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Remifentanil and Etomidate for Laryngeal Mask Airway Insertion*

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Etomidate does not depress the upper airway reflexes, making it difficult to insert a laryngeal mask airway (LMA) when using it for anaesthesia. This study investigated the effect of adding remifentanil to etomidate for LMA insertion. Fifty adult patients, undergoing cystoscopy, were randomized to two groups. The propofol–remifentanil group (*n* = 25) received propofol anaesthesia induction (2.5 mg/kg) and a remifentanil bolus of 0.5 µg/kg, followed by a 2-min remifentanil infusion of 0.05 µg/kg per min. The etomidate–remifentanil group (*n* = 25) received etomidate anaesthesia induction (0.3 mg/kg) and remifentanil as described. The LMA was inserted by a blinded anaesthetist who assessed a number of parameters. Only 13 LMAs were inserted at the first attempt in the etomidate–remifentanil group compared with 23 in the propofol–remifentanil group. Gagging, chest rigidity and myoclonus occurred significantly more frequently in the etomidate–remifentanil group. We conclude that the addition of remifentanil to etomidate anaesthesia induction does not improve LMA insertion.

KEY WORDS: Etomidate; Remifentanil; Anaesthetics; Cystoscopy; Laryngeal mask airway insertion

Introduction

A laryngeal mask airway (LMA) is usually used for short operational procedures, such as cystoscopy, however insertion of the LMA may provoke airway reflexes. Successful insertion of the LMA requires adequate mouth opening and sufficient depth of anaesthesia to minimize the upper airway reflexes and prevent the untoward events of coughing, gagging and laryngospasm.[1,2]

Propofol has been described as the anaesthesia induction agent of choice for the insertion of LMA because of its enhanced depressant effects on the laryngeal reflexes compared with other induction agents, resulting in less gagging, coughing and laryngospasm.[3,4] Remifentanil depresses laryngeal reflexes and its combination with propofol for anaesthesia induction has been shown to provide adequate conditions for laryngoscopy and intubation without the need for concomitant muscle relaxants.[5 – 7]

Etomidate, however, is an anaesthesia induction agent that does not have cardiovascular side effects, which is especially useful for cardiac-compromised patients and for those in whom hypotension

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must be avoided during induction of anaesthesia.[1,2] As short operational procedures, such as cystoscopy, are undertaken in elderly patients with cardiac problems, we wanted to test the hypothesis that the concurrent use of remifentanil with etomidate may reduce the occurrence of airway reflexes and, therefore, increase the success rate of LMA insertion.

Patients and methods

PATIENT POPULATION

This prospective, randomized study enrolled adult patients of American Society of Anesthesiologists (ASA) class I–II, scheduled for elective cystoscopy under general anaesthesia at the Hacettepe University Faculty of Medicine urology operating theatres. All patients who took part provided written informed consent to participate. The study was approved by the ethics committee of Hacettepe University Faculty of Medicine. Exclusion criteria included gastro-oesophageal reflux or hiatus hernia, cardiovascular disease, reactive airway disease, body mass index ≥ 30 kg/m^2, allergy to any of the study drugs, and renal or hepatic impairment. All patients were fasted for over 6 h and no pre-medication was prescribed. The patients were randomly allocated to two groups using a computer-generated random allocation. The propofol–remifentanil group was given propofol 2.5 mg/kg and a remifentanil bolus dose of 0.5 µg/kg followed by a 2-min remifentanil infusion of 0.05 µg/kg per min. The etomidate–remifentanil group was given etomidate 0.3 mg/kg and remifentanil as described.

STUDY METHODS

The anaesthesia induction drugs were injected over 10 s. The patients were not ventilated and after 90 s, a lubricated LMA (size 3 for females or size 4 for males) was inserted by one of the investigators using the technique described by Brain *et al.*[8] The investigator that inserted the LMA and assessed the conditions was blinded to the anaesthesia induction drugs used. Fresenius Propofol 2% (20 mg/ml), (Fresenius Kabi, Graz, Austria) and etomidate-lipuro, (Braun, Melsungen, Germany) are both white in colour and were put in 10 ml syringes to maintain double blindness. Anaesthesia was maintained with sevoflurane 2 – 3% in a mixture of 50% O_2 and N_2O.

The following parameters were investigated on a two-point scale by the anaesthetist who performed the insertion: jaw opening, ease of LMA insertion graded as good or poor, number of attempts (1, 2 or 3), additional propofol use, and unwanted responses such as gagging, coughing, chest rigidity, injection pain and myoclonus. Haemodynamic parameters including heart rate, systolic and diastolic blood pressure and pulse oxymetric measurements were recorded after the initial monitoring, after the induction, after the LMA insertion and 5 min after the start of the operation.

STATISTICAL ANALYSIS

A sample size of 25 per group was required to detect a 45% difference between the groups with a power of 90% and a significance level of 5%. Data analysis was performed by using SPSS® for Windows®, version 11.5 (SPSS Inc, Chicago, IL, USA). Data are shown as the median (range) for continuous variables and frequency with percentage for categorical variables. Mean values were compared using the Mann–Whitney *U*-test. Differences between repeated haemodynamic measurements were evaluated by the Friedman test and a multiple comparison test. For categorical comparisons, the χ^2 or Fisher's exact tests were used. A *P*-value < 0.05 was considered statistically significant.

Results

Fifty patients were enrolled in the study and 25 patients were randomly assigned to each treatment group. The patients in each treatment group were similar with respect to their age, weight, gender and smoking status (Table 1).

The incidence of the parameters that were assessed in relation to LMA insertion are shown on Table 2. There was no significant difference between the two groups with regard to jaw opening but the gagging response was significantly different ($P = 0.034$) (Table 2). The number of attempts

TABLE 1:
Demographic characteristics of patients undergoing laryngeal mask airway (LMA) insertion prior to cystoscopy following induction of anaesthesia with propofol–remifentanil or etomidate–remifentanil

	Propofol–remifentanil ($n = 25$)	Etomidate–remifentanil ($n = 25$)
Gender (male/female)	19/6	19/6
Age (years)		
Mean ± SD	55.6 ± 10.4	59.6 ± 11.6
Range	39 – 85	26 – 84
Weight (kg)		
Mean ± SD	74.5 ± 10.7	77.1 ± 11.9
Range	55 – 99	60 – 105
Smoking status (yes/no)	18/7	16/9

TABLE 2:
Incidence of parameters that were assessed in relation to laryngeal mask airway (LMA) in patients following induction of anaesthesia with propofol–remifentanil or etomidate–remifentanil

	Propofol–remifentanil ($n = 25$)	Etomidate–remifentanil ($n = 25$)	*P*-value
Jaw opening (open/partially open)	18/7 (72%/28%)	14/11 (56%/44%)	NS
Ease of LMA insertion (good/poor)	16/9 (64%/36%)	6/19 (24%/76%)	0.004
Number of attempts (1/> 1)	23/2 (92%/8%)	13/12 (52%/48%)	0.002
Additional propofol (no/yes)	22/3 (88%/12%)	13/12 (52%/48%)	0.005
Gagging (no/yes)	23/2 (92%/8%)	17/8 (68%/32%)	0.034
Coughing (no/yes)	24/1 (96%/4%)	20/5 (80%/20%)	NS
Chest rigidity (no/yes)	19/6 (76%/24%)	11/14 (44%/56%)	0.021
Myoclonus (no/yes)	23/2 (92%/8%)	11/14 (44%/56%)	0.0001
Injection pain (no/yes)	20/5 (80%/20%)	16/9 (64%/36%)	NS

NS, not statistically significant.

at inserting the LMA, additional propofol use and the incidence of unwanted reactions including gagging, chest rigidity and myoclonus were significantly greater in patients who had been given etomidate–remifentanil compared with patients given propofol–remifentanil (P = 0.002, P = 0.005, P = 0.034, P = 0.021, P = 0.0001, respectively). The LMA was more easily inserted in the propofol–remifentanil group (P = 0.004). There was no significant difference in the injection pain scores between the two groups.

Baseline measurements of heart rate,

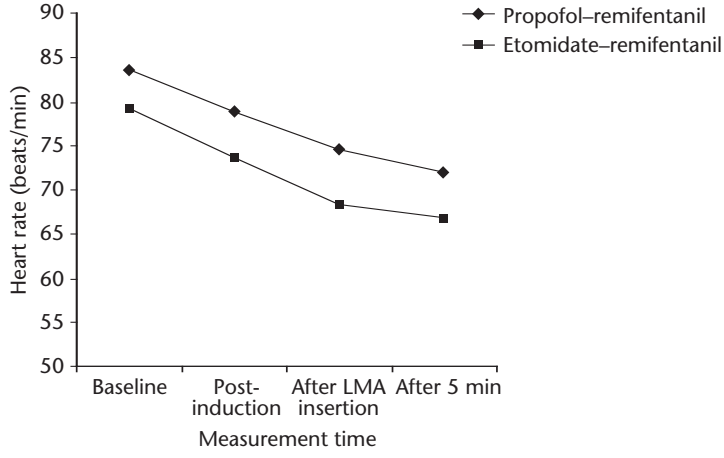

FIGURE 1: Changes in the mean heart rate from baseline up to 5 min after the start of the procedure in patients undergoing laryngeal mask airway (LMA) insertion following induction of anaesthesia with propofol–remifentanil (n = 25) or etomidate–remifentanil (n = 25)

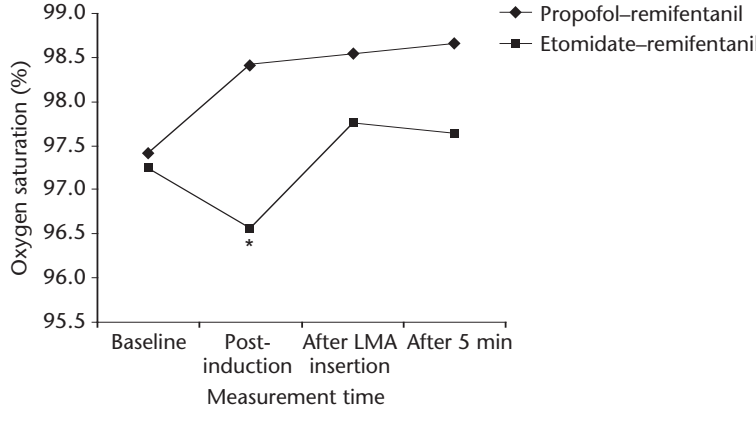

FIGURE 2: Changes in the mean oxygen saturation values from baseline up to 5 min after the start of the procedure in patients undergoing laryngeal mask airway (LMA) insertion following induction of anaesthesia with propofol–remifentanil (n = 25) or etomidate–remifentanil (n = 25). *P = 0.008 compared with baseline

oxygen saturation, and systolic, diastolic and mean arterial blood pressure were not significantly different between the two groups. Heart rate decreased in both groups after the induction of anaesthesia and after insertion of the LMA, but these changes were within clinical limits and required no additional medication (Fig. 1). In the etomidate–remifentanil group, post-induction oxygen saturation was significantly lower compared with the baseline value ($P = 0.008$) but, after LMA insertion, values increased to become not significantly different from baseline levels (Fig. 2). Oxygen saturation levels in the propofol–remifentanil group were not statistically significantly different after the induction compared with baseline. A significant decrease in mean arterial blood pressure compared with the baseline value was observed in the propofol–remifentanil group after induction of anaesthesia ($P = 0.007$) and after LMA insertion ($P = 0.014$) (Fig. 3).

Discussion

Etomidate is a commonly used drug for the induction of anaesthesia in cardiac-compromised patients because of its minimal haemodynamic effects, but LMA insertion can be difficult with this agent.[1,2] We investigated whether the addition of remifentanil to etomidate could facilitate insertion of the LMA, but the findings of our study showed that remifentanil provided no additional benefits for LMA insertion when used with etomidate.

Insertion of the LMA requires suppression of the upper airway reflexes. Propofol is usually the preferred induction agent for this purpose because it readily blocks the upper airway reflexes thereby ensuring suitable conditions for LMA insertion.[9] Additional opioids are used in conjunction with propofol to decrease the upper airway reflexes even further and to potentiate the effects of propofol, enabling the dose of propofol to be reduced.[10,11] Decreasing the

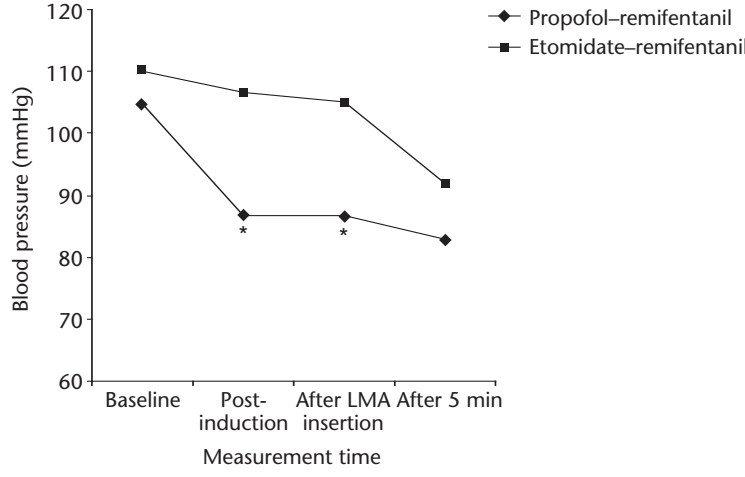

FIGURE 3: Changes in mean arterial blood pressure from baseline up to 5 min after the start of the procedure in patients undergoing laryngeal mask airway (LMA) insertion following induction of anaesthesia with propofol–remifentanil ($n = 25$) or etomidate–remifentanil ($n = 25$). *$P = 0.007$ compared with baseline post-induction; *$P = 0.014$ compared with baseline after LMA insertion

induction dose of propofol helps to reduce any unwanted haemodynamic effects, such as hypotension. Etomidate does not suppress the airway reflexes as much as propofol and additional propofol was required more frequently in our study to suppress the airway reflexes in patients treated with etomidate–remifentanil (12 patients) compared with patients treated with propofol–remifentanil (three patients) (P = 0.005).

Mean arterial blood pressure decreased after induction of anaesthesia in the propofol–remifentanil group and was significantly different from the baseline value; no decrease of mean arterial blood pressure was seen in the etomidate–remifentanil group. In the study by Wilhelm *et al.*,[12] which compared the effects of remifentanil or fentanyl on the anaesthetic induction characteristics of propofol, thiopental or etomidate, mean arterial blood pressure and heart rate decreased significantly after anaesthesia induction with propofol. In our study, heart rate decreased to a similar extent in both treatment groups after the induction agents had been injected, so there was no need for additional drug administration. Oxygen saturation decreased after induction in the etomidate–remifentanil group (P = 0.008) but, in the propofol–remifentanil group it was not significantly different from baseline at any measurement time. The decline in oxygen saturation observed after induction in the etomidate–remifentanil group may be because of the greater number of attempts to insert the LMA and additional propofol use. A study by Lee *et al.*[13] found a longer apnoea interval with propofol and remifentanil at a dose of 0.5 μg/kg compared with a dose of 0.25 μg/kg, hence the lower dose of remifentanil was suggested for LMA insertion in conjunction with propofol.

Remifentanil is an ultrashort-acting potent ester opioid, which is metabolized by non-specific plasma and tissue esterases that are widespread throughout the plasma, red blood cells and interstitial tissues.[14,15]. It has a rapid onset of action (blood–brain equilibration time of 1 min), and a higher clearance and shorter elimination half-life (< 10 min) than alfentanil and fentanyl.[14,15] Remifentanil depresses laryngeal reflexes and its combination with propofol for induction has been shown to provide adequate conditions for laryngoscopy and intubation without the need for concomitant muscle relaxants.[5 – 7] The success of the remifentanil–propofol combination is probably because of apnoeic, analgesic and antitussive effects of the opioid.[16] In the present study, however, the remifentanil–etomidate combination did not show the same benefits as propofol–remifentanil.

One of the major advantages of etomidate is the lack of cardiovascular side effects. Etomidate, when administered at a dose of 0.3 mg/kg, has only minimal effects on cardiovascular parameters or myocardial function.[17] Clinical and experimental data reveal that etomidate is highly suitable for the induction of anaesthesia even in patients who have cardiovascular risk factors.[17,18] Etomidate has been shown to provide stable haemodynamics while blunting the response to laryngoscopy for the induction of anaesthesia.[17,18] Stevens *et al.*[19] investigated intubation conditions with different hypnotics (propofol, etomidate, thiopental) without muscle relaxation using alfentanil. Alfentanil plus etomidate yielded intubation conditions comparable with those achieved with alfentanil and propofol. However, according to our present study, the situation appears to be different for LMA with the addition of remifentanil to etomidate, which

did not show any benefits for LMA insertion.

Myoclonus is one of the most inconvenient side effects experienced during the induction of anaesthesia with etomidate. The incidence of myoclonus has been estimated to be as high as 50 – 80%, especially if etomidate is used without pre-medication.[17] The incidence of myoclonus after etomidate induction, however, has been shown to be reduced by remifentanil pre-treatment,[18] In our present study, a total of 56% of patients treated with etomidate–remifentanil experienced myoclonus, however, as there was no group using etomidate alone, it is not possible to comment specifically on the effect of remifentanil on myoclonus in this study.

Propofol has been described as the anaesthesia induction agent of choice for the insertion of LMA because of its enhanced depressant effects on the laryngeal reflexes compared with other induction agents; for example it has been reported to cause less gagging, coughing and laryngospasm.[3,4] Our study also revealed that a propofol–remifentanil combination was superior to an etomidate–remifentanil combination for LMA insertion.

Many studies have investigated ways to facilitate LMA insertion with different induction agents,[3,4,9,10,13,16,20,21] but only Liou *et al.*[1] and Lui [2] have studied how to improve the success rate of LMA during etomidate induction. In looking at the effect of fentanyl or succinylcholine on LMA insertion conditions they found that 2 μg/kg of fentanyl reduced the occurrence of airway reflexes and increased the success rate of insertion, but concurrent use of 1 mg/kg of succinylcholine might provide better results in terms of a shorter duration for the LMA insertion and a greater success rate of insertion than fentanyl.

In conclusion, the present study comparing concurrent use of etomidate–remifentanil with propofol–remifentanil anaesthesia induction on the ease of LMA insertion, jaw opening and on untoward effects, such as coughing and gagging, found the jaw opening rate to be similar in both groups but the LMA was more easily inserted in the propofol–remifentanil group. A significantly reduced gagging response was observed with propofol–remifentanil compared with etomidate–remifentanil. We conclude that the addition of remifentanil to etomidate anaesthesia induction did not offer any advantages for LMA insertion.

Conflicts of interest

No conflicts of interest were declared in relation to this paper.

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