

Impact of Intra-operative Intravenous Administration of Ketamine, Fentanyl or Propofol in Decreasing Pediatric Post-tonsillectomy Emergence Agitation

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ABSTRACT: **OBJECTIVE :** To evaluate the frequency of emergence agitation after tonsillectomy in children administered ketamine, fentanyl or propofol during surgery. **STUDY DESIGN:** Prospective, doubleblind study. **PLACE AND DURATION:** Queen Rania Hospital for children KHMC, Amman, Jordan from April 2012 to April 2013. **SUBJECTS AND METHODS :** Our study included 273 children patients, of both sexes, aged 3-11 years, classed I by the American society of anesthesiologists and scheduled for tonsillectomy under general endotracheal anesthesia. Patients received intravenous induction of anesthesia using fentanyl 2 mcg/kg, propofol 2 mg/kg and tracrurium 0.5mg/kg, after which a proper endotracheal tube size was secured through which a mixture of nitrous oxide/oxygen with 1 MAC of isoflurane was delivered. At the end of surgical procedure, patients received in a random fashion an intravenous dose of either ketamine 1mg/kg (GI, n=93), fentanyl 1 mcg/kg (GII, n=89) or propofol 1mg/kg (GIII, n=91). Incidence and intensity of post-operative emergence agitation was assessed using the five-step emergence agitation scale where; 1 meant obtunded with no response to stimulation, 2 meant asleep but responsive to movement or stimulation, 3 meant awake and responsive, 4 meant crying and 5 meant thrashing behavior that requires restraint. The patient scale of more or equal to 4 was considered as having emergence agitation. The frequency of emergence agitation was analyzed statistically using Chi-square test. Significant P-value was considered if it was <0.05. **RESULTS:** Post-operative emergence agitation was 4.4% in propofol group, 5.6% in fentanyl group (P>0.05) and 13.97% in ketamine group (P<0.05). **CONCLUSION:** The incidence of postoperative emergence agitation was significantly less in groups using intraoperative fentanyl or propofol compared to group using ketamine. **Key Words :** Intra-operative, Intra venous Fentanyl, Ketamine, Propofol, Sevoflurane, Paediatric, Post-tonsillectomy, Emergence agitation.

INTRODUCTION: Post-operative emergence agitation is also called post-operative emergence delirium and it is a recognized phenomenon happening in children and adults in the immediate post-operative period. It is a dissociated state of consciousness in which the child is inconsolable, irritable, uncompromising or uncooperative, typically thrashing, crying, moaning or incoherent. Additional paranoid ideation has been found with these behaviors. Children with this disorder cannot recognize familiar and known objects. Pediatric post-operative emergence agitation is a frequent hazard. The use of sevoflurane as an inhalational agent in children was associated with a frequency of about 80%. Post-operative emergence agitation in children can be diagnosed by having excitation, disorientation, delirium and crying¹. Post-operative emergence agitation is a self-limited condition with no permanent impacts on child's behavior. Nevertheless, post-operative emergence agitation can lead to self-assault causing psychological injury to relatives and medical persons². Although generally self limiting (5-15 min), it can be severe resulting in physical distress to child. It is not a new phenomenon. The incidence of post-operative emergence agitation in all surgical patients is 5.3% with a more frequent incidence in children (12-13%). There were different protocols in

the hope of reducing the frequency and intensity of post-operative emergence agitation including perioperative drug administration, modification of maintenance of anesthetic method and administration of pre-operative sedative³. Administration of peri-operative drug can be considered the most suitable clinical technique because it doesn't depend on the duration of anesthesia or the type of anesthetics administered during induction and maintenance of anesthesia⁴. Reduced doses of fentanyl 1 mcg/kg or propofol 1 mg/kg were demonstrated significantly to decrease post-operative emergence agitation if were given peri-operatively⁵. The molecular different mechanisms of these agents may affect various parameters of hazards and recovery^{6,7}. The impacts of reducing the frequency and intensity of post-operative emergence agitation and recovery pattern are variable between propofol, fentanyl and ketamine under similar clinical environments. The aim of our investigation was to evaluate the actions of peri-operative ketamine, fentanyl and propofol administration on post-operative emergence agitation in a pediatric population group scheduled for tonsillectomy.

SUBJECTS AND METHODS : Our prospective, double-blind and randomized study enrolled 273 child patients, of physical status I by the American society of

	Group I	Group II	Group III
N	93	89	91
Sex(no)			
M	51	48	54
F	42	41	37
Age (years)			
Mean(range)	5 (3-9)	6 (3-10)	7(4-11)
Weight(kg)			
Mean(range)	16(15-20)	18(17-22)	20(18-24)
ASA I(no)	93	89	91
Duration of surgery(min)			
Mean(range)	30(25-35)	25(24-30)	35(30-40)

Table-1 : Patient demographics.

	Group I	Group II	Group III
Frequency (no-%)	13(13.97)	5(5.6)	4(4.4)
Scale \geq 4			
Severe intensity(no-%)	8(61.5)	0	0
Scale 5			

Table 2. Post-operative emergence agitation incidence and intensity.

anesthesiologists, of both genders, aged 3-11 years and assigned for tonsillectomy under general anesthesia at Queen Rania Hospital for children, KHMC, Amman, Jordan, during the period of April 2012 to April 2013, after obtaining written informed consent from children's parents and approval from the board review ethics committee of Royal Jordanian medical services. Children with past history of psychological disturbances or on antiepileptic drugs were excluded from our study. Induction of general anesthesia was performed using fentanyl 2mcg/kg, propofol 2mg/kg and tracrurium 0.5mg/kg, all via an intravenous line secured by the surgical ward nursing team. After administration of induction agents, a proper endotracheal tube was selected and introduced through which a mixture of oxygen and nitrous oxide (33%-66%) mixed with 1MAC of sevoflurane was given. Anesthesia was maintained using incremental doses of tracrurium 0.1 mg/kg if necessary with 1MAC of isoflurane. Monitoring was accomplished using ECG for pulse rate, SPO2 for O2 saturation and ETCO2 for percentage of CO2 in exhaled breathing. At the end of surgery, children patients were randomly divided in 3 groups using sealed envelopes according to the agent administered between propofol, fentanyl and ketamine. Group I patients (n=93) received intravenous ketamine 1mg/kg, group II patients (n=89) received intravenous fentanyl 1mcg/kg and group III (n=91) patients received intravenous propofol 1mg/kg. After removal of the endotracheal tube in the theatre with airway patency, children were transferred to the recovery room where the post-operative emergency agitation was monitored and assessed between the three groups, every 5 minutes after awakening during the first post-operative hour. The frequency and intensity of post-operative emergence agitation was assessed using the five step emergence agitation scale where 1 indicated obtunded with no response to stimulation, 2 indicated asleep but responsive to movement or stimulation, 3 indicated awake and responsive, 4 indicated crying and 5 indicated thrashing behavior that requires restraint. The recorded scale more than or equal 4 was considered as having post-operative

emergence agitation and patients with scale of 5 were considered to have severe post-operative emergence agitation. Awake children patients with stable vital signs were transferred to the surgical ward. Continuous parameters were recorded as mean with standard deviation and post-operative emergence agitation was recorded as numbers and percentages and analyzed using the chi-square test. A P-value <0.05 was considered significant.

RESULTS : There were no significant discrepancies regarding sex, age, duration of surgery and weight (Table-1). The incidence of post-operative emergence agitation was 13.97% in group I (Ketamine), 5.6% in group II (Fentanyl) and 4.4% in group III (Propofol). There were no significant difference ($P>0.05$) between groups II and III regarding post-operative emergence agitation frequency, nevertheless, it was less significantly less as compared to ($P<0.05$) group I. Patients in propofol group had less (but not significant) post-operative emergence agitation than patients in fentanyl group ($P>0.05$). All patients in groups II and III did not have scale 5 post-operative emergence agitation while 8 patients (61.5%) in group I had severe (scale 5) post-operative emergence agitation. ($P<0.05$) (Table-2).

DISCUSSION : Although the reported incidence of post-operative emergence agitation after sevoflurane anesthesia was 80%, the mean frequency was 34% in other studies⁸. In the same study, post-operative emergence agitation with peri-operative ketamine 0.5mg/kg administration was 16.6%⁸, while we used ketamine 1mg/kg. For that reason we had lower incidence of post-operative emergence agitation in our ketamine group. Assumed causes of this condition are misperception of environmental stimuli with paranoid ideation, differing CNS effects, sympathetic activation or psychomotor effect. Our investigation showed that administration of fentanyl 1 mcg/kg or propofol 1 mg/kg at the end of surgery was similar in decreasing the frequency and intensity of post-operative emergence agitation than ketamine 1mg/kg in children patients undergoing tonsillectomy under general sevoflurane endotracheal anesthesia. Different preventive drugs were used to decrease the incidence and intensity of post-operative emergence agitation, such as fentanyl, ketamine, propofol and alpha² adrenergic agonists⁴. Until now, the potency of one agent over another is still unknown. A study had demonstrated that propofol or midazolam administration with fentanyl was effective in decreasing the incidence of post-operative emergence agitation, where the action of propofol or midazolam is additive or synergistic with fentanyl which reduces the frequency and intensity of post-operative emergence agitation independently. In the previous study, the final frequency of post-operative emergence agitation in the preventive groups was 15-20%⁹. The analgesic characteristics of fentanyl can reduce the frequency and intensity of post-operative emergence agitation and combination of sevoflurane anesthesia with fentanyl may be used although there is no severe post-operative pain. Another investigation showed that

propofol and midazolam reduced the frequency of post-operative emergence agitation by 40% and the final frequency of post-operative emergence agitation in the preventive groups was 40% also¹⁰. In our study we used a single agent in each group in ENT patients not as the previous two studies which used two agents in each group in eye surgery patients. Aouad MT, showed that a single administration of propofol 1mg/kg at the end of surgery can decrease the incidence of post-operative emergence agitation¹. Post-operative emergence agitation may happen in pain free subjects, and post-operative pain is a major factor of post-operative distress and agitation in children patients. So, the impacts of anesthetic methods on post-operative emergence agitation must be studied in pain free patients post-surgery¹¹. The reduced frequency of post-operative emergence agitation in previous investigations could be due to the administration of midazolam as preoperative premedication and parental presence in the recovery room. It was assumed that rapid emergence with lack of adequate pain control before agitation caused this disorder. The incidence of post-operative emergence agitation after halothane, isoflurane, sevoflurane and desflurane ranges from 2-55%. The disorder is more acutely observed with the increased use of sevoflurane and desflurane that have a rapid emergence profile due to their low blood gas solubility profile. The frequency of post-operative emergence agitation is different according to the type of surgery where it is higher in ENT or eye surgery¹². In our study we did not use a controlled study which we think, is out of our limitations. By limiting the kind of surgery, clear comparison between two drugs can be made without the surgical impact on post-operative emergence agitation. Factors incriminating are younger age, no previous surgery, poor adaptability, eye and ENT surgery, sevo and isofluranes, analgesics and short time to awakening. Agent choice for a specific aim is based on potency and also on side effects. post-operative emergence agitation can be investigated using different scales such as the pediatric anesthesia emergence delirium and Aonos scale. post-operative emergence agitation is associated with adverse events such as increased bleeding at the surgical site, pulling out a drain or an intravenous line and increased pain.

CONCLUSION : Administration of propofol or fentanyl at the end of surgery in children patients undergoing tonsillectomy under sevoflurane anesthesia could decrease the frequency and severity of post-operative emergence agitation.

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