



Egyptian Society of Anesthesiologists
Egyptian Journal of Anaesthesia

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Research Article

Effect of oral dextromethorphan versus oral ketamine on sevoflurane related emergence agitation in children undergoing adenotonsillectomy

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Received 2 April 2012; accepted 26 May 2012

Available online 4 July 2012

KEYWORDS

Dextromethorphan;
Ketamine;
Sevoflurane related agitation

Abstract *Background:* Emergence agitation is a popular phenomenon after sevoflurane anesthesia. Our aim was to study the efficacy of oral dextromethorphan compared to oral ketamine on sevoflurane related agitation.

Methods: In a prospective, randomized, double-blinded study 120, ASA I, aged 4–10 years old children undergoing adenotonsillectomy were randomly divided into three groups to receive oral dextromethorphan 1 mg/kg (Group D, $n = 39$), oral ketamine 5 mg/kg (Group K, $n = 39$) or placebo (Group C, $n = 38$) as premedication 1 h before surgery. Standard general anesthesia was induced and maintained with sevoflurane in N_2O/O_2 . The following were recorded by a blinded anesthetist: Child separation and cooperation at induction, duration of operation, duration of anesthesia, duration of extubation, duration of emergence, state of emergence on admission to PACU using emergence agitation scale, number of patients required postoperative fentanyl to control agitation, duration of discharge from PACU, vital signs (heart rate, blood pressure, and SpO_2) in PACU, and side effects (Nausea, vomiting, respiratory depression, and hallucination).

Results: The agitated patients that required fentanyl treatment were statistically significant low in groups D and K compared to group C ($p < 0.05$). Child separation and child cooperation at induction from parents was successful in all children in group K with statistical significant

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Peer review under responsibility of Egyptian Society of Anesthesiologists.



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difference compared to other groups ($p < 0.05$). There were increases in duration of anesthesia, extubation, and emergence in group K compared to other groups without increase in the duration of stay in PACU.

Conclusion: Oral premedication with either dextromethorphan 1 mg/kg or ketamine 5 mg/kg were comparable in reducing significantly the incidence of postoperative sevoflurane related emergence agitation in comparison to placebo treated group without reported side effects in children undergoing adenotonsillectomy.

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1. Introduction

Sevoflurane is a popular inhalational anesthetic agent used for induction and maintenance of anesthesia in pediatric patients. Because of its low blood solubility, it allows rapid induction and emergence from general anesthesia. However, when it is used as sole anesthetic agent, it is associated with a high incidence of emergence agitation (EA) that may be harmful to patients [1]. The exact etiology of EA is unknown, however; many explanations have been postulated including rapid removal of residual anesthetics, lack of adaptation of young children to the environment after awakening, anxiety from separation from their parents, increased pain sensation, and sympathetic hyperactivation [2].

Many authors used many drugs in attempts to reduce the incidence of EA including propofol [3], narcotics [4], alpha 2-agonists such as clonidine [5] or dexmedetomidine [6,7].

Ketamine, a competitive N-methyl D-aspartate (NMDA) receptor antagonist, has been reported in many studies to be effective in reducing the incidence of EA when administered orally [8] or intravenously [2,9].

Dextromethorphan, the D-isomer of the codeine analog levorphanol, is another non competitive NMDA receptor antagonist which has been used for a long period as a central cough suppressant and analgesic adjuvant. The cough suppressant effect and the analgesic effect were attributed to its codeine analog structure and its NMDA receptor antagonistic action respectively [10]. It is metabolised in the liver to active metabolite, dextrorphan, which is responsible for its side effects through acting on phencyclidine receptors [11].

The aim of this study was to study the hypothesis that oral preoperative dextromethorphan can reduce the incidence of sevoflurane related emergence agitation in children, so we compared between oral dextromethorphan and oral ketamine when given one hour before surgery in a controlled double blind study on the incidence of emergency agitation in children undergoing adenotonsillectomy procedures.

2. Methods

After approval of the ethical committee in Dar Alshifa hospital (State of Kuwait), a written informed consent obtained from the parents of 120 children ASA physical status I aged 4–10 years old, undergoing adenotonsillectomy surgeries under general anesthesia during the period from September 2011 to March 2012. Children had history of cardiovascular, pulmonary or neurologic diseases, chronic cough, bronchial asthma, coagulation defects, an allergy to the studied drugs or recent upper respiratory tract infection within the previous 2 weeks, were excluded from this study.

On the morning of operation, the children were randomly divided using closed envelope technique for randomization to one of three groups according to the premedication drugs:

Group C (control) ($n = 40$) received oral water for injection.

Group D ($n = 40$) received oral dextromethorphan 1 mg/kg (Dextrokuf; Kuwait Saudi Pharmaceutical industries Co. 3 mg/ml).

Group K ($n = 40$) received oral ketamine 5 mg/kg (Ketam, Hikma pharmaceutical, Jordan, 50 mg/ml).

The premedication were mixed with apple juice prepared in 5 ml syringes by the nurses of the ward according to the instruction written in the sealed envelop and were given by the parents 60 min before the surgery. Both the anesthesiologists and anesthesia technicians of operating theatre were unaware of the used premedication except in emergency situation in order to ensure the double blind nature of the study.

Anesthesia technician assigned to the case received the child from parents and the observer recorded the separation using a separation score [12] (1 = Excellent: happily separated, 2 = Good: separated without crying, 3 = Fair: separated with crying, 4 = Poor: need for restraint) where 1 or 2 considered successful and 3 or 4 considered unsuccessful. Parents were allowed to attend the induction if separation was unsuccessful.

Children were fasting 4–6 h before surgery. In the operating room the ECG, pulse oximeter and noninvasive arterial blood pressure monitor were attached and the anesthesia was induced in all patients with sevoflurane 8 vol% in 50/50% O₂/N₂O (6 L/min) via face mask and the observer recorded cooperation of the children during induction using cooperation score at induction [12] (1 = Cooperative, 2 = Mildly resistant, 3 = Resistant to placement of face mask). After loss of consciousness, a peripheral venous catheter (22G or 24G) was inserted and dextrose 5% in 0.45% NaCl was infused at rate of 4 ml kg⁻¹ h⁻¹. Orotracheal intubation was done using a suitable size, lubricated, and cuffed preformed tube. Anesthesia was maintained with sevoflurane 3–4 vol% in 50/50% O₂/N₂O. SpO₂, end-tidal carbon dioxide, heart rate, and non-invasive arterial blood pressure were monitored continuously. Immediately after intubation, a suppository of paracetamol (Adol, Julphar Pharmaceutical Industries, UAE) 15 mg/kg was given. Spontaneous breathing was allowed and assisted ventilation had been performed if ETco₂ had exceeded 45 mm Hg. No sedative, muscle relaxant or narcotic was given during the procedure. The same surgeon performed all the operations to ensure the same duration of operation which recorded from application of the mouth gage till removal of the mouth gage (before removal of the mouth gag, the surgeon

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