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RESEARCH ARTICLE

EVALUATION OF THE EMERGENCE AGITATION INCIDENCE IN CHILDREN WHO UNDERWENT DEEP SEDATION FOR TOOTH EXTRACTION.

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Abstract

Purpose: Emergence agitation (EA) is a condition where factors associated with patient, surgery and anesthesia play role in occurrence, and that may occur in any age groups—particularly well-defined in children and delay discharge. Emergence agitation has been investigated for medical interventions under general anesthesia in children, but not for dental treatment under deep sedation. The objective of this study was to investigate the incidence of EA in pediatric cases scheduled for tooth extraction under deep sedation and its relationship with drugs for sedation.

Materials and Methods: 120 cases, less than 12 years old and in ASA I-II group according to “American Society of Anaesthesiologists (ASA)” risk classification were scheduled for elective tooth extraction under deep sedation without premedication. The patients were admitted in operating room just according to our anesthesia protocol. With the aim of achieving Richmond Agitation Sedation Scale (RASS)=(-4), In Group K who allowed IV (Intravenous) cannula insertion: 2-3 mg.kg⁻¹ IV Ketamine was administered. In Group KM who also allowed IV cannula insertion: 0.5 mg of Midazolam was added to 2-3 mg.kg⁻¹ IV Ketamine. In Group S: 8% Sevoflurane in 50% O₂/N₂O through face mask (connected to a Mapleson C circuit) was administered to the Group S who did not allow inserting IV cannula. Detecting the RASS as -4 local infiltration anaesthesia was applied for the extraction of associated teeth. Following the procedure recovery was evaluated at T₀, than 15 min. later (T₁₅), 30 min. later (T₃₀), 45 min later (T₄₅), 60 min later (T₆₀) with RASS.

Results: The RASS values at T₀ were statistically significantly higher in Group K than those of other groups. No significant differences were found between groups for RASS mean at T₁₅ RASS values at T₃₀, T₄₅, T₆₀ minutes were statistically significantly lower in Group S than Group K and Group KM.

Conclusions: We concluded that use of ketamine alone or in combination with low dose of midazolam for short-time surgical procedures did not cause agitation compared to sevoflurane, increased

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quick recovery and child-parent satisfaction and efficiency of operating room.

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Introduction:-

Dental fear and anxiety complicates and sometimes even makes treatment impossible in children (1). It is required to use sedation or general anesthesia in patients for whom dental treatment cannot be performed under local anesthesia and behavioral and psycho-pedagogical techniques remain inadequate (2, 3). The sedation is a method that is often used for dental treatment of children for performing dental treatment in safe and comfortable conditions; reduces the time apart for the child-parent and the occupancy time of patient beds, and increases the efficiency of operating room. The sevoflurane, midazolam and ketamine are therefore commonly used anesthetics. The sevoflurane is the preferred inhalation agent because it has low solubility and low risk for hepatotoxicity, is less irritant, maintains hemodynamic stability, and results in quick recovery (4, 5). However, the sevoflurane is also reported to cause agitation more often in pediatric patients than other anesthetics during recovery from general anesthesia (5, 6). The ketamine is a non-competitive N-methyl-D-aspartate receptor antagonist that is commonly used anesthetics for outside anesthesia. Ketamine allows for sedation, analgesia and amnesia without suppressing the functions of respiratory tract and circulatory system (7). But, hallucinogenic properties of the ketamine is its unwanted effect. Midazolam is one of the benzodiazepine class sedative, and dose-dependent, anxiolytic, sedative-hypnotic and safely used with presence of specific antidote, working by increasing GABA activity in the central nervous system (8). However, low doses of midazolam is reported to cause agitation not sedation in some cases (9).

The EA was first defined in 1960 and is a problem that occurs within the first 30 minutes after surgery, often spontaneously improves within 15 minutes, includes disorientation, agitation, delusion, hallucination, discomfort, unstoppable crying, cognitive changes and impaired memory, and delays the discharge (9-13). It has been reported that selected anesthetics may play role in the incidence of EA in general anesthesia practice for medical reasons (9). Although there is not only one cause for EA, it is important to know the risk factors causing this condition in order to reduce the contributing factors and treat it (7). The factors playing role in occurrence of EA may be grouped in association with patient, surgery and anesthesia (9). The EA has been investigated in detail in the literature for the pediatric population and medical procedures performed under general anesthesia (e.g., strabismus surgery, adenotonsillectomy), but it has not been sufficiently studied for the dental treatment performed under deep sedation (9, 13, 14). Therefore, the objective of this study was to examine the characteristics of postoperative recovery for evaluating the incidence of EA and its relationship with drugs used for anesthesia in pediatric cases scheduled for tooth extraction under deep sedation (15).

Materials and Methods:-

With the approval of local ethics committee of Faculty of Dentistry, Ankara University, this study was performed with data of 120 cases, less than 12 years old, ASA I-II group according to 'American Society of Anesthesiologists (ASA)' risk classification, who were scheduled for tooth extraction under deep sedation because it was not possible to perform tooth extraction under local anesthesia. The informed consent form was read and signed by the children's parents.

The cases whose parents did not provide informed consent, who had drug allergy, mental-motor retardation, uncontrolled systemic disease and psychiatric complaint or diagnosis, and were on antiepileptic or sedative medication and above 12 years of age were excluded from the study.

Patient's age, body weight (kg), height (cm), ASA risk group and number of teeth extracted were recorded in the study protocol. The anesthesia protocol used for tooth extraction in our clinic was followed. After 6-hour fastening time, a topical anesthetic (EMLA®) was applied on the hand dorsal surface of all cases 30 minutes before transferring them to the operating room. All the cases were transferred to the operating room without premedication. Group K allowed to insert intravenous (IV) cannula and intravenously received 2-3 mg.kg⁻¹ of Ketamine (Ketalar®, Pfizer, 50 mg ml⁻¹, Istanbul, Turkey). Group KM (Ketamine-Midazolam, n=40) intravenously received 0.5 mg Midazolam (Dormicum®, Roche, 5 mg.ml⁻¹, Fontenay-sous-Bois, France) in addition to 2-3 mg.kg⁻¹ of Ketamine. Group S disallowed to insert intravenous cannula and received 8% Sevoflurane in the 50% O₂/N₂O (Sevoflurane®, Abbott, Italy) through a face mask (connected to a Mapleson C circuit). The aim was to achieve Richmond Agitation SedationScale(RASS, Table 1): -4 (deep sedation) in all of the groups. Research method was planned to obtain

(RASS: -4) sedation level. For that reason if we could not obtain RASS = -4 level, another doses of ketamine (0.05 mg kg⁻¹ iv ketamine in Group K, KS) or additional Sevoflurane (in Group S) inhalation was planned. The EA was assessed another anesthesia personnel who was blinded to which anesthetic agent was administrated to the patients. The cases were oxygenized through nasal cannula for 4 L/min during the procedure, and noninvasive Systolic Arterial Pressure (SAP), Diastolic Arterial Pressure (DAP), Heart Beat Rate (HR), and peripheral oxygen saturation (SPO₂) were monitored. When desired sedation level (RASS=-4) was obtained, dental surgeon performed infiltration anesthesia (Ultrakain DS[®], 1 mL/40 mg Articaine hydrochloride+0.006 mg epinephrine hydrochloride, Sanofi Aventis, Istanbul) on the teeth planned for extraction, and then dental procedure was performed. The anesthetic gasses were terminated in Group S when RASS was -4; spontaneous breathing was maintained and oxygenation through nasal cannula was performed during the procedure. Anesthetic agents were administered performed by Anesthesiologist to obtain RASS=-4 level. Doses of anesthetics, procedure time and unwanted side effects were recorded by same Anesthesiologist. At the end of the procedure, another anesthesia personnel (allied health staff) who were blinded groups were recorded RASS at minute 0 (T₀) in the operating room and the RASS at minutes 15., 30., 45. and 60. [respectively (T₁₅), (T₃₀), (T₄₅), (T₆₀)] were recorded in the wards with parents. The cases numbered for 2 months were grouped by the anesthetist according to anesthetics administered, and the data of first 40 cases in each group was included in the study.

Statistical Analysis:-

The data was analyzed using SPSS version 20.00. The descriptive analysis was performed to determine mean and standard deviation of data. ANOVA was used to analyze intergroup differences. Tukey test was performed to analyze differences between groups that had equal variances, and post hoc Dunett's test was performed when the variances were not equal between the groups. Normal distribution of data was assessed by Kolmogorov Smirnov test and the data had normal distribution (p<0.005). The homogeneity test was performed to determine whether or not intergroup variances were homogeneous.

Results:-

The data of all cases (n=120) was included in the study. The groups were created according to anesthetics administrated in accordance with our clinical protocols (Group K: Ketamine, n=40, Group KM: Ketamine + Midazolam, n=40, Group S: Sevoflurane, n=40).

No statistically significantly differences were found in comparison of groups for height, body weight, procedure time, and number of teeth extracted. In comparison of groups for the age of cases, the age of cases in Group KM was statistically significantly higher than that of cases in Group K (p< 0.05), No significant differences were found between the Group KM and the Group S (Table 2).

In comparison of study groups for RASS, statistically significantly differences were found between the groups (p<0.001). The RASS values at minute 0 were statistically significantly higher in Group KM than that of other groups. While no statistically significantly differences were found between the groups for mean RASS at 15, the RASS values at minute 30., 45. and 60. were statistically significantly lower in Group S (Table 3).

Comparison of groups by number of cases in RASS score groups (Table 4, 5, 6, 7, 8 and Graphic 1)

Discussion:-

In the study groups, the targeted sedation level [RASS=(-4) score (deep sedation)] was achieved with anesthetics administered and the tooth extraction was successful in all of the cases.

RASS was used by *Kerson et al.* (15) to assess consciousness and awareness in the pediatric population, to titrate sedative agents, and to evaluate childhood delirium, and is one of the validity and safety proven scales that is intuitive, easy to use, includes agitation and sedation scales together, and has the highest adaptation among practitioners (16). The score "0" represents ideal level on the scale, and the values up to "+4" represent increasing agitation, and values up to "-5" represent increasing sedation level (17).

According to the memorandum published by ASA in 1999 and revised in 2004, the *deepsedation* is a sedation manifestation during which consciousness is depressed by or totally disappears by drugs, defense reflexes are partially maintained, patients cannot be easily aroused and occasionally respond to physical and verbal stimulus,

interventions may be required to maintain the airway patency and spontaneous ventilation but no cardiovascular functions are affected (18).

Our clinic practice aims at RASS:-4 (deep sedation) to achieve a proper mouth opening during dental treatment and successfully perform the procedure. We obtained RASS:-4 level in all of the cases, started the procedure and extracted the teeth without any undesirable effects. Upon completion of the procedure, we assessed the emergence agitation with RASS.

The factors establishing the incidence and severity of EA are multifactorial (7). However, one of the factors contributing to the development of EA is *anesthesia time*. No statistically significant differences were found between the groups for the procedure time and number of teeth extracted (7,9, 12, 14).

Children with EA are unaware of the things around them and cannot be calmed by parents and other caretakers (19). Literature reports that EA mostly occurs between the ages of 2 and 5, but preschoolers are at risk (7, 9, 20, 21). In comparison of study groups by mean age, the age of cases in Group KM was statistically significantly higher than that of cases in Group K ($p < 0.05$), but not different from the Group S (Table 2). After the procedure was completed, 12.5% of cases in Group S were agitated, 22.5% of cases were restless at minute 0 (Table 4). None of the cases in two other groups were agitated from the completion of procedure and to the discharge. In our opinion, this may be due to anesthetics selected as well as the age characteristics of children.

One factor responsible for EA is personality traits of child and stressed induction of anesthesia (11). The children in all groups were the cases for who tooth extraction was attempted under local anesthesia but could not be performed due to dental anxiety and fear. Therefore, the fear and anxiety level of all cases in the study was higher than those who were treated under local anesthesia. *Kain et al.* (22) concluded that there was a relationship between the preoperative anxiety and the postoperative behavior disorder. The cases in Group KM and Group K allowed intravenous cannulation but not the cases in Group S, and the number of agitated and restless cases in Group S was greater. We therefore judge that preoperative anxiety level may have an effect on the development of EA.

Another responsible factor among other factors causing EA is the presence of pain (9, 21). However, the surgeon performing the procedure administered infiltration anesthesia to all the cases during tooth extraction, and none of the cases complained about the pain for 60 minutes after the procedure.

Another factor that is associated with EA is a noisy environment distant from family (9, 12, 20, 21). During the study, deep sedation was administered in a quiet and peaceful environment and all the cases were exposed to the same conditions.

The other factors that increase the incidence of EA include quick recovery of patients and possibility of airway obstruction. All of the cases included in this study were in the ASA I risk group and none of them had systemic diseases that might cause airway obstruction. We oxygenated our cases in 4L/min through nasal cannula during the procedure and did not have airway obstruction that might disturb the oxygenation or similar unwanted side effects. When we examine the groups for quick recovery of consciousness in an environment without family, we consider that anxiety caused by preoperative dental anxiety and fear was quickly remembered because midazolam had amnesic effects that was used in standard dose in addition to Ketamine in Group KM, Ketamine used in Group K had amnesic effects, and had no such effect in Group S; therefore the number of agitated and restless cases in Group S was statistically significantly higher than that of other groups.

The factor that is mostly responsible for EA is anesthetics. The pediatric anesthetists underline that they observe higher agitation with Sevoflurane and associate this with low blood/tissue solubility and its EEG (electroencephalography) changes (6, 23). *Işık et al.* suggested that EA was also observed for administration of sevoflurane for MRI where no surgical intervention was performed (24). *Cravero et al.* (25) compared the sevoflurane and halothane anesthesia in children who underwent magnetic resonance imaging, and reported that no agitation was observed in cases received halothane and that 33% of cases received sevoflurane had agitation. The authors concluded that quicker recovery with sevoflurane and sudden awakening of child in a foreign environment resulted in agitation. The studies comparing propofol and sevoflurane reported that recovery was quicker with propofol and the agitation was higher in the sevoflurane group (26, 27). In the present study, 55% of cases in Group K, 20% of cases in Group KM and 0 case in Group S were alert and calm following completion of procedure. The

recovery was quicker in Group KM and Group K than that of Group S, and the number of agitated and aggressive cases was higher in this group as compared to two other groups. Therefore, we consider that recovery time may have an effect on the EA.

There are contradictory data for premedication with midazolam: a number of studies suggest that it is effective in reducing preoperative anxiety and EA in children received anesthesia with sevoflurane (28). Despite this, *Cole et al.* pointed out that EA was higher after isoflurane and halothane anesthesia in children received midazolam for premedication (30%-40%)(19). They explained that this might be due to a gap caused by midazolam in the memory of children, sudden awakening in an environment that was totally strange to children, and an intense sense of fear accompanied by irritating stimulus. *Shrestha S et al.* (29) compared placebo and midazolam by orally administering (0.5 mg/kg) paracetamol, and reported that 96.7% of children in midazolam group and 53.3% of children in placebo group were calm when leaving their parents. The authors also reported that induction of anesthesia was calm in 73.3% of children in midazolam group and 33.3% of children in placebo group, and no differences were found between two groups for recovery. *Lapin et al.* (28) and *Ko et al.* (30) reported that premedication with midazolam reduced the EA; *McGraw et al.* (31) reported that it had no effects on the EA, moreover children developed postoperative unfavorable behavioral changes. We administered 0.5 mg/kg standard dose of midazolam to all of the cases in Group KM in addition to ketamine. We found that less cases were alert and calm and more cases were drowsy and sedated at minute 0 according to RASS at the end of procedure compared to the group received Ketamine alone (Group K). We judge that standard dose of midazolam added to ketamine deepened the anesthesia, slightly prolonged the recovery time, however, we did not have any agitated cases in these two groups for 60 minutes following completion of procedure.

Literature has no studies that evaluate the effect of ketamine on the postoperative agitation in children who underwent dental treatment. On the other hand, there are studies reporting that premedication with ketamine reduced postoperative agitation compared to placebo (7, 32). *Hadi et al.* (7) intraoperatively administered bolus low dose of ketamine to cases undergoing adenotonsillectomy with sevoflurane, and reported reduced incidence and severity of agitation developed with sevoflurane. *Chen et al.* (33) reported that dexmedetomidine and ketamine reduced EA and pain in strabismus surgery. We did not have agitated cases in the groups (Groups KM and K) received ketamine neither.

In comparison of study groups for postoperative RASS values, the cases in Group KM were statistically significantly drowsy at minute 0 compared to the other groups, and we associated this deepened anesthesia with midazolam. In regard to RASS values at minute 30, 45 and 60, we observed that cases in Group S were statistically significantly restless and agitated than other cases. We consider that sevoflurane delays recovery in short-time surgical procedures, which is in consistent with literature, and results in agitation because it has no amnesic effects. Finally, we used anesthetics (Ketamine, Ketamine-Midazolam and Sevoflurane) in cases of tooth extraction to achieve deep sedation, which are not compared alone in the literature for incidence of recovery and agitation. We achieved quicker recovery with ketamine alone (Group K) and did not have any agitated cases. We concluded that use of ketamine alone or in combination with low dose of midazolam for short-time surgical procedures did not lead to agitation compared to sevoflurane, increased quick recovery and child-parent satisfaction and efficiency of operating room, and that preoperative anxiety or agitation level may be an indicator for development of postoperative behavior disorder. However, the limitations of this study include selection of anesthetics according to characteristics of cases and lack of randomization. Secondly, age distribution was not comparable in the groups. Therefore, we consider that postoperative, randomized and controlled studies on similar age groups are needed.

Graphic 1:-Comparison of groups by number of cases in RASS score groups T₀, T₁₅, T₃₀, T₄₅, T₆₀

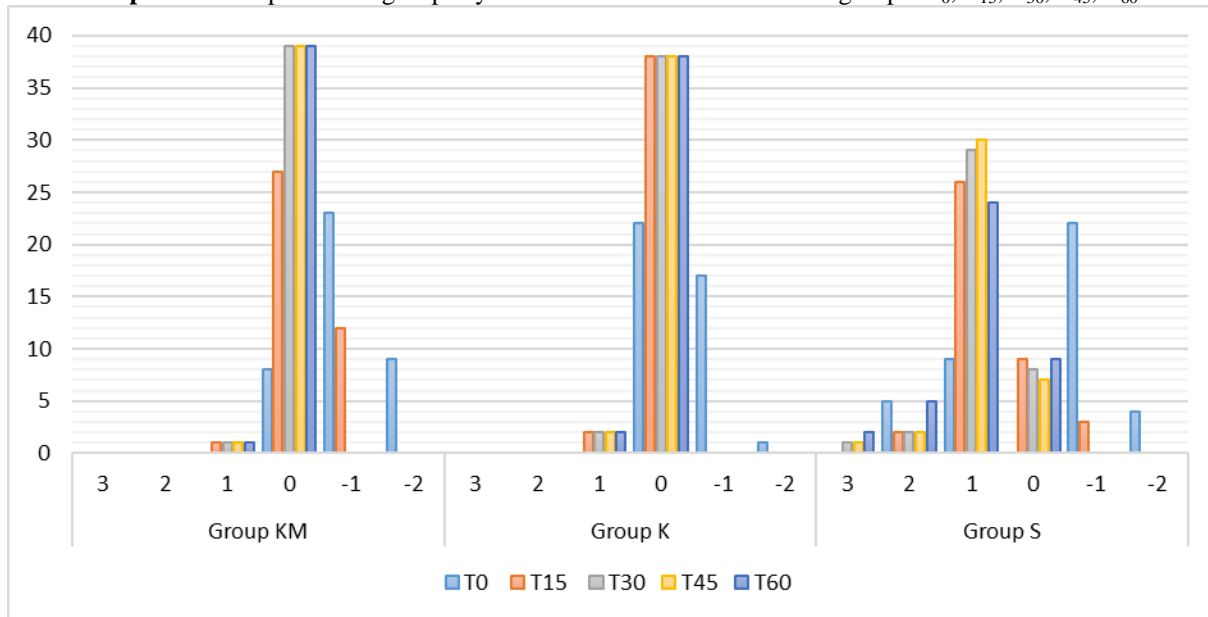


Table 1 :-Richmond Agitation SedationScale (RASS)

Numbers correspondings RASS scoring	Scoring	Clinical status
1	+4	Combative
2	+3	Very agitated, aggressive
3	+2	Agitated (frequent non-purposeful movement)
4	+1	Restless
5	0	Alert and calm
6	-1	Drowsy
7	-2	Light sedation
8	-3	Moderate sedation
9	-4	Deep sedation
10	-5	Unarousable

Table 2:-Demographic characteristics by groups (mean± SD)

	Group KM (n=40)	Group K (n=40)	Group S (n=40)	F	P
Age (year)	6.15 ±1.95*	5.10 ±1.33	5.37 ±1.62	4.30	0.016*
Height (cm)	107.30±18.87	100.00±13.36	107.17±15.48	2.70	0.071
Body weight (kg)	21.83±5.16	20.00±4.89	22.78±6.70	2.49	0.087
Procedure time (minute)	7.87 ±2.77	7.05±2.56	6.75±2.25	2.10	0.126
Number of teeth extracted	2.85 ± 1.99	2.40±1.62	2.67±1.83	0.61	0.541

Table 3:-Groups as in terms numbers of the correspondings RASS scoring (mean± SD)

RASS/Time	Group KM	Group K	Group S	F	P
T ₀	6.02±0.65	5.47±0.55	5.27±1.28	7.596	0.001
T ₁₅	5.27±0.50	4.95±0.22	4.32±0.69	35.596	0.000
T ₃₀	4.97±0.15	4.95±0.22	4.10±0.59	70.484	0.000
T ₄₅	4.97±0.15	4.95±0.20	4.07±0.57	78.561	0.000
T ₆₀	4.97±0.15	4.95±0.22	3.95±0.93	43.507	0.000

Table 4:-Number of cases according to RASS values at T₀ n (%)

Groups	Agitated (+2)	Restless (+1)	Alert and calm (0)	Drowsy (-1)	Light sedation (-2)	Total
Group KM	0	0	8 (20)	23 (57.5)	9 (22.5)	40
Group K	0	0	22 (55)	17 (42.5)	1 (2.5)	40
Group S	5 (12.5)	9 (22.5)	0	22 (55)	4 (10)	40
Total	5	9	30	62	14	120

Table 5:-Number of cases according to RASS values at T₁₅ n(%)

Groups	Agitated (+2)	Restless (+1)	Alert and calm (0)	Drowsy	Total
Group KM	0	1 (2.5)	27 (67.5)	12 (30)	40
Group K	0	2 (5)	38 (95)	0	40
Group S	2 (5)	26 (65)	9 (22.5)	3 (7.5)	40
Total	2	29	74	15	120

Table 6:-Number of cases according to RASS values at T₃₀ n (%)

Groups	Very agitated, aggressive (+3)	Agitated (+2)	Restless (+1)	Alert and Calm (0)	Total
Group KM	0	0	1 (2.5)	39 (97.5)	40
Group K	0	0	2 (5)	38 (95)	40
Group S	1 (2.5)	2(5)	29 (72.5)	8 (20)	40
Total	1	2	32	85	120

Table 7:-Number of cases according to RASS values at T₄₅ n(%)

Anesthetic agent	Very agitated, aggressive(+3)	Agitated (+2)	Restless (+1)	Alert and Calm (0)	Total
Group KM	0	0	1 (2.5)	39 (97.5)	40
Group K	0	0	2 (5)	38 (95)	40
Group S	1 (2.5)	2 (5)	30 (75)	7 (17.5)	40
Total	1	2	33	84	120

Table 8:-Number of cases according to RASS values at T₆₀ n(%)

Groups	Very agitated, aggressive (+3)	Agitated (+2)	Restless (+1)	Alert and Calm (0)	Total
Group KM	0	0	1 (2.5)	39 (97.5)	40
Group K	0	0	2 (5)	38 (95)	40
Group S	2 (5)	5 (5)	24 (60)	9 (22.5)	40
Total	2	5	27	86	120

References:-

- Hallonsten A, Veerkamp J, Rölling I. Pain, Pain control and sedation in children and adolescent: Koch G, Poulsen S. Pediatric Dentistry: A Clinical Approach Oxford: Blackwell Publishing Co,Uk, 2003;147-71.
- Troutman KC: In Pediatric Dentistry: Total Patient Care. SHY Wei ed. Philadelphia: Lea and Febiger. 1988;396-7.
- Ogg TW: Use of anaesthesia. Implications of day-case surgery and anaesthesia. Br Med J 1980;19: 281(6234):212-4.
- Cravero J, Surgenor S, Whalen K. Emergence agitation in paediatric patients after sevoflurane anaesthesia and no surgery: a comparison with halothane. Paediatr Anaesth. 2000;10(4):419-24.
- Guo J, Jin X, Wang H, Yu J, Zhou X, Cheng Y, Tao Q, Liu L, Zhang J. Emergence and Recovery Characteristics of Five Common Anesthetics in Pediatric Anesthesia: a Network Meta-analysis. Mol Neurobiol. 2016 doi:10.1007/s12035-016-9982-3.

6. Kuratani N, Oi Y. Greater incidence of emergence agitation in children after sevoflurane anesthesia as compared with halothane: a meta-analysis of randomized controlled trials. *Anesthesiology*. 2008; 109(2): 225-32.
7. Hadi SM, Saleh AJ, Tang YZ, Daoud A, Mei X, Ouyang W. The effect of KETODEX on the incidence and severity of emergence agitation in children undergoing adenotonsillectomy using sevoflurane based-anesthesia. *Int J Pediatr Otorhinolaryngol*. 2015;79(5):671-6. doi: 10.1016/j.ijporl.2015.02.012.
8. Reves JG, Glass PSA, Lubarsky DA, McEvoy MD: Intravenous nonopioid anesthetics: Anaesthesia. Sixth edition. Miller RD (ed) Churchill Livingstone, Philadelphia 2005, P. 317-379.
9. Moore AD, Angheliescu DL. Emergence Delirium in Pediatric Anesthesia. *Pediatric Drugs*. 2016 Oct 31. doi: 10.1007/s40272-016-0201-5.
10. Eckenhoff, JE., Kneale DH, Dripps RD. The incidence and etiology of postanesthetic excitement: a clinical survey. *Anesthesiology*. 1961;22:667-73.
11. Smessaert A, Schehr CA, Artusio JF. Jr. Observations in the immediate postanesthesia period. II. Mode of recovery. *Br. J. Anaesth*. 1960; 32: 181-5.
12. Veysckemans F. Excitation phenomena during sevoflurane anesthesia in children. *Curr Op Anesthesiol* 2001; 14:339-43.
13. Voepel-Lewis T, Malyvia S, Tait AR. A prospective cohort study of emergence agitation in the pediatric postanesthesia care unit. *Anesth Analg* 2003; 96:1625-1630.
14. Wermelt JZ, Ellerkmann RK. Emergence delirium in children - prophylaxis and treatment. *Anesthesiol Intensivmed Notfallmed Schmerzther*. 2016;51(7-08):448-57
15. Kerson AG, DeMaria R, Mauer E, Joyce C, Gerber LM, Greenwald BM, Silver G, Traube C. Validity of the Richmond Agitation-Sedation Scale (RASS) in critically ill children. *J Intensive Care*. 2016 Oct 26;4:65. doi: [10.1186/s40560-016-0189-5](https://doi.org/10.1186/s40560-016-0189-5)
16. Robinson BR, Berube M, Barr J, Riker R, Gelinas C. Psychometric analysis of subjective sedation scales in critically ill adults. *Crit Care Med* 2013;41:16-29.
17. Sessler CN, Gosnell M, Grap MJ, Brophy GM, O'Neal PV, Keane KA, Tesoro EP, Elswick RK. The Richmond Agitation-Sedation Scale: validity and reliability in adult intensive care unit patients. *Am J Respir Crit Care Med* 2002;166 (10):1338-44.
18. ASA: Continuum of depth of sedation definition of general anesthesia and levels of sedation/analgesia (Approved by ASA House of Delegates on October 13, 1999, and amended on October 27, 2004). <http://www.asahq.org/publicationsAndServices/standards/20.pdf>
19. Cole, JW, Murray DC, McAllister JD. Emergence behaviour in children: defining the incidence of excitement and agitation following anaesthesia. *Paediatr Anaesth*. 2002; 12: 442-7.
20. Aono J, Ueda W, Mamiya K, Takimoto E, Manabe M. Greater incidence of delirium during recovery from sevoflurane anesthesia in preschool boys. *Anesthesiology*. 1997; 87(6): 1298-300.
21. Vlajkovic GP, Sindjelic RP. Emergence delirium in children: many questions, few answers. *Anesth Analg*. 2007; 104(1):84-91.
22. Kain ZN, Wang SM, Mayes LC, Caramico LA, Hofstadter MB. Distress during the induction of anesthesia and postoperative behavioral outcomes. *Anesth Analg*. 1999;88(5):1042-7.
23. Ahrazoğlu MS, Türktan M, Özbek H, Güneş Y. Effects of Sevoflurane and Desflurane Anesthesia on Recovery and Agitation in Children Undergoing Strabismus Surgery. *Çukurova Med J* 2012; 37(4): 186-192.
24. Işık B, Arslan M, Tunga AD, Kurtipek O. Dexmedetomidine decreases emergence agitation in pediatric patients after sevoflurane anesthesia without surgery. *Paediatr Anaesth*. 2006; 16(7):748-53.
25. Cravero J, Surgenor S, Whalen K. Emergence Agitation in paediatric patients after sevoflurane anesthesia and no surgery: a comparison with halothane. *Paediatr Anaesth* 2000;10:419-24.
26. Cohen IT, Finkel JC, Hannallah RS, Hummer KA, Patel KM. Rapid emergence does not explain agitation following sevoflurane anaesthesia in infants and children: a comparison with propofol. *Paediatr Anaesth*. 2003;13(1):63-7.
27. Picard V, Dumont L, Pellegrini M. Quality of recovery in children: sevoflurane versus propofol. *Acta Anaesthesiol Scand*. 2000; 44(3): 307-10.
28. Lapin SL, Auden SM, Goldsmith LJ, Reynolds AM. Effects of sevoflurane anaesthesia on recovery in children: a comparison with halothane. *Paediatr Anaesth*. 1999;9(4):299-304.
29. Shrestha S, Shrestha BR. Oral administration of intravenous solution of midazolam mixed in syrup of paracetamol is an effective way of premedicating children undergoing surgery under general anaesthesia. *Katmandu Univ Med J*. 2007; 5(4): 449-55.

30. Ko YP, Huang CJ, Hung YC, Su NY, Tsai PS, Chen CC, Cheng CR. Premedication with low-dose oral midazolam reduces incidence and severity of emergency agitation in pediatric patients following sevoflurane anaesthesia. *Acta Anaesthesiol Sin.* 2001; 39: 169–177.
31. McGraw T, Kendrick A. Oral midazolam premedication and postoperative behaviour in children. *Paediatr Anaesth* 1998; 8: 117–121.
32. Abu-Shahwan I, Chowdary K. Ketamine is effective in decreasing the incidence of emergence agitation in children undergoing dental repair under sevoflurane general anesthesia. *Paediatr Anaesth.* 2007; 17(9):846-50.
33. Chen JY, Jia JE, Liu TJ, Qin MJ, Li WX. Comparison of the effects of dexmedetomidine, ketamine, and placebo on emergence agitation after strabismus surgery in children. *Can J Anaesth.* 2013; 60(4): 385-92.