EFFECTS OF TRIMETAPAN ON THE CARDIOVASCULAR RESPONSE TO TRACHEAL INTUBATION


SUMMARY

In three groups of 10 patients, we have studied the effect on the cardiovascular responses to laryngoscopy and intubation of bolus doses of saline or trimetaphan 0.05 mg kg⁻¹ or 0.1 mg kg⁻¹ given 1.75 min before the start of laryngoscopy. Anaesthesia was induced with thiopentone 5 mg kg⁻¹ i.v. and tracheal intubation was facilitated with vecuronium 0.2 mg kg⁻¹. During anaesthesia, ventilation was assisted or controlled with 1% enflurane and 50% nitrous oxide in oxygen. Patients receiving saline showed a significant increase in mean arterial pressure and rate-pressure product associated with tracheal intubation. These increases following tracheal intubation were less in trimetaphan-treated patients compared with those of the control group (P<0.05). There was no significant difference in heart rate following tracheal intubation between the three groups. These data suggest that trimetaphan may be used as a supplement during induction, to attenuate the hypertensive response associated with laryngoscopy and tracheal intubation.

KEY WORDS


Considerable interest has focused on the haemodynamic changes following laryngoscopy and tracheal intubation [1]. Increases in mean arterial pressure (MAP) of 20-50 mm Hg compared with awake control values, and of 35–65 mm Hg compared with preintubation values, have been reported after tracheal intubation [2–5]. Such cardiovascular disturbances may be dangerous in some patients, particularly in those suffering from myocardial or cerebrovascular disease. This stress response may be attenuated by low doses of fentanyl [1], local anaesthetics [1], α- or β-adrenergic blocking agents [1], and calcium antagonists [6, 7]. Vasodilators such as nitroglycerine [8], sodium nitroprusside [4], isosorbide dinitrate [9] and prostaglandin E₁ [10] have been shown also to be effective for this purpose. The present study was designed to evaluate the efficacy of a single rapid bolus dose of trimetaphan in attenuating this response.

PATIENTS AND METHODS

This study was approved by the Human Investigation Committee of Kobe University School of Medicine and consent was obtained from all patients after a full explanation of the study. The present study consisted of two experimental methods based on those used by Stoelting [4] and Mikawa and co-workers [6, 7].

The first part of the study investigated 20 patients (ASA physical status I) to determine the time course and magnitude of arterial pressure (AP) and heart rate (HR) changes following tracheal intubation produced by stimulation. Anaesthesia was induced with thiopentone 5 mg kg⁻¹ and the trachea was intubated following vecuronium 0.2 mg kg⁻¹. Anaesthesia was maintained with 1% enflurane and 50% nitrous oxide in oxygen for elective surgery and end-tidal partial pressure of carbon dioxide (PeCO₂) was measured by Datex Capnometer (Datex, Helsinki, Finland). Ventilation was con-
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trolled to maintain $P_{E CO_2}$ at 4.0–5.1 kPa. Twenty patients were allocated randomly to groups A and B. After AP and HR had stabilized, patients received trimetaphan 0.05 mg kg$^{-1}$ (group A) or 0.1 mg kg$^{-1}$ (group B) as a single rapid i.v. injection. MAP was recorded continuously via a radial artery catheter and HR was calculated from a 15-s portion of the ECG. All measurements were completed before surgical incision of the skin.

The second part of the study was conducted on 30 normotensive patients (ASA physical status I) undergoing elective surgery, and was designed to determine the effect of prior administration of trimetaphan on the cardiovascular responses to tracheal intubation. Based on the previously determined time course of MAP change following trimetaphan, it was predicted that the onset of action of trimetaphan administered 1.75 min before laryngoscopy would occur at the same time as the onset of hypertension produced by laryngoscopy and tracheal intubation.

No patient had received sedatives or antihypertensive drugs. The patients were allocated randomly to three groups of 10 patients as follows: group C received saline i.v. (control group); group D received trimetaphan 0.05 mg kg$^{-1}$ i.v.; group E received trimetaphan 0.1 mg kg$^{-1}$ i.v. Premedication consisted of diazepam 0.1 mg kg$^{-1}$ by mouth 1 h and atropine sulphate 0.01 mg kg$^{-1}$ i.v. 30 min before induction of anaesthesia. The study design is shown in figure 1.

On arrival of the patient in the operating room, a radial arterial cannula was inserted under local anaesthesia for continuous monitoring of MAP. Heart rate was calculated from a 15-s portion of the ECG (lead II). In all patients, after stabilization of AP and HR, 100% oxygen was breathed via a mask for 3 min and anaesthesia was induced with thiopentone 5 mg kg$^{-1}$, followed by vecuronium 0.2 mg kg$^{-1}$ to facilitate tracheal intubation. Trimetaphan 0.05 mg kg$^{-1}$, trimetaphan 0.1 mg kg$^{-1}$ or saline (control) was injected rapidly via a peripheral i.v. cannula 1.75 min before starting direct laryngoscopy (15 s after thiopentone–vecuronium). Two minutes after administration of thiopentone and vecuronium, direct laryngoscopy was attempted, and tracheal intubation was completed within 30 s in all patients with the aid of a standard Macintosh laryngoscope blade. All intubations were performed by the first author, who was unaware of the nature of the injection which had been administered.

During anaesthesia, ventilation was assisted as required or controlled with 1% enflurane and 50% nitrous oxide in oxygen and $P_{E CO_2}$ was maintained at 4.1–4.9 kPa, measured with a Datex Capnometer by means of a catheter placed in the nostril until after the insertion of the tracheal tube, when sampling took place from a T-piece connector. Serial measurements of HR and

| Table I. Patient characteristics (mean (SEM)). No significant differences (P < 0.05) |
|-----------------------------------|-----------------------------------|-----------------------------------|---------------------------------|---------------------------------|
|                                   | Part 1                             | Part 2                             |                                 |                                 |
|                                   | Group A                            | Group B                            | Group C                          | Group D                          | Group E                          |
|                                   | Trimetaphan 0.05 mg kg$^{-1}$      | Trimetaphan 0.1 mg kg$^{-1}$        | Control (saline)                 | Trimetaphan 0.05 mg kg$^{-1}$    | Trimetaphan 0.1 mg kg$^{-1}$      |
| n                                 | 10                                 | 10                                 | 10                               | 10                               | 10                               |
| Age (yr)                          | 49.9 (3.3)                         | 46.6 (3.4)                         | 48.2 (3.5)                       | 46.5 (3.1)                       | 50.1 (3.7)                       |
| Weight (kg)                       | 57.8 (3.2)                         | 56.4 (3.5)                         | 57.2 (3.0)                       | 58.1 (3.4)                       | 54.3 (3.8)                       |
AP were obtained immediately before induction and 1, 2, 2.5, 2.75, 3, 3.5, 4, 4.5 and 5 min after induction. MAP, HR and the rate–pressure product (RPP) were compared with preinduction (baseline) measurements within the same group and with corresponding measurements among the three groups (groups C, D and E).

Statistical analysis was performed using analysis of variance and Student's *t* test (paired and unpaired). A *P* value of less than 0.05 was considered significant.

RESULTS
The five groups (A–E) of the study were comparable in respect of age, weight and gender (table I). Figure 2 shows the time course and magnitude of MAP and HR changes following a single i.v. administration of trimetaphan 0.05 and 0.1 mg kg⁻¹ in patients anaesthetized with enflurane and nitrous oxide in oxygen in the absence of stimulation produced by laryngoscopy for tracheal intubation. MAP began to decrease 30–60 s after administration of trimetaphan regardless of the dose, and the decrease was maximal after 2.5 min, with a return toward control apparent by 4 min (fig. 2). HR did not differ significantly with the two doses of trimetaphan.

There were no significant differences in MAP immediately before the start of laryngoscopy or before induction between the three groups (C–E) (fig. 3). In response to laryngoscopy and intubation, MAP increased significantly in control patients, while the increase was significantly less in the trimetaphan-treated groups. Administration of trimetaphan 0.1 mg kg⁻¹ had a greater inhibitory effect on the increase in MAP associated with intubation than the dose of 0.05 mg.
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FIG. 4. Changes in heart rate (mean, SEM) after thiopentone-vecuronium and in response to laryngoscopy and tracheal intubation after trimetaphan 0.05 mg kg\(^{-1}\) (○) or 0.1 mg kg\(^{-1}\) (●) or saline (control) (■). Arrow indicates injection of saline or trimetaphan; dotted area = duration of laryngoscopy and tracheal intubation. There was no difference between the three groups at any time. *P < 0.05 vs baseline value within group.

FIG. 5. Changes in rate-pressure product (RPP) (mean, SEM) after thiopentone-vecuronium and in response to laryngoscopy and tracheal intubation after trimetaphan 0.05 mg kg\(^{-1}\) (○) or 0.1 mg kg\(^{-1}\) (●) or saline (control) (■). Arrow indicates injection of saline or trimetaphan; dotted area = duration of laryngoscopy and tracheal intubation. *P < 0.05 vs control; †P < 0.05 for 0.05 mg kg\(^{-1}\) vs 0.1 mg kg\(^{-1}\).

kg\(^{-1}\). Although HR increased after induction and tracheal intubation in all groups, there was no significant difference in HR among the three groups at any time (fig. 4). In contrast, RPP was significantly less in trimetaphan-treated (0.05 or 0.1 mg kg\(^{-1}\)) patients compared with the control group after laryngoscopy and intubation (fig. 5). Trimetaphan 0.1 mg kg\(^{-1}\) also had a greater inhibitory effect on the increase in RPP following intubation than trimetaphan 0.05 mg kg\(^{-1}\).

There were no abnormal changes in ECG in any patient of the five groups (A–E). No patient required pressor drugs to treat severe hypotension.

DISCUSSION

Trimetaphan has been used to treat hypertensive emergencies and for controlled hypotension during and after anaesthesia [11]. The hypotensive effect is caused by sympathetic block [12]. There is only one previous report on the effect of trimetaphan on the cardiovascular changes following tracheal intubation [13]. In that report, Siedlecki demonstrated that a continuous infusion of trimetaphan 1 mg min\(^{-1}\) for 3–9 min blunted the cardiovascular responses to tracheal intubation. However, a single rapid injection is a more practical and simpler method than continuous infusion and is less likely to cause prolonged hypotension immediately before operation.

This study has confirmed previous reports that intubation of the trachea following thiopentone and a neuromuscular blocking agent is associated with significant increases in HR and MAP. In this study, trimetaphan 0.05 mg kg\(^{-1}\) and 0.1 mg kg\(^{-1}\) was found to attenuate the increases in MAP and RPP compared with those of the control (saline) group. As with other vasodilators which have been reported to have no effect on the increase in HR associated with tracheal intubation, trimetaphan also failed to prevent tachycardia. The maximum mean RPP after intubation in the trimetaphan 0.1 mg kg\(^{-1}\) group was 13286 mm Hg·beat min\(^{-1}\). This value is comparable to values of RPP of 17916 mm Hg·beat min\(^{-1}\) and 15868 mm Hg·beat min\(^{-1}\) in response to intubation in patients given hydralazine and buprenorphine, respectively, before induction [14, 15].

We consider that the decrease in AP after administration of trimetaphan is influenced by three factors. First, existing sympathetic tone. This is illustrated by the fact that AP may be decreased only minimally in recumbent subjects, but may decrease markedly in sitting or standing subjects [11]. Second, because the usual predominant tone at the heart is parasympathetic, the effect of ganglionic block by trimetaphan on the heart causes tachycardia [11] which may minimize the decrease in AP after trimetaphan. Third, the
magnitude of the decrease in AP may depend also on circulating blood volume or venous return.

We believe that undue hypotension following trimetaphan may be avoided if sufficient i.v. fluids are given to recumbent patients. In the present study, profound hypotension did not occur in any patient, regardless of the dose of trimetaphan. As shown in figure 2, the onset of action of trimetaphan was rapid, and duration of action was short; therefore, it seems to be an appropriate drug to attenuate the cardiovascular responses to tracheal intubation.

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REFERENCES


