British Journal of Anaesthesia 1993; 70: 306–310

HAEMODYNAMIC AND CATECHOLAMINE RESPONSES TO INDUCTION OF ANAESTHESIA AND TRACHEAL INTUBATION: COMPARISON BETWEEN PROPOFOL AND THIOPENTONE

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SUMMARY

We have studied the haemodynamic changes, QT intervals and catecholamine responses to induction of anaesthesia and tracheal intubation in 24 ASA I patients allocated randomly to receive either propofol 2.5 mg kg^{-1} or thiopentone 5 mg kg^{-1} over 60 s. After disappearance of the eyelash reflex, the lungs were ventilated with 100% oxygen for 3 min. The trachea was intubated after administration of vecuronium. With thiopentone, heart rate (HR) was greater than with propofol before intubation (P < 0.05). During induction, systolic (SAP) and diastolic arterial pressure (DAP) decreased more with propofol than with thiopentone. The QT interval was prolonged only during induction with thiopentone. In both groups, HR, SAP, DAP and the QT were increased in response to intubation (P < 0.001). The SAP and QT interval responses to intubation were significantly greater with thiopentone than with propofol (P < 0.05). One patient in the thiopentone group with a significantly prolonged QT interval had episodes of bigeminy and ventricular tachycardia. In both groups, concentrations of noradrenaline in mixed venous plasma increased after intubation (P < 0.001). Concentrations of adrenaline increased after intubation only in the thiopentone group (P < 0.001). (Br. J. Anaesth. 1993; **70**: 306–310)

KEY WORDS

Anaesthetics, intravenous: propofol, thiopentone. Intubation, tracheal: haemodynamic response. Sympathetic nervous system: catecholamines.

Vohra and others have shown that induction of anaesthesia with propofol causes a greater decrease in arterial pressure and systemic vascular resistance than induction with thiopentone [1]. The differences were maintained after intubation, which increased systemic vascular resistance and arterial pressure. However, cardiac index, measured non-invasively, decreased with both agents. Therefore, they queried the effect of catecholamines released in response to tracheal intubation. Catecholamine responses with these agents used alone for induction of anaesthesia have not been compared.

We have demonstrated that changes in the QT interval correlate directly with changes in plasma noradrenaline concentrations [2]. Also, mixed venous samples give a more accurate reflection of changes in catecholamine release than peripheral samples [3]. The aim of the present study was to compare, in healthy patients, the cardiovascular, QT interval and sympathoadrenal responses in mixed venous plasma to induction of anaesthesia and tracheal intubation with either propofol or thiopentone.

PATIENTS AND METHODS

We studied 24 (ASA I) patients undergoing minor elective surgery (herniotomy and breast surgery) (table I). The study was approved by the hospital Ethics Committee and informed consent was obtained from all patients. Patients receiving regular medication or with known allergy were excluded.

Patients were given oral oxazepam 15 mg on the night before surgery and were premedicated with oral diazepam 0.2 mg kg^{-1} 1 h before induction of anaesthesia. Simultaneously with administration of premedication, the skin over the basilic veins in both antecubital fossae and the site for cannulation of the radial artery were covered with local anaesthetic cream (EMLA, Astra, Södertälje).

TABLE I. *Patient characteristics (mean (range or SD)). BMI = Body mass index: weight/height*^{2}

	Propofol group	Thiopentone group
Number of patients	12	12
Sex (M/F)	5/7	5/7
Age (yr)	33 (19–44)	33 (18–43)
Weight (kg)	69 (15)	67 (17)
Height (cm)	166 (12)	167 (11)
BMI (kg m^{-2})	24.2 (2.9)	24.1 (3.2)

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Accepted for Publication: September 23, 1992.
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A cannula was inserted in the basilic vein and a 70-cm catheter was inserted via the contralateral basilic vein. The position of the catheter tip in the right ventricle of the heart was verified by the pressure wave form. The radial artery was cannulated for continuous measurement of arterial pressure. The ECG (aVR-lead) was displayed on an oscilloscope and recorded continuously on paper.

The QT intervals were measured manually and retrospectively from the onset of the QRS complex to the end of the T-wave by one of the authors (M.K.) unaware of the anaesthetic method. The mean QT interval of four successive beats was calculated. A heart rate-dependent correction (QTc) was made according to the formula:

$$QTc = QT/\sqrt{RR\ interval}$$

A value less than 440 ms is considered normal [4].

When the monitoring equipment had been attached, the patients were allowed to rest for 20 min. Cardiovascular recordings were then made and the first blood samples obtained (baseline).

Anaesthesia was induced with either propofol 2.5 mg kg^{-1} (12 patients) or thiopentone 5 mg kg^{-1} (12 patients) through the antecubital peripheral cannula. The anaesthetic was chosen randomly and given over 60 s. No anticholinergics were used. After disappearance of the eyelash reflex, the lungs were ventilated with 100% oxygen using intermittent positive pressure ventilation with a fresh gas flow of 10 litre min^{-1} via a face mask until intubation. Two minutes before intubation, vecuronium 0.1 kg^{-1} was given for neuromuscular block. At the same time, all patients received an additional dose of induction agent (propofol 25 mg or thiopentone 50 mg). Laryngoscopy was performed with a Macintosh laryngoscope and intubation was successful at the first attempt within 5–7 s in all patients. Disposable tubes of o.d. 7 mm were used for women and o.d. 8 mm for men. The end-tidal carbon dioxide concentration was recorded immediately after intubation (Cardiocap, Datex Ltd, Finland).

Blood samples (10 ml) for catecholamine measurements were obtained from the right ventricle of the heart simultaneously with recording of ECG, heart rate (HR), direct systolic (SAP) and diastolic (DAP) arterial pressures at the following times: 20, 40, 60, 80, 100, 120 and 210 s after the start of injection of the i.v. anaesthetic, and at 10 and 180 s after intubation. The samples were collected into prechilled polypropylene tubes containing EDTA and placed immediately on ice. They were centrifuged at 0 °C within 30 min and the plasma stored in polypropylene tubes at −70 °C until analysis. Plasma concentrations of catecholamines were measured simultaneously using HPLC with electrochemical detection [5]. The intra-assay coefficients of variation were approximately 2% for noradrenaline and 10% for adrenaline at physiological concentrations.

Statistical evaluation was performed using analysis of variance (two-way ANOVA) for repeated measurements, with one between factor (drug) and one within factor (time). When a statistically significant drug–time interaction was found, the analysis was continued by calculating contrasts between the groups for each time point. Changes over time within a group were tested with analysis of variance (one-way ANOVA) for repeated measurements. If significant differences were found, further analysis was made with the Fisher PLSD test. The time point 210 s after the start of induction was taken as baseline for assessment of the effects of tracheal intubation. The maxima and minima of the cardiovascular variables and QT interval between the groups were compared using Student's t test. Mann–Whitney U test, Student's t test or chi-square test were used for other data when appropriate. The statistical analysis was performed using Stat View 512 software (Brain Power Inc., Calabasas, CA, U.S.A.). $P < 0.05$ was considered statistically significant. Results are presented as mean (SD).

RESULTS

The study groups were comparable in patient characteristics (table I). At baseline, HR, SAP, DAP, QTc, noradrenaline and adrenaline concentrations in mixed venous plasma were comparable in the groups (ns). In all patients, the eyelash reflex disappeared and remained absent throughout the study. One patient complained of pain in the arm during injection of propofol. End-tidal carbon dioxide concentration immediately after intubation was 4.5 (0.8) % in the propofol group and 4.9 (0.7) % in the thiopentone group (ns).

Haemodynamic changes

In the propofol group, HR increased significantly from baseline 60 s after the start of injection ($P < 0.05$) and decreased thereafter. In the thiopentone group, HR increased after induction and remained increased until intubation. At 120 s after the start of induction, HR was greater in the thiopentone group than in the propofol group ($P < 0.05$) (fig. 1). In both groups, a significant increase in HR occurred in response to intubation ($P < 0.001$) (fig. 1).

In both groups, SAP decreased after the start of induction, more significantly with propofol than with thiopentone (fig. 1, table II). In the propofol group, DAP decreased at 60 s ($P < 0.01$) after the start of induction and further decreases were seen until 210 s after induction. In the thiopentone group, DAP did not change during the induction period. DAP was significantly greater with thiopentone than with propofol induction before intubation (fig. 1, table II). With both agents, tracheal intubation caused a significant increase in SAP ($P < 0.001$). The SAP response to intubation was greater with thiopentone than with propofol ($P < 0.05$) (fig. 1). DAP increased in response to intubation ($P < 0.001$) similarly in both groups (fig. 1).

QT interval

In the propofol group, QT interval remained stable during the induction phase. In the thiopentone group, QT interval was prolonged significantly from the baseline at 40 s ($P < 0.05$) and thereafter. After

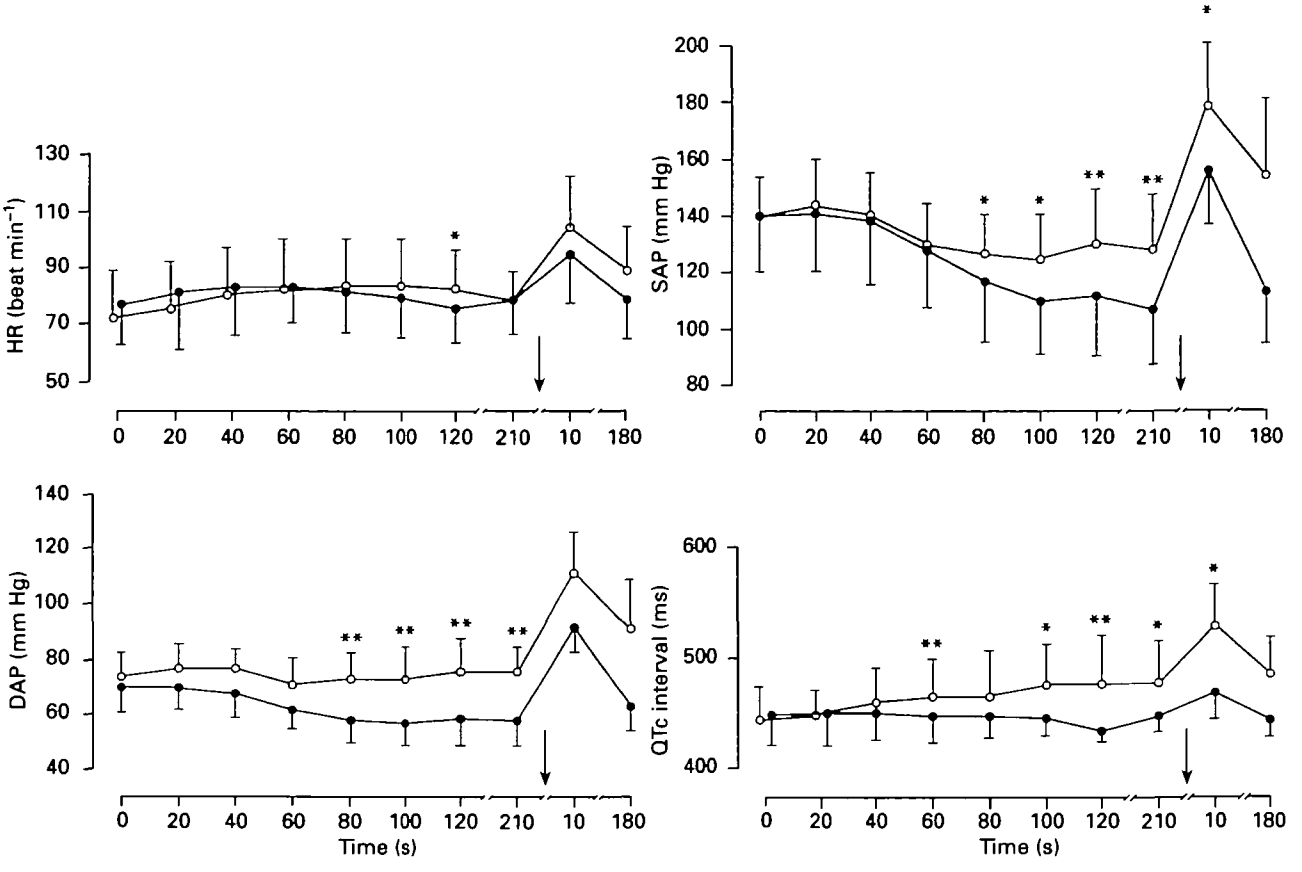

FIG. 1. Cardiovascular responses during induction of anaesthesia and tracheal intubation (arrow). ● = Propofol; ○ = thiopentone. SAP = Systolic arterial pressure; DAP = diastolic arterial pressure. Statistically significant drug–time interaction (two-way ANOVA): $*P < 0.05$; $**P < 0.01$ for contrasts between the groups.

TABLE II. *Heart rate (HR), systolic (SAP) and diastolic (DAP) pressures and QTc interval during induction (mean (SD))*

	Propofol group	Thiopentone group	*P*
HR (beat min⁻¹)			
Max.	97 (16)	106 (15)	ns
Min.	71 (11)	70 (14)	ns
SAP (mm Hg)			
Max.	154 (19)	179 (25)	< 0.05
Min.	97 (12)	120 (17)	< 0.001
DAP (mm Hg)			
Max.	92 (8)	112 (15)	< 0.001
Min.	52 (6)	67 (9)	< 0.001
QTc (ms)			
Max.	480 (18)	528 (38)	< 0.001
Min.	425 (15)	437 (27)	ns

intubation, QT interval was prolonged compared with the values before intubation in both groups (fig. 1). QT intervals were significantly longer with thiopentone than with propofol (fig. 1, table II). One patient in the thiopentone group developed three episodes of bigeminy and ventricular tachycardia 20 s after intubation when the QT interval was 535 ms.

Catecholamine responses

Plasma noradrenaline concentrations were not influenced by induction of anaesthesia (fig. 2). The

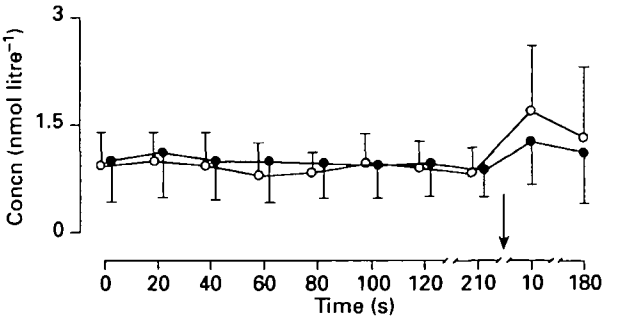

FIG. 2. Concentrations of noradrenaline in mixed venous plasma. ● = Propofol; ○ = thiopentone. ↓ = Intubation.

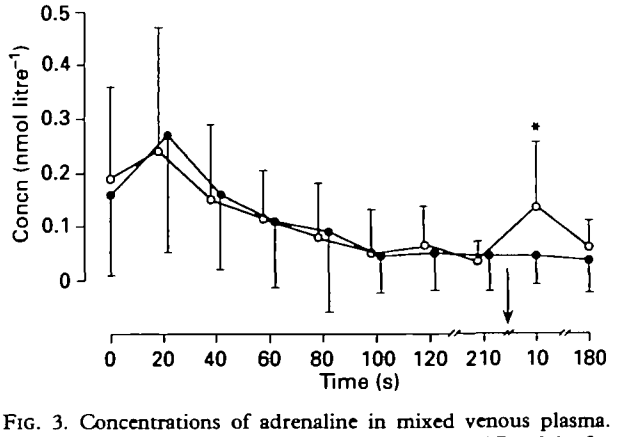

FIG. 3. Concentrations of adrenaline in mixed venous plasma. ● = Propofol; ○ = thiopentone. ↓ = Intubation. $*P < 0.01$ for contrasts between the groups.

plasma concentrations of noradrenaline increased by 46 (26)% (range 13–100%) in the propofol group and by 95 (96)% (range 0–344%) in the thiopentone group in response to intubation ($P < 0.001$ for time factor; ns for differences between groups) (fig. 2). After an initial increase, concentrations of adrenaline in mixed venous plasma declined gradually throughout induction with both agents (fig. 3). In the thiopentone group, plasma adrenaline increased four-fold after intubation ($P < 0.001$). Such a response did not occur in the propofol group ($P < 0.01$ between the groups) (fig. 3).

DISCUSSION

Our results show that haemodynamic responses to induction of anaesthesia and catecholamine responses to tracheal intubation differ with propofol and thiopentone. With each drug, plasma concentrations of both noradrenaline and adrenaline declined during induction and plasma noradrenaline concentrations increased similarly after intubation. However, plasma concentrations of adrenaline increased markedly after intubation in the thiopentone group only.

Heart rate increased 1 min after propofol, but decreased to baseline values thereafter. This is in agreement with the results of Fairfield, Dritsas and Beale [6]. The decrease in heart rate can be explained by the "reset" of the baroreflex function of propofol [7]. In contrast with propofol, heart rate remained increased until intubation in the thiopentone group. This probably results from preservation of the baroreflex activity by thiopentone [8]. With both agents, heart rate increased as a response to intubation—a finding consistent with earlier studies [1, 9–11].

Tracheal intubation after thiopentone induction has been shown to be associated with increases in arterial pressure and in plasma catecholamine concentrations [2, 3, 12–14]. With propofol, the pressor response to intubation is smaller than that with thiopentone [1, 9–11]. Our results show that the diastolic pressor response to intubation was of similar magnitude with both agents; the response with propofol alone started from smaller pressures than that with thiopentone. This haemodynamic change may be related to our finding that, with both agents, the noradrenaline response to intubation was similar. However, plasma adrenaline increased after intubation only with thiopentone. This increase in adrenaline concentration may have caused the greater systolic pressor response with thiopentone than with propofol. Tracheal intubation is a noxious stimulus which can be obtunded by opioids [2] and it appears also that propofol is capable of attenuating intubation-induced adrenomedullary release [15]. Propofol preserves upper airway integrity more effectively than thiopentone [16], which may in part explain the adrenaline response with thiopentone. Coley and others [17] compared haemodynamic and catecholamine responses with propofol or thiopentone in the presence of fentanyl and nitrous oxide. Plasma noradrenaline increased only with thiopentone. No changes in plasma adrenaline concentrations occurred with either agent. Catecholamine concentrations were measured from peripheral samples, whereas we sampled mixed venous blood [3]. The study designs may explain these differences.

Propofol causes marked peripheral vasodilatation [1, 9, 18–21] whereas thiopentone has no such effect [1]. It has been shown that the decrease in cardiac output caused by decreased systemic vascular resistance produced by propofol can be prevented by effective volume loading [21]. In our study, diastolic arterial pressure decreased 60 s after the start of injection of propofol and remained significantly reduced compared with thiopentone throughout the later course of induction. A reduction in plasma noradrenaline concentrations after propofol has been demonstrated also by Valtonen and others [22]. The rapid onset of vasodilatation produced by propofol suggests possible involvement of endothelium-derived relaxing factor, which causes dilatation of peripheral arterioles within seconds [23], but this view awaits investigation.

The QT interval was prolonged 40 s after injection of thiopentone, but remained unchanged after propofol. We have shown prolongation of the QT interval after thiopentone [24–27] as a predictor of cardiac arrhythmia in 10–40% of healthy patients at intubation. We have demonstrated previously a close association between plasma noradrenaline concentrations and prolongation of the QT interval during induction of anaesthesia with thiopentone [2, 14]. After intubation in the present study, the plasma concentrations of adrenaline increased, followed by significant cardiac arrhythmia in one patient. With propofol, QT interval was unchanged during induction, but increased after intubation when the plasma noradrenaline concentration increased also. Increased prolongation of the QT interval after thiopentone compared with propofol was found also by McConachie and others [28].

ACKNOWLEDGEMENTS

The authors are indebted to Dr Riku Aantaa, M.D. for his help in statistical analysis.

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