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**Research Article**

# Use of ketofol to control emergence agitation in children undergoing adenotonsillectomy

**Sherry N. Rizk, Enas M. Samir** *

*Kasr Al Aini Hospital, Department of Anesthesia and Intensive Care, Faculty of Medicine, Cairo University, Egypt*

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**KEYWORDS**

Ketofol;
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**Abstract** *Objective:* To assess the efficacy and safety of ketofol administration in controlling emergence agitation (EA) after sevoflurane-based anesthesia in children undergoing adenoidectomy or adenotonsillectomy.

*Subjects and methods:* This double-blinded randomized study involved 90 children (3–6 years) scheduled for elective adenotonsillectomy or adenoidectomy. They were randomly assigned to receive 10 ml of normal saline (control group, C) or, 1 mg/kg propofol in 10 ml saline (group P) or ketofol as 1 mg/kg propofol and 0.25 mg/kg ketamine in 10 ml saline (group K) 10 min before the end of surgery. In PACU, sedation, behavior, pain and severity of EA were assessed using modified Aldrete score, Aono's scale, Objective Pain Score (OPS) and Pediatric Anesthesia Emergence Delirium (PAED) scale, respectively.

*Results:* In ketofol group, OPS was significantly lower compared to propofol and control groups. Recovery criteria were in favor of ketofol and propofol groups including longer time to eye opening ($p < 0.001$) and time to Aldrete score $\geqslant 9$ ($p = 0.001$). Time to discharge from PACU was comparable in the three groups ($p = 0.079$). EA was significantly more frequent in the control group ($p < 0.001$), but comparable in ketofol and propofol groups. PAED score was significantly higher in control group compared to ketofol and propofol groups. Ketofol and propofol preserved hemodynamic stability.

*Conclusion:* Ketofol provides a promising new option for controlling emergence agitation with adequate postoperative sedative and analgesic effect, good recovery criteria and hemodynamic stability compared to propofol and control groups in children undergoing adenoidectomy or adenotonsillectomy.



## 1. Introduction

Emergence agitation (EA) designates an irritable, uncooperative, and inconsolable child upon emergence. It can be linked with a number of causes including pain, anxiety and psychological compromise in addition to anesthetics side effect [1]. EA may increase the risk of falling, bleeding and self-extubation. Continuous monitoring in the recovery room and drug

* Corresponding author. Tel.: +20 121054817.
E-mail address: enahamdy@yahoo.com (E.M. Samir).

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administration or physical restriction of the patient may be needed to control EA [2].

Sevoflurane has been broadly used in pediatric anesthesia. However, EA is a common side effect of sevoflurane anesthesia with varying incidence from 10% to 66% [3,4]. Rapid recovery is suggested as one of the factors causing EA after sevoflurane anesthesia, which was not proved with gradual decrease in sevoflurane [5] and in comparison with other drugs with rapid awakening [6].

Effective prevention of EA has been previously investigated with fentanyl [7,8], clonidine [9], oxycodone [10], dexmedetomidine [11,12], midazolam [13], ketamine [14,15], propofol [16–18] and remifentanil [19].

Propofol is a non-opioid, non-barbiturate, sedative-hypnotic agent with rapid onset and short duration of action [20]. Ketamine is a phencyclidine derivative classified as a dissociative sedative that provides analgesia and amnesia [21–23]. Combining ketamine with propofol reduces the sedative dose of propofol. The complementary effects of this combination are supposed to produce lower toxicity compared to each drug alone through decreasing required doses [22]. Ketofol; mixed ketamine and propofol has been shown to be effective in emergency room for procedural sedation [24–31] and for induction for rapid sequence intubation.

Both drugs; propofol and ketamine were used separately successfully to control emergence agitation in adults and children. We suggest effective prevention of EA with a combination of ketamine and propofol; "*ketofol*" in pediatric patients undergoing simple surgical procedural in addition to the advantage of better hemodynamic stability.

The aim of this double-blinded randomized study is to assess the efficacy and safety of ketofol administration in decreasing or preventing EA after sevoflurane-based anesthesia in children undergoing adenotonsillectomy in comparison with administration of propofol alone with assessment their hemodynamic stability.

## 2. Subjects and methods

This study was conducted in Abu EI-Rish Hospital, Cairo University from 2010 to 2012. After ethical committee approval and obtaining written parental informed consent, 90 children aged 3–6 years, ASA physical status I or status II scheduled for elective adenotonsillectomy or adenoidectomy were studied. We excluded children with heart disease, chest infection and neuropsychiatric illnesses.

Using closed envelope method, children were randomly assigned to receive 10 ml of normal saline; control group (C), or 1 mg/kg propofol in 10 ml saline; group (P), or ketofol prepared as 1:0.25 mg/kg of propofol to ketamine respectively in 10 ml saline; group (K). An assistant anesthesiologist not involved in the data collection prepared the syringe for each patient. Children received atropine 0.02 mg/kg intramuscularly 30 min before induction of anesthesia as premedication. Upon arrival to the operating room, standard monitors including electrocardiogram, non-invasive blood pressure and pulse oximeter were attached (Infinity SC 8000, Drager medical system, Avenue, Danvers, MA, USA). The baseline readings were recorded as (T0).

Anesthesia was induced in all patients with 5–8% sevoflurane (Sevorane, Abbott Laboratories SA, Abbott Park, IL, USA) in oxygen through facemask. After obtaining a sufficient depth of anesthesia, a peripheral intravenous line (22G) was inserted and fentanyl 2 μg/kg and atracurium 0.5 mg/kg were administered to facilitate endotracheal intubation. Anesthesia was maintained using sevoflurane inhalational anesthetic. Mechanical ventilation was performed to sustain end tidal ET $CO_2$ at 30–35 mmHg. Ondansetron 0.1 mg/kg and dexamethasone 0.2 mg/kg were given as standard antiemetic for all patients.

Ten minutes before the completion of the procedure, the study drugs were administered to the patients by an anesthetist not involved in the study. The syringe of the study drug was wrapped in foil to ensure blindness to the administered agent. Children in group C were given 10 ml saline; those in group P were given 1 mg/kg propofol in 10 ml saline while those in group K received 1 mg/kg propofol mixed with ketamine 0.25 mg/kg in 10 ml saline. Intraoperative HR and MAP were recorded after induction of anesthesia (T1) and 5 min after drug administration (T2).

Sevoflurane anesthesia was discontinued and manual ventilation was performed. Residual muscle relaxation was reversed using prostigmine 0.05 mg/kg and atropine 0.02 mg/kg. Patients were extubated when they opened their eyes with full recovery of spontaneous breathing (tidal volume 8 ml/kg, respiratory rate more than 12/min, normal breathing pattern and good oxygenation $SpO_2$ more than 98%). The time to eye opening from stopping of anesthetics was measured.

Parents were allowed to stay with their children in the PACU. During PACU stay MAP, HR and $SpO_2$ were continuously monitored. MAP and HR were recorded upon arrival to the PACU, at 10, 20 min. postoperatively and on PACU discharge (T3–T6). If oxygen saturation fell below 95%, oxygen facemask was given to the child.

Modified Aldrete score (0–10 point scale) [19] was used to monitor sedation on PACU admission and at 5 min interval. Time to achieve full Aldrete ($\geqslant 9$) was recorded. Children's behavior was evaluated on PACU admission using Aono's scale (Table 1) [32]. Agitation score of 3 or 4 was considered as an agitation episode. The severity of EA was evaluated using Pediatric Anesthesia Emergence Delirium (PAED) scale (Table 2) [33] which provide a score from (0–20) upon arrival to PACU, at 10 and 20 min postoperatively then on PACU discharge (T3–T6). Postoperative pain was assessed at the same time intervals using Objective Pain Score (OPS) (Table 3) [34]. Each criterion scored from (0–2) to give a total score of (0–10). If OPS is 4 or more, 1–2 mg/kg diclofenac suppository was administered. Midazolam 0.1 mg/kg intravenously was given to treat agitation without pain.

Children were discharged from PACU after satisfying discharge criteria of being calm, fully awake, minimum pain, stable vital signs and oxygen saturation $>95\%$ on room air. Discharge time that was defined as the time from PACU admission until the child fulfilled the discharge criteria was recorded. Recovery was assessed in terms of time to eye opening,

**Table 1** Aono's four-point scale [32].

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|---|---|
| Calm | 1 |
| Not calm, but could be easily calmed | 2 |
| Moderately agitated or restless | 3 |
| Combative, excited, disoriented | 4 |