

Comparison of the Effects of Adding of Ketamine to Pre- Incisional Bupivacaine Injection on Postoperative Pain Relief after Tonsillectomy in Children

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ABSTRACT

Pain control in children is still a therapeutic dilemma and preschool patients are affected from undesirable effects of postoperative pain more than adults. The aim of this work was to compare the effects of adding of Ketamine to pre-incisional Bupivacaine injection of post-operative pain relief after tonsillectomy. Sixty-three children that classified as ASA class I and II scheduled for adenotonsillectomy and divided into three groups (every group had 21 patients). Group 1: Bupivacaine (0.5%) 2mg/kg, Group 2: Ketamine 0.5 mg/kg and Group 3: Ketamine 0.5mg/kg and Bupivacaine (0.5%) 2mg/kg was injected into tonsillar bed by the surgeon. Side effects were evaluated at 1, 4 and 24 hours after adenotonsillectomy. The correlation between the data was done by Chi-square test and a $P < 0.05$ was considered significant. One hour after surgery, in group 3, pain score was lower than other groups ($P > 0.05$). Besides, after 4 hours in group 3, there was no severe pain in patients and higher percent of patients (61.9%) had mild pain compared to group 2 ($P > 0.05$) and group 1 ($P < 0.05$). After 24 hours, higher percent of patients without pain were in group 3 compared to group 2 ($P > 0.05$) and group 1 ($P = 0.05$). In conclusion, adding of Ketamine to pre-incisional Bupivacaine injection resulted in post-operative acceptable pain relief with lower side effects after adenotonsillectomy.

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Introduction

Tonsillectomy continues to be one of the most common Otorhinolaryngology surgical procedures for children [1] and is the oldest and most often performed surgical procedure practiced by ear, nose, and throat physicians [2]. Despite advancements in surgical and anesthetic techniques, serious pain and difficulty swallowing are common complaints encountered in children [1]. Pain control in children is even so a therapeutic dilemma and preschool patients are affected from undesirable effects of postoperative pain more than adults [3]. The pain after tonsillectomy is a problem that induces to be solved [4]. It is discovered that reducing post adenoidectomy pain with analgesic drugs has a notable effect on patients. For instance, non-steroid anti-inflammatory drugs are caused gastrointestinal hemorrhage (GIB), or Opioids cause respiratory depression, nausea and vomiting [5]. Ketamine is an intravenous anesthetic in phencyclidine family, which is a noncompetitive antagonist of N-methyl-D-aspartate (NMDA) receptors. Ketamine influences the regulation of central sensitization and opium resistance [6]. Ketamine demonstrates a potent analgesic effect by central blockage of perception of pain with sub-anesthetic doses. Preoperative intramuscular administration of Ketamine for sedation decreases the pain during swallowing after tonsillectomy, while it provides long-term analgesia when applied around the incision [7]. Peri-operative Ketamine peritonsillar infiltration in children can reduce the incidence of postoperative nausea and vomiting, but its postoperative analgesic time is short [8]. Bupivacaine is used as a topical analgesic widely. In terms of construction it is very similar to lidocaine except amine group of butyl pyridine [9]. Topical application of Bupivacaine at a 0.25% concentration appears to a considerable degree of analgesia within the first 24 hours post tonsillectomy [10]. This drug is a suitable combine for long acting anesthesia. Considering that, till now, there was no research on the preemptive effect of Bupivacaine and tramadol combination in post-tonsillectomy pain [11,12]. The purpose of this study was to compare the effects of adding of

Ketamine to pre-incisional Bupivacaine injection for postoperative pain relief after tonsillectomy.

Patients and Methods

This study was approved by Kermanshah University Ethics Committee and was registered at <http://www.irct.ir> (registration number IRCT138903181617N3). In a randomized double-blind study, 63 children that classified as ASA class I and II scheduled for adenotonsillectomy and divided into three groups (every group has 21 patients). Group 1: Bupivacaine (0.5%) 2mg/kg, Group 2: Ketamine 0.5 mg/kg and Group 3: Ketamine 0.5mg/kg and Bupivacaine (0.5%) 2mg/kg, Syringes were encoded. In conclusion of surgery, Surgeon that didn't know syringe contain injected drug to tonsillar fossa. The patients were evaluated for hemodynamic stability, (HR), pain after surgery with NRS and nausea and vomiting at 1, 4 and 24 hours after adenotonsillectomy. Postoperative pain was measured by a Numeric Rating Scale (NRS). Our patients scored pain as know if score was 0, mild if was 1-4, moderate if was 5-7 and severe if was 8-10 [13]. The correlation between the variables was checked by SPSS software v. 19 (Chi-square test) and a p-value equal or less than 0.05 was considered as statistically significant.

Results

The mean age at the time of referral to surgery was 9.71 years (range, 4-12 years). Thirty-six patients (57.1%) were male and 27 (42.9%) were female [Table 1]. After surgery, of 63 patients, 59 patients (93.7%) in the first day were hospitalized and of all patients, 4 (6.3%) for the second day, too. Twenty patients (19%) after surgery had nausea and 6 (9.5%) had vomiting. The mean heart rate in one, 4 and 24 hours after surgery was 115.3, 102.9 and 94.7, respectively. The prevalence of heart rate after surgery for 63 patients has been shown in Figure 1.

Table 2 shows NRS pain after surgery for all patients. One hour after surgery, 23 patients had mild pain, 34 patients had moderate pain and 6 patients had severe pain. After 4 hours, 26, 35 and

2 patients had mild, moderate and severe pain. After 24 hours, just 43 patients had mild pain and

rest of patients didn't have pain.

Table 1. The variables for all patients (n=63).

Variables	Mean	n(%)
Age(year)	9.71	
Sex		
Male		36(57.1)
Female		27(42.9)
Hospitalization after surgery		
The first day		59(93.7)
Second day		4(6.3)
Nausea after surgery		
Yes		12(19)
No		51(81)
Vomiting after surgery		
Yes		6(9.5)
No		57(90.5)
Heart rate after surgery		
After one hour	115.3	
After 4 hours	102.9	
After 24 hours	94.7	

Table 2. The NRS pain after surgery for all patients (n=63)

Score	NRS pain After one hour	NRS pain After 4 hours	NRS pain After 24 hours
No pain	-	-	20
Mild	23	26	43
Moderate	34	35	-
Severe	6	2	-

Table 3. The NRS pain for 3 groups after surgery (Group 1: Bupivacaine, Group 2: Ketamine and Group 3: Bupivacaine and Ketamine)

Score, n(%)	<u>Bupivacaine</u> n=21	<u>Ketamine</u> n=21	<u>Bupivacaine and Ketamine</u> n=21	*Group 1 and Group 2	*Group 2 and Group 3	*Group 1 and Group 3
NRS pain after one hour	-	-	-	0.768	0.822	0.440
No pain	6(28.6)	8(38.1)	9(42.8)			
Mild	12(57.1)	11(52.4)	11(52.4)			
Moderate	3(14.3)	2(9.5)	1(4.8)			
Severe				0.599	0.224	0.035
NRS pain after 4 hours	-	-	-			
No pain	5(23.8)	8(38.1)	13(61.9)			
Mild	15(71.4)	12(57.1)	8(38.1)			
Moderate	1(4.8)	1(4.8)	-			
Severe				0.359	0.170	0.050
NRS pain after 24 hours	4(19)	6(28.6)	10(47.6)			
No pain	17(81)	15(71.4)	11(52.4)			
Mild	-	-	-			
Moderate	-	-	-			
Severe						

*P-value

Table 4. The correlation between the variables for 3 groups (Group 1: Bupivacaine, Group 2: Ketamine and Group 3: Bupivacaine and Ketamine)

Variables	<u>Bupivacaine</u> n=21	<u>Ketamine</u> n=21	<u>Bupivacaine and Ketamine</u> n=21	*Group 1 and Group 2	*Group 2 and Group 3	*Group 1 and Group 3
Hospitalization after surgery	21	17	21	0.038	0.038	1
The first day	0	4	0			
Second day						
Heart rate	120.9	124.1	103.1	0.378	0.001	0.013
After one hour	106.9	107	95	0.960	0.050	0.005
After 4 hours	98.4	98.9	87	0.870	0.001	0.002
After 24 hours				1	1	1
Nausea	4	4	4			
Yes	17	17	17			
No				1	1	1
Vomiting	2	2	2			
Yes	19	19	19			
No						

*P-value

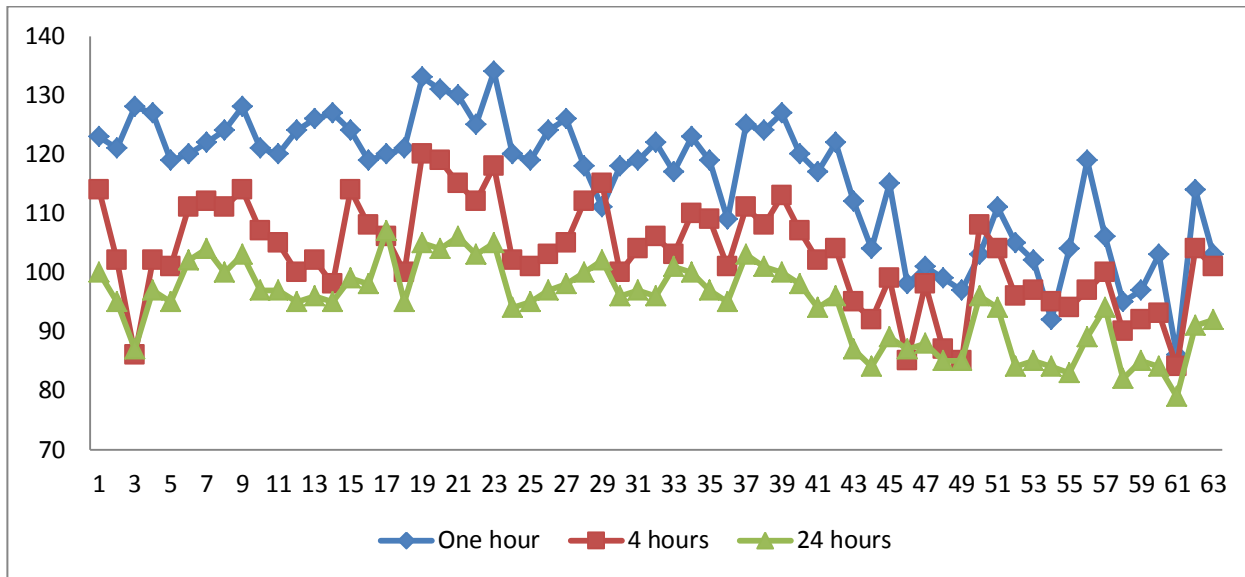


Fig. 1. The prevalence of heart rate for 63 patients (one hour, 4 hours and 24 hours after surgery)

The NRS pain score has been shown in **Table 3** based on 3 groups. One hour after surgery, in group 3, pain score was lower than other groups ($P>0.05$). Likewise, after 4 hours in group 3, there was no severe pain in patients and higher percent of patients (61.9%) had mild pain compared to

group 2 ($P>0.05$) and group 1 ($P<0.05$). After 24 hours, higher percent of patients without pain were in group 3 compared to group 2 ($P>0.05$) and group 1 ($P=0.05$)

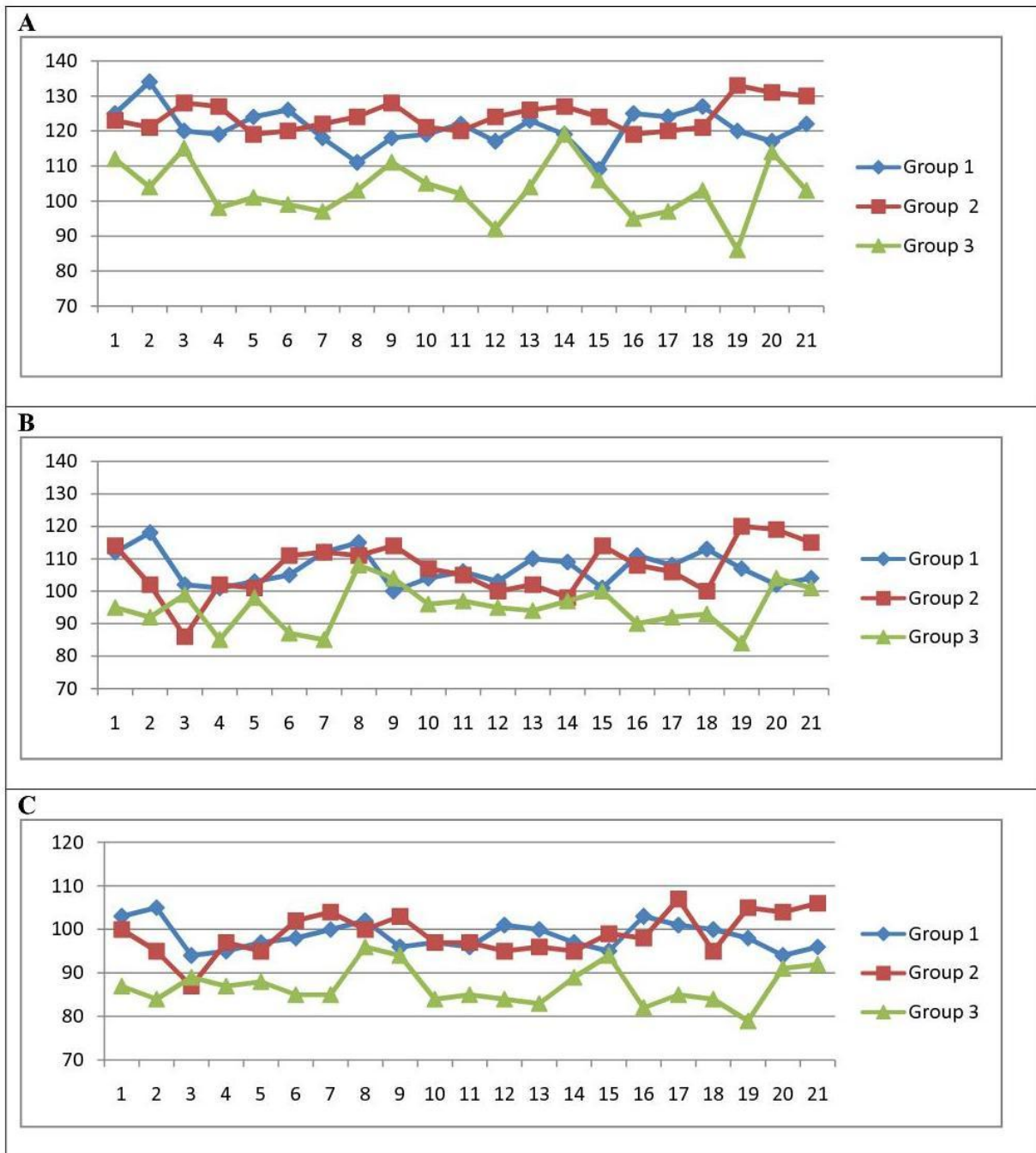


Fig. 2. The prevalence of heart rate after surgery based on groups (A: one hour; B:4 hours; C:24 hours).

Discussion

Post-tonsillectomy pain is one of the most common problems after anesthesia; therefore the use of a good anesthesia technique with minimum side effect is an important aim [4]. A study showed that Ketamine infiltration into the tonsillar region after tonsillectomy was found to be easy and effective [7]. A review study on 24 studies with 1257 participants were included and reviewed for the meta-analysis that the pain score reported by the physician during the first 4 hours and need for analgesics during 24 hours postoperatively was significantly decreased in the Ketamine group versus the control group. In addition, there was no significant difference between Ketamine and control groups for adverse effects during 24 hours postoperatively [14] that Yenigun et al. [2] Resulted the analgesic efficacy of intravenous Ketamine was found especially higher at hours 6 and 24. Umuroğlu et al. [15] Scheduled 60 children for adenotonsillectomy that were randomized into four groups to receive IV either 0.5 mg/kg (-1) Ketamine hydrochloride (K), 0.1 mg x kg (-1) morphine hydrochloride (M), 1.5 mg x kg (-1) tramadol hydrochloride (T) or normal saline (S) in a mass of 4 ml during induction. After tracheal intubation 10 µg x kg (-1). Min (-1) Ketamine hydrochloride in group K and 0.6 ml x kg(-1) x h(-1) saline IV in groups M, K and S were infused preoperatively. Heart rate increased significantly preoperatively only in group K, but Ketamine reduced pain compared to morphine and tramadol in children undergoing adenotonsillectomy. In another study [16], 75 patients were divided into three groups of 25 each and received a local peritonsillar infiltration of 0.9% saline (group S), Ketamine 0.5 mg x kg (-1) (group K1), or Ketamine 1 mg x kg (-1) (group K2). A 0.5 or 1 mg/kg (-1) dose of Ketamine given at roughly 3 min before surgery by peritonsillar infiltration provides efficient pain relief during 24 h after surgery without side-effects in children undergoing adenotonsillectomy. Peritonsillar infiltration of Bupivacaine provided superior immediate postoperative analgesia as reflected by lower recovery room pain scores (P < 0.05) Peritonsillar infiltration of Bupivacaine 0.5% with 1:200,000 epinephrine provided better post-

tonsillectomy pain control in the immediate postoperative period than Bupivacaine spray or placebo [17]. Inanoglu et al. [18] enrolled 90 children undergoing tonsillectomy and divided into three groups. The group I received intravenous and peritonsillar saline, group II received intravenous saline and peritonsillar Bupivacaine, and group III received intravenous 0.5 mg/kg Ketamine and peritonsillar 0.25% Bupivacaine (3-5 ml per tonsil). Intravenous Ketamine and peritonsillar infiltration with Bupivacaine were safe and effective as part of a multimodal regimen in reducing post-tonsillectomy pain. Patients in group III also had significantly lower pain scores than group II at all-time intervals except at 15th min, but analgesic requirements and the time to first analgesia were also significantly better in the Ketamine group. One-hundred patients with the mean age of 10.5 years assigned for adenotonsillectomy [19] that patients were randomly allocated into 4 groups: Group K1: received peritonsillar infiltration of Ketamine (0.5 mg/kg), Group M1: received peritonsillar infiltration of meperidine (1 mg/kg), and groups K2 and M2 received either Ketamine (0.5 mg/kg) or meperidine (1 mg/kg) in combination with Bupivacaine (5 mg/ml). Peritonsillar injection of a combination of Bupivacaine and Ketamine provided efficient postoperative analgesia after adenotonsillectomy and achieved higher parents' satisfaction for the outcome of surgery. In a trial [4], 120 children were candidates for tonsillectomy and randomized into four groups: Peritonsillar infiltration with Bupivacaine 1 mg/kg (Group B), tramadol 2 mg/kg (Group T), a combination of Bupivacaine-tramadol (Group BT) and saline (Group C) was done. One hour after surgery, control of pain in the first three groups was better than Group C. Four hours after surgery, control of pain was better in the second and third groups in comparison to Groups B and Group C and was better in the third group in comparison to the second group. Then, 24 hours after that, only in the group III the control of pain was effective (P<0.05). Therefore, peritonsillar infiltration with a combination of Bupivacaine-tramadol provided less post-surgery pain compared with infiltration of Bupivacaine and tramadol alone in adenotonsillectomy of children. Another study [20],

showed that the pain scores in the Bupivacaine group were lower than those in the saline group at 12 h. Also, the pain scores in the Bupivacaine and lidocaine groups were significantly lower than those in the saline group from 18 to 24 hours until day 7. Therefore, local infiltration of Bupivacaine is a relatively and safe effective method and is equivalent to use of lidocaine for post-tonsillectomy pain. In our study, 63 patients with mean age 9.71 years were divided to three groups (Group 1: Bupivacaine (0.5%) 2mg/kg, Group 2: Ketamin 0.5 mg/kg and Group 3: Ketamin 0.5mg/kg and Bupivacaine (0.5%) 2mg/kg) that one hour, 4 hours and 24 hours after surgery, pain score was lower in group 3 compared to other groups, but except of 4 and 24 hours after surgery between group 3 with group 1 in the rest of times, there is no significant correlation between groups. Also, the time of hospitalization after surgery and heart rate after surgery in group 3 was better than other groups ($P < 0.05$). Totally, side effects and pain score is lower in group 3. The other results and our results showed that combination of Bupivacaine with other drugs (tramadol and Ketamine) has better results compared to Ketamine, Bupivacaine or tramadol alone in adenotonsillectomy of children and Ketamine alone is better than other drugs without combination with each other.

Conclusion:

Adding of Ketamine to pre-incisional Bupivacaine injection resulted in post-operative acceptable pain relief with lower side effects after adenotonsillectomy.

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Conflict of Interests

Authors certify that there is no actual or potential conflict of interest in relation to this article.

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