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# Remifentanil without muscle relaxants for intubation in microlaryngoscopy: a double blind randomised clinical trial

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**Abstract. – OBJECTIVES: We aimed to compare the effect of remifentanil without muscle relaxant with succinylcholine for intubation in microlaryngoscopy.**

**PATIENTS AND METHODS: Eighty patients were randomly divided into two groups: Group R (n=40) and S (n=40) received remifentanil 4 μg/kg intravenously or 1 μg/kg respectively. Anesthesia was induced with 2 mg/kg propofol in both groups. Intubation was performed after bolus administration of 10 ml saline as a placebo or 1 mg/kg of succinylcholine in Group R and S respectively. Remifentanil infusion was initiated at 0.025 μg/kg in each groups.**

**RESULTS: Intubation conditions were similar in both groups. The mean arterial pressure (MAP) values at post-induction period were significantly lower in the Group S than in the Group R ($p$ = 0.001). The requirement for ephedrine in Group R was found to be significantly lower than Group S ($p$ = 0.023). Recovery times were significantly shorter ($p$ = 0.001) and recovery scores were significantly higher ($p$ = 0.021) in Group R. Time to patient could respond to commands was significantly longer in the Group S ($p$ = 0.001). The surgeon's satisfaction score was significantly higher in Group R ($p$ = 0.001).**

**CONCLUSIONS: It was concluded that remifentanil without muscle relaxants provides similar intubating conditions as that provided by succinylcholine, and remifentanil is superior to succinylcholine with regard to haemodynamic stability and recovery duration.**

*Key Words:*
Microlaryngoscopy, Remifentanil, Succinylcholine, Intubation

## Introduction

Endoscopic laryngeal microsurgery is a procedure that requires excellent collaboration between the anaesthesiologist and the surgeon, to manage the patient's airway in a narrow surgical area[1,2]. An ideal anaesthetic technique should provide an immobile larynx, clear and free of secretions. Endoscopic laryngeal microsurgery is a short-term intervention that requires special attention to the anaesthetic technique[2] as blood pressure and heart rate often fluctuate markedly during microlaryngoscopy[3], and myocardial ischemia or infarction may be observed following the intervention[4].

Succinylcholine or short acting non-depolarizing agents[2] are generally used as muscle relaxants in microlaryngoscopy procedures. However, adverse effects such as prolonged paralysis, postoperative myalgia, hyperkalemia, and intraocular and intracranial hypertension may be observed following the use of succinylcholine[5,6]. Short-acting non-depolarizing muscle relaxants have fewer adverse effects when compared to succinylcholine, but have disadvantages such as requiring an antagonist and the impossibility of reversing the block rapidly in cases where tracheal intubation or ventilation through a mask cannot be provided.

Current scientific research focuses on minimizing the dose of neuromuscular drugs or finding alternative methods to achieve endotracheal intubation. Remifentanil is a novel short-acting opioid[7-9]. Several studies have reported that the use of remifentanil, in combination with propofol without using a muscle relaxant, provided adequate intubating conditions[10-12], a good haemodynamic stability and early recovery[13,14]. However, the effects of using remifentanil for intubation without muscle relaxants have not been evaluated adequately in microlaryngoscopy.

The aim of this study is to compare intubating conditions, haemodynamics, and recovery times for patients undergoing microlaryngoscopy who received either remifentanil without muscle relaxants or succinylcholine for intubation.

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## Patients and Methods

### Trial Design and Patients

The present study was a single-centre, balanced randomized [1:1], double-blinded, parallel group, phase IV study conducted at Inonu University Hospital (Malatya, Turkey) between November 2009 and July 2010. After institutional approval by the Ethics Committee of Inonu University Hospital (27.10.2009/N°142) and obtaining written informed consent, 80 American Society of Anesthesiologists (ASA) physical status and Mallampati scores of I and II patients, aged between 18 and 65 years, undergoing scheduled elective microlaryngoscopy were enrolled in this study. Patients with a history of head and neck surgery or being scheduled to undergo head and neck surgery, severe cardiovascular and pulmonary disease, neuromuscular disease or medications effecting the neuromuscular junctions were excluded. Strained patients were excluded from the study and intubated with succinylcholine.

Randomisation and allocation of the patients into intervention groups was performed using computerised numbers (Excel; Microsoft, Remond, WA, USA) by an anaesthesiologist not participating to the trial. Both care providers on the ward and the anaesthesiologists assessing outcomes were blinded to the study groups.

No premedication was administered to any patients. All patients were transferred into the operating room, where our team performed non-invasive tests to monitor the blood pressure, heart rate (HR), peripheral oxygen saturation ($SpO_2$), and electrocardiogram. Following routine monitoring, all parameters were measured three times with two minutes interval and the mean values of this measurements recorded as the baseline.

The patients were randomized into two groups: the remifentanil group (Group R; n = 40) and the succinylcholine group (Group S; n = 40). Following the establishment of intravenous (i.v.) access, patients in Group R were administered 4 $\mu$g/kg of remifentanil over 90 seconds; those in Group S were administered 1 $\mu$g/kg of remifentanil over 90 seconds for induction, and then 2 $mg \cdot kg^{-1}$ propofol was administered over 30 seconds.

Patients were intubated 60 seconds after administration of 10 ml of a saline in Group R and 1mg/kg of succinylcholine in Group S. Patients who strained during the intubation were administered an additional dose of 1 mg/kg succinylcholine and excluded from the study. Maintenance of anesthesia was provided by 1%-2% sevoflurane in a mixture of 65% $N_2O$+35% $O_2$ for both groups.

Remifentanil infusion was initiated at 0.025 $\mu$g/kg in both groups after intubation was performed. If additional muscle relaxants were required intraoperatively, the patients in the Group R were administered 1 $\mu$g/kg of remifentanil and the patients in Group S were administered 10 mg of succinylcholine.

We categorized the patient's intubation condition with the scoring system described by Helbo-Hansen et al[15] (Table I). The HR, mean arterial pressure (MAP), systolic arterial pressure (SAP), and the $SpO_2$ levels were recorded for each patient at pre-induction, post-induction, post-intubation, after installation of the laryngoscope, and at every 3 minutes until the end of the operation. If any change in the MAP or the HR exceeded ±20% to baseline value, a bolus dose of 10 mg ephedrine, or if necessary, a bolus dose of 0.1 mg of nitroglycerine, was administered intravenously. Atropine was administered when the HR decreased to 50 $beats/min^{-1}$. At the end of the surgery, all of the anaesthetic agents were discontinued and the patients were ventilated with 100% $O_2$. The times elapsed from the discontinuation of the anaesthesia to initiation of spontaneous respiration, opening of the eyes, tracheal extubation, responses to commands, and patients' orientation to time, place and person, was recorded as markers along the "recovery" period.

**Table I.** Intubating scoring system.

| | 1 | 2 | 3 | 4 |
|---|---|---|---|---|
| Jaw relaxation | Complete | Tone | Stiff | Rigid |
| Laryngoscopy | Easy | Fair | Difficult | Impossible |
| Vocal cords | Open | Moving | Closing | Closed |
| Coughing | None | Slight | Moderate | Severe |
| Movement | None | Slight | Moderate | Severe |

Adapted from[15].

We evaluated the patients' level of consciousness, activity, respiration, circulation and $SpO_2$ at 1 min, 10 min and 30 min post-extubation using the modified Aldrete Recovery Score. Adverse effects such as hoarseness, sore throat, laryngospasm, nausea and vomiting were recorded.

The surgeon satisfaction was determined as poor (score 1), moderate (score 2), or excellent (score 3).

### Statistical Analysis

At least 40 patients for each group were estimated to be adequate, with a power of 80% and an alpha level of 0.05, in order to reduce the effect of pharyngolaryngeal symptoms due to intubation from 60% to 30%. Statistical analysis of data was performed using Statistical Program for the Social Sciences (SPSS, Inc., Chicago, IL, USA) version 13.0. Continuous variables were expressed as mean±standard deviation (SD), and the categorical variables were expressed as numbers and percentages. The normal distribution of the continuous variables was verified by the Shapiro-Wilk test ($p > 0.05$). Among the parametric tests, the unpaired $t$ test and the paired $t$ test were used for the continuous variables, while the Pearson's chi-square and the Fisher's chi-square test were used for the categorical variables. A $p$ value of $< 0.05$ was considered statistically significant.

## Results

85 patients were eligible for the study. Five of the patients were excluded from the study due to not meeting inclusion criteria. 80 patients completed the study (Figure 1). None of the patients were strained during the study.

Demographic data and intubation conditions were shown in Table II and III. There was no statistical difference between the groups. Coughing was observed in only one patient in each of the two groups. All patients in Group R remained immobile during intubation. However, extremity movements were observed for two cases in Group S. No patients were required additional muscle relaxant.

The SAP and MAP values decreased in both groups, compared to baseline. The MAP values at post-induction were significantly lower in the Group S than in the Group R ($p = 0.001$, Figure 2). There were no differences between groups with respect to SAP and MAP during all monitored periods. The requirement for ephedrine in Group R (2/40) was found to be significantly lower than that in Group S (12/40) ($p = 0.023$). None of the patients in Group R required atropine, but seven patients in Group S required administration of atropine. The post-induction and post-intubation HR values, as well as the HR values measured 6 minutes and 9 minutes after

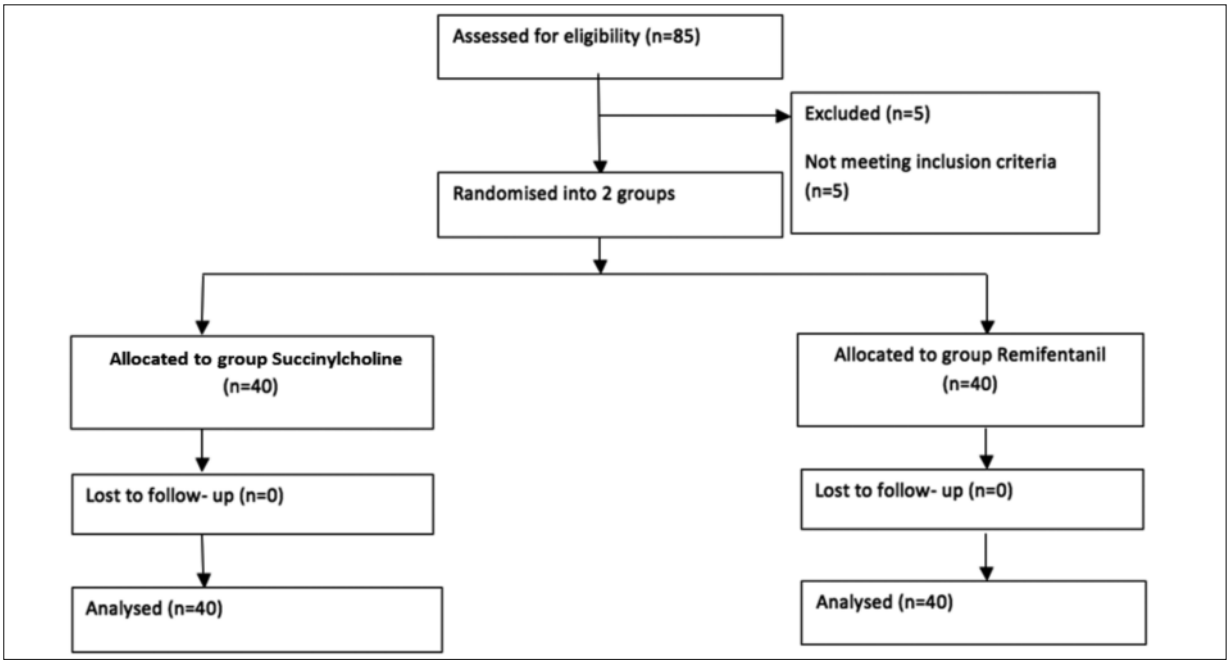


**Figure 1.** Flow chart of the study.

**Table II.** Demographic data for groups. Values are mean (SD) or number (n).

| | Remifentanil (n = 40) | Succinylcholine (n = 40) | *p* value |
|---|---|---|---|
| Age; year | 47.9 (8.7) | 49.6 (8.4) | 0.385 |
| Height; cm | 170 (0.0) | 169 (20) | 0.322 |
| Weight; kg | 73.2 (14.4) | 77.3 (13.1) | 0.182 |
| Time of operation; min | 17.4 (5.3) | 18.5 (6.4) | 0.407 |
| Gender; F/M | 18/22 | 19/21 | 0.451 |
| ASA; I/II; n | 32/8 | 29/11 | 0.485 |

**Table III.** Intubation score of groups. Values are percentage and number.

| | Remifentanil (n = 40) | Succinylcholine (n = 40) |
|---|---|---|
| **Jaw relaxation** | | |
| Complete | 40 (100%) | 29 (72.5%) |
| Tone | 0 | 9 (22.5%) |
| Stiff | 0 | 2 (2.5%) |
| Rigid | 0 | 0 |
| **Laryngoscopy** | | |
| Easy | 39 (97.5%) | 25 (62.5%) |
| Fair | 1 (2.5%) | 10 (25%) |
| Difficult | 0 | 5 (8%) |
| Impossible | 0 | 0 |
| **Vocal cord** | | |
| Open | 38 (95%) | 36 (90%) |
| Moving | 2 (5%) | 3 (7.5 %) |
| Closing | 0 | 1 (2.5%) |
| Closed | 0 | 0 |

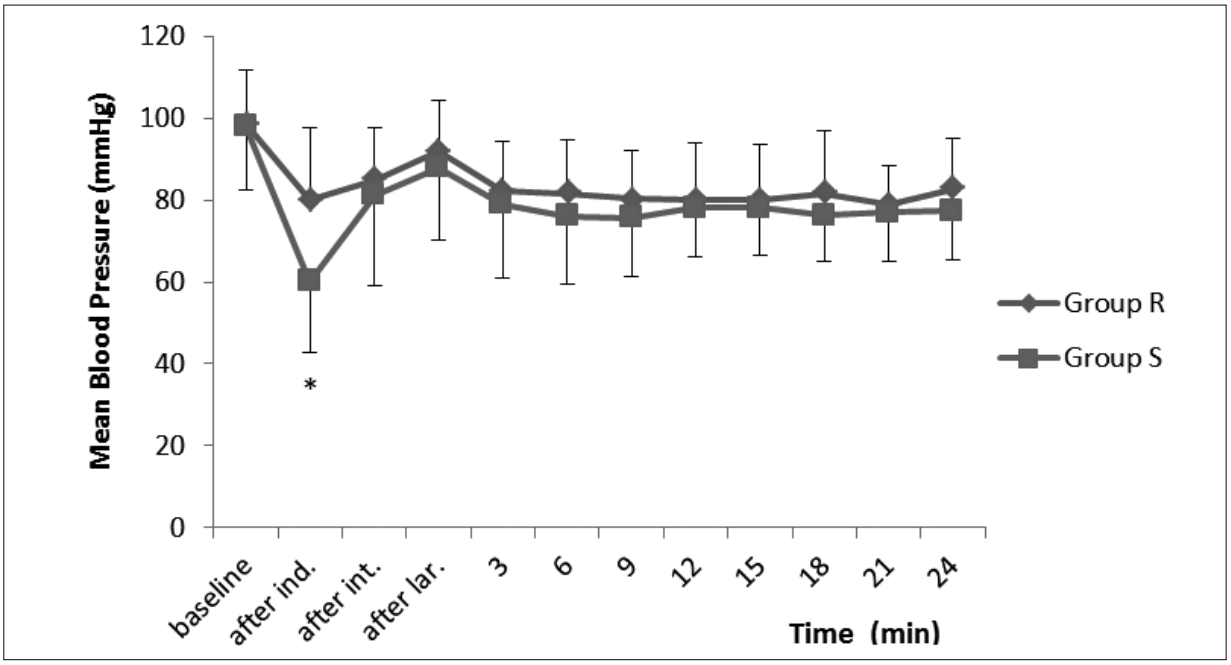


**Figure 2.** Change in mean arterial pressure (MAP) in groups.

**Table IV.** Recovery characteristics and surgeon satisfaction score of groups. Values are mean (SD).

| | Remifentanil (n = 40) | Succinylcholine (n = 40) | *p* value |
|---|---|---|---|
| Spontaneous respiration; min | 5.7 (1.7)* | 8.9 (3.3) | 0.001 |
| Eye opening; min | 9.2 (2.3)* | 14.7 (5.9) | 0.001 |
| Extubation; min | 7.1 (1.9)* | 10.5 (3.3) | 0.001 |
| Response to commands; min | 11.6 (2.9)* | 16.2 (3.6) | 0.001 |
| Regaining orientation; min | 14 (3.3)* | 18.9 (3.8) | 0.001 |
| Aldrete score-1. min | 6.8 (0.6)* | 6.1 (0.5) | 0.021 |
| Aldrete score-10. min | 8.7 (0.5)* | 8.3 (0.8) | 0.023 |
| Aldrete score-30. min | 10 (0.0) | 9.9 (0.1) | 0.496 |
| Surgeon satisfaction score | 3.0 (0.0)* | 2.6 (0.4) | 0.001 |

*= $p < 0.05$ Group R versus Group S.

insertion of the laryngoscope, were found to be significantly higher in the Group R ($p < 0.04$).

The times to spontaneous respiration, open the eyes, and the team could complete extubation were found to be significantly shorter in Group R ($p = 0.001$). Orientation to time, place and person, and for response to commands were found to be significantly longer for patients in the Group S ($p = 0.001$). The Aldrete recovery scores at 1 minute and the 10 minutes were found to be significantly higher in Group R ($p = 0.021$), and the surgeon satisfaction score was significantly higher in Group R ($p = 0.001$), as shown in Table IV.

None of patients complained of nausea or vomited. The rates of adverse effects such as sore throat, laryngospasm and hoarseness were found to be similar in the two groups (Table V).

## Discussion

In the present study, the intubating conditions were more favourable, the haemodynamic control was easier, the recovery times was more rapid, and the surgeon satisfaction scores were higher in patients for whom intubation was performed without muscle relaxant compared to those patients who received 1 mg/kg succinylcholine.

The ability to perform a tracheal intubation easily depends on the experience of anaesthesiologist, the depth of anaesthesia, and the degree of muscle relaxation. Hence, in this study, intubation of all the patients was performed by the same anaesthesiologist, who had at least 2 years of anaesthesia experience. Alexander et al[6] compared propofol with remifentanil or succinylcholine, they determined that the success rate of intubation in the remifentanil group was lower (35%) when compared to the succinylcholine. This may be attributable to low dose of remifentanil leading to the incomplete onset of its effectiveness. In a study performed by Woods et al[12] 2 mg/kg propofol was used in combination with 1 μg or 2 μg remifentanil; more favourable intubating conditions was observed in the remifentanil group (1 mg) in which 1 mg/kg lidocaine was used, as compared to the remifentanil group (2 μg).

By administering a target-controlled infusion of propofol and remifentanil, Ithnin et al[16] reported similar intubating conditions in patients with normal airways, compared to intubating conditions in a paralyzed patient. In contrast to our investigation, Ithnin et al[16] administered all the anaesthetic agents intravenously. In our study, inhalation anaesthesia was performed to maintain the anaesthesia during the operation. We used only an infusion of remifentanil, however, and the infusion was not target-controlled.

Many researches have reported that hypotension and bradycardia may develop following the use of high-dose opioids in combination with propofol[11]. In patients undergoing microlaryn-

**Table V.** Adverse Effects, percentage or number.

| | Remifentanil (n = 40) | Succinylcholine (n = 40) | *p* value |
|---|---|---|---|
| Sore throat (n, %) | 2 (5%) | 2 (5% ) | 1.0 |
| Laryngospasm (n, %) | 0 | 1 (2.5%) | 1.0 |
| Hoarseness (n, %) | 2 (5%) | 0 | 0.494 |

goscopy, an increase in the HR and blood pressure may occur, depending on the surgeon's manipulation of the upper and lower airways. However, although the rapid increase in blood pressure after laryngoscopy would not pose a problem in patients with normal cardiac functions, it may be clinically important in those with coronary artery disease, the elderly and those with pulmonary disease. In these patients, increases in the blood pressure and HR, combined with a decrease in oxygen saturation, cause an increase in the myocardial oxygen consumption, resulting in the development of arrhythmia, ischemia and myocardial infarction[4]. Remifentanil administered as a bolus or i.v. in both groups might have prevented sudden increases in blood pressure.

In the study performed by Ithnin et al[16] the hemodynamics were observed to be stable, as in our remifentanil group, and no significant decreases in blood pressure and HR were noted following induction. A report by Klemola et al[11] referred that they achieved intubation with a success rate of 93% using 4 $\mu$g remifentanil and 2.5 mg propofol, and prevented the cardiovascular response to intubation. In the research by Erhan et al[17] the drugs were administered at doses similar to those of our study; however, they administered 7 ml/kg of 0.9% saline to the patients prior to induction and 0.01 mg/kg atropine to obtain stable hemodynamia.

Similarly, Stevens and Wheatley[10] achieved excellent intubating conditions (80%) by administering 2 mg propofol and 4 $\mu$g/kg remifentanil to the patients, and spontaneous respiration returned less than 5 minutes after the end of surgery. They did not use a remifentanil infusion to maintain the anaesthesia, which may have resulted in the rapid return of spontaneous respiration.

Woods et al[18] reported the time to spontaneous respiration was 270 seconds in the patients to whom 1 $\mu$g/kg remifentanil was administered in combination with 2 mg propofol, and is 487 seconds in the patients to whom 2 $\mu$g/kg remifentanil was administered in combination with 2 mg propofol. In the present study, for the patients 4 $\mu$g/kg remifentanil was administered, the time to initiation of spontaneous respiration was 342 seconds, which was shorter than expected. This may be attributed to the different recovery times of the induction agents we used.

Spontaneous respiration returned after 1 mg/kg succinylcholine in approximately 6 minutes in Mc Neil et al[19] study; this duration also depends on the induction agents used. In the present investigation, spontaneous respiration returned 8.9 minutes after administering succinylcholine. This may be attributed to the use of a remifentanil infusion in our patients.

The limitation of this study was addition of remifentanil 1 $\mu$g/kg to the succinylcholine to obtain balanced anaesthesia during the procedure.

## Conclusions

The administration of remifentanil without muscle relaxants provides similar intubating conditions as those provided by succinylcholine during intubation for microlaryngoscopy, and remifentanil is superior to succinylcholine with regard to haemodynamic stability and recovery times.

### Conflict of Interest

None.

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