

## The Analgesic Effects of Ketamine, Ketorolac and Dexamethasone after Adenotonsillectomy Surgery in Children Aged 4 to 18 Years

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### Abstract

**Background:** This study aimed to investigate the analgesic effects of ketamine, ketorolac and dexamethasone after adenotonsillectomy surgery in children aged 4 to 18 years.

**Methods:** This clinical trial was undertaken on children aged 4 to 18 years who were admitted in Shafa Hospital of Kerman for tonsillectomy and adenotonsillectomy surgeries. Simple randomization was used for sampling and the subjects were randomly divided into three groups. In all three groups, 1-8 mg dexamethasone was administered/ injected. 0.5 mg/kg ketamine, 0.5 mg/kg ketorolac and dexamethasone were administered/ injected in the first, second and third (control) group groups respectively. This means that subjects in the control group did not receive any drug except dexamethasone. The Wong-Baker Faces Pain Rating Scale was used for measuring the level of pain. Statistical analysis was performed using SPSS software, version 21.

**Results:** According to the post-operative pain of patients who used ketamine, ketorolac and dexamethasone during the recovery time, there was a significant difference in six hours after surgery and the time of discharge/release as the highest pain score was related to the control group (the group that only used dexamethasone). Moreover, the pain score of the subjects or the patients who received ketamine at the time of discharge was significantly higher ( $p < 0.05$ ) than the ones who received ketorolac.

**Conclusion:** Administration of ketamine and ketorolac can be beneficial for controlling and decreasing the post-operative pain in patients undergoing adenotonsillectomy surgery.

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### Introduction

Inflammatory and infectious diseases of pharynxes and tonsils in children are common and the costs of their treatment are so high. In many cases, they lead to tonsillectomy and adenotonsillectomy surgeries (1). Currently, tonsillectomy and adenotonsillectomy can be done with various methods and

each of them is with specific side effects including pain, bleeding, laryngospasm, airway obstruction, nausea, vomiting, and aspiration (2). The most important kinds of these side effects are the post-operative pain. In 20-50 percent of children undergoing tonsillectomy/adenotonsillectomy, post-operative pain is reported (3). The level of post-operative pain can

increase the consumption of analgesics, hospitalization, dysphasia and difficulty in doing the daily activities. So, pain reduction can improve the quality of life for these patients after surgeries (4). Moreover, this issue (reduction) can lead to more satisfaction of children (as patients) and their parents and also better recovery and care delivery after these two kinds of surgeries (5, 6). Dexamethasone as an anti-inflammatory and immunosuppressive drug can be used in different cases (7). The administration of dexamethasone in a case of tonsillectomy/adenotonsillectomy, in addition to its analgesic and anti-inflammatory effects, can lead to the earlier oral intake, improve the daily routines and the quality of life (8, 9). Some studies show that intravenous or IV administration of dexamethasone in children affected by tonsillectomy/adenotonsillectomy is safe and it is effective in pain reduction and earlier oral intake (9). Ketorolac tromethamine is also a non-steroid anti-inflammatory drug (NSAID) which is used as an analgesic medicine for treating the inflammatory diseases. Also, it is used for fulfilling the short term control of mild to moderate pains (10). A study comparing pain reduction effects of ketorolac and acetaminophen after tonsillectomy/adenotonsillectomy in children showed that analgesic effects of ketorolac are equal to high rectal doses of acetaminophen, but bleeding control in the patients who received ketorolac was so hard (11). However, another study showed that as there is not a risk of bleeding in children, ketorolac is a safe medicine for this age group and hemorrhagic affects in adults are common (12). Ketamine as an effective medicine on the Central Neuron System or CNS can be used as an anesthetic drug and it is useful for pain reduction and treatment of bronchospasm (13). Ketamine is used as an analgesic medicine (after operation or surgery)

which its low dose can decrease nausea, vomiting and the need for morphine after surgery (14). Since tonsillectomy/adenotonsillectomy are common surgeries in children and post-operative pain leads to the high consumption of opioids and analgesics and increase the hospitalization time as well, it is associated with the impairment of swallowing and daily activities of the patients. In this regard, all related studies did not discuss the analgesic effects of these medicines; and for this reason, we decided to compare these three medicines (ketamine, ketorolac and dexamethasone) and determine the most effective ones which can improve the quality of life and decrease the medical costs. By the same token, literature shows that only the effect of ketamine, ketorolac and dexamethasone is investigated so far (8 -11-15), thus in this study we also compared the analgesic effects of these three medicines.

## Methods

This double blind clinical trial was conducted on 132 children aged 4 to 18 years who were admitted in Shafa Hospital of Kerman University of Medical Sciences for tonsillectomy and adenotonsillectomy surgeries. Simple randomization method was used for sampling and subjects were randomly divided in three groups (44 subjects in each group). 1-8 mg dexamethasone was administered to these three groups prior to the surgery. 0.5 mg/kg ketamine, 0.5 mg/kg ketorolac and dexamethasone were administered/injected to the first, second and third group as the control groups respectively. We have to mention that subjects in the control group did not receive any drug except dexamethasone. The method of anesthesia for all groups was the same. 2µg/kg fentanyl, 4mg/kg thiopental (induction) and

0.5mg/kg atracurium were used. Then, tracheal intubation was done. Additionally, anesthesia was done by 1.2% isoflurane plus 50% O<sub>2</sub> (its dose: 3 L/min) and 50% N<sub>2</sub>O and atracurium (if necessary). Routine included a non-invasive measuring of blood pressure, heart rate, ECG, and arterial saturation. Routine monitoring included NIBP (non-invasive measuring of blood pressure), heart rate, ECG, and arterial saturation percentage. At the end of anesthesia, relaxant revers including 0.02mg/kg atropine and 0.04mg/kg neostigmine were used. All the surgeries were done by one surgeon and a team of surgeries. Then a checklist related to each of these patients was completed at the end of recovery time and 6 hours after discharge or release time.

The inclusion criteria encompassed:

- Informed consent to participate in the study,
- Anesthesia classification (I and II) based on the Anesthesia Association of America,
- Patients having different symptoms such as nocturnal snoring, mouth breathing, apnea during sleep, and infectious symptoms including recurrent pharyngitis related to peritonsillar.

The exclusion criteria included:

- Identified sensitivity to analgesics and topical anesthesia,
- Being affected by asthma, kidney and liver diseases, severe throat infections and coagulopathy.

Informed consent was obtained from all patients or their parents. By the same token, the aims, purposes as well as the steps of the study were completely explained. Patients were assured that their disagreement to participate in the study does not have an effect on their normal treatment pathway and it does not incur any additional costs. For data collection, a

checklist including the demographic information and The Wong-Baker Faces Pain Rating Scale, as the most valid and reliable tool (16-17), were used for pain measurement. For subjects with scores more than five, 5 mg/kg acetaminophen was administrated. For all patients, this scale was measured for three times. The number of times as the patient requires drugs or acetaminophen refers to the scores which are more than 5. Data analysis was done by using SPSS software (statistical package for social science) version 21 (SPSS Inc., Chicago, IL, USA).

Scores for pain and sedation were analyzed using the Kruskal-Wallis and Mann-Whitney U-test. Data were expressed as Frequency (%), or medians (ranges). P is significant if <0.05 at 95% confidence interval. The study was approved by the ethic committee of Kerman University of Medical Sciences with code number: ir.kmu.rec.1394.218.

## Results

The mean age of participants was 7.4 years and the majority of them were males (54.2%). Regarding post-operative side effects, 87.1 percent of subjects had no side effects. Majority of them took analgesics twice (36.5%). Based on the findings, the score of pain considering Wong-Baker FACES scale in the patients who received ketamine, ketorolac and dexamethasone during the recovery time showed a significant difference. The highest pain score (over recovery time) was seen in patients who received only dexamethasone (table 1). Results of Mann Whitney U test showed that there was a significant difference between pain scores in dexamethasone group and ketamine group (p values=0.005) and the pain score in the ketamine group was lower. Moreover, there was a significant difference between pain scores in dexamethasone group and ketorolac group during the recovery time and the

pain score was lower in the ketamine group ( $p$  values =0.002). Although during the recovery time, the pain score was lower in the ketamine group, but this difference was not significant ( $p=0.929$ ) (Tables 2, 3, and 4). During 6 hours following surgery, a significant difference was observed between the patients receiving dexamethasone, ketamine and ketorolac ( $p<0.001$ ), as the highest score was seen in dexamethasone group (table 1). The results of Mann Whitney U test showed that there was a significant difference between pain scores in dexamethasone group and ketamine group during 6 hours after surgery ( $p=0.01$ ) and the pain score in the ketamine group was lower (44.46 vs. 57.41). Moreover, there was a significant difference between pain scores in dexamethasone group and ketorolac group (41.37 vs. 61.63) during 6 hours after surgery ( $p<0.001$ ), but there was not a significant

difference between ketorolac and ketamine groups during 6 hours after surgery ( $p=0.963$ ) (Tables 2, 3, and 4).

Our findings indicated that there was a significant difference between pain score of the patients who received ketamine, ketorolac and dexamethasone during the time of discharge/release ( $p<0.001$ ), as the highest pain score during this time was seen in dexamethasone group (table 1). Results from Mann Whitney U test showed that although the pain score was lower in the ketamine group, but this difference was not significant ( $p=0.09$ ). However, there was a significant difference between dexamethasone and ketorolac (Pain score 37.65 vs. 60.88, and  $p<0.001$ ) and ketamine and ketorolac (Pain score 37.89 vs. 58.33, and  $p<0.001$ ) at the time of discharge (tables 2, 3, and 4).

**Table 1.** The results of kruskal wallis analysis concerning the differences of pain during recovery time, 6 hours after surgery and at the time of discharge

Variable	Group	Mean rank	Pvalue
Recovery time	Dexamethasone	92.99	0.003
	Ketamine	69.96	
	Ketorolac	68.79	
6 hours after surgery	dexamethasone	93.04	<0.001
	ketamine	74.72	
	ketorolac	61.71	
At the time of discharge	dexamethasone	88.03	<0.001
	ketamine	79.45	
	ketorolac	51.03	

**Table 2.** The results of Mann Whitney U test concerning the differences of pain after taking Dexamethasone with ketamine during the recovery time, 6 hours after surgery and at the time of discharge

Variable	Group	Mean Rank	Pvalue
Recovery time	Dexamethasone	59.33	0.005
	ketamine	44.23	
6 hours after surgery	Dexamethasone	57.41	0.01
	ketamine	44.46	
At the time of discharge	Dexamethasone	52.56	0.09
	ketamine	45.12	

**Table 3.** The results of u Mann Whitney u test concerning the differences of pain after taking Dexamethasone with ketorolac during the recovery time, 6 hours after surgery and at the time of discharge

Variable	Group	Mean Rank	P value
Recovery time	Dexamethasone	60.66	0.002
	ketorolac	44.02	
6 hours after surgery	Dexamethasone	61.63	<0.001
	ketorolac	41.37	
At the time of discharge	Dexamethasone	60.88	<0.001
	ketorolac	37.65	

**Table 4:** The results of Mann Whitney U test concerning the differences of pain after taking ketamine with ketorolac during recovery time, 6 hours after surgery and at the time of discharge

Variable	Group	Mean Rank	P value
Recovery time	ketamine	51.23	0.929
	ketorolac	50.77	
6 hours after surgery	ketamine	55.76	0.063
	ketorolac	46.33	
At the time of discharge	ketamine	58.33	<0.001
	ketorolac	37.89	

## Discussion

Our findings showed that post-operative pain score (using Wong-Baker Faces Scale) of adenotonsillectomy in patients receiving dexamethasone, ketamine and ketorolac had a significant difference over the recovery time, as the highest score was observed in control group that received dexamethasone. The score of pain in control group (that received dexamethasone) was significantly higher than ketamine group during the recovery time. But the difference (concerning the score of pain) between ketamine and ketorolac groups was not significant. The post-operative pain score of adenotonsillectomy in patients receiving dexamethasone, ketamine and ketorolac had a significant difference over 6 hours after the surgery as the highest score of pain was observed in control group receiving dexamethasone. The score of pain in control group was significantly higher

than ketamine group and ketorolac group during 6 hours of the following surgery. But the difference of pain score between ketamine and ketorolac groups over 6 hours after surgery was not significant. The half-life of ketamine and ketorolac was 2.5 to 3 and 4 to 6 hours, respectively. Thus, their analgesic effect up to this time was expectable. The score of pain (after adenotonsillectomy surgery) at the time of discharge/release was associated with significant differences among these groups receiving ketamine, dexamethasone and ketorolac, as the highest score of pain during this time belonged to control group. With respect to analgesic effects of ketamine and ketorolac, the rate of recovery among these groups of patients can be so fast which improves their life and increases their quality of life. There was not a significant difference regarding pain score at the time of discharge in control group (receiving dexamethasone) and ketamine group, but pain score in

dexamethasone group was so high. Besides, pain score in the control group was significantly higher than ketorolac group. Since the half-life of ketorolac is more than ketamine, we can conclude that the effects of this medicine are useful in decreasing the level of pain and also it has an effect on the recovery. Regarding the importance of side effects, there are three kinds of bleeding as two of them were limited to the dexamethasone group and the other was attributed to the ketamine group. These findings indicate that ketorolac does not increase the post-operative bleeding rate. The highest rate of analgesics consumption was observed in the control group and the analgesic effects of ketamine and ketorolac were not so high. In a study done on children undergoing adenotonsillectomy in the United States, the authors stated that administration of a single dose of dexamethasone prior to surgery can lead to a considerable level of analgesia (8). Furthermore, in a comparative study on the post-operative analgesic effects of acetaminophen and ketorolac in children (after adenotonsillectomy), results showed that ketorolac had similar analgesic effects which were equal with the rectal doses of acetaminophen (11). However, another study showed that due to the lack of hemorrhagic effect of ketorolac in children, ketorolac can be used safely in this group but in

adults, its hemorrhagic effects can be seen (12). A study showed that ketamine can reduce swallowing evoked pain in children who underwent adenotonsillectomy surgery (18). In erhan et al study, post-tonsillectomy infiltration of ketamine into the tonsillar region has been introduced as an easy and effective strategy (20). Evidence shows that administration of ketamine in children undergoing adenotonsillectomy is associated with few side-effects and it can be a good choice for their treatment (21).

### Conclusion

According to the results of this study, it can be concluded that administration of ketamine and ketorolac can be beneficial in decreasing the post-operative pains of adenotonsillectomy. Regarding this fact that adenotonsillectomy is one of the commonest pediatric surgeries and its post-operative pains can lead to the consumption of opioid drugs, an increase in the hospitalization time, postponing the swallowing of the patients, as well as weakening the daily activities, therefore, the administration of ketamine and ketorolac is suggested to improve the quality of life and decrease the treatment costs.

### References

1. Leiberman A, Stiller-Timor L, Tarasiuk A, Tal A. The effect of adenotonsillectomy on children suffering from obstructive sleep apnea syndrome (OSAS): the Negev perspective. *Int J Pediatr Otorhinolaryngol* 2006; 70(10):1675-82.
2. Dal D, Celebi N, Elvan EG, Celiker V, Aypar U. The efficacy of intravenous or peritonsillar infiltration of ketamine for postoperative pain relief in children following adenotonsillectomy. *Paediatr Anaesth* 2007; 17(3):263-9.
3. Akbay BK, Yildizbas S, Guclu E, Yilmaz S, Iskender A, Ozturk O. Analgesic efficacy of topical tramadol in the control of

- postoperative pain in children after tonsillectomy. *J Anesth* 2010; 24(5):705-8.
4. Ozkose Z, Akcabay M, Kemaloglu YK, Sezenler S. Relief of posttonsillectomy pain with low-dose tramadol given at induction of anesthesia in children. *Int J Pediatr Otorhinolaryngol* 2000; 53(3):207-14.
  5. Donnelly MJ, Quraishi MS, McShane DP. Indications for paediatric tonsillectomy GP versus Consultant perspective. *J Laryngol Otol* 1994; 108(2):131-4.
  6. Burton MJ, Glasziou PP, Chong LY, Venekamp RP. Tonsillectomy or adenotonsillectomy versus non-surgical treatment for chronic/recurrent acute tonsillitis. *Cochrane Database Syst Rev* 2014; (11):CD001802.
  7. ElHag M, Coghlan K, Christmas P, Harvey W, Harris M. The anti-inflammatory effects of dexamethasone and therapeutic ultrasound in oral surgery. *Br J Oral Maxillofac Surg* 1985; 23(1):17-23.
  8. Afman CE, Welge JA, Steward DL. Steroids for post-tonsillectomy pain reduction: meta-analysis of randomized controlled trials. *Otolaryngol Head Neck Surg* 2006; 134(2):181-6.
  9. April MM, Callan ND, Nowak DM, Hausdorff MA. The effect of intravenous dexamethasone in pediatric adenotonsillectomy. *Arch Otolaryngol Head Neck Surg* 1996; 122(2):117-20.
  10. Dsida RM, Wheeler M, Birmingham PK, Wang Z, Heffner CL, Cote CJ, et al. Age-stratified pharmacokinetics of ketorolac tromethamine in pediatric surgical patients. *Anesth Analg* 2002; 94(2):266-70.
  11. Rusy LM, Houck CS, Sullivan LJ, Ohlms LA, Jones DT, McGill TJ, et al. A double-blind evaluation of ketorolac tromethamine versus acetaminophen in pediatric tonsillectomy: analgesia and bleeding. *Anesth Analg* 1995; 80(2):226-9.
  12. Chan DK, Parikh SR. Perioperative ketorolac increases post-tonsillectomy hemorrhage in adults but not children. *Laryngoscope* 2014; 124(8):1789-93.
  13. Green SM, Roback MG, Kennedy RM, Krauss B. Clinical practice guideline for emergency department ketamine dissociative sedation: 2011 update. *Ann Emerg Med* 2011; 57(5):449-61.
  14. Bell RF, Dahl JB, Moore RA, Kalso E. Perioperative ketamine for acute postoperative pain. *Cochrane Database Syst Rev* 2006; 1.
  15. Elhakim M, Khalafallah Z, El-Fattah HA, Farouk S, Khattab A. Ketamine reduces swallowing-evoked pain after paediatric tonsillectomy. *Acta Anaesthesiol Scand* 2003; 47(5):604-9.
  16. Garra G, Singer AJ, Taira BR, Chohan J, Cardoz H, Chisena E, et al. Validation of the Wong-Baker FACES pain rating scale in pediatric emergency department patients. *Academic Emergency Medicine* 2010; 17(1):50-4.
  17. Luffy R, Grove SK. Examining the validity, reliability, and preference of three pediatric pain measurement tools in African-American children. *Pediatr Nurs* 2003; 29(1):54-9.
  18. Fazel MR, Yegane Moghaddam A, Forhani Z, Farahani F. Effect of dexamethasone on postoperative vomiting and oral intake after

- adenotonsillectomy. *Avicenna J Clin Med* 2007; 13(4):39-42 [In Persian].
19. Gunter JB, Varughese AM, Harrington JF, Wittkugel EP, Patankar SS, Matar MM, et al. Recovery and complications after tonsillectomy in children: a comparison of ketorolac and morphine. *Anesth Analg* 1995; 81(6):1136-41.
  20. Erhan OL, Goksu H, Alpay C, Bestas A. Ketamine in post-tonsillectomy pain. *Int J Pediatr Otorhinolaryngol* 2007; 71(5):735-9.
  21. Cho HK, Kim KW, Jeong YM, Lee HS, Lee YJ, Hwang SH. Efficacy of ketamine in improving pain after tonsillectomy in children: meta-analysis. *PLoS One* 2014; 9(6):e101259.
  22. Meimane Jahromi A, Honarvar H, Khalighi AR. The efficacy of antibiotic therapy on recovery of tonsilectomy and adenotonsillectomy. *J Birjand Univ Med Sci* 2006; 13(4):9-15. In Persian