Evaluation of the effect of Bupivacaine (Marcaine) in reducing early post tonsillectomy pain

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ABSTRACT

الأهداف: تقييم مدى فعالية عقار بُوبيفاكايين وذلك كتخدير موضعي من أجل تخفيف الآلام المصاحبة لعملية استئصال اللوزتين جراحياً خلال 24 ساعة بعد إجراء العملية.

الطريقة: أُجريت هذه الدراسة الاستطلاعية العشوائية المغشاة من طرف واحد باستخدام الغفل في قسم الأنف والأذن والحنجرة، مستشفى الملك عبدالعزيز الجامعي، جامعة الملك سعود، الرياض، المملكة العربية السعودية وذلك خلال الفترة من أكتوبر 2009م إلى مارس 2010م. شملت الدراسة 35 مريضاً خضعوا لعملية استئصال اللوزتين بطريقة السكين البادرة. وبعد ذلك تم تخدير أحد الحفر اللوزية بشاش مشبع بعقار البوبيفاكايين وذلك بتركيز 0.25% (مجموعة الدراسة)، واستخدم للحفرة اللوزية الأخرى شاش مشبع بمحلول ملحي طبيعي (مجموعة الشاهد) بغرض المقارنة بين الجانبين. ولقد قمنا بوضع كلي نوعي الشاش لمدة 5 دقائق، وتم تقييم الألم لدى المرضى في كلي الجانبين باستخدام المقياس التماثلي البصري وذلك عند الساعة 2، و4، و6، و12، و24 بعد الخضوع للعملية الجراحية.

النتائج: أشارت نتائج الدراسة إلى أن انخفاض مستوى الألم في مجموعة الدراسة على الساعة الثانية والرابعة بعد العملية لم يكن كبيراً من الناحية الإحصائية وذلك بالمقارنة مع مجموعة الشاهد. وبالمقابل فقد كان انخفاض الألم على الساعة 6، و12، و24 في مجموعة الدراسة واضحاً من الناحية الإحصائية وذلك عند المقارنة مع مجموعة الشاهد.

خاتمة: أظهرت هذه الدراسة بأن تخدير الحفر اللوزية بالشاش المشبع بعقار البوبيفاكايين وذلك بتركيز 0.25% يؤدي إلى انخفاض نسبة الألم خلال 24 ساعة الأولى بعد إجراء عملية استئصال اللوزتين.

Objectives: To evaluate the effectiveness of bupivacaine as topically applied in reducing post tonsillectomy pain within the first 24 hours.

Methods: This prospective, randomized, placebo-controlled, intra-individual, single-blind study was conducted at the Otolaryngology Department, King Abdulaziz University Hospital, King Saud University, Riyadh, Kingdom of Saudi Arabia from October 2009 until March 2010. Thirty-five patients underwent cold knife tonsillectomy. One tonsillar fossa was packed with gauze soaked in plain 0.25% bupivacaine, while the other tonsillar fossa was packed with gauze soaked in normal saline (the control side). Both gauzes were applied for 5 minutes. The patients' pain was evaluated on each side using the visual analog scale at 2, 4, 6, 12, and 24 hours post-operatively.

Results: The reduction in pain at 2 and 4 hours was statistically insignificant compared with the control side. However, at 6, 12, and 24 hours post operatively, the reduction of pain was statistically significant.

Conclusions: Topical application of bupivacaine at a 0.25% concentration appears to a considerable degree of analgesia within the first 24 hours post tonsillectomy.

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Tonsillectomy is by far the most common surgical procedure carried out by otolaryngologists worldwide, and mostly in children. Post-operative pain is the most considerable morbidity in addition to its potential sequels of delays in resuming oral intake, which can lead to post-tonsillectomy infection or hemorrhage. For these reasons, otolaryngologists, and researchers have questioned the role of local anesthetics in reducing post-tonsillectomy pain. For instance,

pre-incisional lidocaine infiltration of the surgical site was tried, and was shown to be beneficial in reducing the post-operative pain.[1] However, because of its short half-life, the effect was limited to the immediate post-operative period. Therefore, the need to investigate a long acting agent was raised. Bupivacaine is a long acting local anesthetic agent, and has been studied either as a pre-incisional infiltration or as post-dissection local application. However, its role is controversial; some studies have proved its effect, while others showed no statistically evidence of its benefit. There have also been reported serious complications after infiltration of Bupivacaine in the tonsillar fossa, such as bilateral vocal cords paralysis, and cervical osteomyelitis.[2] In our paper, we aim to prospectively examine the role of Bupivacaine 0.25%, as a local application to the tonsillar fossa after dissection, in reducing early post-tonsillectomy pain.

Methods. This prospective, randomized, placebo-controlled, intra-individual, single-blind study was conducted at the Otolaryngology Department, King Abdulaziz University Hospital, King Saud University, Riyadh, Kingdom of Saudi Arabia from October 2009 until March 2010. The Institutional Review Board of the College of Medicine, King Saud University approved the study, and the principles of the Helsinki Declaration were applied. Informed consent was obtained from each patient or patient's guardian. It was of an intra-individual design (one tonsillar fossa was the tested side, while the other fossa was the control side). To reinforce the randomization, the tested and control sides were selected based on the last digits in the patients medical records number; namely, if the last digit was even then the tested side was the right, and if the last digit was odd then the tested side was the left. The inclusion criterion was all patients undergoing tonsillectomy in the assigned period of data collection. While the exclusion criteria included: history of unilateral peritonsillar abscess, the current regular use of a systemic steroid or nonsteroidal anti-inflammatory drugs, known hypersensitivity to Bupivacaine, tonsillectomy combined with unilateral myringotomy, poor dental hygiene, or asymmetrical tonsillar enlargement.

After completing the classical cold knife tonsillectomy and achieving hemostasis by electrocautery as needed, the tested tonsillar fossa was packed with a Bupivacaine soaked gauze (Marcaine™, Bupivacaine Hydrochloride Injection, USP, 0.25%, 2.5 mg/mL, Lake Forest, IL 60045, USA); 4ml of 0.25% concentration was used. The controlled tonsillar fossa was packed with normal saline soaked gauze. Both packs were applied for 5 minutes. Post-operatively, pain was evaluated at 2, 4, 6, 12, and 24 hours. Pain was evaluated on each side by a visual analog scale as follows: 0 (no pain), one (hurts a little bit), 2 (hurts a little more), 3 (hurts even more), 4 (hurts whole lot), and 5 (the worst pain ever). The same surgeon carried out all operations, and the tested sides were blinded to the patients and the person who evaluated the pain.

Data were analyzed using McNemar's test to measure (Excel, Versions: 9x/Me/NT/2000/XP/Vista/Win7), and a p-value was set <0.05. The mean and standard deviation were calculated for the control and tested side as well.

Results. After applying the exclusion criteria, 35 patients were included in the study. Ages ranged from 3-53 years (mean 10.3 years). Twenty-three patients were male (66%), and 12 patients were female (34%). The most common indication for surgery was recurrent tonsillitis (82%), and tonsillectomy accompanied with adenoidectomy was carried out in 24 patients, tonsillectomy alone in 7 patients, and adenotonsillectomy with bilateral myringotomy in 4 patients. The tested side (Bupivacaine) was the right tonsillar fossa in 19 patients (54%), and the left tonsillar fossa in 16 patients (46%). Pain was evaluated at 2, 4, 6, 12, and 24 hours post-operatively. The reduction in pain at 2 (p=0.078) and 4 (p=0.146) hours was statistically insignificant compared with the control side. However, at 6 (p=0.024), 12 (p=0.001), and 24 (p=0.001) hours post-operatively, the reduction of pain in the tested side compared with the control side was statistically significant. For the control side, the results of the pain evaluation (Mean±SD) at 2 hours was 3.25±0.70, at 4 hours was 3.0±0.87, at 6 hours was 2.77±0.84, at 12 hours was 2.69±0.76 and at 24 hours was 2.09±0.95, while the results of the tested side at 2 hours was 3.23±0.77, at 4 hours was 2.97±0.71, at 6 hours was 2.71±0.83, at 12 hours was 2.60±0.69 and at 24 hours was 1.97±0.95. None of the patients were complicated by post-tonsillectomy bleeding or infection, all were discharged from the hospital on the first post-operative day, and all showed normal recovery during out-patient follow up.

Discussion. Bupivacaine hydrochloride is available either as a plain solution or mixed with epinephrine 1:200,000. It can be used for local infiltration,

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peripheral nerve block, and lumbar epidural block. For local infiltration, the recommended concentration is 0.25% (2.5mg/ml). Its usage is contraindicated in cases of known hypersensitivity to Bupivacaine or to any amide-type local anesthetic agents. Its mechanism of action is by binding to the intracellular portion of sodium channels and blocking sodium influx into nerve cells, which prevents depolarization. Bupivacaine has a duration of action of approximately 200 minutes after local infiltration.[3]

In our results, at 2 and 4 hours post-operatively the pain reduction was not statistically significant; however, later at 6, 12, and 24 hours this reduction was significant. This may be explained as in the early post-operative hours patients could still be drowsy from the general anesthesia, affecting their input in pain evaluation. However, after fully awakening, their contributions became more accurate.

In this study, we used the same subjects as case and controls, which can eliminate the variation in pain tolerance between different individuals. However, 35 patients may be considered a small sample, which could be one of the limitations of our trial. In addition, our sample included pediatric individuals, which could be considered as another limitation, especially for the accuracy of pain evaluation.

Kader et al[2] conducted a prospective, intra-individual study design on 72 patients. They packed one tonsillar fossa with a (0.5% concentration) plain Bupivacaine soaked swab for 5 minutes and the other tonsillar fossa was packed with a normal saline soaked swab for 5 minutes. Thereafter, pain was evaluated within the first 24 hours, and their results showed a statistically significant pain reduction in the Bupivacaine packed side. They concluded that topical application of Bupivacaine in a 0.5% concentration is effective in reducing post tonsillectomy pain. In our study, our results showed that an even lower concentration of Bupivacaine (0.25%) was effective in providing post tonsillectomy analgesia. It is worth noting that there is no statistical evidence that Bupivacaine in a 0.25% concentration provides the same degree of analgesia as a 0.5% concentration.

In 1993, a prospective double blind trial (including 22 children) was conducted to evaluate pre-incision Bupivacaine infiltration compared with placebo in pain reduction for 10 days.[4] They found that pre-dissection local nerve blockade by Bupivacaine infiltration reduces short- and long-term pain in children undergoing tonsillectomy. The theory behind pre-incision infiltration is that the local anesthetic is thought to act by impeding noxious stimulation of C-fiber afferent neurons, thereby diminishing the excitability of the dorsal horn neurons. The excitability produced by nociceptive stimuli may contribute to postoperative pain, even when procedures are performed under general anesthesia.[5]

Also, a comparison was carried out between infiltration of Bupivacaine and topical application in 1995. As a clinical trial of 43 children compared Bupivacaine 0.5% with epinephrine 1:200,000 as infiltration in peri-tonsillar fossa after tonsillectomy (group 1), and Bupivacaine 0.5% with epinephrine as spray to the tonsillar bed after tonsillectomy (group 2), and group 3, the control group, using normal saline spray to the tonsillar bed after tonsillectomy, and found that peri-tonsillar Bupivacaine infiltration was superior in providing postoperative analgesia.[6]

In contrast, Grainger and Saravanappa,[7] published a systematic review and meta-analysis evaluating the usage of Bupivacaine in providing analgesia post tonsillectomy. They included 13 studies in their meta-analysis, and concluded that overall, either topical application or infiltration of Bupivacaine, can significantly reduce pain scores. In addition, they found that the topical application method appears to provide an equal level of analgesia compared with infiltration of Bupivacaine. However, the former will be without the potential adverse effects. Finally, they recommended topical application of Bupivacaine as the method of choice for providing additional post-operative analgesia.

Generally, most of the clinical trials used Bupivacaine in a 0.5% concentration. However, in1994 a clinical trial was conducted using Bupivacaine in a 0.25% concentration. They prospectively compared pre-incision Bupivacaine infiltration, post-operative Bupivacaine infiltration, and pre-incision normal saline infiltration and found no statistically significant differences between all 3 groups.[8]

In contrast, a recent large clinical trial concluded different results. Moss et al[9] prospectively evaluated the effectiveness, in pain reduction post-tonsillectomy, of lidocaine plus Bupivacaine compared with placebo, when used as a pre-incision injection, and found that local anesthetic agents have no role in post-tonsillectomy pain reduction.

As a clinical implication of this paper, in classical tonsillectomy after dissecting the tonsil from the tonsillar bed, swab packing is commonly used to achieve hemostasis. Therefore, by using a swab soaked in Bupivacaine, the surgeon could achieve both goals of controlling hemostasis and providing analgesia.

Lastly, we suggest further research on the quantitative usage of analgesia post-tonsillectomy with and without Bupivacaine application, or the effect of application of Bupivacaine on the duration needed to resume oral feeding post tonsillectomy. In addition, further research on the cost effectiveness of Bupivacaine application is needed, as well as a clinical comparison between Bupivacaine in a 0.25% and 0.5% concentration in the degree of analgesia provision.

In conclusion, the application of plain Bupivacaine in a 0.25% concentration to the tonsillar fossa after tonsillectomy appears to be effective in reducing post-tonsillectomy pain within the first 24 hours.

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