±12.87	112.35±5.10	171.75±12.45	112.85±5.29
Allam A et al [2] (2018)	174.45±7.50	115.35±3.12	175.80±7.72	115.20±3.03
Present study	166.12±12.24	114.96±8.76	164.36±9.33	112.12±7.84

The mean baseline systolic blood pressure in our study was 166.12±12.24mm of Hg and diastolic 114.96±8.76 mm of Hg which was comparable to studies by other authors. [7,9,10](Table 5). We find work of other authors to compare time taken to achieve target blood pressure. [1,2] (Table 6)

Table 6: Showing mean time taken to achieve target blood pressure in various studies

Author and year of study	Labetalol (Group A) (Time taken in minutes)	Nifedipine (Group B) (Time taken in minutes)
Kumari V R et al[1] (2014)	36.61±5.2	34.77±4.8
Alam A et al [2] (2018)	32.62±12.19	26.25±12.60
Present study	30.00±13.89	34.00±14.14

Table 7: Comparing no of subjects who required cross over treatment in various studies

Author and year of study	%age of subjects in labetalol group (Group A)	%age of subjects in nifedipine group (Group B)
Singh D et al[6] (2013)	05	00
Das S et al [11] (2014)	12	14
Kumari V R et al[1] (2014)	14	14
Devi S R et al [12] (2017)	10	00
Present study	04	08

In present study, in labetalol group (Group A), 2 (4%) subjects required cross over treatment and among these, both target systolic and diastolic blood pressure was not achieved in 1 subject and only diastolic blood pressure was not controlled in other. In nifedipine group (Group B) cross over treatment was required in 4 (8%) subjects and among these, both target systolic and diastolic blood pressure was not achieved in 3 subjects and only target diastolic blood pressure was not achieved in 1 subject. (Table 7) The most common adverse effect in labetalol group (Group A) was dizziness and in nifedipine group (Group B) was palpitations. One subject in nifedipine group developed hypotension. 80% subjects in labetalol group (Group A) and 78% subjects in nifedipine group (Group B) had no notable adverse effects. Alam A et al [2] in their study reported that 80% subjects in labetalol group and 87.5% subjects in nifedipine group had no notable adverse effects.

The mode of delivery in majority of enrolled subjects was vaginal i.e., 62% in labetalol group (Group A) and 66 % in nifedipine group (Group B). While caesarean delivery was conducted in 38 % subjects in labetalol group (Group A) and 34% subjects in nifedipine group (Group B). In a study conducted by Gavit Y et al [10] vaginal delivery was conducted in 62.5% in

labetalol group and 65% in nifedipine group and caesarean delivery was in 37.5% in labetalol group and 35% in nifedipine group which is comparable to present study.

In our study the mean birth weight was 2.10±0.64 kg in labetalol group (Group A) and 2.26±0.73 kg in nifedipine group (Group B) which is comparable with the study conducted by Kumari V R et al [1] where mean birth weight was 2.28±0.5 kg in labetalol group and 2.31±0.24 kg in nifedipine group.

Conclusion

Hypertensive disorders are among major causes of maternal mortality and morbidity. Management of severe hypertension in pregnancy requires strict observation as drastic reduction in blood pressure leads to utero-placental insufficiency and that may cause intrauterine fetal death, and continuation of pregnancy with severe hypertension leads to adverse feto-maternal outcome.

Our study compared efficacy of intravenous labetalol and oral nifedipine in severe hypertension in pregnancy. From the results of our study, we concluded that both intravenous labetalol and oral nifedipine are equally effective and well tolerated in control of blood pressure in severe hypertension in pregnancy. Nifedipine can be used in peripheral centres due to its easy availability, ease of administration and cost effectiveness. Labetalol is costlier but being injectable labetalol can be used in unconscious and drowsy patients.

Bibliography

1. Kumari VR, Saraswathi K, Srilaxmi A. Oral nifedipine versus intravenous labetalol for control of blood pressure in severe preeclampsia. J. Evolution Med. Dent. Sci. 2016; 5 (20):994-7.
2. Alam A and Zakaria S.M.A. Oral nifedipine versus intravenous labetalol for acute blood pressure control in hypertensive emergencies of pregnancy: a randomized controlled trial. International Journal of Reproduction, Contraception, Obstetrics and Gynecology. 2019 May ; 8(5):1921-7
3. Gestational hypertension and preeclampsia. ACOG Practice Bulletin No. 202. American College of Obstetricians and Gynecologists. Obstet Gynecol 2019;133: e1–25.
4. Cunningham F G, Leveno K J, Bloom S L, Dashe J S, Hoffman B L, Casey B M, Spong C Y editors, 2018, Williams Obstetrics ,25th edition, McGraw-Hill, New York, p. 720
5. Padmaja A and Sravanthi VL. A study of oral nifedipine and intravenous labetalol in severe hypertension in pregnancy at teaching hospital. IAIM 2017;4(8):12-19
6. Singh D, Singh S, Singh S, Rani R, Verma U, Nigam AK et al. Comparative Evaluation of Efficacy & Safety of Intravenous Labetalol and Oral Nifedipine in Severe Hypertension of Pregnancy. JMSCR 2017;5(3):18941-947.
7. 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.
8. Duckitt K, Harrington D. Risk factors for pre-eclampsia at antenatal booking: systematic review of controlled studies. BMJ. 2005 March 12; 330 (7491):565
9. Dhali B, Bhattacharya S, Ganguly RP, Bandyopadhyay S, Mondal M, Dutta M. A randomized trial of intravenous labetalol & oral nifedipine in severe pregnancy induced hypertension. International Journal of Reproduction, Contraception, Obstetrics and Gynecology. 2016;1(1): 42-6.
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. International Journal of Reproduction, Contraception, Obstetrics and Gynecology. 2018 February; 7 (2): 719-24 17.
11. Das S, Biswas S, Das P, Mahapatra B. Comparative study of intravenous labetalol and oral nifedipine for control of blood pressure in severe preeclampsia. IOSR Journal of Dental and Medical Sciences 2015;14(10):22-27.
12. Devi SR, Devi RKP, Kumar LA, Devi R, Das S, Deepthambika and Abhipsa. Comparative study between oral nifedipine and intravenous labetalol in management of severe pregnancy induced hypertension. European Journal of Pharmaceutical and Research. 2017; 4(9): 291-6.