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Effects of ketofol and propofol on intubation conditions and hemodynamics without the use of neuromuscular blockers in patients undergoing tympanomastoidectomy

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Abstract

The effect of ketofol, a mixture of ketamine and propofol in various ratios, on hemodynamic, for intubation without the use of neuromuscular blockers, has not been elucidated in patients undergoing tympanomastoidectomy. We evaluated the effects of ketofol and propofol on intubation conditions and hemodynamic without the use of a neuromuscular blocker. The prospective randomized, double-blinded study was scheduled for tympanoplasty or mastoidectomy. The patients were divided randomly into a propofol group (Group P) and a ketofol group (Group KP). Intubation conditions, changes in hemodynamics, HR, MAP, systolic arterial pressure (SAP), and SpO2 values were recorded before induction, after induction, after intubation, and at 3-min intervals during the first 30 min, 5-min intervals for the next 30 min, and 10-min intervals after that. In the intragroup evaluation, SAP, DAP, MAP and HR values were lower in both groups compared to the baseline values. Hemodynamic values were significantly lower in Group P than in Group KP after intubation compared to baseline. DAP at 12 and 18 min, DAP and MAP at 24 min, SAP, DAP and MAP at 27 min, and SAP and MAP at 30 min after the start of the operation were significantly lower in Group P than in Group KP. The need for ephedrine and the number of patients who required ephedrine were significantly lower in Group KP than in Group P. Ketofol provided appropriate intubation conditions similar to propofol, without the use of a neuromuscular blocker, and contributed to better hemodynamic conditions in patients undergoing tympanomastoidectomy.

Keywords: Ketofol, propofol, hemodynamic, neuromuscular blocker, tympanomastoidectomy

Introduction

The use of neuromuscular blocker is not recommended in terms of exposure and protection of the facial nerve in patients undergoing ear surgery [1]. Propofol and thiopental have been used for intubation without the need for neuromuscular blockers. However, propofol reduces heart rate (HR) and mean arterial pressure (MAP) and thiopental is associated with a longer recovery period [2,3].

Ketofol is a mixture of ketamine and propofol in various ratios [4]. Some properties of propofol, including quick recovery due to a short duration of action and decreased nausea-vomiting, compliment several beneficial effects of ketamine, such as long duration of action, analgesic activity, and a hemodynamic stimulatory effect [4,5]. However, the impact of ketofol on hemodynamics, in the absence of a neuromuscular blocker, has not been elucidated in patients undergoing tympanomastoidectomy.

In the study, we evaluated the effects of intubation with propofol or ketofol, without the use of a neuromuscular blocker, on hemodynamic parameters and intubation scores in patients who were scheduled for tympanoplasty and mastoidectomy.

Material and Methods

The present study was a single-center, cross-sectional observational study conducted at Inonu University Hospital (Malatya, Turkey) between April 2015 and March 2016. After receiving institutional approval from the Ethics Committee of Inonu University Faculty of Medicine (Date/No: 2015/81.) and obtaining written informed consent, 60 patients with American Society of Anesthesiologist physical status and Mallampati scores of I and II, aged between 18 and 65 years and scheduled for elective tympanoplasty or

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mastoidectomy, were enrolled in this study.

The patients were divided randomly into a propofol group (Group P) and a ketofol group (Group KP). 2 mg/kg propofol Propofol (2 mL/kg), 4 µg/kg remifentanil, and 1 mg/kg lidocaine were administered to Group P. A ketofol solution (1:1, total 20 mL) was prepared for Group KP, comprising 100 mg ketamine (Ketalar 50 mg/mL; Pfizer, Cambridge, MA, USA) and 100 mg propofol (1% propofol; Fresenius, Bad Homburg, Germany), brought up to 20 mL with saline and administered along with 4 µg/kg remifentanil and 1 mg/kg lidocaine. The final concentrations were 5 mg/mL ketamine and 5 mg/mL propofol. Ketofol (0.2 mL/kg; 1 mg/kg ketamine and 1 mg/kg propofol) was administered to the KP group. Three min. later, the patients were intubated with 7–7.5 ID endotracheal tubes. Patients who strained during the intubation were administered 10 mg rocuronium and excluded from the study. Anesthesia was maintained in both groups by infusion with 6–8% desflurane, 50% O2 + 50% air, and 0.025 µg/kg remifentanil.

Patients with a history of allergy to the drugs used, severe cardiovascular or pulmonary systemic diseases, hepatic or renal dysfunction, a history of psychiatric disorder, or a body weight < 50 kg or > 90 kg were excluded from the study.

The patients were randomized and allocated to groups using computer-generated numbers, via Excel software (Microsoft Corp., Redmond, WA, USA), by an anesthesiologist not participating in the trial.

No patients were premedicated. All patients were accepted into the operating room. Electrocardiogram, HR, peripheral arterial oxygen saturation (SpO2), and noninvasive blood pressure were monitored. Following routine monitoring, all parameters were measured three times at 2 min intervals, and the mean values of the measurements were taken as the baseline.

The primary outcome was to evaluate the effects of the intubation conditions. The secondary outcome was changes in hemodynamics. HR, MAP, systolic arterial pressure (SAP), diastolic arterial pressure (DAP) SpO2 values were recorded before induction (baseline), after anesthesia induction, after intubation, and at 3-min intervals during the first 30 min, 5-min intervals for the next 30 min, and 10-min intervals after that. If the MAP and HR decreased 20% to the baseline value and 45 beats/min, respectively, 10 mg ephedrine or 0.5 mg atropine was administered. At the end of the operation, all anesthetic agents were discontinued, and the patients were ventilated with 100% oxygen. Initiation of spontaneous respiration, opening of the eyes, tracheal extubation time, responsiveness to commands, and orientation to time, place, and person were recorded.

The patients were assessed for consciousness, activity, respiration, circulation, and SpO2 at min 1, 10, and 30 according to the Modified Aldrete Recovery Score. Also, side effects such as nausea, vomiting, sore throat, laryngospasm, hoarseness, and chin laxity, as well as ease of laryngoscopy, vocal cord clearance, and extremity movements, were also recorded. Intubation conditions were evaluated according to the Helbo–Hansen–Raulo intubation scoring system. Surgical satisfaction was assessed with a 3-point scoring system, as follows 1: poor, 2: moderate, 3: good.

Statistical Analysis

SPSS software (ver. 23.0, SPSS Inc., Chicago, IL, USA) was used for the statistical analysis. Continuous quantitative variables are expressed as means and standard deviation and categorical variables as numbers and percentages. The normality of the data was assessed by the Shapiro–Wilk test. Pearson's chi-square test was used to compare categorical variables. The Mann–Whitney U test or unpaired t-test was used to compare continuous quantitative variables. A p-value < 0.05 was considered statistically significant.

Results

Sixty-six patients were enrolled in the study. However, four patients did not meet the inclusion criteria, and two patients declined to participate. Demographic data of the study population was shown in Table 1.

Table 1. Demographics of the groups

	Group P (n=30)	Group KP (n=30)	P values
Age, year	28.3 ± 8.8	31.1 ± 9.1	0.221
Gender, Female (n, %)	15 (%50)	12 (%40)	0.604
Height (cm)	167.5 ± 7.0	166.5 ± 7.9	0.593
Weight (kg)	65.1 ± 9.7	68.0 ± 11.6	0.310
ASA I/II	20/10	16/14	0.197

When SAP, DAP, MAP, and HR values were evaluated between groups, it found that all values were lower compared to the baseline values ($p < 0.05$ for all). SAP, DAP, and HR values were significantly lower in Group P than in Group KP after intubation compared to baseline ($p < 0.05$) (Table 2). DAP at 12 and 18 min, DAP and MAP at 24 min, SAP, DAP, and MAP at 27 min, and SAP and MAP at 30 min after the start of the operation were significantly lower in Group P than in Group KP ($p < 0.05$).

Table 1. Demographics of the groups

	Group P (n=30)	Group KP (n=30)	P values
Baseline			
SAP (mmHg)	129.7 ± 11.6	129.0 ± 18.9	0.857
DAP (mmHg)	80.5 ± 9.0	81.3 ± 8.8	0.742
MAP (mmHg)	97.0 ± 11.3	97.9 ± 14.8	0.793
HR (beats/min)	81.2 ± 15.1	84.3 ± 17.5	0.462
SpO_2 (%)	99.5 ± 0.8	98.9 ± 1.3	0.047
After induction			
SAP, (mmHg)	89.8 ± 14.6	100.3 ± 19.5	0.023
DAP, (mmHg)	49.0 ± 10.6	59.5 ± 10.7	< 0.001
MAP, (mmHg)	64.9 ± 11.2	70.5 ± 11.7	0.066
HR, (beats/min)	66.8 ± 12.3	73.6 ± 12.1	0.035
SpO_2 (%)	99.6 ± 1.4	97.9 ± 8.8	0.311
After Intubation			
SAP (mmHg)	97.6 ± 11.6	98.5 ± 16.7	0.810
DAP (mmHg)	53.9 ± 12.3	62.9 ± 17.1	0.023
MAP (mmHg)	69.7 ± 11.2	73.2 ± 16.1	0.334
HR (beats/min)	70.5 ± 12.2	72.4 ± 13.0	0.564
SpO_2 (%)	99.5 ± 1.3	98.4 ± 7.3	0.424

SAP=Systolic arterial pressure, DAP=Diastolic arterial pressure, MAP=Mean arterial pressure, HR=Heart rate, SpO_2= Peripheral Oxygen saturation

Atropine was not needed in both groups. The need for ephedrine was significantly lower in Group KP (3 patients) than in Group P (12 patients) ($p < 0.05$). The number of patients who required ephedrine was significantly lower in Group KP than in Group P ($p < 0.05$).

Initiation of spontaneous respiration, eye opening, tracheal extubation time, responsiveness to commands, and orientation to time, place, and person were similar between the groups. Modified Aldrete Recovery Score was significantly higher in Group P than in Group KP at min 30 ($p < 0.05$) (Table 3).

Table 3. Data of Aldrete recovery scores.

	Group P	Group KP	P values
Aldrete 1st min	7.5 ± 0.8	7.5 ± 0.8	0.999
Aldrete 10th min	8.9 ± 0.6	8.7 ± 0.6	0.243
Aldrete 30th min	9.7 ± 0.4	9.2 ± 0.5	< 0.001

No difference in surgical satisfaction was observed between the groups. The groups were also similar in terms of side effects, such as sore throat, laryngospasm, and hoarseness. The incidence of nausea/vomiting was significantly higher in Group P than in Group KP ($p = 0.001$). Vomiting/nausea was observed in 18 patients in Group P. No nausea/vomiting was observed in Group KP.

Discussion

In the present study, ketofol provided better hemodynamic conditions; moreover, vomiting/nausea was observed fewer patients receiving ketofol versus group P. Additionally, the intubation conditions (Helbo–Hansen–Raulo intubation scoring) were similar those achieved with propofol, without the use of a muscle relaxant during tympanomastoidectomy.

Several induction agents, such as propofol, thiopentone, and etomidate, in combination with different opioids, such as remifentanil, alfentanil, and fentanyl at different doses, are preferred for laryngoscopy and tracheal intubation without neuromuscular blockers [6-9]. It has been reported that propofol in combination with a short-acting opioid provides satisfactory conditions for tracheal intubation without the use of a neuromuscular blocker [10]. Propofol combined with remifentanil has been used more commonly, and provides more favorable conditions [2,3]. Remifentanil is preferred due to its short half-life, breakdown by esterases, and hemodynamic stability. In addition, biotransformation is sufficiently rapid and complete to render the effect of the duration of remifentanil infusion on wakeup time minimal [11]. In this study, an endotracheal intubation protocol without a neuromuscular blocker was used for anesthetic management of patients scheduled for tympanoplasty or mastoidectomy, to prevent facial nerve paralysis due to surgery and to allow monitoring of complications that may develop. We also used remifentanil as an opioid. Ketamine was added to propofol to provide better hemodynamic stability.

Klemola et al. [10] showed that 3.5 mg/kg propofol combined with 4 mg/kg remifentanil provides good or excellent intubation conditions in children. Another study showed excellent intubation conditions with 2 mg/kg propofol combined with 4 mg/kg remifentanil [1]. In the present study, similar intubation doses of propofol and remifentanil were used and excellent intubation conditions were achieved, as in other studies [1,10].

Erdoğan et al. [12] compared the effects of propofol and ketofol on laryngeal mask airway insertion conditions and hemodynamics in elderly patients. The same laryngeal mask airway insertion conditions were observed with ketofol and propofol, and the number of patients in need of ephedrine and the total doses of ephedrine were significantly lower in the ketofol group, whereas SAP was significantly higher in the ketofol group than in the propofol group. In the present study, the number of patients in need of ephedrine (3 patients) in Group KP was lower than in Group P (12 patients). This was likely because ketamine stimulates the nervous system and inhibits norepinephrine reuptake. Co-administration of propofol and ketamine is more favorable than propofol alone due to hemodynamic stabilization.

Previous studies demonstrated that propofol combined with remifentanil decreases mean blood pressure and HR after induction, without the use of a neuromuscular blocker [1,13,14]. Similarly, in the present study, HR, SAP, and DAP values decreased significantly in Group P after induction compared to baseline, and better hemodynamic stability was provided by ketofol. The likely reason for this is that propofol leads to a loss of sympathetic stimulation on induction. A propofol-opioid-ketamine combination provided better hemodynamic stability, which can be explained by the antagonistic properties of propofol and ketamine.

Recovery times were reportedly prolonged in a ketamine/propofol group compared to a alfentanil/propofol [15]. Similarly, in the present study, the Aldrete score was significantly lower in Group KP at 30 min, suggesting that recovery from propofol may be faster because the rate of clearance of the drug exceeds the hepatic blood flow [13].

No nausea/vomiting was observed in Group KP. However, nausea/vomiting was seen in 18 patients in Group P. This was likely due to the tympanoplasty and mastoidectomy surgeries, which are associated with a high incidence of nausea/vomiting [16-18]. We believe that ketamine produces effects, such as stable hemodynamics and inhibition of hypotension and analgesia, which may inhibit nausea/vomiting [19,20].

Conclusion

Ketofol provided appropriate intubation conditions similar to propofol, without the use of a neuromuscular blocker and contributed to better hemodynamic conditions in patients undergoing a tympanomastoidectomy. We suggest that the studies should be replicated with larger groups and multicentric studies are required to make a final decision.

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Ethical approval
After receiving institutional approval from the Ethics Committee of Inonu University Faculty of Medicine (Date/No: 2015/81.)

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