



Research Article

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## ***Comparing the level of effect of pre-incisional topical injections of two drugs of Bupivacaine and Ketamine in pain reduction after Tonsillectomy***

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### ABSTRACT

**Introduction** – Pain after surgery is one of the more suffering aspects of Tonsillectomy surgery. Although various types of painkillers have been used to alleviate the pain after the surgery, this issue is yet to be solved efficiently. Hence, this study has been undertaken with the purpose of comparing the level of effect of pre-incisional topical injections of two drugs of bupivacaine and ketamine in pain reduction after Tonsillectomy. **Methodology** – This double-blind study and clinical trial was performed on 60 patients with class I and II ASA after Tonsillectomy surgery. In this study, patients were divided in two groups of 30 members and were put under similar Anesthesia procedures. After the anesthesia procedure, the level of pain in patients were determined in hours 1, 6, 12, and 24 after the surgery using the Verbal pain score (VPS) questionnaire. Data Analysis was performed using SPSS software version 21 and with the support of clinical trial studies such as K square;  $P < 0.05$  was considered to be significant. **Findings** – in the first hour after surgery, patients of group 2 (who had received bupivacaine) experienced no pain compared to the first group (receivers of Ketamine) with higher percentage (pain severity score of 0). 6 and 12 hours after the surgery also yielded similar results. Twenty four hours after the surgery had also similar results but they were not significant statistically ( $P > 0.05$ ). **Conclusion** – Results indicated that the topical injection of Bupivacaine in tonsillectomy provided better pain-relief compared to Ketamine.

**Keywords:** Bupivacaine, Ketamine, pain reduction, Tonsillectomy

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### INTRODUCTION

Tonsillectomy is considered to be one of the most prominent operations for treatment of infection and inflammation of tonsils, and it is among prominent surgeries for children [1]. One of the most significant side-effects of this surgery is pain which may result in further hospitalization of the patient in hospital [2]. Pain after surgery is one of the more suffering aspects of Tonsillectomy surgery. Although various types of painkillers have been used to alleviate the pain after the surgery, this issue is yet to be solved efficiently [3]. Utilization of topical anesthesia has been suggested as a method to decrease pain after the operation [4]. Pulmonary complications include bronchopneumonia, lung abscess, atelectasis, embolism, aspiration, and bronchospasm that are of secondary importance [5]. In an study undertaken in 2011, the topical injection of Bupivacaine and Levobupivacaine was proven to be more effective in reducing pain after surgery in comparison to the placebo (normal saline) [6]. In another study in 2010, the topical injection of Levobupivacaine paired with Epinephrine has been shown to be

effective in reduction of pain after surgery and bleeding during the operation [7]. In yet another study in 2009, the combination of intravenous Ketamine and topical injection of Bupivacaine was evidently effective in reducing pain after surgery [8]. Ketamine is an NMDA (n-Methyl-di-Aspartate) receptor antagonist with 30 years of background in clinical use. Ketamine has the ability to provide analgesia and amnesia, while its feature to help the automatic respiration of patients has turned this drug to an ideal solution for procedures related to pain and trauma. In clinical trials, the effect of ketamine was highlighted in pain reduction, halting the tolerance to opioids and reduced usage of Morphine. Moreover, the simultaneous usage of ketamine and morphine has shown to be significantly effective in reducing pain after operation [10]. Considering that ketamine has effective analgesia features, we are trying to compare the analgesic effects of topical injection of ketamine with topical injections of bupivacaine.

### METHODOLOGY

This study is a clinical trial that was performed on 60 patients with ASA (American Society of Anesthesia) score of class I and II who were under Tonsillectomy surgery, after being approved by research council of Jahrom Medical Sciences University and verified by ethics committee with code jus.rec. The population under study in this research were patients whom visited Jahrom's Paymanie Hospital and were handpicked by ENT specialist for tonsillectomy operation. The volume of samples were chosen with considering previous studies and sampling was done randomly. In this study, patients were divided in to 2 groups of 30 went under the same anesthesia. In the 1st group: 0.5 - 1 mg/kg of Ketamine and in 2nd group: 0.25 - 0.5 mg/kg of Bupivacaine were injected in the base of tonsil. Anesthesia drugs were: 0.1 - 0.2 mg/kg of Midazolam, 1 - 2 ug/kg Fentanyl, 4 - 6 mg/kg Thiopental and 0.4 - 0.6 Atracorium. These drugs were used as intravenous injection. Maintaining anesthesia was done by Isoflurane gas. Before anesthesia, patients were give 10 - 20 cc/kg of Hydrate Saline. In the 1st group 0.5 - 1 mg/kg of Ketamine and in 2nd group 0.25 - 0.5 mg/kg of Bupivacaine were injected in the base of tonsil before incision. All the tonsillectomy operations were done by the same surgeon. The inclusion factor for this study was reception of patients to hospital and the its exclusion factor were neglect of treatment by patient, inability of study for a patient, patients having homodynamic problems ( congenital cardiopulmonary ) and patients having upper respiratory system infection. After anesthesia, amount of patients' pain caused by surgery was determined by VPS (Verbal pain score) questionnaire at 1, 6, 12 and 24 hours after surgery. Patients were asked to score their pain. If there was no pain no point, low level of pain 1 point, medium level of pain 2 points and high level of 3 points were considered. The amount of pain was measured by the researcher and the study was Double blind, because patients were not informed of the type of medicine they receive and also statistical analyzer in both group didn't have any knowledge about the medicines. Finally, analyzing the information was done by SPSS ver. 21 and medical trial studies such as K square.

### FINDINGS

In this study 60 patients were divided into 2 groups of 30. 27 of them were male and the rest were female. At 1 hour after surgery, group 2 patients (Bupivacaine receiving patients) had more percentage of painlessness (pain severity score of 0) in comparison to group 1 patients (Ketamine receiving patients). (13.3% to 3.3%)

At the same hour 47.7% of group 2 patients experienced low level of pain (pain severity score of 1), which was equal to group 1 percentage. 36.7% of group 1 patients experienced medium level of pain (pain severity score of 2), while this amount for 2nd group was 26.7%. 13.3% of patients of both groups determined their pain as high level (pain severity score of 3).

**Table 1:** Comparison of the amount of pain in ketamine and bupivacaine one hour after surgery

Drug name	Pain severity			
	Without pain	Low	Moderate	High
<b>Ketamine</b>	3.3%	46.7%	36.7%	13.3%
<b>Bupivacaine</b>	13.3%	46.7%	26.7%	13.3%
<b>P-V</b>	0.518			

After six hours after the operation, the intensity of analgesia (pain severity score of 0) was also higher in group 2 than it was in group 1 (40% to 30%). At the same time, 60% of group 1 patients expressed the severity of pain as low (pain severity score 1), the value of which for group 2 was 53.3%. Also, 10% of patients in group 1 experienced moderate pain (pain severity score 2), while the same value was 3.3% in group 2. However, 3.3% of patients in group 2 expressed their pain as severe (pain severity score 3), whereas in group 2, no patient suffered severe pain (table 2).

**Table 2:** Comparison of the amount of pain of ketamine and bupivacaine 6 hour after surgery

Drug name	Pain severity			
	Without pain	Low	Moderate	High
<b>Ketamine</b>	30%	60%	10%	0%
<b>Bupivacaine</b>	40%	53.7%	3.3%	3.3%
<b>P-V</b>	1			

After twelve hours after the operation, the intensity of painlessness (pain severity score of 0) was also higher in group 2 than it was in group 1 (86.7% compared to 70%). At the same hour, 30% of group 1 patients expressed the severity of pain as low (pain severity score 1), the value of which for group 2 was 10%. Also, 3.3% of patients in

group 2 experienced moderate pain (pain severity score 2), whereas in group 1, no patient suffered moderate pain. At this hour, none of the patients of both groups expressed their pain as severe (pain severity score 3, table 3).

**Table 3:** Comparison of the amount of pain of ketamine and bupivacaine 12 hour after surgery

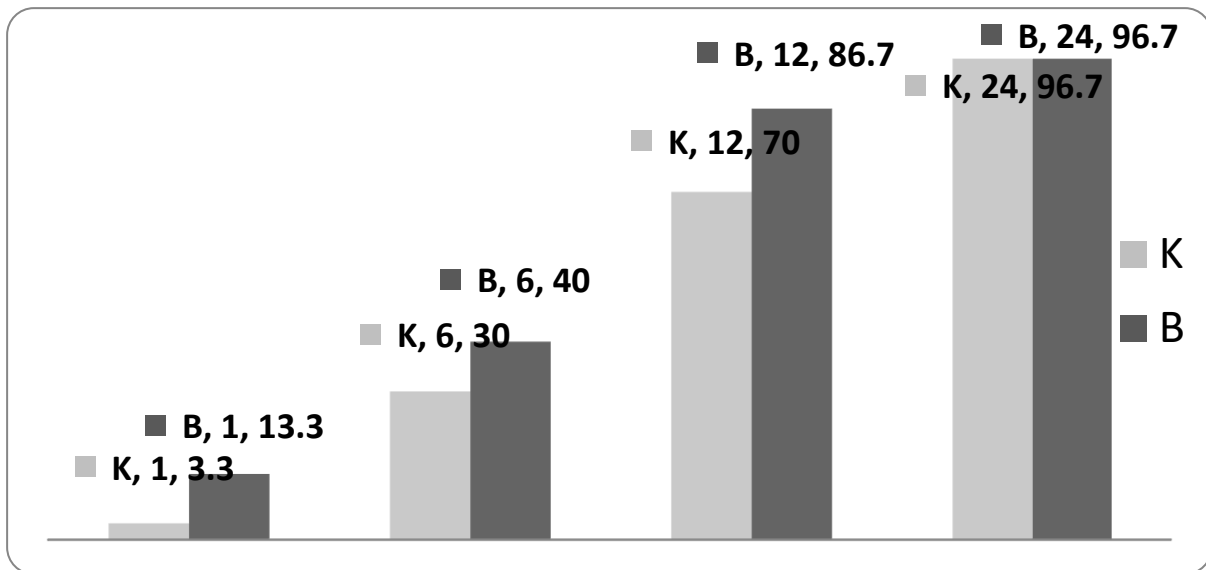
Drug name	Pain severity			
	Without pain	Low	Moderate	High
<b>Ketamine</b>	70%	30%	0%	0%
<b>Bupivacaine</b>	86.7%	10%	3.3%	0%
<b>P-V</b>	0.104			

In 24 hours after the operation, the value of intensity of painlessness (pain severity score of 0) was similar in both groups (96.7%). Also at the same hour, 3.3% patients of both group expressed the severity of pain as low (pain severity score 1). At this hour, none of the patients of both groups expressed their pain as moderate or severe (table 4). Nonetheless, the aforementioned results are not statistically significant ( $P > 0.05$ ).

**Table 4:** Comparison of the amount of pain in ketamine and bupivacaine 12 hour after surgery

Drug name	Pain severity			
	Without pain	Low	Moderate	High
<b>Ketamine</b>	96.7%	3.3%	0%	0%
<b>Bupivacaine</b>	96.7%	3.3%	0%	0%
<b>P-V</b>	1			

In the following chart the level of painlessness (pain severity score of 0) for ketamine and bupivacaine are compared with each other at hours 1, 6, 12, and 24.



**Figure 1:** comparison of painlessness (pain severity score 0) of ketamine and bupivacaine in different hours

#### DISCUSSION

During the study, two drugs of ketamine and bupivacaine were injected in the base of tonsils to two groups of 30 patients respectively. In the first hour after surgery, patients of group 2 (who had received bupivacaine) experienced no pain compared to the first group (receivers of Ketamine) with higher percentage (pain severity score of 0). 6 and 12 hours after the surgery also yielded similar results. Twenty four hours after the surgery had also similar results but they were not significant statistically ( $P > 0.05$ ). Ketamine is an NMDA (n-Methyl-di-Aspartate) receptor antagonist with 30 years of background in clinical use. Ketamine has the ability to provide analgesia and amnesia, while its feature to help the automatic respiration of patients has turned this drug to an ideal solution for procedures related to pain and trauma. This amnesic effect of ketamine helps patients to forget event occurred before or during the surgery, and considering the powerful analgesia and automatic respiration that is provided by ketamine, we decided to use ketamine as a suitable anti-pain with retrospective effects in this study. This drug has powerful analgesic effects on doses less than that of anesthesia, and the analgesic effects of ketamine in pain after surgery for drug users has been shown in various studies[9].

In a research conducted by Canbay et al. (2008) at turkey, the result showed that topical use of Ketamine is a safe and simple way to reduce pain after tonsillectomy[11]. Pain-relieving effects of Ketamine is proven in numerous studies like Inanoglu et al (8), El Sonbatay et al [12], Levanen J [13], Murry [14] and Ayatollahi et al[15]. Bupivacaine is a topical anesthetic drug. Initiation of its effect is slow and its effectiveness is gradual. Due to having longtime effects on nerve system rather than mobility system, it is an appropriate medicine for long-term pain relief and after-surgery period [14]. In research done by Goldsher et al. (1996), results showed that removing tonsils with Bupivacaine decreases the severity of pain after surgery[16]. Also, effects of Bupivacaine on after-surgery pain reduction is proven in numerous studies like Wong et al [17], Somdas [18] and Kasapoglu [19]. As Bupivacaine effect on pain relief is proven in studies and is mentioned in pharmacological books of Goodman- Gillman and Martindale, this medicine can be compared with Ketamine.

In 2007, Erhan et al. in turkey used Ketamine as a topical injection medicine in tonsils. The results showed that there is not any significant difference in pain relief between Ketamine, magnesium, morphine and clonidine and Ketamine couldn't provide a significant pain-relief, which is compatible with our study [20].

In study conducted by Ertugrul et al. (2006 Turkey), Ketamine was used Intermuscular to reduce pain after tonsillectomy and results showed that there is no difference in amount of pain after surgery between Ketamine and morphine or meperidine [21]. In another study by Taheri et al. (2011 Tabriz) Ketamine was used as intravenous injection and result showed that Ketamine and fentanyl reduce after-surgery pain similarly [22].

In a research conducted by Canbay et al. (2008) at Turkey, Ketamine was compounded with Saline. They compared this compound with Morphine, Saline and Ketamine plus Morphine and come to this conclusion that topical separate use of Morphine and Ketamine is a safe and sound method to reduce pain after tonsillectomy operation which is in contrast to our study [11]. In a study done 1 hour after the operation, there was a significant difference between Ketamine, Morphine groups and Ketamine groups compounded with Morphine or Saline group, which again our result was different. In this study Ketamine is used as a compound with Saline. As Ketamine is solvable in water and fat, its mixture with saline increases its dilution and volume. This increased volume of liquid can be concentrated in tissues around tonsil and due to high solvability of Ketamine in fat it is gradually released from surrounding tissues. As a result, more time is required for Ketamine to clean the tissues around tonsil [9].

In another study conducted by Murry (1987), Ketamine was used as intravenous and was compared with saline. The results showed that Ketamine doses were safer and more effective which is different with our study. Although Ketamine is considered as a powerful and well-known pain-killer, he compared Ketamine with saline and no study has ever shown that saline is effective in pain reduction after surgery. We have compared Ketamine with bupivacaine, both of which are proved as effective painkillers [23].

In a study conducted by Inanoglu et al. (2009) in turkey the effects of intravenous injection of Ketamine and topical injection of Bupivacaine on pain after operation were analyzed and the result showed that a regime consisting of intravenous injection of Ketamine and topical injection of Bupivacaine is appropriate for decreasing after-operation pains. This study has an obvious difference with ours, and it is because of adding topical injection of Bupivacaine to intravenous injection of Ketamine. Combination of painkilling abilities of these to medicines yielded more after-operation pain reduction [8]. This combination was again studied by El Sonbatay et al. (2011) in Egypt, in which the result showed that it provides a significant pain relief after operation [12].

In a study conducted by Safavi et al. (2012) effects of intravenous injection of Ketamine and dexamethasone, both separately and as a compound, on after-operation pain relief were analyzed. The results that single-dose intravenous injection of profligacy dexamethasone while compounded with Ketamine is more effective than separate use of intravenous Ketamine and dexamethasone which has an obvious difference with our study of Ketamine. One hour after operation there is a significant difference between Ketamine group compounded with dexamethasone and Ketamine group alone, but in our study this difference was insignificant. Tonsillectomy can damage tissues around tonsil. As a result, chronic inflammation responses in tissues surrounding tonsil are triggered which can lead to pharyngeal tissues spasm and irritability of nerves end. Thus, this damaged tissue disrupt the balance in swallowing mechanism and cause dysphagia and pain. If in aforementioned effects, tissue damages are stopped, Normal physiological mechanisms are stabilized. Glucocorticoids can decrease degree of inflammation by decreasing levels of bradykinin, prostaglandin and leukotrienes. Decrease of inflammation responses can decrease symptoms and pains. As a result effect of dexamethasone-Ketamine combination on after-operation pain relief is evident due to decrease in level of inflammation [24].

## CONCLUSION

The results show that topical injection of Bupivacaine in tonsils provide better pain relief in comparison to Ketamine, although this finding was insignificant statistically. As both medicine are effective in pain relief after operation and with regard to previous studies, it seems that combination of these 2 medicines is an effective way to quell chronic pain after operation but still further studies are required.

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