Original Research Article

Comparative study of oral nifedipine versus intravenous labetalol in severe hypertension in pregnancy: A randomized controlled study

Rekha Sahai[1], Anupam Nidhi[1], Rita Ranjan[2], Shyam Lal[3,*]

[1]*Guru Gobind Singh Government hospital Raghubir Nagar, New Delhi, India*
[2]*Deen Dayal Upadhyay Hospital, New Delhi, India*
[3]*Dept. of Surgery, ESIC Postgraduate Institute of Medical Sciences and Research, New Delhi, India*

ARTICLE INFO

ABSTRACT

Objective: To compare the efficacy of oral nifedipine with intravenous labetalol in the treatment of severe hypertension in pregnancy.

Materials and Methods: It was a double-blind, randomized, controlled study conducted in pregnant women with blood pressure ≥160/110 mm Hg. Total 60 patients were enrolled from October 2016 to September 2017. Patients were randomized to receive nifedipine (10 mg tablet orally up to five doses) and intravenous placebo saline injection or intravenous labetalol injection in doses of 20, 40, 80, 80, and 80 mg and a placebo tablet every 20 minutes until the target blood pressure of $\leq$ 150/100 mmHg was achieved. The primary outcome of the study was time necessary to achieve target blood pressure. Secondary outcome were number of doses required, onset of labour, mode of delivery, adverse maternal and neonatal effects, side effect, and perinatal outcome.

Results: The time to achieve the blood pressure goal was significantly shorter with nifedipine (mean $\pm$ SD, 34.67 ± 20.297 minutes) than with labetalol (52.00 ± 29.054minutes; P <.017). Nifedipine group required significantly lower doses (mean $\pm$ SD, 1.73 ± 1.015) as compared to labetalol (2.60 ± 1.453, p<0.017). Urine output was significantly increased in nifedipine group (mean $\pm$ SD, 2296 ± 210.483 ml) compared with labetalol group (1374 ± 155.798 ml, P < .0001) and remained significantly increased 24 hours after initial administration. No patients required crossover therapy. The adverse effects were infrequent. There were no significant differences in maternal age, gestational age, and blood pressures between the groups.

Conclusion: Oral nifedipine and intravenous labetalol both are effective in the management of severe hypertension of pregnancy; however, nifedipine controls hypertension more rapidly with less number of doses and was associated with a significant increase in urinary output.

1. Introduction

Hypertension in pregnancy is one of the common medical disorder. It complicates 6 to 10% of pregnancies and is the third common cause for maternal mortality and morbidity next to haemorrhage and infections in India.[1] Severe pregnancy induced hypertension (PIH) requires prompt treatment because of risk of cardio-vascular accident, to prevent intracerebral haemorrhage, hypertensive encephalopathy and other target organ damage.[2] It also pose an increased risk of complication for the fetus such as prematurity, low birth weight, neonatal ICU admission and even fetal death.[3]

The optimal management of PIH somewhat controversial. Most guidelines recommend labetalol, hydralazine and nifedipine as first line alternatives for the treatment of severe PIH.[2] Previously, the hydralazine was preferred drug; but it has higher incidence of ' overshoot ' hypotension.[4,5] However, labetalol and nifedipine have fast emerged as drugs of choice.

Vermilion and Shekhar et al[6,7] demonstrate that both oral nifedipine and intravenous labetalol are effective in

* Corresponding author.
E-mail address: slaldr@gmail.com (S. Lal).

the management of severe hypertensive emergencies of pregnancy; however, nifedipine controls hypertension more rapidly and is associated with a significant increase in urinary output. A meta-analysis by Shekhar et al[8] for severe PIH, showed that oral nifedipine was associated with less risk of persistent hypertension and is as efficacious and safe as intravenous labetalol. However, in study of Raheem,[9] concluded that oral nifedipine and intravenous labetalol regimens were similarly effective in the acute control of severe hypertension in pregnancy. Lakshmi and Chawla D et al[10,11] found that though both oral nifedipine and intravenous labetalol are effective in the treatment of hypertensive crisis during pregnancy, intravenous labetalol may have benefits because it is more effective in reducing the BP to target levels with a lower number of doses. Therefore, due to controversies in the treatment present study was undertaken to evaluate and compare oral nifedipine and intravenous labetalol in severe PIH.

2. Materials and Methods

This was a, randomized, double-blind clinical study conducted in patients with severe pregnancy induced hypertension (PIH) from October 2016 to September 2017 at Deen Dayal Upadhyay Hospital New Delhi. Institutional ethical committee approval was obtained.

2.1. Inclusion criteria

Pregnant women of age between 20 to 45 years with ≥ 34 weeks of gestation, blood pressure of $\geq 160/110$ mmHg and with or without proteinuria ($\geq +1$ or ≥ 300 mg in a 24 hours urine collection), were included in this study after informed consent.

2.2. Exclusion criteria

Patients with chronic hypertension, asthma, cardiogenic shock, cardiac failure, pulmonary oedema, chronic obstructive pulmonary disease, bradycardia and exposure to either medication within the preceding 24 hours or absolute contraindication to labetalol and nifedipine were excluded from study.

2.3. Sample size calculation and Randomization

Sample size calculation was done on the basis of previous study which reveals, patients received oral nifedipine achieved the target BP in 25.0 ± 13.6 minutes (mean $\pm$ SD]) as compared with 43.6 ± 25.4 minutes (mean $\pm$ SD) in patients of labetalol group.[6] Using these results as guidance data, with an alpha value of 0.05 and 90% power, the required sample size calculated using Open epi CDC tool was 25 patients in each arm. Assuming the possibility of outcome statistics to be non-parametric, and dropouts of participants, we increased our sample size by 10% for

each assumption. The final sample size calculated was 30 participants in each arm.

Participants were randomized on 1:1 basis. We did block randomization for two treatment arms of the block size 4. The order of treatments within each block was determined by a computer-generated random sequence and placed in numbered sealed envelopes with allocated drugs. Two packages, A and B were made. Package A consist of injection labetalol 60 ml (5mg/ml) and placebo tablets, which were identical to oral nifedipine tablets, or 60ml sodium chloride solution (0.9%) in a syringe and 10 mg nifedipine tablets. Package B contained the opposite regimen; for crossover, if needed. Envelopes were opened by a ward nurse, who was in the research team, and both the gynecologist and patients were blinded. All patients were received magnesium sulfate for seizure prophylaxis. (loading doses of 4g IV and 10g IM, and maintenance dosing of 5g IM/4hr)

Patients were placed in a semirecumbent position on bed. Nurse was instructed to administer 4 ml intravenously from syringe A and one tablet to swallow as the initial treatment. After 20 minutes, (if blood pressure >150/100 mmHg), a second tablet and 8 ml from syringe A was administered. After another 20 minutes, if the target blood pressure was not achieved, a third tablet and 16 ml from syringe A was given. This can be repeated for another two cycles, if required. If after five cycles of regimen A the target blood pressure was not achieved; crossover to regimen B was carried out. Regimen B was carried out in identical fashion to that described for regimen A. If the treatment goal was not achieved after completion of five cycles of regimen B, then open-label treatment was carried out.

All patients were subjected to detailed history and examination. Routine hematological, biochemical and urine test were done. Urine output and vitals were monitored. Fundus examination was done. Cardiotocography and ultrasound scan for fetal well-being was done.

The primary outcome of the study was time required to achieve target blood pressure ($\leq 150/100$ mm Hg). Patients were monitored till delivery or 48 hours after control of blood pressure and followed up till 6 weeks after delivery.

Secondary outcome were number of doses required, onset of labour, mode of delivery, adverse maternal and neonatal effects, side effect, and perinatal outcome.

3. Results

Total of 76 concordant patient were enrolled in this study in which one patient of bronchial asthma and 15 patients with history of exposure to anti-hypertensive medication in preceding 24 hours were excluded.(Figure 1)

As shown in theTable 1, two groups were similar with respect to maternal age, parity and period of gestation. A high systolic BP or diastolic BP alone or both were also comparable among two groups. Age distribution in the

study groups, has shown that the mean age of nifedipine group was 23.42± 4.768 years and 22.90±4.213 years in labetalol group, (p<0.648). Nine (30.0%) patients in nifedipine group and 12(40.0%) in labetalol were booked; rest of the patient in study were un -booked.

Maximum patients were primigravida in both the groups (54.3% in the nifedipine and 56.7% in the labetalol group). Moreover, 14 (46.70%) patients in nifedipine and 13(43.3%) patients in labetalol group were multigravida. (p< 0.795) Most of the patients in our study were at mean gestational age of 37.4 ± 1.799 and 37.7 ± 2.063 weeks in nifedipine and labetalol group respectively. (p< 0.328) The mean systolic BP was 182.40 ± 15.804 mmHg in nifedipine and 184.67 ± 17.462 mmHg in labetalol group. (p<0.600) The mean diastolic BP was 116.07 ± 8.493 mmHg and 114.87 ± 6.447 mmHg in nifedipine and labetalol group respectively. (p<0.500)

The mean arterial blood pressure was 138.178 ± 8.716 mmHg in nifedipine and 146.200 ± 31.813 mmHg in labetalol group. (p<.0.188) Twenty six patients (86.66%) in nifedipine and 24 (80.00%) patients in labetalol group showed proteinuria.(p<0.907)

The mean time needed to achieve the target BP in women received nifedipine was 34.67 ± 20.297 minutes as compared to 52.00 ± 29.054 minutes for those received intravenous labetalol. (Table 2) Patients on oral nifedipine were more rapidly achieved target blood pressure, as compare to labetalol. The finding was statistically significant. (p <.017) The mean dose required to achieve target BP was 1.73 ± 1.015 in nifedipine group while 2.60 ± 1.453 in la betalol group. The required doses was less in nifedipine group. The difference was statistically significant (p <.017). The mean urinary output in 24 hours in nifedipine and labetalol group was 2296.17 ± 210.483 ml and 1374.00 ± 155.798) ml respectively ; which were statistically significant. (p < 0.0001)There was no difference noted in the mode of delivery as 5 patient underwent caesarean section and 25 delivered vaginally in each group.

The various side effects of the drugs like nausea, dizziness, palpitations, headache, flushing and fatigue showed no statistical significance among the two drugs. Maternal hypotension or foetal tachycardia was not seen in either of the study groups.

The mean birth weight of babies in nifedipine group was 2.666 (± 0.337) kg and for the labetalol group was 2.660 (± 0.191) kg. The p value was 0.929 which was not statistically significant. The APGAR score of <7 at 5 minutes was seen in 10% of the nifedipine group and 16.66% of the labetalol group. Ninety percent of the nifedipine group and 83.33% of the labetalol group showed APGAR score of ≥ 7 at 5 minutes. (p < 0.448) The neonatal complications like prematurity, neonatal ICU admissions, IUGR was comparable among the two groups

as no statistically difference was noted.(Table 2)

Table 2: Outcomes

Characteristics	Nifedipine n=30	Labetalol N=30	*P value*
Primary outcome			
Mean time taken to achieve blood pressure< 160/110mg	34.67 ± 20.297	52.00 ± 29.054	0.017
Secondary Outcomes			
Mean dosages to achieve blood pressure <160/100 mmHg	1.73 ± 1.015	2.60 ± 1.453	0.017
Urine output in 24 hours(ml)	2296.17 ± 210.483	1374.00 ± 155.798	0.0001
Onset of Labour			
Spontaneous	9(30.0)	9(30.0)	1.000
Induced	21(70.0)	21(70.0)	1.000
Mode of delivery			
Caesarean	5(16.66)	5(16.66)	1.000
Vaginal(including instrumental)	25(83.33)	25(83.33)	1.000
Birth weight (kg)	2.9 (2.2 – 3.1)	2.9 (2.7 – 3.2)	0.95
Side Effects			
Nausea	6(20.0)	8 (26.7)	0.542
Dizziness	4(13.3)	8 (26.7)	0.197
Headache	15(50.0)	6 (20.0)	0.015
Flushing	3 (10.0)	4 (13.3)	0.688
Fatigue	00	4(13.3)	0.038
Hypotension	00	00	-
Shortness of breath	00	00	-
Chest Pain	00	00	-
Perinatal Outcome			
Birth weight (kg)	2.666 ± 0.337	2.603 ± 0.191	0.929
APGAR Score (5 minutes)			
< 7	3(10.0)	5(16.66)	0.448
>7	27(90.0)	25(83.33)	
Prematurity	5(16.66)	3(10.0)	0.59
IUGR	2(6.7)	4(13.3)	0.389
Neonatal intensive care admission	3(10.0)	5(16.66)	0.448

Figure in parentheses denote percentages

4. Discussion

Hypertension remains the most commonly encountered medical condition in pregnant women. Various etiological theories for the pregnancy induced hypertension has been proposed. The common pathophysiological changes seen are imbalance between vasoconstrictor thromboxane A2 and vasodilator prostacyclin resulting in generalized vasospasm. This leads to endothelial damage resulting in release of vasoactive substances. This causes decreased

Table 1: Characteristics of pregnancy in both the groups

Characteristics	Nifedipine	Labetalol	*P* value
Age in years ,(mean ±SD)	23.43 ± 4.768	22.90 ± 4.213	0.648
Parity:			
Primigravida	16(54.3)	17(56.7)	0.795
Multigravida	14(46.70)	13(43.3)	
Booked /Un-booked			
Booked	9(30.0)	12(40.0)	0.417
Un-booked	21(70.0)	18(60.0)	
Gestational age in weeks (mean ±SD)	37.4 ± 1.799	37.7 ± 2.063	0.328
Systolic Blood Pressure (mmHg) (mean ±SD)	182.40 ± 15.804	184.67 ± 17.462	0.600
Diastolic Blood Pressure (mmHg) (mean ±SD)	116.07 ± 8.493	114.87 ± 6.447	0.500
Mean arterial Blood pressure (mean ±SD)	138.178 ± 8.716	146.200 ± 31.813	0.188
Proteinuria	26(86.66)	24(80.00)	0.907

Figure in parentheses denote percentages
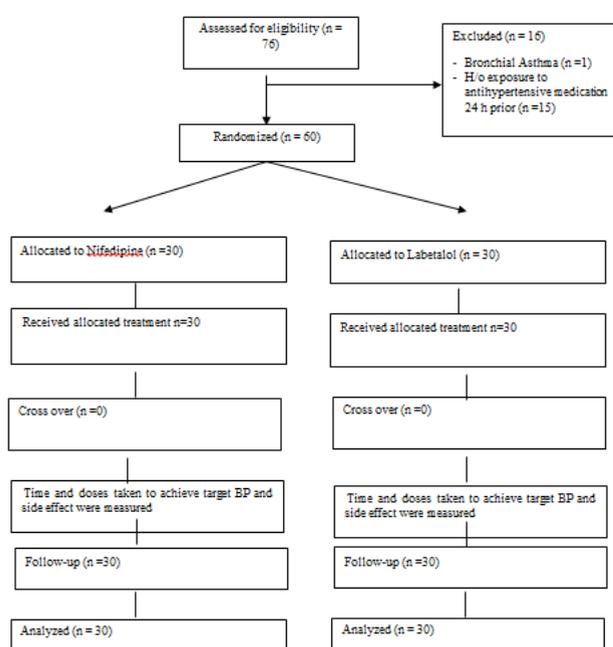
Fig. 1: Flow chart of randomized trial of nefidipine vs labetalol

intravascular volume and increased extravascular volume. The effects of this are placental insufficiency leads to complications.[12]

The main strategy in the management of severe pre-eclampsia is reduction of blood pressure for the prevention of both maternal and fetal adverse events. The recommended drugs for treatment of hypertensive crisis are oral nifedipine, intravenous labetalol and hydralazine.[13] Various randomized control trials has been conducted with the use of these drugs. Nifedipine has been found to have a rapid onset, longer duration of action and the advantage of oral route.[10] It selectively increases renal perfusion and thereby has a diuretic effect.[14] Intravenous labetalol is a fast-acting antihypertensive with few adverse effects on

mother and fetus.[6,15] It also potentially decreases cerebral perfusion pressure thereby decreasing the incidence of eclampsia.[16]

In the present study both nifedipine and labetalol were found to be effective in the treatment of hypertensive crisis and this is consistent with the reports of the previous studies.[6,11,15–17] In our study, pregnant women allocated to oral nifedipine achieved target blood pressure significantly more rapidly and with fewer doses as compared with those receiving intravenous labetalol.

Vermillion et al,[6] demonstrates the mean times needed to achieve target blood pressure was 25 minutes and 43.6 minutes for nifedipine and labetalol group, respectively. We found mean times of 34.67 ± 20.297 and 52.00 ± 29.054 minutes, in nifedipine and labetalol group respectively. (p <.017) Although, longer time needed to achieve target BP in the present study might be attributable to a flat dose of nifedipine (10mg) used in our study. A similar effect was also seen in the study by Shekhar et al.[7] although they reported longer times taken to achieve the target BP than our study.

However, in the study of Raheem et al[9] reveals, both nifedipine and labetalol to be equally efficacious as median times needed to achieve the target BP was 30 minutes and 45 minutes in the nifedipine and labetalol group, respectively (P= 0.59).

Shi et al[18] reported that the use of nifedipine and labetalol for severe PIH and found that oral nifedipine was more effective for safely reducing BP to target levels and with lower number of doses compared with intravenous labetalol. Therefore, oral nifedipine can be an alternative to intravenous labetalol for lowering BP during hypertensive emergencies in pregnancy. Oral nifedipine may also be preferable because of its ease of oral administration, low cost and a flat dosing regimen. The network meta-analysis and trial sequential analysis of randomized clinical trials conducted by Shridhran et al[19] also showed similar results.

The number of doses required to control the BP indirectly reflects the time required to reach the desired BP, the probability of persistent severe hypertension and the side-effects, all increasing with increasing dose requirements. Our data indicate that we achieved the therapeutic goal blood pressure with less number of doses in nifedipine group as compare to labetalol. The mean dose in nifedipine and labetalol group was 1.73 ± 1.015 and 2.60 ± 1.453) respectively. (p <.017). Similar finding was demonstrated by Dhali[20] This less time and dose requirement was because of nifedipine has rapid onset, oral bioavailability and longer duration of action. Moreover, nifedipine >90% metabolized in liver, excreted in urine and has very few side effects. Studies also have demonstrated that nifedipine lowers blood pressure without any reduction in uteroplacental blood flow and abnormal heart rate.[6,7,21]

Decreased in both urine output and renal perfusion is common in patient of PIH due to intravenous volume depletion. Randomized controlled trials reveals, a significant increase urine output in nifedipine group as compare to patients receiving labetalol.[6,22] Nifedipine increases urine output after selective renal arteriolar vasodilatation.[6,23,24] In our study mean urinary output in 24 hours in nifedipine and labetalol group was 2296.17 ± 210.483 ml and 1374.00 ± 155.798 ml respectively. (p < 0.0001). The increase in urine output was persisted at least 24 hours after initial dose.

Nifedipine has been used safely in the treatment of hypertensive emergencies and as a tocolytic agent in several randomized clinical trials.[6,23,25] Our patients achieved the targeted blood pressure after 1 to 2 doses of nifedipine and due to smaller concentration of nifedipine was insufficient to evaluate the tocolytic effect.

For seizure prophylaxis magnesium sulphate is commonly used in severe pre-eclampsia[9,22,26] Therefore, the possibility of interaction between antihypertensive agents and magnesium sulphate is to be considered. Some cases of severe hypotension,[27] neuromuscular blockade,[28] and symptomatic hypocalcaemia[29] were reported, when nifedipine was used concurrently with magnesium- sulphate in hypertensive pregna ncies. However, various studies suggest that the use of nifedipine and magnesium sulphate together does not increase the risk of serious magnesium-related effects and is well tolerated.[26,30] We used magnesium sulphate as prophylaxis in all patients of both the groups, none of them had a significant adverse event.

In our study no significant adverse effects on maternal or foetal health were reported in both the groups. However, minor side effects, such as nausea, dizziness, headache, cutaneous flushing, and fatigue, were reported which were infrequent, transient, and did not warranted for discontinuation of medication in either groups. None of the randomized studies reported significant maternal side effect.[6–10] Fetal side effects were rare and occurred with similar frequencies in both groups. The findings were similar in previous studies.[4,13,14,30] Meta-analysis done by S Shekhar[8] shows a significantly reduced risk of maternal side effects with nifedipine.

Nifedipine also lowers BP without any apparent reduction in uteroplacental blood flow[12,14] and without any significant fetal heart rate abnormalities.[6] There were no significant differences in maternal and perinatal outcome, which makes nifedipine an ideal or better than equal alternative to labetalol.

All patients responded to antihypertensive agents in our study. Further, there were no cases of overshoot hypotension, cerebrovascular accidents, eclampsia or abruption after initiation of antihypertensive treatment reported. There was no case of maternal mortality.

5. Conclusion

Intravenous labetalol and oral nifedipine both are effective in controlling BP. Nifedipine reduced blood pressure more rapidly and had a favourable effect on urine output. No significant maternal and fetal adverse effects were noted with either drug. Oral nifedipine may be a better alternative due to its ease of oral administration and a flat dosing regimen.

6. Source of funding

None.

7. Conflict of interest

None.

8. Ethical approval

Yes

References

1. WHO reproductive health library. WHO recommendation on antihypertensive drugs for women with severe hypertension during pregnancy. *World Health Organization*. 2011;.
2. National Institute for Health and Clinical Excellence (NICE). Hypertension in Pregnancy: the management of hypertensive disorders during pregnancy. *NICE Clin Guideline*. 2010;107:1–295.
3. Sibai BM, Stella CL. Diagnosis and management of atypical preeclampsia-eclampsia. *Am J Obstet Gynecol*. 2009;200.
4. Fenakel K, Fenakel G, Appelman Z, Lurie S, Katz Z, et al. Nifedipine in the treatment of severe preeclampsia. *Obstet Gynecol*. 1991;77:331–337.
5. Mabie WC, Gonzalez AR, Sibai BM, Amon E. A comparative trial of labetalol and hydralazine in the acute management of severe hypertension complicating pregnancy. *Obstet Gynecol*. 1987;70:328–333.
6. 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;181:858–861.
7. 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;122:1057–1063.

8. Shekhar S, Gupta N, Kirubakaran R, Pareek P. Oral nifedipine versus intravenous labetalol for severe hypertension during pregnancy: a systematic review and meta-analysis. *BJOG*. 2016;123:40–47.

9. 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.

10. Lakshmi BS, Dasari P. Oral nifedipine versus intravenous labetalol in hypertensive urgencies and emergencies of pregnancy: a randomized clinical trial. *Obstet Med*. 2012;5:171–175.

11. Chawla D, Khatri R, Minal, Nayyer PS. A comparative study of intravenous labetalol versus oral nifedipine in severe hypertension in pregnancy in a tertiary hospital. *J Dent Med Sci*. 2018;17(3):56–59.

12. Granger JP, Alexander BT, Llinas MT, Bennett WA, Khalil RA. Pathophysiology of hypertension during preeclampsia linking placental ischemia with endothelial dysfunction. *Hypertension*. 2001;38(3):718–722.

13. Pampus MGV, Wolf H, Westenberg SM, Post JAVD, Bonsel GJ, et al. Maternal and perinatal outcome after expectant management of the HELLP syndrome compared with pre-eclampsia without HELLP syndrome. *Eur J Obstet Gynecol Reprod Biol*. 1998;76:31–36.

14. Ganzevoort W, Rep A, Bonsel GJ, Fetter WP, Soderen LV, et al. A randomised controlled trial comparing a temporising management strategy with plasma volume expansion with one without plasma volume expansion. *Br J Obstet Gynaecol*. 2005;112:1358–1368.

15. Gracia PVD, Lasso M, Ruiz E, Vega-Malek JC, Mena FT, et al. Severe hypertension in pregnancy: hydralazine or labetalol. A randomized clinical trial. *Eur Obstet Gynecol Reprod Biol*. 2006;128:157–162.

16. Belfort MA, Tookie-Miller C, Jr JCA, Dizon-Townson D, Varner MA. Labetalol decreases cerebral perfusion pressure without negatively affecting cerebral blood flow in hypertensive gravidas. *Hypertens Pregnancy*. 2002;21:185–197.

17. Pampus MGV, Wolf H, Ilsen A, Treffers PE. Maternal outcome following temporizing management of the (H)ELLP syndrome. *Hypertens Pregnancy*. 2000;19:211–220.

18. Shi Q, Leng W, Yao Q, Mi C, Xing A. Oral nifedipine versus intravenous labetalol for the treatment of severe hypertension in pregnancy. *Int J Cardiol*. 2015;178:162–164.

19. Sridharan K, Sequeira RP. Drugs for treating severe hypertension in pregnancy: a network meta- analysis and trial sequential analysis of randomized clinical trials. *Br J Clin Pharmacol*. 2018;84(9):1906–1916.

20. Dhali B, Bhattacharya S, Ganguly RP, Bandyopadhyay S, Mondal M, et al. A randomized trial of intravenous labetalol & oral nifedipine in severe pregnancy induced hypertension. *Int J Reprod Contracep Obstet Gynecol*. 2012;1:42–46.

21. Lurie S, Fenakel K, Freidman A. Effect of nifedipine on fetal heart rate in the treatment of severe pregnancy induced hypertension. *Am J Perinatol*. 1990;7:285–291.

22. Momina Z, Radha T. Sowjanya Ravella IV labetalol and oral nifedipine in acute control of severe hypertension in pregnancy–A randomized controlled trial;Available from: ejogrb.2019.01.022.

23. Thalamati S, Bandaru S, Bhumireddy D. Assessment of safety and efficacy of oral nifedipine and intravenous labetalol in management of increased blood pressure in severe preeclampsia. *Int J Reprod Contracept Obstet Gynecol*. 2018;7:2645–2649.

24. Venkat-Raman G, Feehally J, Elliot HL. Renal and haemodynamic effects of amlodipine and nifedipine in hypertensive renal transplant recipients. *Nephrol Dial Transplant*. 1998;13:2612–2616.

25. Scardo JA, Vermillion ST, Hogg B, Newman RB. Hemodynamic effects of oral nifedipine in preeclamptic hypertensive emergencies. *Am J Obstet Gynecol*. 1996;175:336–338.

26. Altman D, Carroli G, Duley L, Farrell B, Moodley J, et al. Do women with pre-eclampsia, and their babies, benefit from magnesium sulphate? The Magpie Trial: a randomised placebo-controlled trial. *Lancet*. 2002;359:1877–1890.

27. Waisman GD, Mayorga LM, Camera MI, Vignolo CA, Martinotti A. Magnesium plus nifedipine: potentiation of hypotensive effect in preeclampsia? *Am J Obstet Gynecol*. 1988;159:308–309.

28. Ben-Ami M, Giladi Y, Shalev E. The combination of magnesium sulphate and nifedipine: a cause of neuromuscular blockade. *Br J Obstet Gynaecol*. 1994;101:262–263.

29. Koontz SL, Friedman SA, Schwartz ML. Symptomatic hypocalcemia after tocolytic therapy with magnesium sulfate and nifedipine. *Am J Obstet Gynecol*. 2004;190:1773–1776.

30. Magee LA, Cham C, Waterman EJ, Ohlsson A, Dadelszen PV. Hydralazine for treatment of severe hypertension in pregnancy:meta-analysis. *BMJ*. 2003;327:955–960.

Author biography

Rekha Sahai Senior Resident

Anupam Nidhi Specialist

Rita Ranjan Specialist

Shyam Lal Professor