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ORIGINAL ARTICLE

Target controlled remifentanil infusion for smooth laryngeal mask airway removal during emergence from desflurane–remifentanil anesthesia

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Abstract
Purpose Administration of remifentanil can be a reliable method for preventing airway reflex responses during emergence. We therefore investigated the effect of maintaining target controlled infusion (TCI) of remifentanil for smooth cLMA removal during emergence from desflurane–remifentanil anaesthesia.
Methods Forty-one patients undergoing uretero-renoscopy under general anesthesia with desflurane and at 1–4 ng/ml TCI remifentanil infusion were randomly assigned to a control group ($n = 20$) or a remifentanil group ($n = 21$). At the end of the surgery, desflurane and remifentanil infusion were stopped in group C and remifentanil was maintained at the effect-site concentration of 1.5 ng/ml TCI in group R. When LMA removal was accomplished without coughing, teeth clenching, gross purposeful movements, breath holding, laryngospasm, and desaturation to SpO_2 less than 90%, removal was regarded as smooth (successful). The emergence and recovery profiles were also evaluated.
Results The incidence and number of complications (coughing, teeth clenching, gross purposeful movements, breath holding, laryngospasm, desaturation to SpO_2 <90%) were significantly higher in the control group than in the remifentanil group ($p = 0.002$).
Conclusion Maintaining effect-site TCI of remifentanil at 1.5 ng/ml during emergence from anaesthesia enabled smooth removal of cLMA without any delay in recovery time.

Keywords Analgesics opioid · Remifentanil · Complications · LMA removal · Target-controlled infusion

Introduction

Airway reflexes must be depressed to prevent complications such as bronchospasm or laryngospasm during cLMA removal in emergence [1]. In the state of deep anesthesia, however, elimination of airway protection may lead to airway obstruction and aspiration [2, 3].

Hence providing a balanced anesthesia technique as a calm arousal state without agitation may cause smooth cLMA removal. Although this ideal state can be achieved with opioid administration, opioids have some risks, for example respiratory depression and delayed emergence [4]. Remifentanil, a short acting, potent opioid, may eliminate those risks during emergence [5]. Additionally, target controlled infusion (TCI) of remifentanil can provide a stable blood concentration [6].

This prospective, randomized, controlled, double-blind study was designed to determine whether maintaining TCI

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of remifentanil during emergence after desflurane–remifentanil anaesthesia could enable smooth cLMA removal.

Methods

Approval for this study (Ethics Committee 2011/16) was provided by the Ethics Committee of the Faculty of Medicine, Mersin University, Mersin, Turkey (President Professor Bahar Tuncdal) on 02.02.2011. The study took place in the department of 1. Anesthesiology and Reanimation Clinic, Ministry of Health Diskapi Yildirim Beyazit Research and Training Hospital, Ankara, Turkey. After obtaining the patients' written consent, we enrolled 41 patients ASA I–II, aged 18–60 years, scheduled for elective uretero-renoscopy under general anaesthesia. Exclusion criteria included signs of a difficult airway, history of chronic respiratory disease, hypertension, hepatic or renal disease, recent respiratory tract infection, current smoking, increased risk of perioperative aspiration, and BMI of more than 30. The patients were randomly allocated to one of two groups on the basis of a computer-generated random table.

All patients were premedicated with midazolam 0.05 mg/kg, intramuscularly, 20 min before induction of anesthesia. Routine monitoring with ECG, pulse oximetry, and non-invasive blood pressure measurement was applied to all. End-tidal CO_2 and end-tidal desflurane concentrations were continuously measured in the breathing cycle with a precalibrated gas monitor (Scio Four Oxi plus Medibus Fabius GS; Drager Medical, Lubeck, Germany). The gas sampling flow rate was 200 ml/min. For effect-site TCI of remifentanil, a TCI pump (Space TCI; B. Braun, Melsungen, Germany) using Minto's pharmacokinetic model was used. Intravenous induction was performed with propofol 2.5 mg/kg and a effect-site TCI of remifentanil set at 4 ng/ml; no muscle relaxant was used. An LMA Classic (cLMA) appropriate for the patient's body weight was inserted once the ciliary reflex was lost. Anaesthesia was maintained with 50% nitrous oxide in oxygen, desflurane, and effect-site TCI of remifentanil at 1–4 ng/ml, to maintain blood pressure and heart rate within 20% of baseline values. Ventilation was adjusted to maintain the end-tidal CO_2 at 35–45 mmHg. After urinary catheterization, nitrous oxide and desflurane were ceased in both groups (T0). In the control group (group C) remifentanil infusion was also stopped, but in remifentanil group (group R) TCI effect-site remifentanil at 1.5 ng/ml was continued until cLMA removal. Mechanical ventilation was continued with 100% oxygen. When the patients fulfilled the criteria of eye opening or response to verbal commands, cLMA was removed without the cuffs' deflated. Remifentanil was stopped after cLMA removal in group R. Paracetamol 1 g intravenously was administered 20 min before the end of surgery for postoperative analgesia in both groups.

Duration of anaesthesia, time to cLMA removal (between T0 and LMA removal), and end-tidal concentrations of desflurane at cLMA removal were recorded. The emergence phase was described as the time between T0 and 5 min after cLMA removal. Heart rate, MAP, and SpO_2 were recorded at baseline (preoperative), T0, cLMA removal (T1), 2 min after cLMA removal (T2), and 5 min after cLMA removal (T5).

cLMA removal was accepted as successful if none of the complications coughing, teeth clenching, gross purposeful movements, breath holding, laryngospasm, and desaturation to SpO_2 <90% was observed. If any of these complications was observed it was regarded as unsuccessful [7]. The respiratory rate at T2 and total amount of remifentanil were also recorded.

All patients were monitored in the post-anesthesia care unit (PACU). Ten minutes after PACU arrival the patients were questioned for spontaneous respiratory rate, verbal numerical rating scales scores for pain (0, no pain; 10, as worst possible pain), nausea and vomiting, and sore throat. Patients with a modified Aldrete score [8] of at least 9 were transferred to the related clinic and PACU discharge time was recorded.

Patients' data collected from removal of cLMA to PACU discharge time were estimated by two different anaesthesiologists who were blinded to the groups.

The incidence of complications on removal of the cLMA has been reported to be 54% for the awake patients group [1]. A power analysis indicated that a minimum 16 patients in each group were required to demonstrate a difference of 50% reduction of complications (a power of 80% and α error 0.05). Statistical analysis was performed with SPSS 15.0 for (SPSS, Chicago, IL, USA). Data are presented as mean (SD), numbers and percentage or medians and ranges. Statistical analysis was with a t test or analysis of variance for multiple comparisons and Bonferroni for post hoc analysis, with χ^2 test or Mann–Whitney U test as appropriate. A p value of <0.05 was considered statistically significant.

Results

A total of 41 patients completed the study. One patient in the control group was excluded from the study because of failure while performing URS (Fig. 1). There were no differences between the groups for patients' characteristics, duration of anaesthesia, total dose of remifentanil, and end-expiratory desflurane concentration at LMA removal (Table 1).

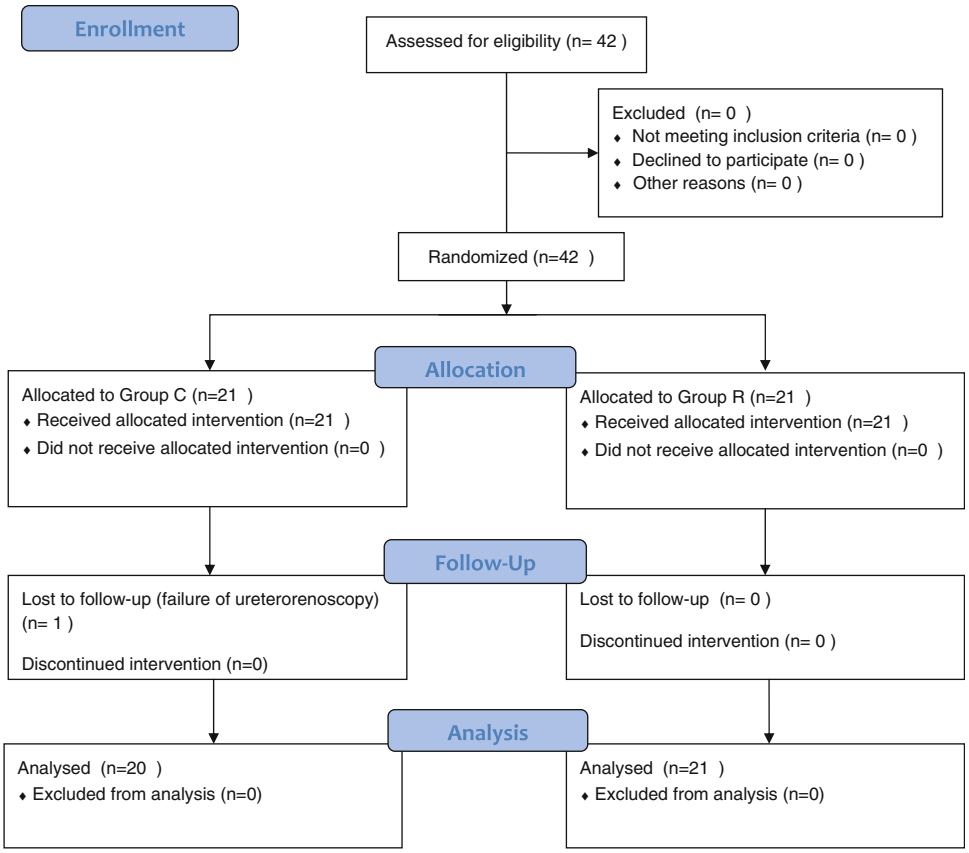

Fig. 1 CONSORT diagram (*C* control, *R* remifentanil)

Table 1 Demographic data and details of operation

	Control group ($n = 20$)	Remifentanil group ($n = 21$)	p
Sex (M/F)	14/6	19/2	NS
Age (years)	38 (12)	41 (13)	NS
ASA physical status (I/II)	12/8	16/5	NS
BMI (kg m^{-2})	26 (4)	27 (3)	NS
Duration of anaesthesia (min)	48 (20)	46 (11)	NS
Total dose of remifentanil (mcg)	260 (111)	248 (52)	NS
End-expiratory desflurane concentration at LMA removal (%)	0.3 (0.1)	0.3 (0.2)	NS

Values are mean (SD), or number (proportion)

During emergence, between the two groups, MAP values were comparable. HR was significantly higher in the control group than in the remifentanil group 2 min after cLMA removal ($p = 0.019$) (Fig. 2).

The incidence and number of complications (coughing, teeth clenching, gross purposeful movements, breath holding, laryngospasm, and desaturation to SpO_2 <90%) were significantly higher in the control group than in the remifentanil group ($p = 0.002$) (Table 2). There were no differences in time to cLMA removal and respiratory frequency at T2 between the groups (Table 2).

The duration of PACU stay, nausea, sore throat, and VAS scores were similar between the groups (Table 3).

Discussion

We observed that maintaining TCI of remifentanil of 1.5 ng/ml at an effect-site during emergence reduces the incidence of complications of cLMA removal compared with the control group. In addition neither PACU discharge time nor cLMA removal time were delayed as a result of the applied dose.

Adequate depth of anesthesia with proper mouth opening must be provided for the successful placement of the LMA without any complication. Therefore, propofol has been successfully combined with different opioids, for example remifentanil, alfentanyl, and fentanyl, as reported

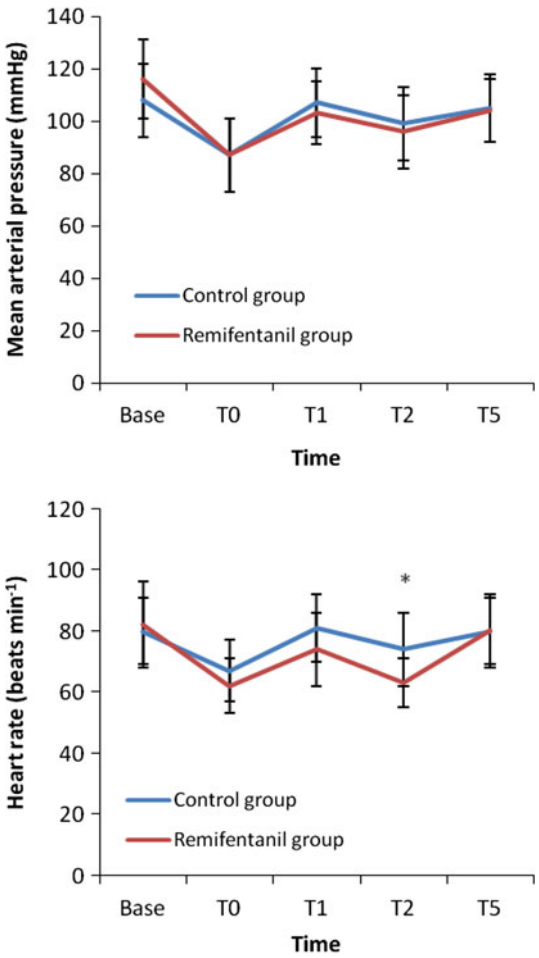

Fig. 2 Changes in MAP and HR during emergence from anaesthesia. *Base* before induction of anaesthesia, *T0* at urine catheter removal, *T1* at cLMA removal, *T2* 2 min after cLMA removal, *T5* 5 min after cLMA removal. Data are expressed mean (SD). $*p < 0.05$ versus remifentanil group

in the literature [9, 10]. Therefore, during insertion of the LMA because anesthesiologists do not need to worry about early emergence, they are comfortable with the doses of drugs used. In contrast, during emergence, providing adequate depth of anesthesia without complication with early emergence is the main concern. So remifentanil, a potent opioid with short acting time, may be an ideal agent.

Opioids' antitussive effects are mediated by m and κ-opioid receptors in the central nervous system (CNS) and peripheral nerve endings [11, 12]. Opioids may reduce CNS excitation generally [13]. Remifentanil has high clearance and short blood–brain equilibration time [14]. This pharmacologic profile of remifentanil enables easy titration of the infusion rate to the desired depth of anaesthesia and makes it an ideal agent for emergence.

TCI is safe and more predictable method than manually controlled infusion by means of overdosing [15].

The reported incidence of problems with removal of the cLMA after the patient has awakened is 10–54% [1]. Therefore, to prevent those complications of cLMA removal is as important as ETT extubation. Despite demonstrating higher incidence of complications in our study (60%) we did not observe any major complication (desaturation, laryngospasm). We included minor complications (teeth clenching, breath holding) in our complication criteria to assess the optimum cLMA removal conditions. This might lead to a higher incidence of complications. In addition, if these relatively minor complications were excluded, the statistical difference in smooth cLMA removal conditions between the two groups might be reduced or considered less significant.

While reviewing the literature we found studies about TCI remifentanil dose for ETT extubation; we could not find TCI remifentanil dose for cLMA removal. Therefore, in our study we decided to use the recommended dose of 1.5 ng/ml remifentanil infusion during emergence period of tracheal extubation by the other investigators.

Aouad and colleagues, showed that continuous infusion of low-dose remifentanil during emergence resulted in smooth emergence and suppressed coughing [16].

Lee and colleagues compared the effects of maintaining a effect-site TCI of remifentanil at 2 ng/ml to lidocaine i.v. bolus in emergence and extubation. They concluded that remifentanil administration even in 2 ng/ml doses did not effect recovery status, suppressed coughing, and resulted in stable hemodynamics [17].

In contrast with other studies, Jun and colleagues maintained TCI 1.5 ng/ml during emergence after sevoflurane–remifentanil anesthesia in thyroidectomies and found the cough reflex could be suppressed but, different from our study, emergence and PACU discharge time were delayed [18]. We thought this delay might be because of their i.v. fentanyl application in PACU for pain control. In our study, during the PACU period none of the patients required analgesics and PACU discharge time was similar in both groups. This can be explained by our type of surgery, which was less invasive than the thyroidectomies.

In a multicenter study remifentanil was administered for postoperative analgesia and a dose-related relationship between high incidence of respiratory depression and nausea–vomiting was observed [19]. We did not observe any respiratory depression at 1.5 ng/ml TCI dose and found no difference in the incidence of nausea–vomiting.

A limitation of our study is age and ASA status of the included patients'. The relatively older or ASA status III, IV population may interfere the effect-site concentration TCI of remifentanil. In the future, dose-finding studies for remifentanil will be helpful for smooth cLMA removal.

In conclusion, maintaining an effect-site TCI of remifentanil at 1.5 ng/ml during emergence from anesthesia has

Table 2 Time to LMA removal and LMA removal conditions

	Control group ($n = 20$)	Remifentanil group ($n = 21$)	p
Time to LMA removal (min)	6 (2)	7 (2)	NS
Ventilatory frequency at T2 (bpm)	13(2)	12 (3)	NS
Smooth removal condition (%)	40	86	0.002
Total number of patients with complication (n) (%)	12 (60)	3 (14)	
Coughing (n)	3	2	
Teeth clenching (n)	6	3	
Gross purposeful movements (n)	3	0	
Breath holding (n)	1	0	
Laryngospasm (n)	0	0	
Desaturation (SpO_2 <90) (n)	0	0	

Values are mean (SD), or number (proportion)

Table 3 Duration of PACU stay, nausea, sore throat, and VAS values

	Control group ($n = 20$)	Remifentanil group ($n = 21$)	p
Duration of PACU stay (min)	20 (4)	22 (3)	NS
Nausea (n) (%)	3 (15)	5 (23)	NS
Sore Throat (n) (%)	3 (15)	3 (14)	NS
VAS	3 [0–4] (0–5)	3 [0–4] (0–6)	NS

Values are mean (SD), median IQR (range) or number (proportion)

enabled smooth removal of cLMA without any delay in recovery.

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Conflict of interest No author has a conflict of interest.

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