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The Effect of Ketamine and Fentanyl on Emergence Agitation after Sevoflurane-Based Anesthesia in Children Undergoing Tonsillectomy with or without Adenoidectomy: A Randomized Blind Comparison Study.

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Abstract

Emergence agitation (EA) has many potential etiologies and remains a significant clinical issue in children postoperatively, Adenoidectomy and tonsillectomy are the most common operations done on children, Sevoflurane is the inhalational anaesthetic agent of choice in the pediatric age group, and it has a higher incidence of emergence agitation in children, it reaches up to 80% when used alone. Method: After obtaining our institutional ethics committee approval and written informed consent from parents, in a prospective, randomized, blind study, we enrolled 80 children 2-10 years old undergoing tonsillectomy with or without adenoidectomy under sevoflurane-based anaesthesia. We assigned children to one of two groups, Group A (n=40) received ketamine 0.5mg/kg, and Group B (n=40) received fentanyl 2mcg/kg intravenously at induction. Anesthesia protocol was standardized for all children, time to extubating, emergence time, duration of surgery, anaesthesia, and post-anaesthetic care unit stay, and incidence of emergence agitation were recorded and compared in both groups, aiming to compare the effect of ketamine and fentanyl on the post-operative EA in children. Results: 80 patients participated in this study, in the fentanyl group 75% of the children had emergency agitation as compared to 20% in the ketamine group (P= 0.000), post anaesthetic care unit stay time was significantly less in the ketamine group, the two groups were comparable in age, sex, durations of surgery, durations of anaesthesia, and time to extubating. Conclusion: in children undergoing tonsillectomy with/without adenoidectomy under sevoflurane-based anaesthesia, administration of intravenous ketamine at induction of anaesthesia significantly reduces the incidence of emergence agitation as compared with fentanyl.

1. INTRODUCTION

In childhood adenoidectomy and tonsillectomy are the foremost common operations and speak to more than 15 percent of all surgical strategies in children under the age of 15 a long time (Cullen KA, Lobby MJ, Golosinskiy A. 2006). Disturbance postoperatively has numerous etiologies and remains a significant clinical issue within the post-anesthetic care unit (PACU) setting. Caring for the disturbed child requires a careful evaluation and calls for focus on intercessions. (Patel HH, Straight CE, Lehman EB. 2014).

Development tumult (EA) in children is generally short-lived with no after-effect, however, it could be a troublesome wonder, because it may cause an increment in the chance of falling, damage to the surgical site, removal of dressings and channels leading to the disappointment of the guardians, and needs additional care and nonstop observing within the recuperation room and medicate organization may be required to control EA. EA has higher frequency in children anaesthetized with Sevoflurane alone with a frequency of up to 80% in those children. (Vlajkovic GP, Sindjelic RP. 2014),(Kuratani N, Oi Y. 2008),(Uezono S, Goto T, Terui K, Ichinose F, Ishiguro Y, Nakata Y, et al. 2000). The most prominent frequency of tumult is watched amid the primary 30 minutes(min) after the rise, and length is for the most part brief and the recuperation happen unconstrained. In any case, long scenes of disturbance enduring for up to 2 days have been described. (Uezono S, et al. 2000) . Numerous diverse clarifications for rise disturbance have been recommended, like the fast return of consciousness in a new environment, torment, stretch, aviation route obstacles, the term of anaesthesia, the child's identity, anaesthetic premedication and the strategy utilized. (Veyckemans F. 2001), Sevoflurane: Sevoflurane (1,1,1,3,3,3-hexafluoro-2-(trifluoromethoxy)propane) may be a colourless, volatile, and non-flammable fluid with a characteristic scent. It is steady at room temperature and has a bubbling point of 58.6°C and a vapour weight of 157 mm Hg. Subsequently, in differentiation to desflurane, it can be used in standard vaporizers. Sevoflurane has an oil/gas parcel coefficient of 47.2 and its negligible alveolar concentration (MAC) is 2.05%, these values of MAC alter with age, from 3.3% in neonates and 2.5% in newborn children and youthful grown-ups to 1.58% to 2.05% in middle-aged grown-ups and 1.45% in grown-ups who are more than 70 a long time ancient. MAC values for sevoflurane decrease by 50% in grown-ups when blended with 65% nitrous oxide within the propelled gas mixture.(Fragen RJ, Dunn KL. 1996) . 98% of sevoflurane is eliminated through the lung. The driving constraint for this end is the distinction in fractional weights between the motivated gas blend and the aspiratory capillary blood. In people, 2% of the retained dosage of sevoflurane is metabolized by the liver, coming about through the formation of inorganic fluoride and the natural fluoride metabolite hexafluoroisopropanol. The last mentioned is conjugated with glucuronic corrosive and excreted quickly through the kidneys. (Kharash ED. 1995).

Fentanyl: Fentanyl is a built, lipophilic phenylpiperidine opiate agonist with pain-relieving and narcotic properties. Fentanyl particularly ties to the mu-receptor within the central tactile framework (CNS) in this way imitating the impacts of endogenous opiates. A feeling of the mu-subtype opiate receptor invigorates the exchanging of Guanosine triphosphate (GTP) for Guanosine diphosphate (Net household item) on the G-protein complex and consequently controls adenylate cyclase. This result may be a lessening in intracellular cyclic adenosine monophosphate (cAMP) and prompts a diminish within the entry of neural connections like substance P, Gamma - Amino Butyric Destructive (GABA), dopamine, acetylcholine and noradrenaline. Bioavailability is 92% when given transdermally and half taken after the verbal course. Most opiates lessen mindful and update vagal and parasympathetic tone subsequently patients who are volume-exhausted or unexpected upon tall astute tone or exogenous catecholamines to keep up with cardiovascular capability are slanted toward hypotension after the organization of opiates. Fentanyl conveys essentially zero alter in myocardial contractility.(Kawakubo A, Fujigaki T, Uresino H, et al. 1999) . Fentanyl might thrust down cardiovascular conduction by an instrument interceded by coordinate layer exercises instead of opiate receptor intelligence. (Weber G, Self-evident G, Particular U. 1995) . Opiates appear to definitively influence coronary vasomotion or myocardial absorption, do not convey take quirks, and do not decrease the capacity of gigantic coronary arterioles to reply to vasoactive operators. (Blaise GA, Witzeling TM, Edge JC, et al. 1990) . KETAMINE: The Ketamine molecule contains a disproportionate carbon particle with two enantiomers: The S(+) isomer and the R(−) isomer.

Ketamine is an outstanding lipid dissolvable and goes through quick breakdown and reallocation to periphery tissues. It is prepared within the liver by N-demethylation and ring hydroxylation pathways. Norketamine is the basic metabolite and is 33% to one-fifth as solid as ketamine as a narcotic. Ketamine is released in pee and defecation. Ketamine quickens the cardiovascular system bringing almost tachycardia, hypertension and extended heart abdicate. It irrelevantly influences the central respiratory drive and makes the flying course loosen up by taking after up on diverse receptors red hot wellsprings and bronchial smooth muscles. It builds salivation and muscle tone. It has cataleptic, amnestic, noteworthy pain-relieving, and portion-subordinate narcotic exercises.

The dissociative state made by ketamine is curiously where the patient seems cautious be that as it may is isolated from the natural components with open eyes. Ketamine is a noncompetitive danger to the N-methyl D-aspartic destructive (NMDA) receptor. (Persson J. 2010). Overview of composing: (Lee YS, Kim WY, Choi JH, Child JH, Kim JH, Stop YC. 2010) analyzed ketamine 0.25mg/kg and 0.5 mg/kg i.v. coordinated to youths who went through adenotonsillectomy 10 mins sometime recently the wrap-up of a restorative strategy and uncovered a reduction within the event of EA since of the solidified pain-relieving and opiate effect. They also famous lower torment scores with the higher parcel of ketamine and prescribed that raising the ketamine parcel was successful as a pain-relieving without conceding the recovery. (Eqhbal MH, Tareqh S, Amin A, Sahmeddini Mother. 2013) controlled ketamine 0.25mg/kg i.v. for youths who went through adenotonsillectomy amid acknowledgement of sedation and saw that low-portion ketamine was compelling in reducing EA and postoperative torment. (Kawara guchi Y, Miyamoto Y, Fukumitsu K, Taniguchi A, Hirao O, Kitamura S, et al. 2002) investigated the effect of ketamine on reducing postoperative unsettling influence after sevoflurane sedation in adolescents who went through elective strabismus therapeutic method, assumed that organization of ketamine 1mg/kg after the enrollment of sedation taken after by implantation of ketamine 1mg/kg/hr amid pediatric strabismus restorative strategy lessens EA. (Kararmaz A, Kaya S, Turhanoglu S, Ozyilmaz MA 2004) administered a high dose of oral ketamine (6mg/kg) as a premedication30 minutes before induction of anaesthesia for children who underwent adenotonsillectomy with or without bilateral myringotomy and insertion of tubes, and reported reduced incidence of EA in children after desflurane anaesthesia without a delay in recovery.

2. METHOD

The inquiry included 80 youngsters, ranging in age from 2 to 10 years, who were scheduled for a surgical operation to remove their tonsils, either alone or with the adenoids, under sedation with sevoflurane at Alhwari Medical Center, University of Benghazi, Libya. Before the start of the investigation, the necessary approvals from the ethics committee were secured, and the caregivers were granted written consent. The youths involved in the study had a physical status of I-II according to the American Society of Anesthesiologists.

To be included in the study, the children needed to fulfil certain criteria, such as not having a history of snoring, obstructive sleep apnea, a compromised airway, upper respiratory infections, cognitive or developmental impairments, seizure disorders, CNS depressant medications, or other drugs that impact the central nervous system, allergies to the medications under investigation, or signs of agitation at the start of the research.

The children were randomly split into two groups, with each comprising 40 participants. Group A was administered ketamine at a dose of 0.5mg/kg, while Group B was given fentanyl at a dosage of 2 mcg/kg intravenously. The relaxation plan stayed the same for all

Before the operation, the kids were told to refrain from consuming solid foods for 6 hours and transparent fluids for 2 hours. Anesthesia was started with sevoflurane in 100% oxygen through a facial mask. The subjects also received atropine 0.01mg/kg and dexamethasone 0.25mg/kg via intravenous (IV) injection, followed by the examination drug

Necessary monitoring equipment was set up, and atracurium was given intravenously to assist in the intubation of the trachea. During the procedure, sedation was maintained with oxygen and sevoflurane, while the pain was managed with intravenous (IV) acetaminophen at a dose of After the procedure, the reversal of neuromuscular blockade was achieved with neostigmine 0.05mg/kg and atropine 0.01mg/kg. The process of decannulation started once the patients showed they could breathe independently, had a gag reflex, and were able to move purposefully.

- Extubation time: The amount of time that passed after the procedure before the tracheal tube was removed was recorded. - Emergence time: The amount of time that passes after the tracheal tube is removed and a command is given or an eye-opening occurs. - Length of surgery: The amount of time that passed between the beginning and end of the operation was noted as its duration. - Length of anaesthesia: The duration of anaesthesia was measured as the interval between the insertion of basic monitors and the tracheal extubation. - Post-anesthesia care unit observation period: Upon admission to the post-anesthesia care unit, each patient was watched for sixty minutes. - Emergence agitation assessment: Aono's four-point scale was used every five minutes to gauge the degree of emergence agitation:

(1) sleep.
(2) awake but calm;
(3) agitated but consolable; and
(4) severe agitation and difficulty in consoling.

Grades 3 and 4, which lasted longer than or equal to five minutes, were classified as having emergence agitation, while grades 1 and 2 were deemed to have no emergence agitation. As a rescue drug, midazolam 0.02-0.1 mg/kg was given. All unfavourable outcomes, such as oxygen desaturation, respiratory depression, hallucinations, and postoperative nausea and vomiting (PONV), were noted. After 30 minutes of stable vital signs, no bleeding, no pain, and no nausea or vomiting, patients were considered ready to be released from the post-anesthesia care unit.

3. RESULT

Table 1: ages of patients [mean (±SD)]

Variables	Groups		T- Test	p-value
	Ketamine Mean (±SD)	Fentanyl Mean (±SD)		
Age in years	4.90(1.27)	5.00(1.41)	0.323	0.464

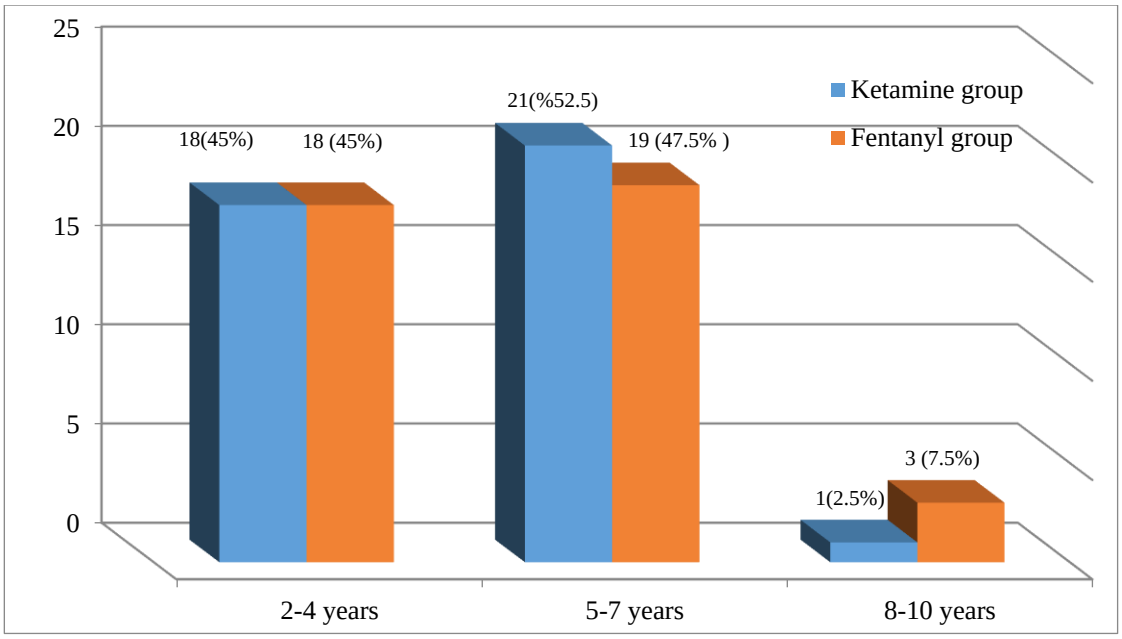

Figure 1: Distribution of the patients by their age group.

Table 2: Distribution of the patients according to ASA classification

ASA Classification	Groups		Total
	Ketamine	Fentanyl	
1	36 (90%)	36 (90%)	72
2	4(10%)	4(10%)	8
Total	40 (100%)	40 (100%)	80

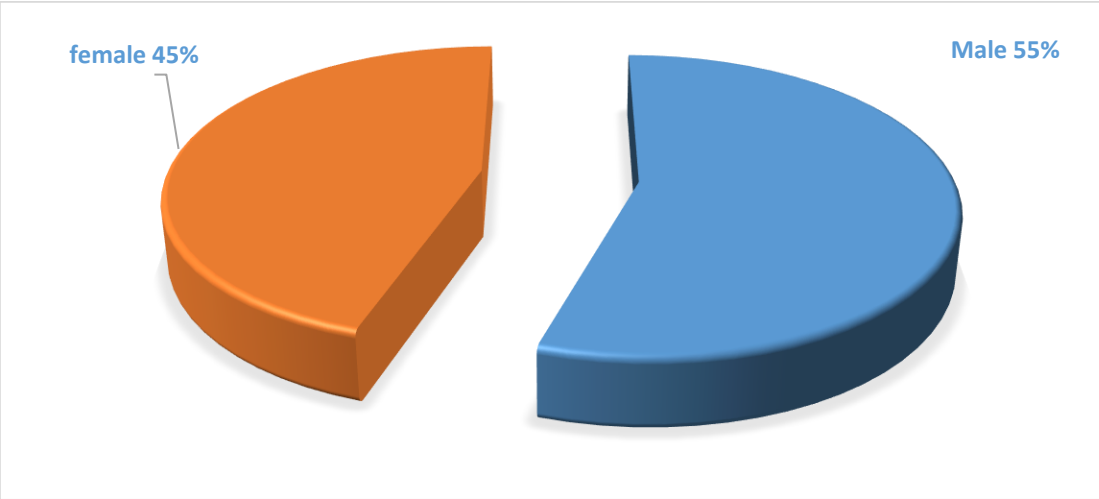

Figure 2: Gender distribution of Ketamine group.

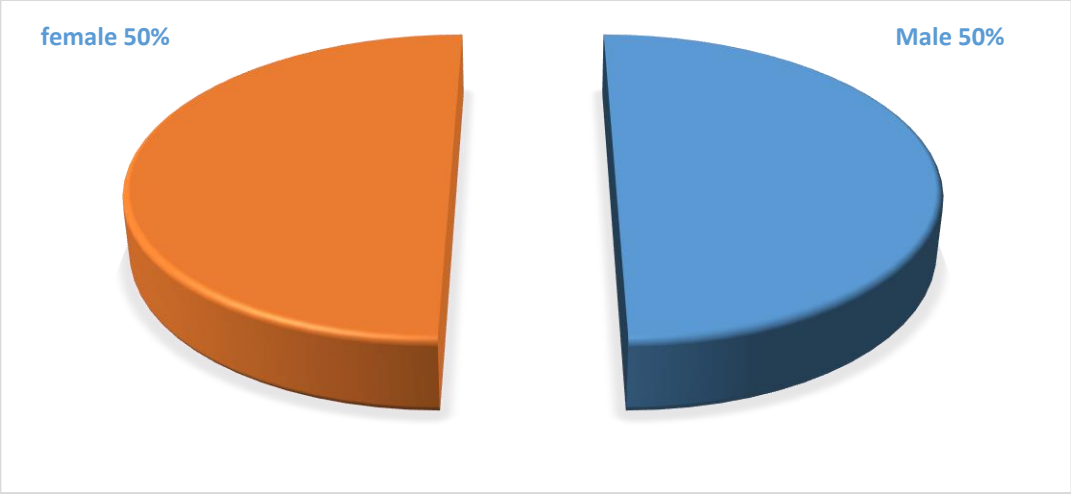

Figure 3: Gender distribution of the Fentanyl group.

Table 3: Comparison of durations

Variables	Groups		T- Test	p-value
	Ketamine Mean (±SD)	Fentanyl Mean (±SD)		
Duration of anaesthesia in minutes	40.20(4.62)	39.88 (3.99)	3770.	0.737
Duration of the surgery in minutes	29.10 (3.76)	27.55 (3.99)	1.787	0.78
Time to extubation in minutes	5.80 (1.30)	6.00 (1.13)	0.732	0.466
PACU stay in minutes	65.30(5.59)	69.58(4.96)	3.615	0.001
Emergence time in minutes	4.45 (0.87)	3.05(0.87)	7.151	0.000

Table 4: Distribution of the patients by type of Drug and the occurrence of emergency agitation

Emergence agitation	Groups		X^2	p-value
	Ketamine	Fentanyl		
No	32(80%)	10 (25%)	24.26	0.000
Yes	8(20%)	30(75%)		
Total	40(100%)	40(100%)		

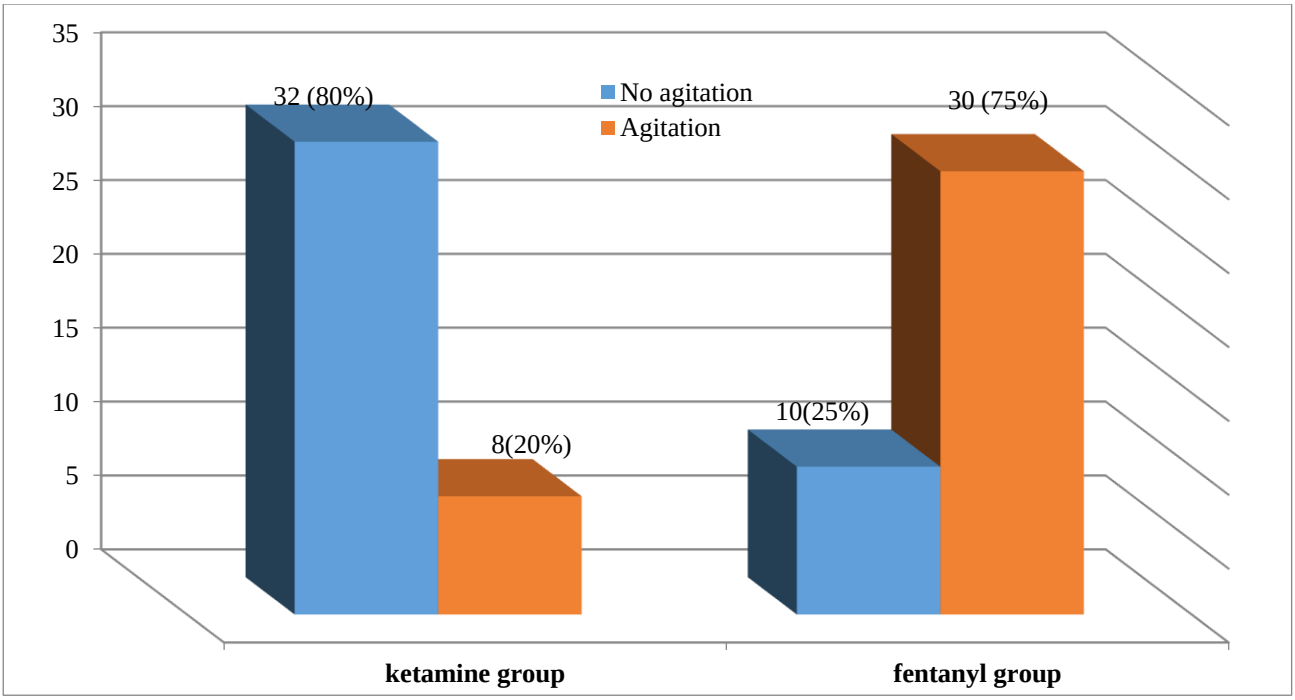

Figure 4: Distribution of the patients by type of Drug and the occurrence of emergency agitation

Table 5: Distribution of the patients by occurrence of emergence agitation and gender

Gender	Emergence agitation		Total	X^2	p-value
	No	Yes			
Male	24 (57.1%)	18 (47.4%)	42 (52.5%)	0.764	0.382
Female	18 (42.9%)	20(52.6%)	38(47.5%)		
Total	42(100%)	38(100%)	80(100%)		

Table 6: Distribution of the patients in the Ketamine group by the occurrence of emergence agitation and gender

Gender	Emergence agitation		Total	X^2	p-value
	No	Yes			
Male	18(56.2%)	4(50%)	22(55%)	0.101	0.751
Female	14(43.8%)	4(50%)	18(45%)		
Total	32(100%)	8(100%)	40(100%)		

Table 7: Distribution of the patients in the Fentanyl group by occurrence of emergency agitation and gender

Gender	Emergence agitation		Total	X2- Test	p-value
	No	Yes			
Male	6(60%)	14(46.7%)	20 (50%)	0.533	0.465
Female	4(40%)	16 (53.3%)	20(50%)		
Total	14(100%)	30(100%)	(100%)		

Table 8: Comparison of various study outcome variables according to EA (with/without)

	Ketamine Mean (±SD)	Fentanyl Mean (±SD)	Total (80) Mean (±SD)
Age in years			
Without EA	4.88(1.33)	4.80(1.61)	4.86 (1.38)
With EA	5(1.06)	(1.36)5.07	5.05 (1.29)
P-value	0.808	0.612	0.158
Duration of surgery (min)			
Without EA	28.94 (3.61)	(3.09)29.70	29.12 (3.48)
With EA	29.75 (4.49)	(4.04)26.83	27.45(4.25)
P-value	0.591	0.048*	0.057
Duration of anaesthesia (min)			
Without EA	40.16 (4.58)	(3.26)42.70	40.76(4.40)
With EA	40.38(5.09)	(3.80)38.93	39.24(4.07)
P-value	0.906	0.008*	0.113
Time to extubation (min)			
Without EA	5.75(1.32)	(0.91)6.80	6.00(1.30)
With EA	6(1.30)	(1.08)5.73	5.79(1.11)
P-value	0.634	0.008*	0.444
Time to consciousness (emergence) (min)			
Without EA	4.50 (0.84)	(1.07)3.40	4.24(1.00)
With EA	4.25 (1.03)	(0.78)2.93	3.21(0.99)
P-value	0.477	0.147	0.000*
Duration of PACU stay(min)			
Without EA	62.88(2.79)	(2.50)62.60	62.81(2.69)
With EA	75.00(2.39)	(2.96)71.90	72.55(3.09)
P-value	0.000*	0.000*	0.000*

4. DISCUSSION

Central nervous system inflammation, neurotoxic effects of damage products, and an imbalance between synaptic inhibition and excitability have been shown to cause EA17. Many factors contribute to the development of EA, including induction of anesthesia (rapid-onset, insoluble anesthetics), ancillary medications (benzodiazepines, opioids, anticholinergics), neck, tonsils, thyroid, eye surgery, pain, and patient care. (age, prenatal stress, child's condition) 18. We found that children receiving IV ketamine had significantly fewer cases of EA (20% of the ketamine group) compared to children receiving IV fentanyl (75% of the fentanyl group). The results of this study are comparable to those of Lee et al.13 comparing 0.25 mg/kg and 0.25 mg/kg ketamine. 5 mg/kg i. v. They gave 10 minutes before the end of the surgery and said that the decrease in EA disease in both groups was due to the effect of the treatment and the decrease in its severity. They also showed lower pain scores with higher doses of ketamine, suggesting that the increased dose of A was effective as an antidote. Speedy recovery. In the study of Lee et al.13, unlike studies in which ketamine was administered during anesthesia induction, ketamine was administered before surgery. Similar to this study, Eqhbal et al.14 administered ketamine during anesthesia induction and found that 0.25 mg/kg IV ketamine was effective in reducing EA. The results of this study were similar, but a higher dose of ketamine was used in this study. High doses of ketamine (1 mg/kg) followed by ketamine infusion (1 mg/kg/hour) can be applied after induction until the time of strabismus surgery in children, as used by Kawaraguchi et al. (15). Improve Reduce EA, similar to results from studies. Like IV-administered drugs, oral ketamine reduced the incidence of EA; Karamaz et al. (16) used it in children who underwent adenotonsillectomy with bilateral myringotomy and intubation under desflurane anesthesia; intravenous ketamine was administered orally 30 min before anesthesia induction rather than induction, and the dose was higher than in this study (6 mg/kg).

5. CONCLUSION

in children undergoing tonsillectomy with/without adenoidectomy under sevoflurane-based anaesthesia, administration of iv. ketamine 0.5 mg/kg at the time of induction of anaesthesia significantly reduces the incidence of emergence agitation as compared with iv. fentanyl 2 mcg/kg.

6. RECOMMENDATION

Based on the results of this study, it is recommended to consider the use of ketamine to reduce agitation in children undergoing tonsillectomy by sevofluraine-based anaesthesia.

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