Nicardipine and verapamil attenuate the pressor response to laryngoscopy and intubation

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In a prospective, double-blind study, we compared the efficacy of iv nicardipine hydrochloride and verapamil hydrochloride in attenuating the cardiovascular responses to laryngoscopy and tracheal intubation, in 45 patients undergoing elective surgery with general anaesthesia. Patients were allocated randomly to one of three groups of 15 patients. Patients in Group I received saline while those in Groups II and III received nicardipine hydrochloride, 0.03 mg · kg⁻¹ or verapamil hydrochloride, 0.1 mg · kg⁻¹ iv three minutes before laryngoscopy and intubation. Patients in Group I showed the greatest increase in SBP 25.4 ± 2.2 mmHg and HR 35.7 ± 3.8 beats · min⁻¹ at one minute after intubation (P < 0.001), and these changes persisted throughout the study period albeit with decreasing magnitude. After drug administration, patients in Groups II and III demonstrated increases in HR of 26 ± 2.4 and 15.1 ± 2.2 beats · min⁻¹ and decreases in SBP of 24.8 ± 2.0 and 18.8 ± 2.4 mmHg respectively (P < 0.001). It is concluded that nicardipine and verapamil are effective in attenuating pressor responses to laryngoscopy and intubation but did not control the tachycardia.

Cette étude prospective et à double insu compare l'efficacité de l'hydrochlorure de nicardipine et de l'hydrochlorure de verapamil utilisés pour atténuer la réponse cardio-vasculaire à la laryngoscopie et à l'intubation de la trachée chez 45 patients soumis à une chirurgie programmée sous anesthésie générale. Les patients sont répartis au hasard à un de trois groupes de

15 patients. Les patients du groupe I reçoivent du soluté physiologique alors que les groupes II et III reçoivent soit de l'hydrochlorure de nicardipine 0,03 mg · kg⁻¹ ou de l'hydrochlorure de verapamil 0,1 mg · kg⁻¹ trois minutes avant la laryngoscopie et l'intubation. Les patients du groupe I manifestent l'augmentation la plus importante de PAS à 25,4 ± 2,2 mmHg et de Fc 35,7 ± 3,8 b · min⁻¹ une minute après l'intubation (P < 0,001) et ces changements persistent pendant la période d'étude mais en diminuant. Après l'administration de la drogue, les patients du groupe II et III manifestent des augmentations de la Fc de 26 ± 2,4 et de 15,1 b · min⁻¹ et des baisses de PAS de 24,8 ± 2,0 et de 18,8 ± 2,4 mmHg respectivement (P < 0,001). En conclusion, la nicardipine et le verapamil atténuent la réponse vaso-pressive de la laryngoscopie et de l'intubation mais ne contrôlent pas la tachycardie qui en résulte.

Laryngoscopy and tracheal intubation are known to result in transient hypertension, tachycardia and arrhythmias which can be deleterious in patients with systemic hypertension, coronary artery disease, aortic aneurysms, intracranial aneurysms and cerebrovascular disease.¹⁻⁵ Various pharmacological attempts have been made to attenuate these responses. These include opioids,⁶ deep anaesthesia,⁷ local anaesthetics,⁸ vasodilators,⁹ alpha and beta sympathetic blocking agents¹⁰ and calcium channel blocking drugs.¹¹

The calcium channel blocking drugs used for attenuation of these cardiovascular responses include intravenous verapamil,^{11,12} intravenous diltiazem¹³ and intravenous nicardipine hydrochloride.^{14,15} In the present study we compared the efficacy of two calcium channel blocking agents, nicardipine hydrochloride, a dihydropyridine derivative and verapamil hydrochloride, a papaverine derivative, for attenuation of the pressor responses to laryngoscopy and intubation.

Methods

Forty-five adult patients of ASA grades I–II, undergoing elective surgery, were selected for the present study. Eth-

Key words

ANAESTHETIC TECHNIQUES: laryngoscopy, tracheal intubation;

PHARMACOLOGY: verapamil, nicardipine.

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ical clearance was obtained from the institute ethics committee and informed consent was obtained from the patients. Those with major systemic illness, pregnant women and lactating mothers, and patients in whom intubation took more than 30 sec were excluded from the study. Premedication was with diazepam $0.15 \text{ mg} \cdot \text{kg}^{-1}$ *po* the night before surgery and repeated 90 min before surgery. In addition, morphine sulphate $0.15 \text{ mg} \cdot \text{kg}^{-1}$, promethazine hydrochloride $0.5 \text{ mg} \cdot \text{kg}^{-1}$ were administered *im* 45 min before surgery.

In the operating theatre each patient was connected to a multichannel monitor Horizon 1000 for continuous ECG display and non-invasive blood pressure and heart rate measurements. Base line recordings of systolic, diastolic and mean blood pressure and heart rate were made. Blood gas analysis was also done at this time. A separate ECG recorder was connected to patients for recording of any relevant ECG changes.

Patients were randomized to receive either normal saline (Group I), $0.03 \text{ mg} \cdot \text{kg}^{-1}$ nicardipine hydrochloride (Group II), or $0.1 \text{ mg} \cdot \text{kg}^{-1}$ verapamil hydrochloride (Group III), three minutes before tracheal intubation. Each injection was made up to a volume of 5 ml and its nature was unknown to the observer. The drug/saline injection was followed two minutes later by thiopentone $5 \text{ mg} \cdot \text{kg}^{-1}$, *iv* over 30 sec, followed by succinylcholine, $1.5 \text{ mg} \cdot \text{kg}^{-1}$. Artificial ventilation was commenced via a face mask using a Magill circuit. Thirty seconds later, i.e., three minutes after the drug/saline injection, laryngoscopy was performed and the trachea was intubated. Anaesthesia was maintained with 67% nitrous oxide in O_2 and pancuronium was used for muscle relaxation. No other inhalational agent was used.

A second ABG analysis was done after intubation and analysed to ensure normocarbida. Readings of systolic, diastolic and mean blood pressures and heart rate were taken after the injection of the drug/saline at the following times:

- D 60: 60 sec after administration of drug/saline.
- D 120: 120 sec after administration of drug/saline and coinciding with administration of thiopentone.
- D 150: 150 sec after administration of drug/saline and coinciding with administration of suxamethonium.
- L: At laryngoscopy.

I_1, I_2, I_3, I_5 every minute for five minutes and then $I_{10}, I_{15}, I_{20}, I_{25}, I_{30}, I_{35}$ every five minutes thereafter for up to 35 min after intubation.

The data collected were analysed using paired Student's *t* test for comparison within the group, repeated measures ANOVA for differences among the three groups and Student's unpaired *t* test for differences between individual groups. Post Hoc test (Newman Keul's) was also applied for pair wise comparison.

FIGURE 1 Changes in systolic blood pressure.

Results

There were no differences between the three groups with respect to mean age and weight (32.3 ± 3.4 yr and 52.7 ± 3.5 kg in Group I, 30.1 ± 2.9 yr and 54.7 ± 3.2 kg in Group II and 33.0 ± 2.9 yr and 53.4 ± 3.3 kg in Group III). The baseline cardiovascular variables (SBP, DBP, MBP and HR) were comparable ($P > 0.05$).

Changes in systolic blood pressure (SBP)

In Group I, a marked increase in SBP occurred during laryngoscopy (L), which reached its peak, 25.4 ± 2.2 mmHg ($P < 0.001$) above basal value, at I_1 and the peak was sustained until I_2 . The SBP remained above basal level until I_{30} ($P < 0.001$) (Figure 1). In Groups II and III the mean maximum decrease in SBP was seen at D150, measuring 24.8 ± 2.08 mmHg ($P < 0.001$) and 18.8 ± 2.4 mmHg ($P < 0.001$) respectively. In Group II, following laryngoscopy and intubation, SBP always remained below the basal value, until the end of the study period ($P < 0.05$, Figure 1). In Group III, SBP was comparable to the basal value at I_1 , after which it decreased and remained so throughout the study (Figure 1).

Changes in diastolic blood pressure (DBP)

Apart from changes in magnitude and duration, the changes of DBP were similar to those of SBP. The maximum change seen in DBP was $+23 \pm 3.0$ mmHg ($P < 0.001$) at I_1 in Group I, -14.5 ± 1.4 mmHg ($P < 0.001$) at D150 in Group II and -12.73 ± 1.1 mmHg ($P < 0.001$) at D150 in Group III. In Groups II and III, DBP was same at all times except for a greater decrease in Group II at D120 (Figure 2).

Changes in mean blood pressure (MBP)

The pattern of changes in MBP was similar to SBP and DBP (Figure 3).

FIGURE 2 Changes in diastolic blood pressure.

Changes in heart rate (HR)

Group I had the greatest increase in heart rate (HR) after tracheal intubation, compared with Groups II and III (Figure 4). In Group I, HR increased with laryngoscopy and intubation (35.7 ± 3.8 beats min^{-1} , $P < 0.001$) and remained above the basal levels throughout the study. In Groups II and III, HR increased after drug administration, but the peak increase in HR was seen at I₁ measuring 26 ± 2.5 beats min^{-1} in Group II and 15.1 ± 2.17 beats min^{-1} in Group III (Figure 4). The HR remained higher in Group II than in Group III ($P < 0.05$) except at I₁ (Figure 1).

Discussion

Calcium channel blocking agents are widely used for their cardiovascular and cerebrovascular actions.¹⁶ Verapamil is the treatment of choice in supraventricular tachycardias and a useful antihypertensive and antianginal agent. It has also been used for successful attenuation of the cardiovascular responses to laryngoscopy and intubation.^{11,12} However, it cannot be administered safely with volatile anaesthetic agents,¹⁷ or beta adrenergic blocking agents,^{18,19} in patients who have poor left ventricular function. It can also potentiate neuromuscular blockade.²⁰

In this respect, nicardipine has been combined with digoxin²¹ and beta blocking agents^{22,23} and has no neuromuscular blocking effect. However, when used with inhalational agents it may cause excessive hypotension.²⁴

Puri *et al.* (1986), using higher doses of morphine ($0.2 \text{ mg} \cdot \text{kg}^{-1}$) and thiopentone ($5.5 \text{ mg} \cdot \text{kg}^{-1}$), achieved better control of heart rate responses using verapamil $0.1 \text{ mg} \cdot \text{kg}^{-1}$ *iv* one min before induction.¹¹ Nishikawa and Namiki (1989), on the other hand, using the same dose of verapamil after succinylcholine could not control hypertension and tachycardia.¹² This could have been due

FIGURE 3 Changes in mean blood pressure.

FIGURE 4 Changes in heart rate.

to two factors. First, the time allowed for verapamil to act (one min) was not sufficient for its peak action. Secondly, precurarisation may result in tachycardia and hypertension.²⁵ In our study, we achieved control of hypertension with verapamil but the tachycardia could not be controlled.

Our patients showed a greater decrease in systemic blood pressure with nicardipine than described by Mikawa *et al.* (1990)¹⁴ and Omote *et al.* (1992),¹⁵ perhaps because, in these two studies, opioid premedication was not used.

Our study shows that nicardipine and verapamil are effective in attenuating the hypertensive response to laryngoscopy and tracheal intubation, but neither controlled the resulting tachycardia.

In summary, calcium channel blockers provide satisfactory control of hypertension but some other agents,

e.g., opioids, may be needed to attenuate the tachycardia resulting from laryngoscopy and intubation.

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