J Anesth (2003) 17:129–132

Journal of
Anesthesia

Clinical reports

Comparison of the effects of neuroleptanesthesia and enflurane or sevoflurane anesthesia on neuromuscular blockade by rocuronium

İrfan Gungor, Füsun Bozkirli, Hülya Çelebi, and Berrin Günaydin

Department of Anesthesiology and Reanimation, Faculty of Medicine, Gazi University, 06500 Ankara, Turkey

Key words Rocuronium · Neuroleptanesthesia · Enflurane · Sevoflurane

Introduction

Neuromuscular blocking agents are administered to facilitate endotracheal intubation for a variety of surgical procedures. The durations of their relaxing effects can be altered with different anesthesia regimens, such as inhalational anesthesia (halothane, enflurane, isoflurane, or sevoflurane), total intravenous anesthesia (TIVA), or neuroleptanesthesia [1–3].

Rocuronium is a steroidal, nondepolarizing muscle relaxant with an intermediate onset of action lacking histamine-releasing and cardiovascular effects [4,5]. It has been reported that muscle paralysis by rocuronium (Org 9426) is potentiated during enflurane anesthesia as compared with TIVA or balanced anesthesia [6,7]. Sevoflurane, a widely used volatile anesthetic agent possessing rapid and smooth induction and recovery characteristics, has been demonstrated to potentiate vecuronium- and rocuronium-induced neuromuscular blockade compared with balanced anesthesia using propofol or midazolam [8–11]. Not only was the neuromuscular blocking action of rocuronium significantly potentiated, but also the duration of action of, and the recovery from, rocuronium were significantly prolonged by sevoflurane [12]. In the present study, we compared the effect of enflurane or sevoflurane on neuromuscular blockade by a single bolus dose of rocuronium $0.6\,mg{\cdot}kg^{-1}$ in comparison with the effect of neuroleptanesthesia.

Address correspondence to: B. Günaydin
Received: February 19, 2002 / Accepted: November 28, 2002

Materials and methods

Forty-five unpremedicated ASA class I or II patients scheduled to undergo either orthopedic or ear, nose, and throat surgery under general anesthesia with an anticipated duration of approximately 1.5–3 h were enrolled in this study after approval of the hospital ethics committee and written informed consent from the patients had been obtained. All patients were free from neuromuscular, endocrine, liver, or renal diseases and were not receiving drugs known to interact with neuromuscular blocking agents. They required muscle relaxation only for endotracheal intubation.

An intravenous infusion of 0.9% sodium chloride solution was given initially via the basilic vein on one of the arms, while the other arm was kept for monitoring neuromuscular block. The heart rate (HR), mean arterial pressure (MAP), peripheral oxygen saturation (SpO_2) (Odam Physiogard SM 785, Wissenbourg, France), and end-tidal concentrations of CO_2 and volatile anesthetics (Artema MM 256, Sundbyberg, Sweden) were monitored. Each patient was allocated to one of three groups: enflurane (group E, $n = 15$), sevoflurane (group S, $n = 15$), and neuroleptanesthesia (group NA, $n = 15$). The induction of anesthesia was performed with i.v. fentanyl $2\,\mu g \cdot kg^{-1}$ and thiopentone $5–7\,mg{\cdot}kg^{-1}$, followed by a volatile anesthetic, either enflurane or sevoflurane, with assisted ventilation by mask in groups E and S, respectively. The volatile anesthetics (enflurane or sevoflurane) were administered in 66%/33% : nitrous oxide/oxygen at the end-tidal concentration corresponding to 1 minimum alveolar concentration (MAC) in the present study. One MAC of enflurane and sevoflurane was assumed to be 0.57% and 0.66% in approximately 66% nitrous oxide, respectively [13]. In group NA, anesthesia was induced with i.v. droperidol $0.2\,mg \cdot kg^{-1}$, fentanyl $5\,\mu g \cdot kg^{-1}$, and thiopentone $1–2\,mg \cdot kg^{-1}$ during inhalation of 66%/33% : N_2O/O_2. Stable end-tidal anesthetic concen-

trations were maintained for at least 10 min before administration of i.v. rocuronium 0.6 mg · kg^{-1} (2×ED_{95}) [14]. End-tidal CO_2 was kept between 35 and 40 mmHg throughout the operation.

Neuromuscular blockade was monitored by an electromyograph (Datex Relaxograph NMT 100, Helsinki, Finland) following immobilization of the hand and forearm in abduction on a splint with the fingers fixed in extension. The arm was wrapped with cotton to prevent the temperature of the thenar muscle from decreasing to below 32°C. Following calibration, the electromyographic response of the thenar muscle to stimulation of 70 mA every 10 s was recorded. Then, the ulnar nerve was stimulated transcutaneously at the wrist via surface electrodes. Supramaximal stimuli of 2 ms duration at 2 Hz were delivered every 10 s in a train-of-four (TOF) mode until the end of the study. The first twitch of the TOF was considered as the twitch height (T1). Endotracheal intubation was performed when a T1 value of 0% was achieved. T1 (0%, 5%, 25%, 75%, and 95%) and TOF (25%, 50%, and 75%) values were displayed and recorded. Spontaneous recovery of TOF to 75% (TOF75) and 95% (TOF95) was evaluated. The onset time (time from administration of the intubating dose to the development of maximum depression of the T1 value to 0%) and clinical duration (time from administration of the intubating dose to 25% recovery of T1) were assessed as previously described [15]. The total duration (time from administration of the intubating dose to 95% recovery of T1) and recovery index (time from 25% to 75% recovery of T1) were determined.

The results were expressed as means ± SD. Statistical analysis of the data was performed by the Friedman test within groups, and the χ^2 and Kruskall–Wallis tests were used among groups. To detect significance for the Friedman test, all treatments compared to control were examined by the post hoc test suggested by Wolson [16]. *P* values less than 0.05 were considered to indicate statistical significance.

Results and discussion

The three groups of patients were comparable with respect to sex, age, weight, and height (Table 1).

The hemodynamic parameters (HR and MAP) showed significant changes during anesthesia, possibly resulting from the type of anesthesia, which were within the acceptable clinical limits in all groups.

The onset times in groups NA, E, and S were 96.47 ± 16.15, 102.53 ± 25.44, and 90.67 ± 21.07 s, respectively, which were indicated in terms of minutes as T1 0% in Fig. 1A. There were no significant differences among them.

Many studies have demonstrated that with different muscle relaxants, volatile anesthetics do not alter the dose requirements for endotracheal intubation and anesthesia induction and the resulting onset time, but may prolong the clinical duration and recovery times [1,2,6,11,17–19]. In daily practice, muscle relaxants are administered before or simultaneously with the start of inhalation anesthetics. Therefore, equilibration of the inhalation anesthetic is not present at this point and the onset time is unaffected, but potentiation is apparent during 25% recovery of twitch height by most of the volatile anaesthetics. In the present study, the onset time of rocuronium was unaffected by inhalation of enflurane or sevoflurane compared with neuroleptanesthesia, even if the muscle relaxants were given under the stable end-tidal concentration.

These resuts are in accordance with those of other recent studies [5,12,20–22], which showed no significant differences in the onset times of rocuronium under volatile anesthetics. In our study, the shortest onset time (90.67 s) was observed in the sevoflurane group. Lowry et al. [23] reported that the average time for the onset of block following rocuronium 0.6 mg · kg^{-1} under sevoflurane anesthesia was 89 s. We performed endotracheal intubation when the T1 value reached 0%, and this time was found to be longer than the recommended intubation times for rocuronium in all groups. Therefore, the intubation conditions of the present study were evaluated as excellent according to Fahey scoring in all groups [15].

In the present study, the prolonging effect of sevoflurane on rocuronium started from 5% of twitch height recovery, whereas it became evident at 25% recovery of twitch height with enflurane. In group S, the spontaneous recovery time of the first twitch response to 5% was significantly longer (40.73 ± 11.20 min) than in groups E and NA (29.20 ± 5.66 and 23.33 ± 4.65 min, respectively). This might be due to its smaller muscle–gas partition coefficient as compared with enflurane, which allows earlier uptake into the muscle compartment.

Table 1. Demographic data on the patients (means ± SD)

Characteristic	Group NA (n = 15)	Group E (n = 15)	Group S (n = 15)
Sex (Male/Female)	4/11	4/11	4/11
Age (yr)	53 ± 9	52 ± 11	50 ± 17
Weight (kg)	70 ± 7	69 ± 10	71 ± 8
Height (cm)	168 ± 6	165 ± 8	167 ± 6

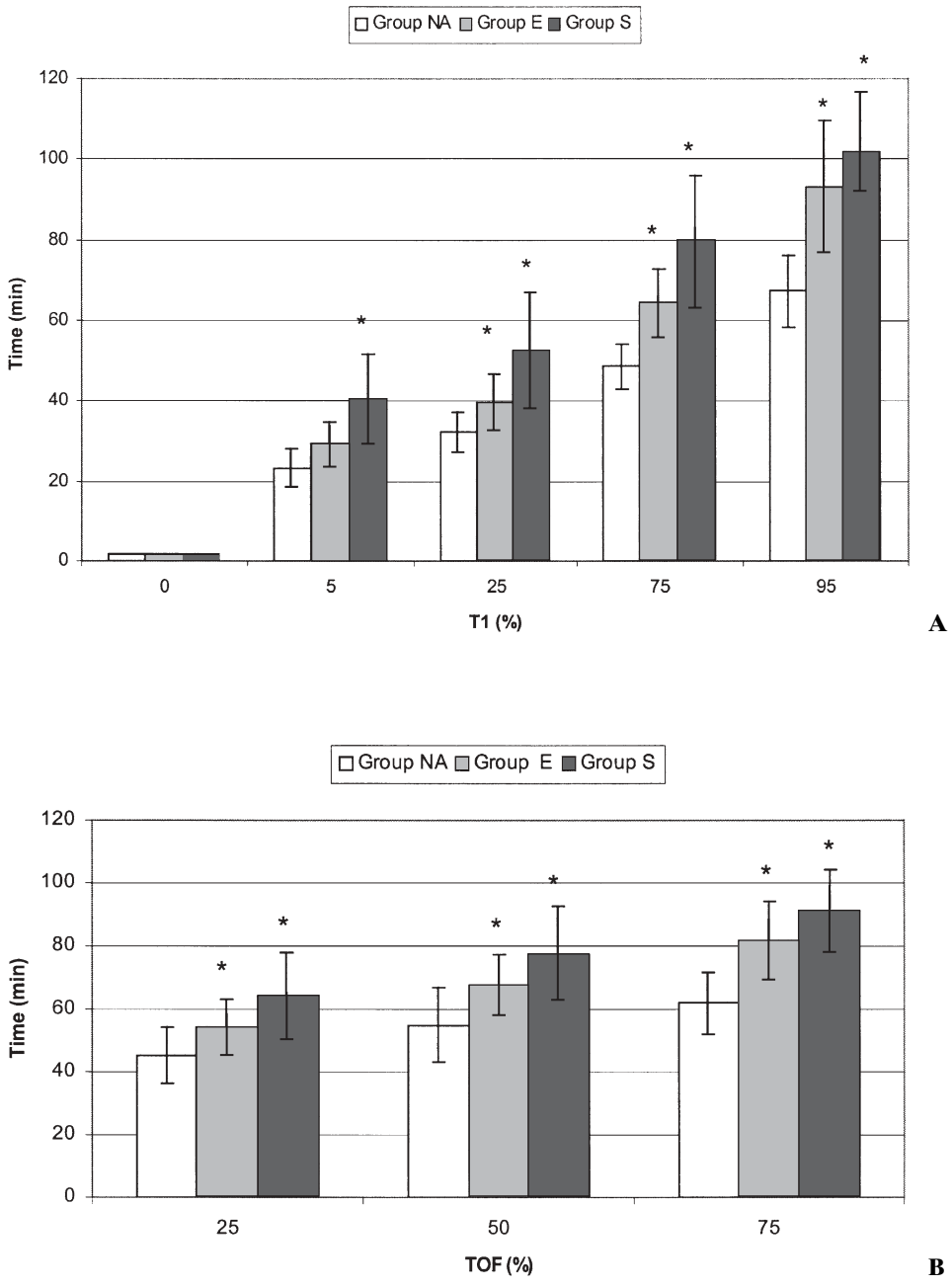

Fig. 1. A 0% (onset time), 5%, 25% (clinical duration), 75%, and 95% (total duration) recovery of T1 of the groups (*$P <$ 0.05 *vs* group NA). **B** Distribution of 25%, 50%, and 75% recovery of train-of-form (TOF) values with respect to groups (*$P < 0.05$ *vs* group NA)

Potentiation of neuromuscular block by volatile anesthetics is a well-known phenomenon, which is usually not evident on induction but becomes significant as anesthesia becomes more prolonged [5]. Interaction of rocuronium with volatile anesthetics (desflurane, isoflurane, and sevoflurane) resulted in augmentation of the intensity of neuromuscular blockade but did not result in a significant effect on duration or recovery from the block, and this effect was seen in only one study that compared the interaction of rocuronium with volatile anesthetics [12]. Bock et al. [24] found that the infusion rate of rocuronium was reduced by 30%–40% during isoflurane, desflurane, and sevoflurane anesthesia compared with propofol, and that the recovery index was longest (28 ± 13 min) with sevoflurane.

In the present study, recovery times of 25%, 75%, and 95% of control twitch height (T1) were prolonged by either enflurane or sevoflurane anesthesia. The recovery indexes (the time in minutes required for 25%–75% recovery of T1) in groups E and S (23.93 ± 4.79 and 26.87 ± 6.39 min, respectively) were significantly longer than that in group NA (15.53 ± 1.92 min) (Fig. 1A). The longest recovery index for sevoflurane was consistent with the results of Bock et al. [24]. Similarly,

25% and 75% recovery times of TOF were significantly longer in groups E and S than in group NA (45.07% ± 8.96% and 61.93% ± 9.69%), as shown in Fig. 1B. In this regard, the results with enflurane and sevoflurane were not significantly different.

The neuromuscular blocking action and pharmacodynamic profile of rocuronium were significantly altered during inhalation anesthesia. Shanks et al. [7] found that there was a 40% reduction in the dose requirements of rocuronium during enflurane and isoflurane anesthesia, and Xue et al. [11] concluded that there were significant increases in the duration of the peak effect (recovery of T1 to 5%), clinical and total duration, and recovery index during sevoflurane anesthesia. We found similar results by comparing both enflurne and sevoflurane in the present study. In parallel with our study, the rocuronium infusion rate required to maintain stable 90%–99% T1 depression was reduced by approximately 20% with halothane and isoflurane anesthesia, and by 50% with sevoflurane anesthesia, when compared with fentanyl–nitrous oxide anesthesia [25].

In conclusion, the clinical and total duration times of rocuronium were prolonged by both sevoflurane and enflurane as compared with neuroleptanesthesia, but the potentiating effect of sevoflurane on rocuronium-induced neuromuscular blockade started from the 5% recovery of T1 when compared with either neuroleptanesthesia or enflurane. Therefore, meticulous attention should be paid to the monitoring of neuromuscular transmission during sevoflurane inhalation to avoid rocuronium overdose.

Acknowledgments. We would like to thank Dr.Ertan Öztürk for his help with statistical analyis.

References

1. Naguib M, Seraj M, Abdulrazik E (1992) Pipecuronium induced neuromuscular blockade during nitrous oxide–fentanyl, enflurane, isoflurane, and halothane anesthesia in surgical patients. Anesth Analg 75:193–197
2. Rupp S, Miller RD, Gencarelli PJ (1984) Vecuronium-induced neuromuscular blockade during enflurane, isoflurane, and halothane anesthesia in humans. Anesthesiology 60:102–105
3. Saitoh Y, Toyooka H, Amaha K (1993) Recoveries of post-tetanic twitch and train- of-four responses after administration of vecuronium with different inhalation anaesthetics and neuroleptanesthesia. Br J Anaesth 70:402–404
4. Abouleish E, Abboud T, Lechevalier T, Zhu J, Chalian A, Alford K (1994) Rocuronium (Org 9426) for caesarean section. Br J Anaesth73:336–341
5. Agoston S (1994) Interactions of volatile anaesthetics with rocuronium bromide in perspective. Eur J Anaesthesiol 11[Suppl 9]:107–111
6. Van Aken H, Oris B, Crul JF (1994). Muscle paralysis by rocuronium bromide during halothane, enflurane, isoflurane and total intravenous anesthesia. Eur J Anaesthesiol 11[Suppl 9]:101–102
7. Shanks CA, Frager RJ, Ling DL (1994) Continuous intravenous infusion of rocuronium (Org 9426) in patients receiving balanced, enflurane, or isoflurane anesthesia. Anesthesiology 78:649–651
8. Muray JM, Fee JPH (1997) Volatile anesthetic drugs. In: McCaughey W, Ckake RSJ, Fee JPH, Wallace WFM (eds) Anaesthetic physiology and pharmacology. Churchill Livingstone, New York, 1997, pp 147–168
9. Jones RM (1996) Inhalational anaesthetics: an update. Acta Anaesthesiol Belg 47:3–6
10. Suzuki T, Munakata K, Watanabe N, Katsumata N, Saeki S, Ogawa S (1999) Augmentation of vecuronium-induced neuromuscular block during sevoflurane anesthesia: comparison with balanced anesthesia using propofol or midazolam. Br J Anaesth 83:485–487
11. Xue FS, Liao X, Tong SY, Liu JH, An G, Luo LK (1998) Dose-response and time-course of the effect of rocuronium bromide during sevoflurane anesthesia. Anaesthesia 53:25–30
12. Wulf H, Ledowski T, Linstedt U, Proppe D, Sitzlack D (1998) Neuromuscular blocking effect of rocuronium during desflurane, isoflurane and sevoflurane anaesthesia. Can J Anaesth 45:526–532
13. Mushambi MC, Smith G (2001) Inhalation anaesthetic agents In: Aitkenhead AR, Rowbotham DJ, Smith G (eds) Textbook of anaesthesia. Harcourt Publisher, London, pp 157–159
14. Smith CE, Donati F, Bevan DR (1987) Dose response curves for succinylcholine: single versus cumulative techniques. Anesthesiology 67:A358
15. Fahey MR, Morris RB, Miller RD, Sohn YJ, Conelly R, Genceralli R (1981) Clinical pharmacology of Org NC45 (Norcuron): a new nondepolarizing muscle relaxant. Anesthesiology 55:6–11
16. Wolson RF (1988) Statistical methods for the analysis of medical data. Wiley and Sons, New York, p 379
17. Miller RD, Way WL, Dolan WM, Stevens WC, Eger EI (1971) Comparative neuomuscular effects of pancuronium, gallamine and succinylcholine during forane and halothane anesthesia in man. Anesthesiology 35:509–514
18. Miller RD, Way WL, Stevens WC, Eger EI (1971). Comparative neuromuscular effects of forane and halothane alone and in combination with d-tubocurarine in man. Anesthesiology 35:38–42
19. Miller RD, Way WL, Dolan WM, Stevens WC, Eger EI (1972) The dependence of pancuroniumand d-tubocurarine induced neuromuscular blockades on alveolar concentration of halothane and forane. Anesthesiology 37:573–581
20. Wierda JMKH, Richardson FJ, Agoston S (1989) Dose response relation and time course of action of pipecuronium bromide in humans anaesthetized with nitrous oxide and isoflurane, halothane, or droperidol and fentanyl. Anesth Analg 68:208–213
21. Swen J, Rashkowsky OM, Ket JM, Koot HWJ, Hermans J, Agoston S (1989) Interaction between non-depolarizing neuromuscular blocking agents and inhalational anesthetics. Anesth Analg 69:752–755
22. Lambalk LM, de Wit APM, Wierda JMKH, Hennis PJ, Agoston S (1991) Dose response relationship and time course of action of Org 9426. Anaesthesia 46:907–911
23. Lowry DW, Mirakhur RK, McCarthy GJ, Carroll MT, McCourt KC (1998) Neuromuscular effects of rocuronium during sevoflurane, isoflurane, and intravenous anesthesia. Anesth Analg 87:936–940
24. Bock M, Klippel K, Nitsche B, Bach A, Martin E, Motsch J (2000) Rocuronium potency and recovery characteristics during steady-state desflurane, secoflurane, isoflurane or propofol anaesthsia. Br J Anaesth 84:43–47
25. Woloszczuk-Gebicka B, Lapczynski T, Wierzejki W (2001) The influence of halothane, isoflurane and sevoflurane on rocuronium infusion in children. Acta Anaesthesiol Scand 1:73–77