British Journal of Anaesthesia **106** (3): 410–15 (2011)
Advance Access publication 2 January 2011 · doi:10.1093/bja/aeq396
BJA

Differential effects of lidocaine and remifentanil on response to the tracheal tube during emergence from general anaesthesia

J. H. Lee[1,2], B.-N. Koo[1,2], J.-J. Jeong[3], H.-S. Kim[1] and J.-R. Lee[1,2]*

[1] Department of Anesthesiology and Pain Medicine, [2] Anesthesia and Pain Research Institute, [3] Department of Surgery, Yonsei University College of Medicine, 250 Seongsan-no, Seodaemun-gu, 120-752 Seoul, Republic of Korea

* Corresponding author. E-mail: leejeongrim@gmail.com

Editor's key points

- During emergence from general anaesthesia, coughing (or bucking), hypertension and tachycardia may result in complications such as postoperative haemorrhage, intracranial and intraocular hypertension or haematoma.
- Remifentanil administration by effect-site target-controlled infusion suppressed cough, hypertension and tachycardia during anaesthetic emergence more effectively than i.v. bolus administration of lidocaine.

Background. I.V. lidocaine administration and target-controlled infusion (TCI) of remifentanil may each be used to reduce cough and haemodynamic stimulation during emergence from general anaesthesia. We therefore compared the effects of these two treatments on patients' responses to the tracheal tube during recovery from general anaesthesia after thyroid surgery.

Methods. Seventy female patients undergoing thyroidectomy under general anaesthesia using sevoflurane and remifentanil were randomly assigned to i.v. lidocaine (Group L, $n=35$) or remifentanil by TCI (Group R, $n=35$). At the end of surgery, sevoflurane was turned off, and the remifentanil infusion was stopped in Group L and maintained in Group R at an effect-site concentration of 2.0 ng ml^{-1} until extubation. At the same time, i.v. lidocaine 1.5 mg ml^{-1} was administered in Group L. The incidence and severity of cough, haemodynamic parameters, and recovery profiles were evaluated during the emergence.

Results. The incidence of cough during the emergence was significantly higher in Group L than in Group R (72.7% *vs* 20.6%, $P<0.001$) and so was the grade of cough ($P<0.001$). The mean arterial pressure and heart rate were significantly lower in the R group than in the L group during the emergence period ($P<0.05$), although the two groups showed comparable recovery profiles.

Conclusions. TCI of remifentanil reduces responsiveness to the tracheal tube during emergence from general anaesthesia more effectively than does i.v. lidocaine in female patients undergoing thyroid surgery.

Keywords: anaesthesia, general; anaesthetics local, lidocaine; analgesics opioids, remifentanil; complications, extubation tracheal; drug delivery; infusion

Accepted for publication: 12 November 2010

During emergence from general anaesthesia, responses that result from the airway reflex such as coughing (or bucking) are common, and the incidence of cough is reported to be 76–80%.[1 2] Occasionally, cough is accompanied by hypertension and tachycardia,[3 4] and they may result in postoperative haemorrhage,[5] intracranial hypertension,[3] or intraocular hypertension.[6] After thyroid surgery, it is important to prevent such responses because they may induce postoperative haemorrhage and a potentially fatal cervical haematoma.[7]

Techniques used to reduce coughing during emergence include lidocaine[4 8] and opioids.[9 10] I.V. lidocaine has been thoroughly investigated and is reported to suppress emergence cough without risk for serious complication.[4 8 11] On the other side, remifentanil via target-controlled infusion (TCI) has recently proved to reduce cough and haemodynamic stimulation during recovery from general anaesthesia without delaying emergence.[12 13]

We designed the present study to compare the antitussive effects of the conventionally used lidocaine and the newly investigated TCI of remifentanil during recovery from general anaesthesia. In addition, we aimed to evaluate and compare the effects of these two treatments on haemodynamic response and recovery profiles.

Methods

The study was approved by the institutional review board of Severance Hospital, Yonsei University Health System (ref: 4-2009-0519) and registered at ClinicalTrials.gov (ref: NCT01082458). We obtained written informed consent from all subjects.

For this study, we enrolled 70 consecutive patients, all females aged 20–65 yr and ASA physical status I–II, who underwent general anaesthesia for elective thyroidectomy due to thyroid neoplasm. Exclusion criteria included signs of a difficult airway, increased risk of perioperative aspiration, history of chronic respiratory disease such as chronic obstructive pulmonary disease or asthma, recent respiratory tract infection, chronic coughing, current smoking, and significant cardiovascular, hepatic, or renal disease. This randomized, double-blinded, controlled trial took place at the operating theatre of Severance Hospital in Seoul, Korea, from February 2010 to May 2010.

Patients were randomly assigned to one of the two treatment groups according to a computer-generated random numbers table. Patients received either i.v. lidocaine 1.5 mg kg^{-1} (Group L) or a predicted effect-site concentration (Ce) of 2.0 ng ml^{-1} of remifentanil by TCI (Group R) for emergence from anaesthesia. For effect-site TCI of remifentanil, a commercial TCI pump (Orchestra® Base Primea, Fresenius Vial, France) was used, and pump operation was based on Minto and colleagues' pharmacokinetic model for remifentanil. Our protocol was based on targeted effect-site concentration.

All patients were premedicated with i.v. midazolam 0.05 mg kg^{-1} 30 min before induction and i.v. glycopyrrolate 0.2 mg just before induction of anaesthesia. Electrocardiogram, peripheral oxygen saturation (Sp_{O_2}), non-invasive arterial pressure, end-tidal carbon dioxide (E'_{CO_2}), and nasopharyngeal temperature were monitored at 5 min intervals. Anaesthesia was induced using i.v. propofol 1.5 mg kg^{-1} and effect-site TCI of remifentanil. After the patient was unable to respond to verbal response, i.v. rocuronium 0.6 mg kg^{-1} was administered. Tracheal intubation was performed in all patients using a 7.0 mm (internal diameter) reinforced tracheal tube and cuff pressure was maintained at 20–25 mm Hg with a hand pressure gauge (Hi-Lo™ Hand Pressure Gauge, VBM Medizintechnik GmbH, Germany) throughout the procedure. Anaesthesia was maintained with sevoflurane and effect-site TCI of remifentanil, which were titrated to maintain arterial pressure and heart rate (HR) within 10–20% of pre-induction values. Sevoflurane and remifentanil were kept within the range of 1.2–2.5% and 2–5 ng ml^{-1}, respectively. Mechanical ventilation was maintained with a tidal volume of 8 ml kg^{-1}, and ventilatory frequency was adjusted to maintain E'_{CO_2} at 4.6–5.3 kPa. Temperature was maintained at 36–37°C.

Two practitioners were involved during the emergence phase. The first anaesthetist knew which group the patient was in, but the second anaesthetist did not. When a surgeon started to suture the subcutaneous tissue, the first anaesthetist shielded the TCI pump from the second anaesthetist and stopped the TCI of remifentanil in patients assigned to Group L, but maintained Ce 2.0 ng ml^{-1} by TCI of remifentanil in patients assigned to Group R. At the same time, the second anaesthetist adjusted sevoflurane to 0.8 minimal alveolar concentration (MAC) (1.4–1.6%, adjusted to age) in all patients. The second anaesthetist performed all tasks related to emergence from general anaesthesia, as well as the monitoring and recording needed for this study except for control of the TCI pump and i.v. lidocaine or i.v. saline administration. After completion of skin suture, ketorolac 0.5 mg kg^{-1} was given for pain control and glycopyrrolate 0.004 mg kg^{-1} with neostigmine 0.02 mg kg^{-1} was given to reverse the neuromuscular block. Reversal was confirmed as a train-of-four response greater than 90%. After the end of surgery and return from the fully extended position to the neutral position, the first anaesthetist administered 0.15 ml kg^{-1} of i.v. saline to the patients of Group R and 1.5 mg kg^{-1} of i.v. lidocaine to the patients of Group L. At the same time, the second anaesthetist turned sevoflurane off. Mechanical ventilation was then converted to manual ventilation and E'_{CO_2} was maintained at 4.6–5.9 kPa in both groups. Manual ventilation continued until the patients breathed spontaneously, and mild hypercapnia was permitted to restore spontaneous respiration during manual ventilation. The patients were not disturbed, except by continual verbal requests to open their eyes, and all other stimuli were avoided. When the patients opened their eyes, they were encouraged to breathe deeply. After spontaneous respiration, adequate tidal volume, and ventilatory frequency were confirmed, the trachea was extubated and oxygen was immediately supplemented via a facemask for 5 min. After confirmation of stable respiratory and circulatory conditions, patients were transported to the post-anaesthetic care unit (PACU).

The time periods from the end of surgery (sevoflurane discontinuation) to eye opening and to extubation were recorded. During emergence, which was defined as the time interval from the end of surgery to 5 min after extubation, the level of cough was assessed and recorded by the following cough grading system: Grade 0, no cough; Grade 1, single cough with mild severity; Grade 2, cough persistence less than 5 s with moderate severity; Grade 3, severe, persistent cough for more than 5 s (bucking). Cough was defined as a sudden contraction of the abdomen. The mean arterial pressure (MAP) and HR were also recorded at the following time points: T0, before induction of anaesthesia (baseline); T1, the end of surgery; T2, immediately before extubation; T3, 5 min after extubation. In addition, the level of sedation and the ventilatory frequency were estimated and recorded at the T3 point. Sedation was graded by the following sedation grading system (SGS): Grade 0, deeply sedated and unresponsive; Grade 1, sedated but responsive to light glabellar tap or loud voice; Grade 2, sedated but responsive to normal voice; Grade 3, awake and responding.

A third anaesthetist investigated the occurrence of hypertension, postoperative pain, sedation, and nausea in the patients during their PACU stay. The parameters of interest were defined by the following criteria: hypertension, an increase of 30% from MAP to T0 shown by estimation at successive 5 min intervals; pain, more than five points on the visual analogue scale; residual sedation, less than Grade 2 on the SGS at 10 min after PACU admission; nausea, need for antiemetic treatment.

The incidence of cough after general anaesthesia is ~76%.[1] A power analysis indicated that a sample size of 35 patients in each group would be required to detect a difference in cough-suppressive capacity with α=0.05 and a power of 80% with the assumption that a 2.0 ng ml^{-1} effect-site concentration of remifentanil by TCI could decrease the incidence of cough by 90%[12] and i.v. lidocaine 1.5 mg kg^{-1} could reduce it by 50%.

All data are expressed as mean (SD), median (range), or number (proportion, %). Data were analysed using SPSS version 15.0 (SPSS Inc., Chicago, IL, USA). Normally distributed continuous variables were compared using an unpaired two-tailed Student's *t*-test or by repeated measures analysis of variance with the Bonferroni correction. Continuous data not normally distributed were analysed using the Mann–Whitney *U*-test. Categorical data were analysed using the χ^2 test or Fisher's exact test where appropriate. A *P*-value of $<$0.05 was considered statistically significant.

Results

Of 82 patients assessed, 70 patients were enrolled in the study. Among the enrolled patients, three patients were dropped from this study on the day of operation. Sixty-seven patients were able to complete all the assessments for this study [Group L (n=33); Group R (n=34)] (Fig. 1). Physical characteristics and the duration of anaesthesia in these patients were comparable between the two groups (Table 1).

The incidence of cough during emergence from general anaesthesia was significantly higher in Group L than in Group R (72.7% *vs* 20.6%, $P<0.001$). Also the grade of cough during the emergence was significantly higher in Group L than in Group R ($P<0.001$) (Table 2).

Estimates of other parameters related to emergence from general anaesthesia are shown in Table 3 and Figs 2 and 3. The time periods from sevoflurane discontinuation to eye opening (7.3 min in Group L *vs* 7.2 min in Group R) and to extubation (8.3 min in Group L *vs* 8.3 min in Group R) were comparable between the two groups. In addition, the groups did not differ in sedation grade and ventilatory frequency at 5 min after extubation, whereas the MAP and HR were significantly lower in the R group than in the L group during the emergence period ($P<0.05$).

The duration of PACU stay and the between-groups comparison of adverse outcomes at the PACU are summarized in Table 4. The groups did not differ significantly in the duration of PACU stay or incidence of hypertension, pain, and nausea at PACU. However, the number of patients with residual sedation during the first 10 min at PACU was

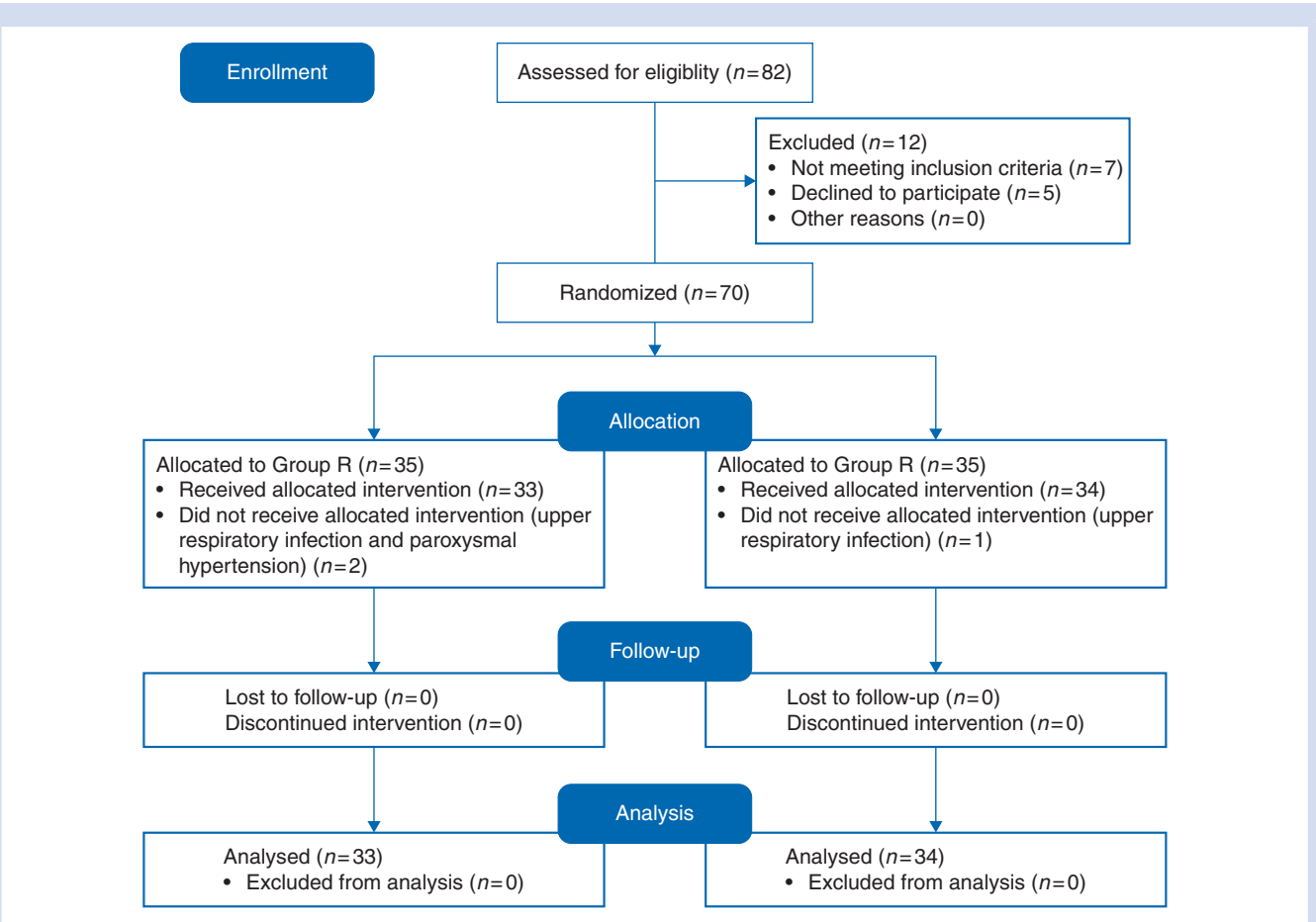

Fig 1 CONSORT diagram showing the flow of participants through each stage of our randomized trial. L, i.v. lidocaine; R, TCI of remifentanil.

Table 1 Patient characteristics and the duration of anaesthesia by group. Values are mean (range), mean (SD) or numbers. L, i.v. lidocaine; R, TCI of remifentanil

	Group L ($n=33$)	Group R ($n=34$)
Age (yr)	45.8 (29–65)	43.0 (26–60)
ASA physical status (I/II)	28/5	29/5
Height (cm)	158.8 (5.9)	159.4 (5.5)
Weight (kg)	59.5 (8.8)	57.6 (8.1)
Duration of anaesthesia (min)	109.8 (21.7)	117.7 (27.5)

Table 2 Cough profiles by group. Values are number (proportion) or median (range). L, i.v. lidocaine; R, TCI of remifentanil; Grade of cough: Grade 0, no cough; Grade 1, single cough with mild severity; Grade 2, cough persistence less than 5 s with moderate severity; Grade 3, severe, persistent cough for more than 5 s. *$P<0.001$ *vs* lidocaine group

	Group L ($n=33$)	Group R ($n=34$)
Cough occurrence	24 (72.7%)	7 (20.6%)*
Grade of cough	1 (1–3)	0 (0–2)*
Total number of patients according to cough grade		
Grade 0	9 (27.3%)	27 (79.4%)
Grade 1	9 (27.3%)	3 (8.8%)
Grade 2	7 (21.2%)	4 (11.8%)
Grade 3	8 (24.2%)	0 (0%)

significantly greater in Group L than in Group R (27.3% *vs* 0%, $P=0.001$).

Discussion

In the present study, remifentanil administration by effect-site TCI suppressed cough, hypertension, and tachycardia during anaesthetic emergence more effectively than i.v. bolus administration of lidocaine in female patients undergoing thyroid surgery. The two treatments did not differ in their recovery profiles, which included the time interval from sevoflurane discontinuation to extubation, level of sedation, and ventilatory frequency after extubation.

The effects of lidocaine to prevent cough during recovery from general anaesthesia have been thoroughly investigated and have been conventionally used. The newly investigated remifentanil TCI may be used during emergence for cough suppression because of its short half-life and expected offset. Several studies showed that i.v. lidocaine at 1–2 mg kg^{-1} is effective without risk for serious complications.[4 8 11] In the previous study, 2.14 and 1.46 ng ml^{-1} of remifentanil Ce were represented as EC_{95} and EC_{50} to abolish cough, and patients who received Ce 2.0 ng ml^{-1} of remifentanil did not suffer significant respiratory complications during anaesthetic induction[14] or emergence.[12] We compared the method of i.v. bolus lidocaine 1.5 mg kg^{-1} and Ce 2.0 ng ml^{-1} of remifentanil by TCI.

Table 3 Recovery profiles by group. Values are mean (SD) or median (range). L, i.v. lidocaine; R, TCI of remifentanil; Time to eye opening, time period from the end of surgery to eye opening; Time to extubation, time period from the end of surgery to extubation; Grade of sedation: Grade 0, deeply sedated and unresponsive; Grade 1, sedated but responsive to light glabellar tap or loud voice; Grade 2, sedated but responsive to normal voice; Grade 3, awake and responding; T3, 5 min after extubation. Both groups show comparable recovery profiles

	Group L ($n=33$)	Group R ($n=34$)
Time to eye opening (min)	7.3 (1.8)	7.2 (2.2)
Time to extubation (min)	8.3 (1.9)	8.3 (2.4)
Grade of sedation at T3	2 (2–3)	2 (2–3)
Ventilatory frequency at T3 (beats min^{-1})	10.6 (3.0)	10.3 (3.2)

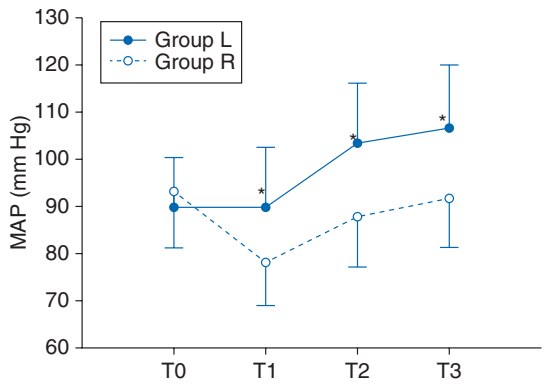

Fig 2 Change in MAP during emergence from general anaesthesia. L, i.v. lidocaine; R, TCI of remifentanil; MAP, mean arterial pressure; T0, before induction of anaesthesia; T1, the end of surgery; T2, immediately before extubation; T3, 5 min after extubation. The mean change in arterial pressure during emergence of Group R is significantly different from that of Group L ($P<0.001$). *$P<0.05$ *vs* Group R.

The lesser efficacy of i.v. bolus lidocaine compared with remifentanil TCI is possibly due to the administration of lidocaine as an i.v. bolus. Sodium channel blockers such as lidocaine or mexiletine suppress cough by inhibiting action potential formation in tracheal touch-sensitive Aδ fibres (cough receptors) at specific concentrations.[15] A serum lidocaine concentration of more than 3 μg kg^{-1} may completely suppress the cough reflex,[16] although this relatively high concentration is difficult to achieve in a timely manner by bolus administration. On the other hand, remifentanil administration via TCI can maintain a predictable plasma concentration or effect-site concentration with an acceptable level of bias and inaccuracy;[17 18] and at this effect-site concentration, remifentanil effectively attenuates coughing

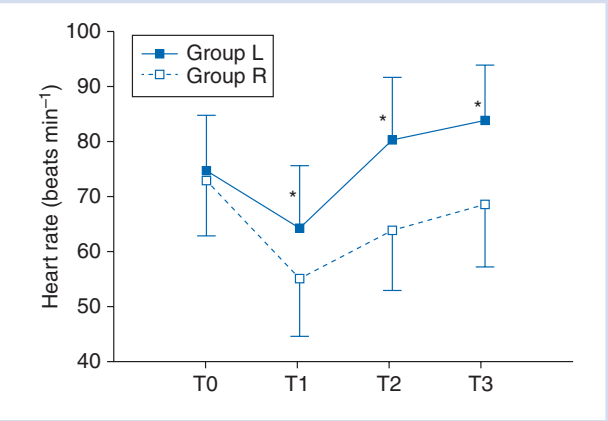

Fig 3 Change in HR during emergence from general anaesthesia. L, i.v. lidocaine; R, TCI of remifentanil; T0, before induction of anaesthesia; T1, the end of surgery; T2, immediately before extubation; T3, 5 min after extubation. Data are expressed as the mean (SD). The change in HR during emergence of Group R differed significantly from that in Group L ($P<0.001$). *$P<0.05$ *vs* Group R.

Table 4 Duration of PACU stay and adverse outcomes at the PACU. Values are mean (SD) or number (proportion). PACU, post-anaesthetic care unit; L, i.v. lidocaine; R, TCI of remifentanil; Hypertension, increase by 30% from mean arterial pressure, estimated at successive 5 min intervals before induction of anaesthesia; Postoperative pain, more than five points on the visual analogue scale; Residual sedation, less than Grade 2 on the SGS at 10 min after PACU admission; Nausea, need for antiemetic drug treatment. *$P<0.005$ *vs* lidocaine group

	Group L ($n=33$)	Group R ($n=34$)
Duration of PACU Stay (min)	42.7 (12.6)	39.6 (11.2)
Residual sedation	9 (27.3%)	0 (0%)*
Hypertension	3 (9.1%)	1 (2.9%)
Postoperative pain	13 (39.4%)	13 (38.2%)
Nausea	1 (3%)	2 (5.9%)

because the probable site of antitussive action for the opioid lies within the central nervous system.[15]

In addition to this advantage, the effect-site TCI of remifentanil showed acceptable recovery profiles for sedation and ventilatory frequency after extubation and for adverse outcomes at the PACU. In contrast, although i.v. lidocaine induced a grade of sedation immediately after surgery comparable with that of remifentanil TCI, it also increased the incidence of residual sedation at the PACU. This is consistent with animal studies showing that i.v. lidocaine at a serum concentration of only 1 μg ml^{-1} may reduce the MAC of halothane by 40%.[19] Some studies also describe sedation or delayed emergence related to i.v. lidocaine in clinical settings.[11 20]

In the context of thyroid surgery, cervical haematoma is a well-known and dreaded complication. Possible causes of this event include coughing during recovery from anaesthesia and increased arterial pressure in the immediate postoperative period.[21] In particular, coughing during and after removal of the tracheal tube may cause a ligature to slip or non-ligated small vessels to bleed profusely because of increased venous pressure.[7] To reduce the risk of a fatal complication in thyroid surgery, it is therefore important to achieve a smooth emergence.

Our study is first limited by the inclusion of only young or middle-aged females in the patient population. This is due to the greater prevalence of thyroid cancer in females[22] and is further complicated due to a gender-related difference in recovery time after sevoflurane anaesthesia.[23] These factors should be considered when interpreting our data. Secondly, there is no control group to which we might compare the effects of i.v. lidocaine on response to the tracheal tube. Hence, it was difficult to find out whether i.v. lidocaine actually attenuated coughing or not; the incidence of cough in the lidocaine group was about 73%, which is similar to the overall incidence of cough in a previous study.[1] During thyroid surgery, however, the trachea is physically manipulated, which may result in a higher incidence of cough than in general surgery overall.

In conclusion, TCI of remifentanil reduces responsiveness to the tracheal tube during the emergence from general anaesthesia more effectively than does i.v. bolus administration of lidocaine in female patients undergoing thyroid surgery. In addition, TCI of remifentanil and i.v. bolus lidocaine show comparable recovery profiles.

Conflict of interest

None declared.

Funding

This work was supported by Yonsei University Research Fund of 6-2010-0004.

References

1 Kim ES, Bishop MJ. Cough during emergence from isoflurane anesthesia. *Anesth Analg* 1998; **87**: 1170–4

2 Aouad MT, Al-Alami A, Nasr VG, Souki FG, Zbeidy RA, Siddik-Sayyid SM. The effect of low-dose remifentanil on responses to the endotracheal tube during emergence from general anesthesia. *Anesth Analg* 2009; **108**: 1157–60

3 Leech P, Barker J, Fitch W. Proceedings: changes in intracranial pressure and systemic arterial pressure during the termination of anaesthesia. *Br J Anaesth* 1974; **46**: 315–6

4 Bidwai AV, Bidwai VA, Rogers CR, Stanley TH. Blood-pressure and pulse-rate responses to endotracheal extubation with and without prior injection of lidocaine. *Anesthesiology* 1979; **51**: 171–3

5 Irwin RS. Complications of cough: ACCP evidence-based clinical practice guidelines. *Chest* 2006; **129**: 54–8

6 Saghaei M, Reisinejad A, Soltani H. Prophylactic versus therapeutic administration of intravenous lidocaine for suppression of post-extubation cough following cataract surgery: a randomized double blind placebo controlled clinical trial. *Acta Anaesthesiol Taiwan* 2005; **43**: 205–9

7 Rosenbaum MA, Haridas M, McHenry CR. Life-threatening neck hematoma complicating thyroid and parathyroid surgery. *Am J Surg* 2008; **195**: 339–43

8 Venkatesan T, Korula G. A comparative study between the effects of 4% endotracheal tube cuff lignocaine and 1.5 mg/kg intravenous lignocaine on coughing and hemodynamics during extubation in neurosurgical patients: a randomized controlled double-blind trial. *J Neurosurg Anesthesiol* 2006; **18**: 230–4

9 Nishina K, Mikawa K, Maekawa N, Obara H. Fentanyl attenuates cardiovascular responses to tracheal extubation. *Acta Anaesthesiol Scand* 1995; **39**: 85–9

10 Mendel P, Fredman B, White PF. Alfentanil suppresses coughing and agitation during emergence from isoflurane anesthesia. *J Clin Anesth* 1995; **7**: 114–8

11 Gefke K, Andersen LW, Friesel E. Lidocaine given intravenously as a suppressant of cough and laryngospasm in connection with extubation after tonsillectomy. *Acta Anaesthesiol Scand* 1983; **27**: 111–2

12 Lee B, Lee JR, Na S. Targeting smooth emergence: the effect site concentration of remifentanil for preventing cough during emergence during propofol–remifentanil anaesthesia for thyroid surgery. *Br J Anaesth* 2009; **102**: 775–8

13 Nho JS, Lee SY, Kang JM, *et al.* Effects of maintaining a remifentanil infusion on the recovery profiles during emergence from anaesthesia and tracheal extubation. *Br J Anaesth* 2009; **103**: 817–21

14 Lee JR, Jung CW, Lee YH. Reduction of pain during induction with target-controlled propofol and remifentanil. *Br J Anaesth* 2007; **99**: 876–80

15 Mazzone SB, Undem BJ, Cough sensors V. Pharmacological modulation of cough sensors. *Handb Exp Pharmacol* 2009: 99–127

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

17 Mertens MJ, Engbers FHM, Burm AGL, Vuyk J. Predictive performance of computer-controlled infusion of remifentanil during propofol/remifentanil anaesthesia. *Br J Anaesth* 2003; **90**: 132–41

18 Moerman AT, Herregods LL, De Vos MM, Mortier EP, Struys MMRF. Manual versus target-controlled infusion remifentanil administration in spontaneously breathing patients. *Anesth Analg* 2009; **108**: 828–34

19 DiFazio CA, Neiderlehner JR, Burney RG. The anesthetic potency of lidocaine in the rat. *Anesth Analg* 1976; **55**: 818–21

20 Gonzalez RM, Bjerke RJ, Drobycki T, *et al.* Prevention of endotracheal tube-induced coughing during emergence from general anesthesia. *Anesth Analg* 1994; **79**: 792–5

21 Shaha AR, Jaffe BM. Practical management of post-thyroidectomy hematoma. *J Surg Oncol* 1994; **57**: 235–8

22 Cook MB, Dawsey SM, Freedman ND, *et al.* Sex disparities in cancer incidence by period and age. *Cancer Epidemiol Biomarkers Prev* 2009; **18**: 1174–82

23 Tercan E, Kotanoglu MS, Yildiz K, Dogru K, Boyaci A. Comparison of recovery properties of desflurane and sevoflurane according to gender differences. *Acta Anaesthesiol Scand* 2005; **49**: 243–7