Egyptian Journal of Anaesthesia (2012) **28**, 281–286

Egyptian Society of Anesthesiologists

Egyptian Journal of Anaesthesia

www.elsevier.com/locate/egja
www.sciencedirect.com

Research Article

Effect of systemic lidocaine infusion on train-of-four ratios during recovery from general anesthesia

Ahmed M. Omar *

King Fahd Military Hospital, Dhahran, Saudi Arabia

Received 17 May 2012; accepted 7 July 2012
Available online 5 August 2012

KEYWORDS

Lidocaine;
Rocuronium;
Neuromuscular monitoring

Abstract *Introduction:* In spite of introduction of intermediate-acting neuromuscular blocking drugs (NMBDs), incidence of postoperative residual muscle weakness is still high. The aim of this trial is to study the effect of systemic lidocaine infusion on intraoperative consumption of rocuronium and TOF ratios at extubation and on arrival to postanesthesia care unit (PACU).
Methods: Forty-six ASA I–III patients aged 16–60 yr were randomly allocated into two groups: lidocaine (L) group ($n = 23$) and control (C) group ($n = 23$). After induction of standard endotracheal general anesthesia with fentanyl, propofol and rocuronium, patients of group L were given i.v. lidocaine bolus (1.5 mg kg^{-1}) followed by continuous infusion (1.5 mg kg^{-1} h^{-1}) till time of endotracheal extubation while patients in group C were given equal volumes of normal saline. Rocuronium was titrated based on clinical signs. On conclusion of surgery, neostigmine was given to reverse the effects of rocuronium if TOF count was two or more. Immediately before extubation, TOF ratio was measured and recorded and considered the primary outcome.
Results: There were no significant differences between the two study groups regarding intraoperative fentanyl doses or core temperature at the end of surgery. End-tidal sevoflurane concentrations were significantly lower in group L than in group P ($P < 0.01$). The dose of rocuronium was significantly less in group L than in group C ($P = 0.001$). Train-of four ratios were significantly higher in group L than in group C either before extubation ($P < 0.001$) or on arrival to PACU ($P = 0.001$).
Conclusion: The current study shows that intraoperative use of i.v. lidocaine infusion in generally anesthetized patients can result in higher TOF ratios at time of extubation and on arrival to PACU when rocuronium was given based on clinical signs.

* Address: King Fahd Military Medical Complex, PO Box 946, Dhahran, Saudi Arabia. Tel.: +966 569527320; fax: +966 38440000.
E-mail address: ahmedmommer@yahoo.com

Peer review under responsibility of Egyptian Society of Anesthesiologists.

Production and hosting by Elsevier

1110-1849 © 2012 Egyptian Society of Anesthesiologists. Production and hosting by Elsevier B.V. Open access under CC BY-NC-ND license.
http://dx.doi.org/10.1016/j.egja.2012.07.002

1. Introduction

In spite of introduction of intermediate-acting neuromuscular blocking drugs (NMBDs), incidence of postoperative residual muscle weakness is still high [1–6]. There is evidence that qualitative monitoring of neuromuscular function does not affect the postoperative train-of-four (TOF) ratios in comparison to relying on clinical signs per se [7]. Surveys of clinical practice in Europe and USA suggest that NMBDs are often administered without proper monitoring [8,9]. Systemic lidocaine infusion has been used effectively to decrease the requirements of analgesics perioperatively [10–12].

However, the effect of systemic lidocaine infusion on intraoperative consumption of NMBDs or TOF ratios at extubation and on arrival to postanesthesia care unit (PACU) was not studied before. The aim of this investigation is to study this effect on one of the intermediate-acting NMBD.

2. Methods

After Local Ethics Committee approval and patients' informed consent, forty-six ASA I–III patients aged 16–60 yr were enrolled. The enrollment period lasted from September 2011 to March 2012 in King Fahd Military Hospital in Dhahran, KSA. Inclusion criteria included surgeries expected to last more than 1 h with positioning that permits access to a forearm and a hand for neuromuscular monitoring. Exclusion criteria included surgeries that needed moderate to intense muscle paralysis or sudden movement of the patient would induce detrimental effects e.g. intracranial, eye and laparoscopic surgeries and bronchoscopy. Patients with known allergy to amide local anesthetics or seizure activity, those with known or expected difficult airway or body mass index $>35\ kg\ m^{-2}$, and those with renal, hepatic or muscle disease (or taking drugs affecting neuromuscular function) were also excluded.

Patients were randomly allocated to two groups using computer-generated codes. These codes were kept in sequentially numbered opaque envelopes. In the morning of surgery, a member of the pharmacy who was not involved in the study opened the allocation envelopes and then prepared either lidocaine 2% or normal saline in "coded" 50-ml syringes. Clinical monitoring included electrocardiography, pulse oximetry, noninvasive arterial blood pressure, depth of anesthesia by bispectral index monitor (BIS VISTA, Aspect Medical Systems, Newton, MA USA) and core temperature via an esophageal probe inserted after endotracheal intubation. Intravenous induction was achieved by propofol 2–3 mg kg^{-1} and fentanyl 100–150 mcg. Endotracheal intubation was facilitated by IV rocuronium 0.6 mg kg^{-1} (based on lean body weight). Immediately after endotracheal intubation, patients were randomly assigned to receive either lidocaine (group L) or placebo saline (control group C). The syringe contained either lidocaine 2% to be given to patients in group L as a 1.5 mg kg^{-1} bolus then 1.5 mg $kg^{-1}\ h^{-1}$ infusion or normal saline to be given to patients in group C in equal volumes. Infusion was kept running until endotracheal extubation. The primary anesthesiologist was blinded to the patient's group assignment. Anesthesia was maintained with sevoflurane and 40% oxygen in medical air to maintain BIS from 40 to 60. Lungs were mechanically ventilated to normocarbia as monitored by capnography. Core body temperature was kept in the range of 35.5–37 °C and the arm with neuromuscular monitoring >33 °C by covering the patients with forced-air mattress (Bair Hugger, Eden Prairie, MN). Intraoperative analgesia was accomplished with intermittent doses of fentanyl 50–100 if blood pressure and heart rate showed sustained elevations (>20% of baseline) for more than 2 min.

Neuromuscular blockade was monitored at the adductor pollicis by using acceleromyography (TOF Watch SX®, Organon, Inc., Dublin, Ireland). The acceleration transducer was taped to the distal interphalangeal joint of thumb with the study arm being immobilized with a splint. The 2 stimulating electrodes were put on the volar medial side of the forearm over the ulnar nerve just proximal to the wrist crease after cleaning the skin with an alcohol swab. Uncalibrated TOF stimulation (four pulses of 0.2-ms duration at a frequency of 2 Hz) was used. The screen area of the acceleromyography was covered with a sheet of paper to conceal the TOF ratio. Rocuronium was not given based on train-of-four (TOF) count but on one of these clinical signs: 1- any spontaneous movement of the patient 2-dipping in capnography indicating trials of breathing 3- more than 20% increase in peak inspiratory preassure after excluding bronchospasm and mechanical obstruction of the endotracheal tube or breathing circuits 4-sustained increase of blood pressure and heart rate after giving one fentanyl bolus.

The top-up dose of rocuronium given was 5–10 mg. No muscle relaxant was given if the expected time of end of surgery was 20–30 min. During this period, boluses of i.v. propofol 20–40 mg were given if needed. Total cumulative dose of rocuronium and number of top-up doses were recorded.

On conclusion of surgery and a few minutes, sevoflurane was discontinued and all patients were given neostigmine 0.05 mg kg^{-1} mixed with glycopyrrolate 10 mcg kg^{-1} if TOF count was $\geqslant 2$. Extubation criteria included TOF count of 4 with objective tactile evaluation of absence of fade, obeying simple commands (e.g. eye opening to orders), strong hand grip, adequate regular breathing and adequate areterial oxygenation ($SpO_2 > 95\%$). At that time and immediately before extubation, the sheet of paper was removed from the screen of TOF Watch SX® and TOF ratio was measured and recorded. Two consecutive TOF ratios (separated by 15 s) were obtained, and the average of the two values was recorded. If measurements differed by more than 10%, additional TOF ratios were obtained (to four TOF values), and the closest two ratios were averaged. Any event of post-extubation laryngospasm was recorded.

Patients were transferred to postanesthesia care unit (PACU) with oxygen mask during transfer (4–6 L min^{-1}). Peripheral oxygen saturation (SpO_2) was continually measured in the PACU. An anesthesiologist who was blinded to patients' allocation recorded TOF ratio on arrival (the same way done before extubation). Peripheral oxygen saturation (SpO_2) on arrival to PACU was recorded. Any adverse respiratory events (defined as $SpO_2 < 95\%$ or airway obstruction requiring intervention i.e. oropharyngeal airway, neck extension, chin lift or jaw thrust) occurring in the PACU was recorded. Number of patients showing mild hypoxemia (SpO2 94–90%) or critical hypoxemia (SpO2 < 90%) were also recorded.

Primary outcome of the study was the TOF ratio at time of tracheal extubation. Murphy et al. [13] found that mean TOF ratio immediately before extubation was 0.67(±0.2).

Table 1 Patients characteristics. Data are mean (±SD), median (range), or number. No statistically significant differences between the 2 study groups. Group C: Control, group L: Lidocaine.

	Group C (n = 23)	Group L (n = 23)
Age (yr)	42.6(11.8)	44.1(12.9)
Sex (M/F)	13/10	11/12
Weight (kg)	79.5(16.9)	81.7(19.1)
Height (cm)	167(15.5)	170.5(13)
ASA (I/II/III)	5/11/7	6/9/8
Surgical procedure		
General	5	6
Ear, nose and throat	5	4
Plastic	3	2
Orthopedic	4	3
Spine	2	3
Urological	4	5
Surgery time (min)	114(67–211)	109(70–215)
Anesthesia time(min)	144(79–240)	148(80–249)

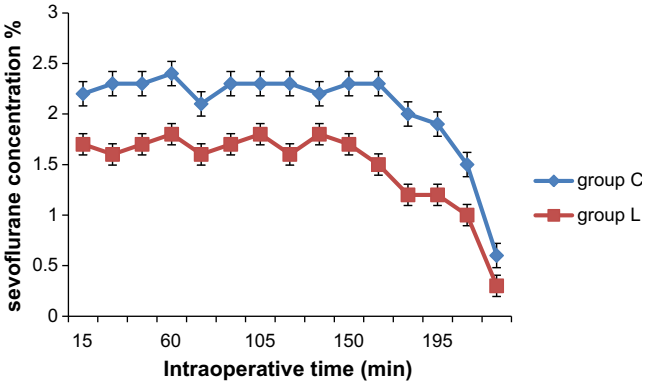

Figure 1 End-tidal sevoflurane concentration intraoperatively. Sevoflurane concentration in the control group (group C) is significantly higher than in lidocaine group (group L) [analysis of variance, $P < 0.01$]. Data are mean (±SD). Time points are 15-min intervals.

Assuming that difference of 0.2 in TOF ratio between the groups would be clinically significant, the sample size was calculated to be 21 in each group at alpha error of 0.05 and beta error of 0.1. Twenty-three patients were allocated per group to accommodate for drop-outs.

Secondary outcomes included cumulative doses of rocuronium, number of top-up doses, end-tidal sevoflurane concentrations, TOF count at time of reversal, time from reversal to extubation, intraoperative doses of fentanyl, incidence of postextubation laryngospasm, TOF ratio on arrival to PACU and time the patients were ready to discharge from PACU based on Aldrete score [14].

Statistical analyses were performed using the SPSS for Windows, version 15 (SPSS Inc., Chicago, IL). Data were first tested for normality by Klomogorov-Smirnov test. Normally distributed continuous data were analyzed by using student t-test. Non-normally distributed continuous and ordinal data were analyzed using Mann–Whitney U test. End-tidal sevoflurane concentrations were analyzed by analysis of variance (ANOVA) test. Categorical data was analyzed by chi square or Fisher's exact test as appropriate. The results are presented as mean ± SD, median (range), or number of patients (percentages) as appropriate. A P value < 0.05 was considered statistically significant.

3. Results

Seventy-one patients were found eligible for the study. Sixteen patients met the exclusion criteria and 9 patients refused participation. Forty-six patients were randomized to 2 groups: group C (n = 23) and group L (n = 23). No patient was excluded from the study.

There were no significant differences between the two groups as regards to age, gender, weight, height, ASA classification, and surgical procedures (Table 1). As depicted in Fig. 1, end-tidal sevoflurane concentrations were significantly lower in group L than in group P ($P < 0.01$).

As shown in Table 2, there were no significant differences between the 2 study groups regarding intraoperative fentanyl doses or core temperature at the end of surgery. The dose of rocuronium and the number of its top-up doses were significantly less in group L than in group C. The time from neostigmine reversal to extubation was significantly longer in group C than group L.

Train-of four ratios were significantly higher in group L than in group C either before extubation or on arrival to PACU (Table 3). Number of patients with TOF ratios less than 0.7 or 0.9 was always more in group C than group L either at extubation or on arrival to PACU yet not statistically significant with TOF < 0.7 on arrival to PACU (Table 3).

Tow patients in group C had post-extubation laryngospasm while no patients in group L had ($P = 0.24$). However the

Table 2 Intraoperative variables. Data are mean (±SD) or median (range). PACU: postanesthesia care unit. Group C: Control, group L: Lidocaine. TOF: train of four.

	Group C (n = 23)	Group L (n = 23)	P value
Fentanyl dose(mcg)	200(100–400)	200(100–400)	0.9
Rocuronium dose (mg)	55.2(7.9)	47.4(6.5)	0.001*
Rocuronium top-ups	2(0–6)	1(0–4)	0.002*
Temperature at end of surgery (C°)	36.2(0.3)	36(0.4)	0.24
TOF count at reversal	3(2–4)	4(2–4)	0.11
Reversal to extubation (min)	11(5.8)	7.2 (3.6)	0.01*
Extubation to transfer to PACU (min)	17.5(4.2)	15.1(4.8)	0.086

* Significant P value (<0.05).

Table 3 Train-of-four (TOF) ratios at extubation and on arrival to postanesthesia care unit (PACU). Data are mean (±SD) or number (percentage). Group C: Control, group L: Lidocaine.

	Group C (n = 23)	Group L (n = 23)	P value
TOF at extubation	0.76(0.07)	0.87(0.09)	<0.001*
TOF on arrival to PACU	0.89(0.18)	1.08(0.16)	0.001*
TOF < 0.7 at extubation	8(35)	1(4)	0.011*
TOF < 0.9 at extubation	18(78)	9(39)	0.008*
TOF < 0.7 on arrival to PACU	3(13)	0(0)	0.12
TOF < 0.9 on arrival to PACU	8(35)	2(8)	0.035*

* Significant P value (<0.05).

Table 4 Postanesthesia care unit variables. Data are number (proportions). Group C: Control, group L: Lidocaine.

	Group C (n = 23)	Group L (n = 23)	P value
Critical hypoxia	1(4)	0(0)	0.5
Mild hypoxia	5(22)	1(4)	0.09
Need for airway intervention	2(9)	0(0)	0.24

laryngospasm was partial and treated with applying continuous positive airway pressure.

Table 4 shows that PACU hypoxic events were more common in group C than in group L albeit not reaching a statistical significance. Two patients in group C needed oropharyngeal airway insertion to relieve airway obstruction. Patients in group L needed shorter time (min) to be ready for discharge from PACU than control group [49.9(16.3) vs. 56.3(13.3), P = 0.15].

4. Discussion

The current study shows that intraoperative use of i.v. lidocaine infusion in generally anesthetized patients can result in higher TOF ratios at time of extubation and on arrival to PACU when rocuronium was given based on clinical signs.

Pederson et al. [7] found that intraoperative qualitative monitoring of neuromuscular block did not affect the intraoperative dose of neuromuscular blocking drug (NMBD) nor did it increase the TOF ratios measured in PACU when compared to patients who have received NMBD based on clinical criteria.

However, the authors did not mention exactly what were the clinical criteria they relied on to titrate the NMBD (pancuronium and vecuronium). On the contrary, four clinical signs were predefined to guide the anesthesiologist to titrate rocuronium in the current trial. It was prudent to predefine these clinical signs to decrease the inter-individual variations of NMBD titration among the 9 attending anesthesiologists who supplied anesthesia to patients in this study. Because the operations in which patients' movement or straining could result in catastrophes were excluded, use of NMBD in the current investigation can be described as "conservative". This conservative approach may be beneficial in decreasing the incidence of postoperative residual recurarization (PORC) which is still high even with use of intermediate-acting NMBDs [1–6]. When comparing the mean doses of rocuronium (SD) in all study patients [51.3(7.1)mg] to one recent study by Murphy et al. [15], it was found that it was nearly 25% less in spite of slight differences in anesthesia durations between the 2 studies. This may be attributed to the different methods guiding the titration of rocuronium in the 2 studies. Murphy et al. [15] used either conventional peripheral nerve stimulator or acceleromyography to guide repeat doses of rocuronium in comparison to the clinical criteria used in the current study. It is clear that reliance on clinical criteria to titrate the NMBDs is not possible in procedures that need deeper levels of muscle relaxation and this can explain the lower doses of rocuronium used because patients undergoing theses procedures were excluded from the study.

Train-of-four ratios were always higher either at extubation time or on arrival to PACU in lidocaine group. Considering TOF ratio less than 0.7 is a critical value at which dangerous respiratory events can occur [16], 13% of patients in control group had recordings less than this value in comparison to zero percent in lidocaine group. However, this difference does not reach a statistical significance may be because the study was not powered enough to detect that difference. Nevertheless, 35% of patients in control group showed TOF ratios <0.9 on arrival to PACU in comparison to 8% in lidocaine group (P = 0.035). When comparing TOF ratios on arrival to PACU in this study with their counterparts in a recent study by Murphy et al. [17], it was found that 13% in all study patients had TOF ratios <0.7 compared to 23% in their study and 43% had TOF ratios <0.9 in all study patients compared to 64% in their study. Putting in mind that times of reversal to TOF ratio measurement were relatively comparable in both studies, this difference can be attributed to the conservative clinical guidance of rocuronium titration in the current study in relation to the use of qualitative and quantitative methods of neuromuscular monitoring in their study. In spite of using a quantitative method (acceleromyography) by Murphy et al. [17] in one group, 14.5% of this group arrived to PACU with TOF <0.9 compared to 8% of lidocaine group in the current study.

Cumulative dose of rocuronium used intraoperatively was found to be 15% less in lidocaine group than in control group. It seems that this difference was probably responsible for shorter time of reversal to extubation and the higher TOF ratios in lidocaine group compared to placebo. This difference could not be explained on pharmacokinetic basis because

Czarnetzki et al. found that continuous intravenous infusion of lidocaine has no impact on the time course of the neuromuscular blockade induced by a standard intubation dose of rocuronium [18]. They gave lidocaine infusion (2 mg kg^{-1} h^{-1}) to one group and saline to the other group and used rocuronium to facilitate endotracheal intubation. They found no differences between the groups as regards to onset time (to 95% depression of first twitch), total recovery time (TOF ratio 0.9), clinical duration (until first twitch has recovered to 25%), recovery index (time between 25% and 75% recovery of the first twitch) and recovery time (between 25% recovery of the first twitch and TOF ratio 0.9).

The probable explanation of decreased needs of rocuronium in lidocaine group is the ability of lidocaine to blunt the cough airway's reflexes to endotracheal tube. Steinhaus JE and Gaskin L found that lidocaine prevented coughing in 8 from 10 anesthetized patients stimulated by manual displacement of the endotracheal tube [19]. Poulton TJ and James FM III found that lidocaine could significantly decrease the cough responses of awake unmedicated persons [20]. Blunting of airway reflexes was speculated to be the mechanism of this favorable effect. Based on these early studies, investigators have shown that lidocaine could be useful in preventing cough related to endotracheal intubation [21] and extubation [22].

The dose of lidocaine bolus and infusion used in the study was based on many previous studies that showed that range of 1.5–2 mg kg^{-1} h^{-1} did not result in plasma concentration higher than 4 mcg ml^{-1} [11,23,24] which is still below the toxic levels (5 mcg ml) [25].

Decreased end-tidal concentrations of sevoflurane required to keep BIS between 40 and 60 in lidocaine group may be explained by its inhibitory effects on central nervous system. Systemic local anesthetics reduce minimum alveolar concentration (MAC) of volatile anesthetics in animals by 20–40% [26,27]. However the study was not powered or designed to detect the effect of lidocaine on MAC.

The results of this study may be encouraging to use lidocaine infusion in general anesthesia to decrease NMBD doses in places lacking quantitative neuromuscular monitors. However one limitation of this study is inappropriateness of this conservative use of NMBD in surgeries that necessitate deep muscle relaxation.

In conclusion, intravenous lidocaine infusion can increase TOF ratios at time of extubation and on arrival to PACU compared to placebo when rocuronium was titrated based solely on clinical criteria.

References

[1] Baillard C, Gehan G, Reboul-Marty J, Larmignat P, Samama CM, Cupa M. Residual curarization in the recovery room after vecuronium. Br J Anaesth 2000;84:394–5.

[2] Cammu G, De Witte J, De Veylder J, Byttebier G, Vandeput D, Foubert L, et al. Postoperative residual paralysis in outpatients versus inpatients. Anesth Analg 2006;102:426–9.

[3] Gätke MR, Viby-Mogensen J, Rosenstock C, Jensen FS, Skovgaard LT. Postoperative muscle paralysis after rocuronium: less residual block when acceleromyography is used. Acta Anaesthesiol Scand 2002;46:207–13.

[4] Naguib M, Kopman AF. Neuromuscular monitoring and postoperative residual curarisation: a meta-analysis. Br J Anaesth 2007;98:302–16.

[5] Hayes AH, Mirakhur RK, Breslin DS, Reid JE, McCourt KC. Postoperative residual block after intermediate-acting neuromuscular blocking drugs. Anaesthesia 2001;56:312–8.

[6] McCaul C, Tobin E, Boylan JF, McShane AJ. Atracurium is associated with postoperative residual curarization. Br J Anaesth 2002;89:766–9.

[7] Pedersen T, Viby-Mogensen J, Bang U, Olsen NV, Jensen E, Engboek J. Does perioperative tactile evaluation of the train-of-four response influence the frequency of postoperative residual neuromuscular blockade? Anesthesiology 1990;73:835–9.

[8] Grayling M, Sweeney BP. Recovery from neuromuscular blockade: a survey of practice. Anaesthesia 2007;62:806–9.

[9] Naguib M, Kopman AF, Lien CA, Hunter JM, Lopez A, Brull SJ. A survey of current management of neuromuscular block in the United States and Europe. Anesth Analg 2010;111:110–9.

[10] McKay A, Gottschalk A, Ploppa A, Durieux ME, Groves DS. Systemic lidocaine decreased the perioperative opioid analgesic requirements but failed to reduce discharge time after ambulatory surgery. Anesth Analg 2009;109:1805–8.

[11] Koppert W, Weigand M, Neumann F, Sittl R, Schuettler J, Schmelz M, et al. Perioperative intravenous lidocaine has preventive effects on postoperative pain and morphine consumption after major abdominal surgery. Anesth Analg 2004;98:1050–5.

[12] McCarthy GS, Megalla SA, Habib AS. Impact of intravenous lidocaine infusion on postoperative analgesia and recovery from surgery: a systematic review of randomized controlled trials. Drugs 2010;70:1149–63.

[13] Murphy GS, Szokol JW, Marymont JH, Franklin M, Avram MJ, Vender JS. Residual paralysis at the time of tracheal extubation. Anesth Analg 2005;100:1840–5.

[14] Aldrete JA, Kroulik D. A postanesthetic recovery score. Anesth Analg 1970;49:924–34.

[15] Murphy GS, Szokol JW, Marymont JH, Greenberg SB, Avram MJ, Vender JS, et al. Intraoperative acceleromyographic monitoring reduces the risk of residual neuromuscular blockade and adverse respiratory events in the postanesthesia care unit. Anesthesiology 2008;109:389–98.

[16] Brull SJ, Murphy GS. Residual neuromuscular block: lessons unlearned. Part II: Methods to reduce the risk of residual weakness. Anesth Analg 2010;111:129–40.

[17] Murphy GS, Szokol JW, Avram MJ, Greenberg SB, Marymont JH, Vender JS, et al. Intraoperative acceleromyography monitoring reduces symptoms of muscle weakness and improves quality of recovery in the early postoperative period. Anesthesiology 2011;115:946–54.

[18] Czarnetzki C, Lysakowski C, Elia N, Tramèr MR. Intravenous lidocaine has no impact on rocuronium-induced neuromuscular block. Acta Anaesthesiol Scand 2012;56:474–81.

[19] Steinhaus JE, Gaskin L. A study of intravenous lidocaine as a suppressant of cough reflex. Anesthesiology 1963;24:285–90.

[20] Poulton TJ, James FM. Cough suppression by lidocaine. Anesthesiology 1979;50:470–2.

[21] Yukioka H, Yoshimoto N, Nishimura K, Fujimori M. Intravenous lidocaine as a suppressant of coughing during tracheal intubation. Anesth Analg 1985;64:1189–92.

[22] Mraovic B, Simurina T, Mikulandra S, Seric J, Sonicki Z. Effects of IV lidocaine administered prior to extubation on early and late recovery after breast surgery. Eur J Anaesthesiol 2010;27:8.

[23] Birch K, Jorgensen J, Chraemmer-Jorgensen B, Kehlet H. Effect of i.v. lignocaine on pain and the endocrine metabolic responses after surgery. Br J Anaesth 1987;59:721–4.

[24] Cepeda MS, Delgado M, Ponce M, et al. Equivalent outcomes during postoperative patient-controlled intravenous analgesia with lidocaine plus morphine versus morphine alone. Anesth Analg 1996;83:102–6.

[25] Mostafa SM, Murthy BV, Hodgson CA, Beese E. Nebulized 10% lignocaine for awake fibreoptic intubation. Anaesth Intensive Care 1998;26:222–3.
[26] DiFazio CA, Neiderlehner JR, Burney RG. The anesthetic potency of lidocaine in the rat. Anesth Analg 1976;55:818–21.
[27] Pypendop BH, Ilkiw JE. The effects of intravenous lidocaine administration on the minimum alveolar concentration of isoflurane in cats. Anesth Analg 2005;100:97–101.