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RESEARCH ARTICLE

Alfentanil Use in Rapid Sequence Induction

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ABSTRACT

Objective: In our study, the effects of using different doses of alfentanil on intubation conditions and hemody-namic parameters were investigated to provide rapid-sequence intubation (RSI) conditions.

Materials and Methods: Fifty-six female patients between the ages of 24–73 who would undergo a medium surgical procedure with a risk of ASA I-II were divided into two groups of 28 each. Intravenous anesthetic and rocuronium doses were standardized for anesthesia induction, and 3 µg/kg alfentanil was given to Group I and 10 µg/kg alfentanil to Group II for anesthesia induction. Furthermore, after intuba-tion, inhalation anesthesia was standardized, electrocardiography, non-invasive-blood-pressure, peripheral oxygen saturation, end-tidal carbon dioxide, and inspiratory sevoflurane concentration, temperature, and train-of-four (TOF) monitoring were performed. All patients were intubated at 60 s and monitorization was recorded until the 10th min (1st-2nd-3rd-4th-5th-7th-10th min) and after skin incision.

Results: We found no significant differences between the two groups according to intubation scores and TOF scores (p=0.052, all p's>0.39, respectively). However, all measured mean-arterial blood pressure values were lower in Group II (all p's<0.012). When the heart rate (HR) of the groups were compared, it was found that Group II was not statistically different from the baseline value (all p's>82) at the 3rd min and after intubation, but HRs of Group I were higher than the baseline HR (all p's<0.32) were observed.

Conclusion: It was observed that the use of alfentanil at a dose of 10 µg/kg in RSI improved hemodynamic parameters without affecting the intubation conditions compared to the use of 3 µg/kg in RSI.

Keywords: Alfentanil, opioid, rapid sequence induction, rapid sequence intubation

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INTRODUCTION

In emergency situations, the time between anesthesia induction and tracheal intubation should be kept as short as possible due to the risk of pulmonary aspiration of gastric contents. [1] To achieve this goal, the intubation time is kept short and referred to as the rapid sequence intubation (RSI) method. RSI is mostly necessary for individuals with a high risk of aspiration of gastric contents, lung disease, chronic illness, or in situations where hypoxia, acidosis, and increased risk of death may occur as a result of trauma, and it should be performed in <2 min.[2] Anesthesia drugs used to ensure RSI are referred to as rapid sequence induction.[3,4] Although there is no exact procedure for rapid sequence induction, it requires a rapid transition to anesthesia. Hypnotics used for rapid sequence induction include thiopental, propofol, and etomidate, neuromuscular blockers such as succinylcholine and rocuronium, and auxiliary drugs such as opioids such as fentanyl and alfentanil to reduce the hemodynamic effects of intubation and lidocaine.[3]

During RSI, it is crucial to prevent the changes in hemodynamic parameters caused by laryngoscopy and intubation

The Effects of Different Doses of Alfentanil on Hemodynamic Parameters and Rapid-Series Induction "(Alfentanilin Farklı Dozlarının Hemodinamik Parametreler ve Hızlı-Seri İndüksiyon üzerindeki Etkileri (Uzmanlık Tezi)) conducted in Şişli Etfal Training and Research Hospital, Department of Anesthesiology and Reanimation in 2010. Pınar Küçükdemirci Kaya İstanbul 2010" was produced from the thesis.

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from harming the patient. For this purpose, many different combinations of anesthetic agents have been investigated.[3,4] Opioids are generally used to eliminate the stress response caused by intubation.[5] The effects of opioid doses on neuromuscular transmission are unclear. Muscular rigidity caused by opioids may interfere with patient ventilation.[6] The opioid doses that cause rigidity are controversial. Opioids reduce the hemodynamic response to laryngoscopy by inhibiting the activation of the sympathetic system.[7] Therefore, they are considered to be useful in intracranial bleeding, tumors, and aortic dissection. However, there is no definitive evidence supporting the use of the dosage of opioids in RSI.[8] Many studies have been conducted to develop a procedure for rapid sequence induction.[8–10] In most of these studies, rocuronium bromide has been shown to provide the best hemodynamic stability for RSI.[11–15] While there is agreement on muscle relaxants, there is no definitive recommendation for opioids due to a limited number of studies conducted. Opioids are used to reduce tracheal stimulation and provide optimal intubation conditions.[1,6,16] However, remifentanil and alfentanil are recommended for RSI due to their short-term effects.[8,17] Alfentanil, fentanyl, sufentanil, and remifentanil prevent the activation sympathetic system and prevent hemodynamic response during laryngoscopy.[11,16–18]

There are very few studies on the use of alfentanil, a short-acting opioid, in RSI and its effect on muscle rigidity.[17,18] In our study, we aimed to compare the effects of 3 μg/kg and 10 μg/kg doses of alfentanil on intubation quality, heart rate, blood pressure, and neuromuscular transmission.

MATERIALS and METHODS

Our study was conducted on ASA I-II classification female patients with planned intermediate-duration surgical procedure. The present study was approved by the Ethics Committee of the Sisli Hamidiye Etfal Training and Research Hospital (decision number: SEEAH/2010 17–2). No study-related interventions were performed on human subjects; our study was conducted in accordance with the Declaration of Helsinki, and informed consent was obtained from all patients when they applied to our department for pre-operative anesthesia examination. Patients were informed about the study that the results of clinical status, laboratory, and radiological examinations can be used for scientific publications without specifying the descriptive characteristics (name, surname, and ID number) of the patients. Patients with cardiovascular, neuromuscular, renal, and hepatic diseases or those using drugs that could affect neuromuscular function (such as magnesium sulfate, anticonvulsants, or polypeptide antibiotics), those who had received radiotherapy or chemotherapy, malnourished patients, and those with alcohol addiction were excluded from the study. Patients who had errors during neuromuscular monitor calibration and whose peripheral temperature was below 33°C were also excluded from the study. In this prospective, randomized, and double-blind study, no premedication was given to the patients. An 18-gauge cannula was used to open vascular access in the patients who were taken to the operating room. Electrocardiogram, heart rate (HR), peripheral oxygen saturation (SpO_2), non-invasive arterial blood pressure, end-tidal carbon dioxide ($ETCO_2$), and inspiratory sevoflurane concentration (Fi Sevoflurane) were monitored (Datex-Ohmeda S/5). The musculus adductor pollicis longus muscle and the ulnar nerve were used for neuromuscular monitoring. Before placing the nerve stimulator electrodes (train-of-four [TOF] Watch SX-Organon T), the skin area where the electrodes were to be placed on the wrist was cleaned and wiped with alcohol. The negative electrode of the nerve stimulator was placed on the ulnar nerve tract, about 2–3 cm. Proximal to the skin crease formed during wrist flexion and positive electrodes was placed about 2–3 cm proximal to the negative electrodes. The receiver of the stimulator was attached to the pulp of the thumb and the thermocouple was attached to the thenar area. The palm of the monitored hand was facing upward, and the thumb was allowed to move freely, while the other four fingers were immobilized. The temperature of the skin of the hand undergoing neuromuscular monitoring was carefully maintained above 33°C and was wrapped with cotton and heated if necessary. No sedation was given to any of the patients. After anesthesia induction, the contraction of the adductor pollicis muscle was controlled by ulnar nerve stimulation with acceleromyographic tetanic stimulation (TOF, 50 mA current, 2 Hz frequency, and 2 ms duration). The patients were randomly divided into two groups using a closed envelope method: Group I was planned to receive 3 μg/kg alfentanil, 7 mg/kg thiopental sodium, and 1 mg/kg rocuronium bromide for anesthesia induction, and Group II was planned to receive 10 μg/kg alfentanil, 7 mg/kg thiopental sodium, and 1 mg/kg rocuronium bromide. After anesthesia induction, the patients were intubated at the 60^{th} s and their intubation scores were recorded according to the modified Cormack-Lehane classification system. The TOF value during intubation, the time to TOF ≤5%, and the time to TOF=0 were recorded for each patient. The time of intubation was considered 0, HR, SpO_2, non-invasive arterial blood pressure, and $ETCO_2$ were recorded at 0, 1, 2, 3, 4, 5, 6, 7, 8, 9^{th}, and 10^{th} min.

Table 1. Demographic characteristics of groups

	Group I n=28 Mean±SD	Group II n=28 Mean±SD	p
Age	46.56±6.99	43.36±10.63	0.195
BMI	29.30±4.93	27.42±4.84	0.156
ASAI	21	14	
ASAII	7	14	

SD: Standard deviation; BMI: Body mass index; ASAI: American Society of Anesthesiologist class I; ASAII: American Society of Anesthesiologist class II

Statistical Evaluation

Data analysis was conducted using SPSS statistical software (SPSS 10.0: SPSS; Chicago, IL, USA), statistical package program was used for data evaluation. Independent samples t-test was used for comparison of demographic characteristics, intubation scores, simultaneous TOF values, and hemodynamic parameters between groups, while non-parametric Chi-square tests were used for ASA values, post-operative sore throat, and hoarseness. P<0.05 was considered significant.

RESULTS

Fifty-six female patients with ASA I-II classification, aged between 24 and 73 years, were included in our study. When the demographic data of two groups consisting of 28 individuals each were examined, no statistically differences were observed. The demographic characteristics of patients are shown in Table 1. There were no statistically significant differences between Group I and Group II in terms of mean intubation scores. The study found no statistically differences between Group I and Group II in terms of TOF values during intubation, the time when TOF ≤5, and the time when TOF value is 0 (all p's>0.06). While there was no statistically significant difference in terms of basal mean-arterial blood pressure (MAP) between the groups, the decrease in simultaneous MAP measurements after anesthesia induction was significantly lower in Group II than in Group I (all p's<0.012) (Fig. 1). While there was no statistically significant difference in terms of basal heart rate between the groups, it was observed that Group II was not significantly different from the basal value after 3 min and later after anesthesia induction (all p's>0.82), but Group I's values were higher than the basal value (all p's<0.0302) (Fig. 2).

Post-operative nausea and vomiting were questioned in patients and no difference was found between the two groups (p>0.05). Of the patients included in the study, 17.9% had hoarseness on the 1st day, 7.1% on the 2nd day, 3.6% on the 3rd day, and 3.6% on the 1st week. Hoarseness did not last for 1 month in any of patients. Throat pain was present in 48.2% of patients on the 1st day, 25.4% on the 2nd day, 5.4% on the 3rd day, and 3.6% on the 1st week and no throat pain was observed in any patients after 1 month. There was no statistically difference between the two groups in terms of throat pain and hoarseness (all p's>0.14) (Fig. 3).

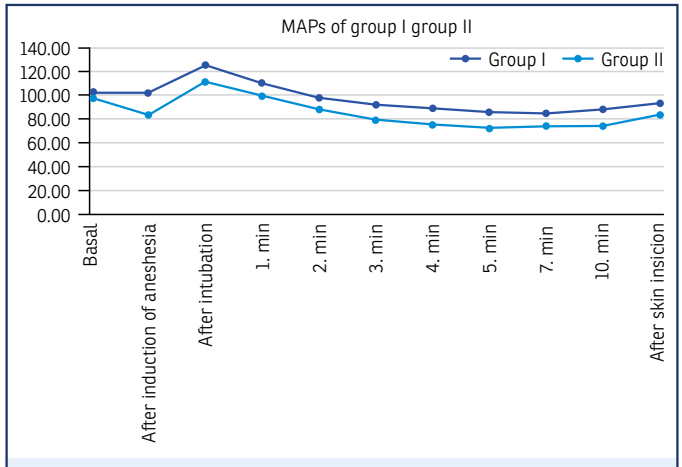

Figure 1. Mean arterial pressures (mm/Hg) of Group I and Group II

MAPs: Mean arterial pressures; Group I: 3µg/kg alfentanil, 7 mg/kg thiopental sodium and 1 mg/kg rocuronium bromide were given for anesthesia induction; Group II: 10µg/kg alfentanil, 7 mg/kg thiopental sodium and 1 mg/kg rocuronium bromide were given for anesthesia induction

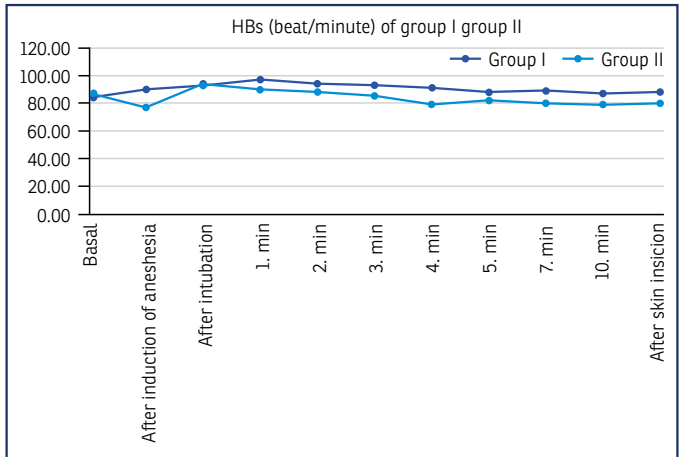

Figure 2. Heart beats (beat/minute) of group I and group II

HBs: Heart beats; Group I: 3µg/kg alfentanil, 7 mg/kg thiopental sodium and 1 mg/kg rocuronium bromide were given for anesthesia induction; Group II: 10µg/kg alfentanil, 7 mg/kg thiopental sodium and 1 mg/kg rocuronium bromide were given for anesthesia induction

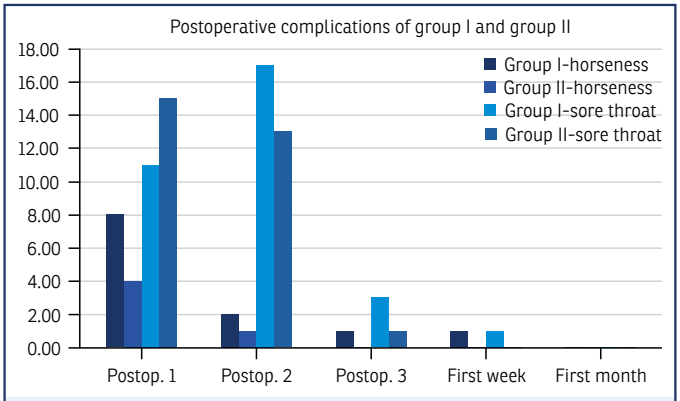

Figure 3. Postoperative complications of Group I and Group II

Group I: 3μg/kg alfentanil, 7 mg/kg thiopental sodium and 1 mg/kg rocuronium bromide were given for anesthesia induction; Group II: 10μg/kg alfentanil, 7 mg/kg thiopental sodium and 1 mg/kg rocuronium bromide were given for anesthesia induction

DISCUSSION

RSI requires a fast induction and transition period to anesthesia, which does not have a definitive procedure.[1,2] There is no definitive evidence supporting to use of opioids in RSI.[11,16] However, if used, remifentanil and alfentanil are recommended due to their short-term effects.[8] Opioids are used to reduce tracheal stimulation and provide optimal intubation conditions.[1,6,17] In addition to these beneficial effects, opioids can cause muscle rigidity when used at high doses during intubation.[6] Thoracic rigidity can cause ventilation difficulty, especially in intubations that need to be performed without neuromuscular blockers.[19] Benthuysen et al.[19] found a significant increase in rigidity in the upper extremities 47 s after the administration of alfentanil, as determined by EMG. In this study, it was stated that muscle rigidity could be seen at doses above 5 μg/kg, where very high doses of alfentanil (170 μg/kg) were given to the patients. These high doses of alfentanil caused apnea periods to last 2–3 min in some patients and an increase in MAP was observed, which could be due to the increase in systemic vascular resistance caused by alfentanil. There are also studies indicating that the use of opioids in combination with rocuronium provides intubation conditions and hemodynamic stability.[17,20] Recent study by Abou-Arab et al.,[17] varying doses of rocuronium (1 mg/kg), pentothal (4 mg/kg), and alfentanil (0, 5, 10, 15, 30, 45, or 60 μg/kg) were used to provide the best intubation conditions. This study was emphasized that increasing doses of alfentanil provided better intubation conditions and the optimal intubation dose was 36.4 μg/kg of alfentanil. However, this dose caused significant hypotension and bradycardia, requiring vasopressor treatment. TOF stimulation has been suggested for demonstrating muscle relaxation and resistance.[8,17,21] In our study, different doses of alfentanil were compared for appropriate muscle relaxation using TOF-Watch values and the modified Cormack-Lehane scoring system and no statistically significant difference was found between the TOF values and intubation scores obtained. In addition, none of the patients included in the study experienced muscle rigidity.

During the placement of an endotracheal tube into the trachea, the infraglottic receptors are stimulated.[20] An increase in blood pressure and heart rate is observed in response to laryngoscopy and intubation.[6] The hemodynamic response initiates afferent stimuli transmitted through the glossopharyngeal and vagal pathways, resulting in the activation of hypothalamic sympathetic centers, leading to a peripheral sympathetic response that causes the release of adrenaline and noradrenaline.[18] These effects can be tolerated in normal healthy individuals, but in patients with limited cardiac reserves, hypertension, and tachycardia may cause serious problems by increasing myocardial oxygen demand and shortening coronary perfusion time.[22] Alfentanil, fentanyl, sufentanil, and remifentanil prevent the activation of the sympathetic system, thereby preventing the hemodynamic response during laryngoscopy.[5,11,16,23] Therefore, the use of opioids in RSI can be beneficial in selected patients where an increase in intracranial pressure, such as with an intracranial bleeding and tumors, and an increase in MAP, such as with leaky aortic aneurysms and aortic dissections.[7,18,20] Alfentanil is a potent opioid with a rapid onset and short duration of action.[22,23] Similar to fentanyl, alfentanil is effective in preventing the hemodynamic response during tracheal intubation and surgical interventions.[24] Studies have reported that alfentanil effectively reduces the hemodynamic catecholamine response and suppresses the hemodynamic response during intubation.[5,22] Recent study of elective cesarean cases, patients given alfentanil before induction had lower levels of catecholamines in their blood and higher oxygen levels were detected in the umbilical cord blood of their babies compared to those not given the drug.[5] Pathak et al.[25] compared lidocaine 2 mg/kg with alfentanil 15 μg/kg and 30 μg/kg doses and 2 mg/kg dose of lidocaine was found to be insufficient to prevent hemodynamic response to laryngoscopy and intubation. However, all doses of alfentanil were shown to be effective. Kirby et al.[26] investigated the optimal dose of alfentanil to suppress the hemodynamic response to laryngoscopy and intubation in elderly patients, doses of 400,

600, 800, and 1000 µg were compared. The study concluded that a dose of 600 µg of alfentanil was the optimal dose that prevented the hemodynamic response to laryngoscopy and intubation and caused minimal cardiovascular depression in elderly patients. Hiller et al.[27] investigated the hemodynamic responses and best intubation conditions in children aged 2–6 years without the use of neuromuscular blocking agents during tracheal intubation and found that alfentanil at a dose of 40 µg/kg resulted in better stability and better suppression of hemodynamic responses during intubation. Hartley et al.[22] conducted a study on 60 patients and found that during fiberoptic tracheal intubation, 10 µg/kg of alfentanil minimized the hypertensive response intubation. In our study, it was determined that the hemodynamic parameters of the patients in it were observed that the patients in Group II who received 10 µg/kg alfentanil maintained hemodynamic stability better than the patients in Group I who received 3 µg/kg alfentanil. In addition, no bradycardia or hypertension was observed in either group. Moreover, there was no difference between the two groups in terms of post-operative nausea, vomiting, sore throat, and hoarseness. The limitations of our study were that it was conducted in elective obstetric cases rather than emergency cases requiring RSI and hemodynamic parameters were measured with non-invasive monitoring tests. We believe that future studies, even if conducted in elective cases, could obtain more accurate results regarding the use of opioids in RSI by increasing the number of cases and using invasive hemodynamic monitoring tests.

CONCLUSION

In our study, we examined the effects of different doses of alfentanil on intubation conditions, TOF values during intubation, and hemodynamics. It was observed that the use of alfentanil at a dose of 10 µg/kg in RSI maintained hemodynamic stability without affecting intubation conditions compared to a dose of 3 µg/kg. Based on these results, we recommended the use of opioids in RSI, especially in selected cases such as intracranial hemorrhage and aortic dissection where hemodynamic stability is crucial.

Disclosures

Ethics Committee Approval: The study was approved by the University of Health Sciences Sisli Hamidiye Etfal Training and Research Hospital Clinical Research Ethics Committee (No: SEEAH/2010 17–2, Date: 07/02/2023).

Informed Consent: Written informed consent was obtained from all patients.

Peer-review: Externally peer reviewed.

Authorship Contributions: Concept: P.K.K.; Design: P.K.K.; Supervision: G.U.S., A.H.; Funding: P.K.K.; Materials: G.U.S., P.K.K.; Data Collection or Processing: P.K.K., G.U.S.; Analysis or Interpretation: P.K.K., A.H.; Literature Search: P.K.K., G.U.S.; Writing: P.K.K.; Critical review: P.K.K., G.U.S., A.H.

Conflict of Interest: No conflict of interest was declared by the authors.

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