British Journal of Anaesthesia 1992; **69**: 444–446

ETOMIDATE SHORTENS THE ONSET TIME OF NEUROMUSCULAR BLOCK

R. S. GILL AND R. P. F. SCOTT

SUMMARY

We have studied 30 healthy patients allocated randomly to receive thiopentone, propofol or etomidate in equipotent doses followed by vecuronium 0.1 mg kg^{-1}. Haemodynamic variables and time to 100% neuromuscular block were measured. The patients receiving etomidate had a significantly shorter onset time of neuromuscular block compared with those receiving the two other i.v. induction agents. There was a significant negative correlation between onset time of neuromuscular block and the maximum percent change in mean arterial pressure.
(Br. J. Anaesth. 1992; **69**: 444–446)

KEY WORDS

Anaesthetics, intravenous: etomidate, propofol, thiopentone. Neuromuscular relaxants: vecuronium. Pharmacodynamics: onset time, neuromuscular block.

The rate of onset of neuromuscular block is determined by the rate at which a pharmacologically effective concentration is achieved in the biophase, in this case the neuromuscular junctional cleft [1]. This is influenced by the dose of drug, its pharmacokinetic profile (volume of distribution, buffering by non-specific binding to mucopolysaccharides and elimination half-life), the rate of association with cholinoceptors, the rate of perfusion of the junctional cleft and drug potency [2].

The rate of equilibration between plasma and junctional cleft concentrations is governed by the dose of neuromuscular blocker, the speed of injection (bolus effect) and by the amount of muscle perfusion. Muscle perfusion may be affected by altered cardiovascular physiology, particularly during the period of induction of anaesthesia.

Enhanced muscle blood flow has been shown to shorten the onset time of neuromuscular block [3], whilst decreased muscle perfusion secondary to hypothermia or low cardiac output delays onset time [4, 5].

Most research into the onset of neuromuscular block for different neuromuscular blockers has been comparative. This paper presents data from a randomized prospective study, designed to test the hypothesis that etomidate, with its favourable haemodynamic characteristics, may be associated with a shorter onset time of neuromuscular block compared with other i.v. induction agents.

PATIENTS AND METHODS

The study was approved by the Hospital Ethics Committee. Thirty ASA class I or II patients gave informed consent for the study and were allocated randomly to one of three groups, to receive thiopentone 5 mg kg^{-1}, etomidate 0.3 mg kg^{-1} or propofol 2.5 mg kg^{-1}. The patients were aged 18–65 yr, weighed 50–110 kg, and were undergoing elective surgical procedures. We excluded any patient suffering from cardiovascular or neuromuscular disorders, or taking medications which might interfere with normal cardiovascular physiology or neuromuscular transmission.

Premedication consisted of oral temazepam 10–20 mg and metoclopramide 10 mg. Before i.v. induction, baseline mean arterial pressure (MAP) and heart rate (HR) were recorded using a Datascope Accutorr 3Sat non-invasive pressure and pulse oximeter monitor. MAP and HR were used as indirect indicators of muscle perfusion. The different i.v. induction agents were administered into a fast flowing infusion of sodium chloride over 5–10 s. After i.v. induction, the ulnar nerve was stimulated supramaximally using surface electrodes at the wrist, with repetitive train-of-four stimuli. The evoked compound electromyogram of thumb adduction was recorded using a Datex Neuromuscular Transmission Monitor (NTM). After baseline calibration of this device, vecuronium 0.1 mg kg^{-1} was administered over 5 s.

MAP and HR were measured non-invasively and recorded every 1 min until 100% depression of the first twitch of the train-of-four was observed. During this time anaesthesia was maintained with 50% nitrous oxide in oxygen.

TABLE I. *Patient data (mean (range or SEM))*

	Etomidate	Thiopetone	Propofol
Age (yr)	42.8 (25–56)	48.3 (31–64)	41.2 (26–65)
Weight (kg)	74.2 (3.86)	65.3 (3.09)	73 (5.06)

R. S. GILL*, B.M., F.R.C.ANAES.; R. P. F. SCOTT, B.SC., M.B., CH.B., F.R.C.ANAES., M.D.; Department of Anaesthesia, Odstock Hospital, Salisbury, Wiltshire. Accepted for Publication: May 26, 1992.

*Present address: Critical Care Programme, University Hospital, University of W. Ontario, London, Ontario, Canada.

Correspondence to R.P.F.S.

Downloaded from https://academic.oup.com/bja/article/69/5/444/303500 by guest on 20 March 2024

TABLE II. *Onset time, maximum percent changes in mean arterial pressure (MAP) and heart rate (HR) (mean (SEM) [range]). Baseline = actual value of mean baseline MAP or HR. * P < 0.05; *** P < 0.001—ANOVA and linear contrast*

	Etomidate ($n = 10$)	Thiopentone ($n = 10$)	Propofol ($n = 10$)
Mean onset time (s)	144 (16)* [40–220]	197 (21.1) [80–300]	206 (21.2) [80–280]
MAP			
Max. % change	12.1 (6.5)*** [−14 to 44]	−16.3 (2.2) [−5 to −28]	−30.2 (4.6) [−2 to −56]
Baseline (mmHg)	91.2	92.9	98.2
HR			
Max. % change	4.39 (8.9) [−44 to 48]	13.3 (5.13) [−24 to 29]	9.18 (4.9) [−12 to 26]
Baseline (beat min^{-1})	83.4	81.5	79.2

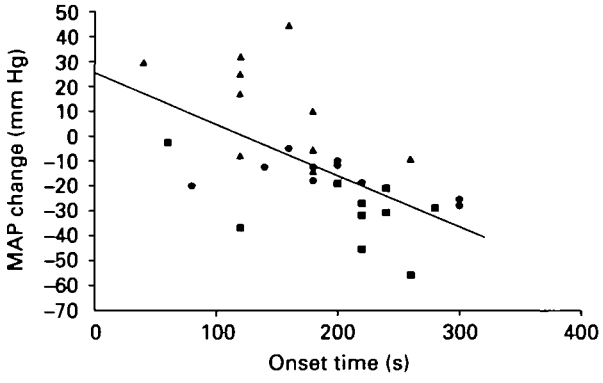

FIG. 1. Correlation between onset time and maximum percent change in MAP in the etomidate (▲), thiopentone (●) and propofol (■) groups. $r = -0.56$; $P < 0.001$.

The results were analysed with the Systat statistical package (Systat Inc, Evanstone Il), using a two-way analysis of variance and linear contrast to calculate the differences between the three groups. Differences were taken to be statistically significant at $P < 0.05$. Results are expressed as mean (SEM).

RESULTS

There were no significant differences between the three groups (table I).

Maximum changes in MAP and HR that occurred between induction and maximal block (100% depression of the first twitch of the train-of-four) were calculated as percentage of baseline value (table II).

Patients in the etomidate group had a significantly shorter onset time than patients in the two other groups ($P < 0.05$). There was a significant difference in the maximum percent change in MAP between all three groups ($P < 0.001$). In addition, there was a significant negative correlation between onset time and the maximum percent change in MAP (fig. 1) ($r = -0.56$, $P < 0.001$).

DISCUSSION

Onset time of neuromuscular block may be influenced by several factors. Standardization of anaesthetic technique is important before any effective comparison is made. In particular, the starting point and end-point in the measurement of onset time, the mode of neuromuscular monitoring and the anaesthetic agents used should be clearly defined. Previous research has shown significantly shorter onset times during nitrous oxide–opioid [6] and nitrous oxide–volatile agent [7] anaesthesia than those associated with thiopentone alone.

In this study the patients received only nitrous oxide and oxygen during the study period. Supplementary opioids and volatile agents were given when the study was complete. Vecuronium was chosen as the neuromuscular blocking drug as it has been shown to have virtually no cardiovascular effects [8]. These anaesthetic agents were selected to minimize changes in haemodynamic variables in order to highlight the effect of the induction agent on the cardiovascular system.

Both thiopentone and propofol in equipotent doses have been shown to have adverse cardiovascular effects, secondary to decreased cardiac output and peripheral vasodilatation. Propofol may be the more haemodynamically unstable of the two drugs [9, 10]. In contrast, etomidate has been shown to have a very stable cardiovascular profile when used for i.v. induction [11]. Furthermore, it has been suggested that etomidate potentiates the non-depolarizing blocking effects of pancuronium [12].

In conclusion, the results of this study suggest that the onset of neuromuscular block may be affected by the amount of muscle perfusion, which in turn can be affected by the choice of i.v. induction agent. If rapid intubation of the trachea is required with a non-depolarizing neuromuscular blocking drug, etomidate may be the induction agent of choice, because of its favourable haemodynamic characteristics.

REFERENCES

1. Bowman WC. Pharmokinetics. In: Bowman WC. *The Pharmacology of the Neuromuscular Junction*. London: Butterworths, 1990; 16.
2. Bowman WC, Rodger IW, Houston J, Marshall RJ, McIndewar I. Structure:action relationships among some desacetoxy analogues of pancuronium and vecuronium in the anesthetized cat. *Anesthesiology* 1988; **69**: 57–62.
3. Goat VA, Yeung ML, Blakeney C, Feldman SA. The effect of blood-flow upon the activity of gallamine triethiodide. *British Journal of Anaesthesia* 1987; **48**: 69–73.
4. Ham J, Stanski DR, Neufield P. Pharmacokinetics and dynamics of d-tubocurarine during hypothermia in humans. *Anesthesiology* 1981; 55: 631–635.
5. Harrison GA, Janis F. Effect of circulation time on the neuromuscular action of suxamethonium. *Anaesthesia and Intensive Care* 1972; 1: 33–40.

Downloaded from https://academic.oup.com/bja/article/69/5/444/303500 by guest on 20 March 2024

6. Scott RPF, Savarese JJ, Basta SJ, Embree P, Ali HH, Sunder N, Hoaglin C. Clinical pharmacology of atracurium given in high dose. *British Journal of Anaesthesia* 1986; **58**: 834–838.
7. Stanski DR, Ham J, Miller RD. Pharmacokinetics and pharmacodynamics of d-tubocurarine during nitrous oxide–narcotic and halothane anesthesia in man. *Anesthesiology* 1979; **51**: 235–241.
8. Robertson EN, Booij LHDJ, Fragen RJ, Crul JF. Clinical comparison of atracurium and vecuronium (Org NC 45). *British Journal of Anaesthesia* 1983; **55**: 125–129.
9. Prys-Roberts C, Davies JR, Caverly RK, Goodman NW. Haemodynamic effects of infusions of diisopropyl phenol (ICI 35 868) during nitrous oxide anaesthesia in man. *British Journal of Anaesthesia* 1983; **55**: 105–101.
10. Grounds RM, Morgan M, Lumley J. Some studies on the properties of the intravenous anaesthetic propofol—a review. *Postgraduate Medical Journal* 1985; **61** (Suppl. 3): 90–95.
11. Doenicke A. Etomidate, a new intravenous hypnotic. *Acta Anaesthesiologica Belgica* 1974; **25**: 307–315.
12. Booij LHDJ, Crul J. The comparative influence of gamma-hydroxy butyric acid, Althesin and etomidate on the neuromuscular blocking potency of pancuronium in man. *Acta Anaesthesiologica Belgica* 1979; **30**: 219–223.

Downloaded from https://academic.oup.com/bja/article/69/5/444/303500 by guest on 20 March 2024