Nifedipine attenuates the hypertensive response to tracheal intubation in pregnancy-induced hypertension

Nanda Kumar MD MNAMS, Y.K. Batra MD MNAMS,
Indu Bala MD, S. Gopalan FRCOG PhD

Thirty women with pregnancy-induced hypertension (PIH) scheduled for Caesarean section under general anaesthesia were studied to evaluate the efficacy of sublingual nifedipine in attenuating the pressor response to laryngoscopy and tracheal intubation. The patients were randomly given either the contents of a nifedipine capsule 10 mg or placebo sublingually 20 min before induction of anaesthesia. Blood pressure and heart rate were recorded at various time intervals. There was a decrease in mean arterial blood pressure (MAP) after pretreatment with nifedipine ($P < 0.01$). The increase in MAP during laryngoscopy and intubation was higher in the control group compared with nifedipine pretreatment group ($P < 0.01$). During laryngoscopy and intubation, MAP decreased by 3 mmHg in the nifedipine pretreatment group, while there was an increase of 14 mmHg in the control group. Heart rate increased in both the groups during the laryngoscopy and tracheal intubation ($P < 0.01$) but the increase was higher in the nifedipine group than in the control group ($P < 0.05$). Neonatal Apgar scores in both the groups were comparable. These results suggest that sublingual nifedipine is effective in attenuating the hypertensive response to laryngoscopy and intubation but not the tachycardiac response in parturients with PIH.

L'efficacité de la nifédipine administrée en sublingual pour atténuer la poussée hypertensive due à la laryngoscopie et à l'intubation endotrachéale a été évaluée chez trente femmes souffrant d'hypertension d'origine gestationnelle (PIH) et programmées pour une césarienne sous anesthésie générale. Les patientes ont reçu aléatoirement soit une gélule de 10 mg de nifédipine, soit un placebo, par voie sublinguale, vingt minutes avant l'induction de l'anesthésie. La pression artérielle et la fréquence cardiaque ont été enregistrées à des intervalles de temps variés. Il y a eu une diminution de la pression artérielle moyenne (MAP) après le prétraitement à la nifédipine ($P < 0,01$). L'augmentation de la MAP pendant la laryngoscopie et l'intubation a été plus importante dans le groupe contrôle par rapport au groupe prétraité à la nifédipine ($P < 0,01$). Pendant la laryngoscopie et l'intubation, la MAP a diminué de 3 mmHg dans le groupe prétraité à la nifédipine, tandis qu'il y a eu un accroissement de 14 mmHg dans le groupe contrôlé. La fréquence cardiaque a augmenté dans les deux groupes lors de la laryngoscopie et de l'intubation ($P < 0,01$) mais cette augmentation a été supérieure dans le groupe nifédipine ($P < 0,05$). Les scores d'Apgar dans les deux groupes étaient comparables. Les résultats suggèrent que la nifédipine en sublingual est efficace pour atténuer la réaction hypertensive mais pas la tachycardie lors de la laryngoscopie et l'intubation chez les parturientes atteintes de PIH.

Key words

ANAESTHESIA: obstetrical;

INTUBATION: complications – cardiovascular;

PHARMACOLOGY: calcium channel blockers, nifedipine.

From the Departments of Anaesthesiology and Obstetrics and Gynaecology, Postgraduate Institute of Medical Education and Research, Chandigarh-160012 (India).

Address correspondence to: Dr. Y.K. Batra, Department of Anaesthesiology, PGI, Chandigarh-160012 (India).

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The pressor response to intubation is markedly exaggerated in hypertensive pregnant patients, with increases in systemic and pulmonary arterial pressures and pulmonary capillary wedge pressure.^{1,2} Transient but severe hypertension during tracheal intubation has been associated with increased maternal intracranial pressure, cerebral haemorrhage and cardiac failure with pulmonary oedema, resulting in increased morbidity and mortality in both mother and child.³

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hypertension both acutely⁴ and in the long term.⁵ It has also been used to treat acute episodes of severe hypertension during pregnancy and puerperium without causing any adverse fetal effects.⁶

Nifedipine has been found to attenuate the reflex cardiovascular responses to laryngoscopy and tracheal intubation in normotensive patients.⁷ The present investigation was planned to study the effectiveness of nifedipine in attenuating the pressor responses associated with laryngoscopy and intubation in pregnancy-induced hypertensive patients undergoing Caesarean section.

Methods

The study was approved by the Human Ethics Committee of the Nehru Hospital PGIMER, Chandigarh and informed written consent obtained from all the patients.

Thirty women with pregnancy-induced hypertension (diastolic blood pressure of 100–120 mmHg) scheduled for Caesarean section under general anaesthesia were selected for the study. The patients were receiving treatment with antihypertensive drugs such as hydralazine and methyldopa. They were randomly assigned to control (Group I, $n = 15$) or nifedipine groups (Group II, $n = 15$) with random number charts. Patients with preexisting cardio-respiratory diseases, morbid obesity and diabetes were excluded from the study.

Twenty minutes before the induction of anaesthesia the patients were given either the contents of a nifedipine gelatin capsule 10 mg or a placebo capsule of a similar physical characteristic sublingually by the fourth author who was not involved in rest of the study.

On arrival in the operating theatre, patients were placed supine with a 15° left lateral tilt. A 5% dextrose infusion was started and the patients were preoxygenated for five minutes. Anaesthesia was induced rapidly in all the patients with thiopentone 5 mg · kg⁻¹, followed by succinylcholine hydrochloride 1.5 mg · kg⁻¹. Any patient in whom tracheal intubation proved to be difficult or who strained or coughed during intubation was excluded from the study.

Anaesthesia was maintained with 50:50 mixture of N₂O and O₂ until the delivery of the baby after which the O₂ concentration was reduced to 33%. Pancuronium bromide 0.07 mg · kg⁻¹ was the muscle relaxant used in all the patients.

The blood pressure and heart rate were recorded at the following intervals:

- (A) Before nifedipine pre-treatment (Control value).
- (B) Twenty minutes after pre-treatment, i.e., just before induction of anaesthesia.
- (C) After injection of thiopentone.
- (D) During laryngoscopy and tracheal intubation. E, F, G, H, I at one, two, three, five and ten minutes

respectively following laryngoscopy and tracheal intubation.

Heart rate and blood pressure were monitored using a digital blood pressure meter (OMRON MODEL-HEM, 58). The mean arterial pressure (MAP) was calculated using the formula diastolic blood pressure + 1/3 pulse pressure. At delivery, the Apgar score of the baby, maternal blood gas values and pH, induction-delivery and uterine incision to delivery intervals were also recorded.

Analysis of variance and Student's *t* test were used to analyse changes within and between the groups. The Mann-Whitney test was used for analysing nonparametric data for Apgar score. $P < 0.05$ was considered to indicate statistical significance.

Results

Age, weight, base line blood pressure and heart rate induction-delivery intervals, uterine incision to delivery intervals and preoperative antihypertensive medications were similar in the control and treatment groups (Table I).

The changes in MAP and heart rate in both groups during the induction sequence are presented in Figure 1 and Figure 2 respectively. There was a decrease in MAP after pretreatment with nifedipine in Group II ($P < 0.01$). In both groups MAP decreased after administration of thiopentone but there was no difference between the two groups at that time. The increase in MAP during laryngoscopy and intubation was greater in Group I than in Group II ($P < 0.01$). During laryngoscopy and intubation MAP decreased by 3 mmHg from the basal value in Group II while there was an increase of 14 mmHg in Group I (Figure 1).

There was an increase in heart rate after pretreatment with nifedipine in Group II ($P < 0.01$) (Figure 2). During laryngoscopy and tracheal intubation there was an increase in heart rate in both the groups ($P < 0.01$) but the increase was greater in Group II and the difference between the two groups was statistically significant ($P < 0.05$). The increase in heart rate over the basal value at one minute after intubation was 27 beats per minute in Group II and 18 beats per minute in Group I. The heart rate was higher in Group II than that in Group I throughout the study period ($P < 0.01$) (Figure 2).

Maternal and arterial blood gas analysis at delivery were similar in both groups (Table II) and Table III illustrates the neonatal Apgar scores in both the groups were not different.

Discussion

Pregnancy-induced hypertensive patients require close control of blood pressure during anaesthesia for Caesarean section for both maternal and fetal well being.

TABLE I Maternal variables in the control and nifedipine treatment groups (mean $\pm$ SD)

	Control group (n = 15)	Nifedipine group (n = 15)
Age (yr)	27.2 $\pm$ 4.0	28.2 $\pm$ 3.5
Weight (kg)	74.3 $\pm$ 1.4	75.4 $\pm$ 1.5
Base line mean BP (mmHg)	124.0 $\pm$ 6.0	128.0 $\pm$ 8.0
Base line heart rate (bpm)	90.0 $\pm$ 11.0	92.0 $\pm$ 15.0
Induction to delivery time (min)	7.2 $\pm$ 1.2	6.6 $\pm$ 1.2
Uterine incision to delivery time (sec)	64.5 $\pm$ 12.7	61.8 $\pm$ 13.8
Pre-op drugs		
- Methyldopa (n)	8	7
- Hydralazine (n)	6	9

No significant difference.

TABLE II Maternal arterial blood gas values

	Control group (n = 15)	Nifedipine group (n = 15)
pH	7.4 $\pm$ 0	7.4 $\pm$ 0
PaO ₂ (mmHg)	145.6 $\pm$ 16.3	140.0 $\pm$ 15.1
PaCO ₂ (mmHg)	35.3 $\pm$ 3.7	35.6 $\pm$ 4.6
HCO ₃ ⁻ (meq $\cdot$ L ⁻¹)	23.0 $\pm$ 3.1	23.8 $\pm$ 2.0

No significant difference.

TABLE III Newborn Apgar score (Mean $\pm$ SD)

	Control group (n = 15)	Nifedipine group (n = 15)
1 Minute	6.4 $\pm$ 1.3 (4-8)	6.2 $\pm$ 1.4 (3-8)
5 Minute	7.9 $\pm$ 1.2 (6-10)	8.2 $\pm$ 1.3 (5-10)

No significant difference.

Nifedipine, a dihydropyridine, is well absorbed by oral or sublingual routes. After a single sublingual administration of nifedipine 10 mg, an antihypertensive action is obvious within five to eight minutes with peak effect at 20 to 30 min.⁸ It has been used to attenuate the cardiovascular responses to laryngoscopy and tracheal intubation in normotensive patients.⁷ It has also been used to treat acute episodes of severe hypertension during pregnancy and puerperium without any adverse fetal effects.⁶ Nifedipine has also been found to have beneficial effects on urinary output during the first 24 hr postpartum in patients with severe eclampsia.⁹

In our study nifedipine smoothly and gradually reduced the SBP, DBP and MAP by approximately 10% of the control value within 20 min of sublingual administration. This smooth and gradual reduction mitigated

FIGURE 1 Mean arterial pressure (MAP) changes in control (Group I, n = 15 ...) and nifedipine pretreatment (Group II, n = 15 ...) patients at various times. A - Before nifedipine pretreatment (control value); B - twenty minutes after pre-treatment; C - after thiopentone; D - During laryngoscopy and tracheal intubation, E,F,G,H,I - one, two, three, five and ten minutes after laryngoscopy and intubation. Within group comparison **P* < 0.05, ***P* < 0.01. Between group comparison **P* < 0.05, ***P* < 0.01. (All values mean $\pm$ SEM).

FIGURE 2 Heart rate changes in control (...) and nifedipine (...) treated patients at various time intervals. (All values mean $\pm$ SEM.) For symbols see Figure 1.

the risk of unintentional hypotension. This 10% reduction in blood pressure following sublingual nifedipine buffered the increase in blood pressure following endotracheal intubation in Group II.

An increase in heart rate was observed in the patients treated with nifedipine. The heart rate during laryngoscopy, one minute and two minutes after laryngoscopy was higher ($P < 0.05$) in Group II than in Group I. In previous studies where nifedipine was used to attenuate the cardiovascular responses to laryngoscopy and tracheal intubation in normotensive⁷ and in patients with coronary artery disease,¹⁰ there was an increase in heart rate in both groups but the heart rates of the control group did not differ from the nifedipine group at any time during the investigation. This discrepancy in heart rate compared with our study could be explained because the central venous pressure in PIH is low and varies inversely with the severity of hypertension.^{11,12} Plasma volume in PIH is 10% less than in normal pregnant women.¹¹ This diminished intravascular volume leads to increased baroreceptor activity and augmentation of sympathetic nervous system activity.¹¹ Moreover, nifedipine by virtue of its blood pressure lowering effects activates baroreceptors leading to an increased heart rate.¹³ Both of these factors might have been responsible for the greater increase in heart rate seen in Group II patients compared with Group I. It is also possible that the haemodynamic response which persisted after intubation can be due to the added effect of both intubation and surgical stimuli.

Many other drugs have been tried to attenuate the hypertensive response to tracheal intubation in PIH patients. The relatively slow onset and long duration of action of hydralazine prevents rapid adjustment of blood pressure.¹⁴ Trimethaphan acts rapidly¹⁵ and has a short duration of action but may prolong muscle paralysis after succinylcholine.¹⁶ Other undesirable side effects of trimethaphan include histamine release, reduction of splanchnic blood flow and cardiac output.¹⁵ Sodium nitroprusside also has a rapid onset of action but carries the risk of both maternal and fetal cyanide toxicity.¹⁷ It also increases maternal intracranial pressure.¹⁸ Nitroglycerine has been found to be effective in preventing the hypertensive response but it crosses the placenta and may also increase maternal intracranial pressure.¹⁹

In a preliminary study intravenous labetalol pretreatment had been evaluated to attenuate the pressure response to laryngoscopy and intubation with moderate success.²⁰ The disadvantage of labetalol pretreatment was that in the event of sudden excessive blood loss, patients might not be able to compensate by an increase in heart rate and peripheral vascular resistance. Moreover, labetalol can cause neonatal bradycardia and hypotension.²¹

In the present study two patients in Group II com-

plained of headache. No other adverse effect was noticed. The Apgar scores were comparable in both groups and no adverse neonatal effects were noted in our study.

In conclusion, sublingual nifedipine when employed as a pretreatment in a dose of 10 mg attenuates the hypertensive response but not the tachycardic response to laryngoscopy and tracheal intubation in PIH patients.

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