Post-tonsillectomy infiltration with bupivacaine reduces immediate postoperative pain in children

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Pain management after tonsillectomy in children remains a dilemma for the anaesthetist. A previous study demonstrated that the administration of lidocaine 1% topical spray to the peritonsillar fossae before tracheal extubation provided considerable immediate postoperative pain relief in infants and children. However, the pain relief was of short duration. We were hopeful that the use of bupivacaine would offer more prolonged pain relief because of its pharmacological characteristics. Therefore, this study was designed to compare the effects of bupivacaine 0.5% with 1:200,000 epinephrine administered after tonsillectomy either as topical spray or submucosal infiltration on postoperative pain in children. Forty-three patients aged two to ten years were randomized into three groups after tonsillectomy was performed. Group (1) received 0.5 ml · kg^{-1} normal saline spray; (2) received 2 mg · kg^{-1} bupivacaine 0.5% with 1:200,000 epinephrine peritonsillar infiltration in a similar volume to Group 1 and; (3) received 2 mg · kg^{-1} bupivacaine 0.5% with 1:200,000 epinephrine spray to both tonsillar beds. The patients in each group were compared postoperatively with regard to the quality of pain control using the Objective Pain Score, and their analgesic requirements. Peritonsillar infiltration of bupivacaine provided superior immediate postoperative analgesia as reflected by lower recovery room pain scores ($P < 0.05$) and opioid requirements ($P < 0.01$). Ward pain scores and analgesic requirements were similar among groups. Peritonsillar infiltration of bupivacaine 0.5% with 1:200,000 epinephrine provides better post-tonsillectomy pain control in the immediate postoperative period than bupivacaine spray or placebo.

La gestion de la douleur après l'amygdalectomie chez l'enfant constitue pour l'anesthésiste un problème complexe. Une étude antérieure à montré que l'administration de lidocaïne topique à 1% en vaporisation sur la fosse périamygdalienne immédiatement avant l'extubation procurait un soulagement notable et immédiat de la douleur postopératoire chez l'enfant. Cependant, le soulagement était de courte durée. Les auteurs ont cru que la bupivacaïne offrirait un soulagement de plus longue durée à cause de ses caractéristiques pharmacologiques. Cette étude a donc été entreprise pour comparer les effets sur la douleur postamygdalectomie de l'administration de bupivacaïne à 0,5% adrénalinée à 1:200,000 soit en vaporisation topique, soit en infiltration sous-muqueuse. Quarante-trois jeunes patients de deux à dix ans ont été répartis au hasard en trois groupes après l'amygdalectomie. Le groupe 1 a reçu 0,5 ml · kg^{-1} de soluté physiologique en vaporisation; le groupe 2 a reçu 2 mg · kg^{-1} de bupivacaïne 0,5% adrénalinée à 1:200,000 en infiltration périamygdalienne en volume identique aux groupes 1 et 3; le groupe 3 a reçu 2 mg · kg^{-1} de bupivacaïne 0,5% adrénalinée à 1:200,000 en vaporisation sur les deux fosses amygdaliennes. Les patients de chaque groupe ont été comparés au regard de la qualité du contrôle de la douleur avec un score de douleur objectif et leurs besoins en analgésique. L'infiltration périamygdalienne de bupivacaïne 0,5% adrénalinée à 1:200,000 a procuré une meilleure analgésie comme l'ont démontré, en salle de réveil, des scores de douleur moins élevés ($P < 0,05$) et des besoins de morphiniques moins prononcés ($P < 0,01$). Au retour dans le service, les scores de douleurs et les besoins analgésiques sont été les même pour les groupes. L'infiltration périamygdalienne de bupivacaïne 0,5% adrénalinée à 1:200,000 procure un meilleur contrôle de la douleur périamygdalienne à la période postopératoire immédiate que la bupivacaïne en vaporisation ou le placebo.

Key words
ANAESTHETICS, LOCAL: bupivacaine;
ANAESTHESIA: paediatric;
PAIN: postoperative;
SURGERY: ENT, tonsillectomy.

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Tonsillectomy was described by Penn in 1952 as "... an operative procedure which ... may lead to apathy on the part of the physician ... Postoperative pain and its sequelae are amongst universal complaints of the patients. The rapid advances in anaesthetic and surgical techniques have left this factor as one of the most distressing aspects of the entire procedure."[1] He also emphasized that post-tonsillectomy pain in children remains a most difficult management problem.[1] The oropharynx and the tonsillar fossae are exquisitely sensitive. They are well innervated locally by the branches of the trigeminal and glossopharyngeal nerves and are highly represented in the somatic cerebral cortex. Many treatment modalities for post-tonsillectomy pain have been used, ranging from systemic opioids to different surgical techniques, even radiation.[2-5] Because of the absence of any respiratory depressant effect there has been a renewed interest in local anaesthetic techniques in children as an effective means of postoperative pain control.[6-7]

A previous study utilizing lidocaine 1% topical spray, 4 $mg \cdot kg^{-1}$ evenly distributed on the tonsillar beds, showed considerable improvement in pain scores in the immediate postoperative period after tonsillectomy when compared with codeine 1.5 $mg \cdot kg^{-1}$ *im.*[8] Bupivacaine should be more effective because of its longer duration of action. In addition, it has been suggested that the topical use of this local anaesthetic following tonsillectomy was effective in reducing postoperative pain.[9]

The purpose of this study was to compare the efficacy of bupivacaine 0.5% with 1:200,000 epinephrine on postoperative pain in children when administered after tonsillectomy either by a topical spray or submucosal infiltration.

Methods

Following approval from the Human Subjects Review Committee and after informed written parental consent was obtained, 43 children aged two to ten years, ASA physical status 1-2, scheduled for elective tonsillectomy and adenoidectomy, were studied. Exclusion criteria included the presence of known allergy to bupivacaine.

All patients were fasted and unpremedicated. Routine monitoring devices (ECG, blood pressure cuff, radial Doppler probe. oxygen saturation monitor, end-tidal CO_2 and temperature probe) were used. Induction of anaesthesia was performed with *iv* administration of atropine 0.02 $mg \cdot kg^{-1}$ and thiopentone 5 $mg \cdot kg^{-1}$. Succinylcholine 2 $mg \cdot kg^{-1}$ was used to facilitate tracheal intubation. Anaesthesia was maintained with 70% nitrous oxide to oxygen and isoflurane. All children were allowed to breathe spontaneously throughout the surgical procedure.

At completion of the tonsillectomy and after haemostasis was achieved, children were randomly allocated by means of code numbers to one of three groups: Group (1) received 0.5 $mg \cdot kg^{-1}$ normal saline spray; (2) received 2 $mg \cdot kg^{-1}$ bupivacaine 0.5% with 1:200,000 epinephrine by peritonsillar infiltration; and (3) received 2 $mg \cdot kg^{-1}$ bupivacaine 0.5% with 1:200,000 epinephrine spray to both tonsillar beds. The infiltration or spray solution was prepared in a room separate from the surgical suite and only the attending anaesthetist knew what solution was administered. The infiltration was performed by RMM. The volume of solution given was similar in each group. Five minutes elapsed before obtaining the first blood sample. All patients had their tracheas extubated when awake and with intact gag reflex and were transferred to the post-anaesthetic recovery room.

In the recovery room, comfort level in all patients was assessed using the Objective Pain Scale (OPS)[10] by a nurse who was unaware of the treatment that each had received. Assessments were performed at the time of admission, at 30 min and immediately before discharge from the post-anaesthetic recovery area. Codeine 1.5 $mg \cdot kg^{-1}$ *im* was given for an OPS ≥ 6 and acetaminophen 15 $mg \cdot kg^{-1}$ *pr* was given for any OPS ≤ 5. The pain assessments were continued on the ward every four hours until discharge from hospital the next day.

In each patient, blood samples for systemic bupivacaine concentrations were drawn at 5, 10, 15, 30 and 60 min following the administration of bupivacaine or placebo. The analysis of the bupivacaine plasma concentration was performed by a relatively simple and rapid method of determination of serum or plasma levels of bupivacaine concentration using high-pressure liquid chromatography (HPLC).[11,12] Most published methods for the determination of bupivacaine in blood use gas-liquid chromatography. Its accessibility is limited because of the complexity of the equipment required and the expertise for this technique is not widely available. The HPLC method shows excellent precision. The assay for quantitation of bupivacaine is linear to 5 $mg \cdot kg^{-1}$. The lower limit of detection which is obtained by replicate analysis of extracted standards in the range 0 to 0.25 $mg \cdot L^{-1}$ is 0.025 $mg \cdot L^{-1}$. The coefficient of variation for between-run assay imprecision is 5.4%. The efficiency of extraction (% recovery) for bupivacaine is 98% (±8%) at 0.1 $mg \cdot L^{-1}$.

Statistical analysis

Data with parametric values are expressed as mean ±SD. Based on a previous study performed in children[8] the sample size (d) determination was obtained from a power analysis calculation. For an alpha value of 0.05 and a beta value of 0.20, the calculated number of patients to reject the null hypothesis was 15 per group. Demographic

data and the differences among the groups for postoperative analgesic requirements and blood loss at each stage were compared using one-way ANOVA and the Student-Newman Keuls for multiple comparison. The Kruskal-Wallis test was used to compare the groups with respect to the recovery room and ward pain scores. $P < 0.05$ was accepted for statistical significance.

Results

There were no differences in age, weight, sex or volume of solution administered among the three groups. Peritonsillar infiltration of bupivacaine provided superior postoperative analgesia to placebo (Group 1) and bupivacaine spray (Group 3) as indicated by a lower average recovery room admission score of 4.8 compared with 7.8 and 7.4 respectively ($P < 0.05$) (Figure 1). Furthermore, the children who had received peritonsillar infiltration of bupivacaine were given less opioids than the other groups ($P < 0.05$) (Figure 2). Objective pain scores at the time of recovery in the postanaesthetic recovery room were similar among the three groups ranging between 2.4 and 3.6. Pain scores on the ward were no different (Figure 3). There were no differences among the three groups with respect to the amount of acetaminophen administered postoperatively. Finally, there were no differences in the blood loss recorded amongst the groups. Although the mean bupivacaine plasma concentration was higher in the patients receiving submucosal infiltration ($0.56 \pm 0.26\ \mu g \cdot ml^{-1}$) than in those receiving topical spray ($0.19 \pm 0.22\ \mu g \cdot ml^{-1}$) ($P < 0.05$), they were well below the toxic range of $1.5\ \mu g \cdot ml^{-1}$ in all patients studied.

There were no complications as a result of this study.

Discussion

This study shows that post-tonsillectomy infiltration of bupivacaine 0.5% with 1:200,000 epinephrine reduces immediate postoperative pain in children compared with a similar concentration of bupivacaine administered by spray or placebo.

Although the use of *im* codeine was less in the bupivacaine infiltration group, pain scores on discharge from the recovery room were not different from the other groups. This would suggest that the clinical analgesic effect of the infiltrated bupivacaine after tonsillectomy is limited to less than one hour, after which time assessment may have become unreliable.

Recently, Jebeles showed that in patients who had peritonsillar infiltration with bupivacaine before surgical stimulation there was less pain with the placebo even on the tenth postoperative day.[13] Although the duration of action of bupivacaine is usually limited to a few hours, it was suggested that this long-lasting pain relief might have been related to the phenomenon of neuroplasticity.

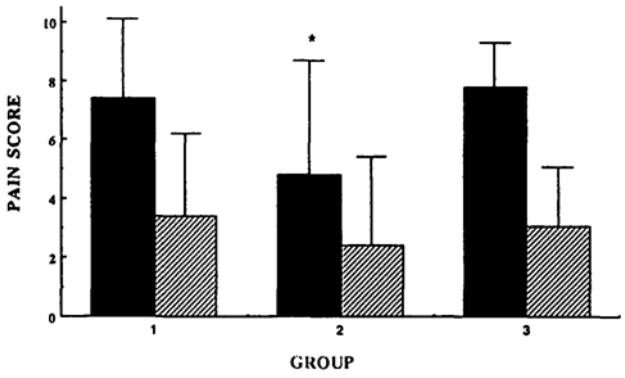

FIGURE 1 Pain score upon arrival at the recovery room and at discharge. The pain score is different between patients receiving bupivacaine 0.5% with 1:200,000 infiltration and the other two groups ($P < 0.05$). ■ Pain score on admission to the post-anaesthetic recovery room, □ discharge pain score.

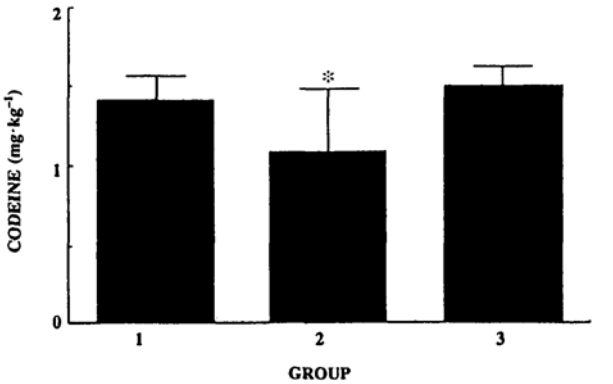

FIGURE 2 The postoperative use of codeine was less in patients receiving peritonsillar infiltration of bupivacaine.

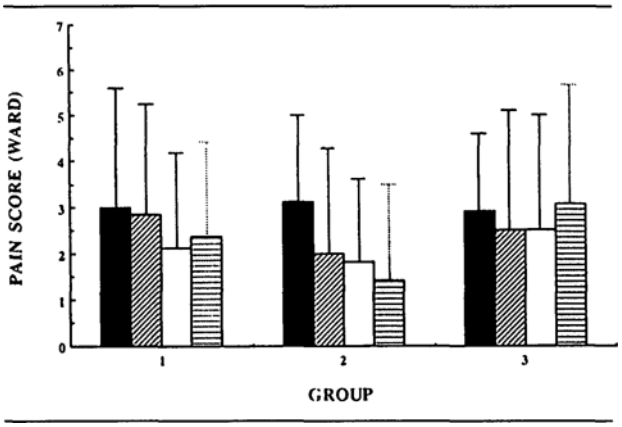

FIGURE 3 The level of pain on the ward was not different among the groups between discharge from the recovery room and up to twelve hours postoperatively. The time after discharge is presented by: ■ 0 hr; □ 4 hr; □ 8 hr and □ 12 hr.

This theory proposes that the pre-emptive blockade of the release of nociceptive neuromediators may contribute to the elimination of the hyperexcitable state responsible for the maintenance of postoperative pain.[14] Therefore, one may speculate that the shorter analgesic effect observed with patients receiving bupivacaine 0.5% with 1:200,000 epinephrine by submucosal infiltration is due to the administration of the local anaesthetic after the surgical stimulation.

The infiltration of the peritonsillar beds for post-tonsillectomy pain control was suggested in 1953 by Allen.[2] He used a solution called "efocaine" which consisted of procaine 1%, procaine hydrochloride 1% and butylaminobenzoate 5% in a solvent composed of polyethylene glycol 300 2% and propylene glycol 78%. A solution initially used for postoperative pain control following haemorrhoidectomy, it proved to be inappropriate due to major allergic reaction. As the same time, a solution known as Smith's solution consisting of a mixture of penicillin-lidocaine-methylprednisolone suspension, was used on 800 patients to infiltrate the tonsillar beds.[15] The advantages of this solution were believed to be related to a high diffusibility and prolonged duration of action without the toxicity of the previous one. Although, at the time, clinical reports were favourable about this technique of postoperative pain relief[15] it became necessary to describe the possible hazards associated with the infiltration of this pain-relieving medication. Subsequently, in a report of 1,086 patients receiving Smith's solution, the possible complications were described.[16] Although it was used safely in this study, several possible complications including inadvertent intravascular or intra-arterial (carotid artery) injection leading to central nervous system and cardiovascular toxicity, haemorrhage, airway obstruction, allergy, vocal cord paralysis and mucosal sloughing were related to its administration. The result of the present series demonstrates that it is essential that the administration of the local anaesthetic be performed by a knowledgeable person. The safest site is just underneath the anterior pillar in the mid portion of the tonsillar bed which corresponds to the farthest distance from the vessels.

The administration of bupivacaine 0.5% with 1:200,000 epinephrine either by submucosal infiltration or as spray on traumatized tissue did not lead to an increase in blood concentrations to toxic levels. The systemic concentration of bupivacaine measured was well below the toxic level of 1.5 $\mu g \cdot ml^{-1}$ confirming that at this dosage and with the concomitant use of 1:200,000 epinephrine, the absorption was limited. This study suggests that both careful administration as well as the addition of epinephrine may contribute to reduce the systemic absorption of bupivacaine.

Another possible clinical disadvantage of the use of a local anaesthetic in the peritonsillar area includes an increase in bleeding caused by induced vasodilatation. None of the three groups studied showed a measurable increase in blood loss.

Finally, the potential risk of postoperative airway difficulties due to inhibition of the laryngeal reflex mechanisms and the possible dysfunction of the airway protective system as a result of the effect of bupivacaine were not encountered. All patients had their tracheas extubated once they were clinically awake after confirmation that the laryngeal reflexes were intact. There were no episodes of laryngospasm, delayed emergence from anaesthesia or pulmonary aspiration.

In summary, post-tonsillectomy pain remains a considerable clinical problem in children. The ideal analgesic should be effective, safe, easy to administer, and free from respiratory depression. In this study, peritonsillar infiltration of bupivacaine 0.5% with 1:200,000 epinephrine appears to be an effective method of providing superior analgesia in the immediate postoperative period when compared to topical bupivacaine spray or placebo. In addition, adequate postoperative pain control may include the blockade of nociceptive transmission to the brain immediately before the beginning of the surgical procedure. Elective tonsillectomy and adenoidectomy are being increasingly performed as outpatient procedures which implies that the use of a regional anaesthesia technique for postoperative pain control may be the most useful new approach for investigation in further studies.

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