Does Topical Anesthetic Reduce Pain During Intraosseous Pin Removal in Children? A Randomized Controlled Trial

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Background: The purpose of this study was to determine the effectiveness of topical liposomal lidocaine in reducing the pain perceived by children undergoing percutaneous intraosseous pin (PP) removal in the outpatient orthopaedic clinic.

Methods: A triple-blinded, randomized, placebo-controlled clinical trial comparing topical liposomal lidocaine to a placebo was conducted at the Stollery Children’s Hospital between September 2008 and February 2011. Subjects undergoing the removal of PP in the orthopaedic outpatient clinic between ages 3 and 16 years were recruited. A computer-generated variable-block randomization scheme was used to determine each subject’s group assignment. Pain was recorded just before randomization and immediately after the procedure using the Oucher Scale (for subjects) and a 10-cm Visual Analog Scale (for parents and an observing orthopaedic technician). In a subset of individuals, follow-up telephone calls were made 24 hours postprocedure to inquire about any adverse event from the use of the topical liposomal lidocaine. Data were analyzed using the Student t test.

Results: Of a total of 296 recruited subjects, complete data were available on 281 subjects (140 intervention and 141 control). There were no significant differences between the 2 groups with regards to baseline characteristics, including preprocedure pain scores. Although postprocedure pain scores demonstrated an increase in pain in both groups (2.3 points in the treatment group and 2.0 points in the placebo group), no statistically significant difference was seen in postprocedure pain scores between groups (P = 0.81). No adverse events were observed or reported.

Conclusions: Topically applied liposomal lidocaine was not effective in reducing pain during this procedure, compared with a placebo. However, this study demonstrates that PP removal is a painful procedure in children. Given the large volume of patients who undergo this procedure and the long-term consequences of experiencing painful procedures in childhood, it is important to find safe and fast-acting methods to decrease procedural pain associated with PP removal.

Level of Evidence: Level I—therapeutic trial.

Key Words: procedural pain, pediatric orthopaedics, percutaneous pins, topical anesthetic or analgesic, liposomal lidocaine

Smooth intraosseous percutaneous pins (PP) are commonly used to stabilize osseous structures after orthopaedic surgery in children, including fractures. Once adequate healing is present, these pins are usually removed in the outpatient clinic without analgesic administration. However, this procedure has been reported as painful by over 90% of children and adults, with up to 2% of patients experiencing sufficient pain to require general anesthesia.1–4 Although the pain experienced appears short lived,1,4 long-term sequelae of poorly controlled procedural pain ranges from increased pain and analgesic requirements with subsequent medical procedures,5–7 to health care avoidance and needle phobias in adulthood.8–10 As such, minimization of procedure-related pain in pediatric care is an important consideration for both health promotion and ethical reasons.

Options to reduce the pain associated with this procedure include the use of oral analgesics, distraction therapy, local anesthetics, and systemically administered sedatives or anesthetics.1,3,11 Previous studies evaluating the efficacy of oral analgesics have cited issues with the longer onset of action, poor patient compliance, and failure to provide significant analgesic benefit.1,3 In contrast, both distraction therapy (eg, role playing, clowns, music therapy, etc.) and procedural sedation (eg, entonox gas) have been shown to be effective in reducing procedural pain; however, the required resources and monitoring make these methods more costly and less practical options.1,3,11 The efficacy of topical anesthetic preparations has been previously demonstrated in various percutaneous procedures including venipuncture, intravenous catheterization, circumcision, lumbar punctures, bone marrow aspirations, dermatologic procedures (eg, skin graft harvesting), dental wire removals, and various otolaryngology and urology procedures.12–15

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Lidocaine is the most commonly used topical anesthetic but due to its hydrophilic properties, it is combined into either a eutectic mixture or encased within a micro-phospholipid vesicle so that it can penetrate the epidermis and become topically absorbed. The efficacy and safety profile of liposomal lidocaine is well established, with the most common reported adverse effects being localized skin reactions. However, to our knowledge, no previous studies have investigated the use of topical anesthetics such as lidocaine for pain relief during percutaneous introsseous pin extraction in children.

The primary purpose of this study was to evaluate the efficacy of a fast-acting topical preparation of liposomal lidocaine in reducing the pain experienced by pediatric patients during PP extraction in the orthopaedic clinic. The secondary study objectives were to evaluate the magnitude of pain reported during the removal of PPs and to examine the impact of age, pin locations (upper vs. lower limb), mechanism of injury, duration for which the pins were in situ, and time from topical anesthetic administration to pin removal, on reported pain levels.

**METHODS**

**Design**

A single-centre, triple-blinded, randomized clinical trial comparing the efficacy of topical liposomal lidocaine to a placebo control for reducing pain experienced during PP removal in the outpatient setting was conducted between September 2008 and February 2011 at the Stollery Children’s Hospital (Edmonton, Canada). CONSORT guidelines were followed in undertaking and reporting of this trial. Enrollment continued until the predetermined sample size was obtained.

Computer-generated variable-block randomization was used for group allocation. Tubes of topical ointment were blinded (tube contents were not identifiable) and sequentially numbered as per randomized allocation. Study randomization occurred in the orthopaedic outpatient clinic following consent of subjects and/or their parents by the pediatric orthopaedic nurse practitioner or orthopaedic clinical nurse or orthopaedic research assistant. This study was approved by the Health Research Ethics Board of the University of Alberta. This randomized control trial was registered with clinicaltrials.gov (NCT01542125).

**Sample Size**

An a priori sample size calculation determined that 264 subjects (132 per group) were required for a non-inferiority analysis that would detect a difference of >10% with 90% power and an α error of 0.05. This was based on a conservative assumption that a difference of <20% would not likely be clinically meaningful, but that minimally important differences would not be missed. We aimed to recruit 300 subjects to allow for 10% attrition and unexpected variability in outcome measurements.

**Subjects**

Subjects aged 3 to 16 years presenting to the pediatric orthopaedic clinic for removal of smooth (ie, nonthreaded) PPs were eligible. Parents provided consent for all subjects, but subjects older than 10 years also provided signed assent. The age interval was selected based on the appropriateness of the employed Visual Analog Scales (VAS) to reliably allow self-reporting of pain. Younger children are not able to demonstrate adequate cognitive ability to participate in self-reporting, and patients older than 16 years of age were outside the normal range of the pediatric population being studied.

Exclusion criteria included contraindications to topical anesthetic (ie, evidence of infection at the pin site or of surrounding dermalatoma area; known allergy or adverse reaction to lidocaine), failure to obtain study consent/assent, language barriers, or developmental delay that could prevent comprehension and/or completion of the outcome measurement, known history of neurological impairment/abnormalities, analgesic or anxiolytic use within the past 24 hours, and requirement of general anesthetic for PP removal.

**Procedure**

Before randomization, baseline information [age, sex, number of PPs, time since pin insertion, mechanism of injury, and reason for pin insertion (ie, fracture, osteotomy, joint fusion)] were collected. Contact information was also obtained for a telephone call at 24-hour postpin removal to document any late-presenting adverse events.

A baseline assessment of pain before pin removal was performed. The Oucher Scale was used for pediatric subjects, whereas their parent(s) and the orthopaedic technician were asked to independently record their assessment on a 10-cm VAS.

As per standard practice, after removing the cast/splint and dressing from the affected limb, the skin around the insertion site(s) and the exposed portions of the pins was prepared with an antimicrobial solution. According to group assignment, liposomal lidocaine or placebo was applied to the area immediately surrounding the pin site(s) by the pediatric orthopaedic nurse practitioner and the site was then covered with a Tegaderm dressing. Sufficient liposomal lidocaine was applied to cover the site, but did not exceed 2.5 g (half a tube), as recommended by the manufacturer (RGR Pharma, La Salle, ON; Ferndale Laboratories Inc., Ferndale, MI). The creams and tubes for both liposomal lidocaine and placebo were visually identical, and identified by a unique number. Application of the topical cream (liposomal lidocaine or placebo-control) was performed 30 to 60 minutes before PP extraction. All raters were blinded to group allocation.

PPs were removed by the pediatric orthopaedic nurse practitioner as per usual standard of care. Immediately following pin removal, subjects, the same parent, and orthopaedic technician who completed the preprocedural pain assessment independently rated the subject’s pain using the Oucher scale or VAS assessment, as appropriate.
Outcome Measures

The Oucher Scale is used to assess pain intensity in children as young as 3 years old, and includes 2 separate scales. One scale is a series of 6 photographs showing a child in varying degrees of discomfort, which is used by children who are still unable or unfamiliar number scales. In contrast, children who are able to count to 100 by ones or tens, and who can identify the larger of 2 numbers, use the vertical numeric scale (0 to 100) that is printed next to the faces. The Oucher Scale has been shown to be a valid reliable tool, and has been shown to have a strong correlation with the VAS for pain ($r = 0.89, \ P < 0.01$).\textsuperscript{24,25} The VAS is a reliable and validated method of pain measurement, consisting of a horizontal 100-mm line, where “0” means “no pain” and “100” means the worst possible pain.

The primary outcome of interest was the difference in pain scores between the 2 groups as assessed by the VAS and Oucher scales immediately following pin removal. Secondary outcomes were changes within groups in pain measures before and immediately after pin removal.

Analysis

After the generation of descriptive statistics, independent $t$ tests were used to identify differences in baseline characteristics and to assess for differences in preprocedure and postprocedure pain ratings between the 2 groups. Paired $t$ tests were used to compare preprocedure and postprocedure pain ratings within groups. A priori determined subgroup analyses were performed to assess for the effects of variables identified as potential confounders. These included the subject’s age, pin location (upper vs. lower limb), mechanism of injury, duration that the pins were in situ, and the length of time between cream application and pin removal.

Results

Subjects

A total of 480 children were screened of which 296 subjects were eligible and agreed to participate (Fig. 1). Complete outcome data were collected on 281 subjects, of whom 140 were allocated to the treatment group and 141 were allocated to the placebo group (Fig. 1).

Males comprised the majority of subjects and ages ranged from a minimum of 2 to a maximum of 16 years (Table 1). Fractures were the most common reason for pin insertion, with elective procedures (osteotomy/fusion) only accounting for 2.5% of cases. Falls and accidents accounted for $>75\%$ of the injuries (Table 1). The majority of subjects had $<3$ pins that had been in place for 28 days on an average (Table 1).

Topical Anesthetic Compared With Placebo

Almost all patients, parents, and orthopaedic technicians, rated the subject’s pain as minimal before pin removal (Fig. 2). No significant differences were found among postprocedure pain scores as reported by subjects, their parents, and the orthopaedic technicians (Table 2). No adverse events were reported from the use of liposomal lidocaine.

Changes in Pain Before and After PP Removal

Comparison of preprocedure and postprocedure pain scores within each group demonstrated a significant increase in pain with pin removal in both the groups (Table 2). On average, children reported a 2.18 (SD =
2.92) increase in pain ($P < 0.001$) and parents reported a 2.10 (SD = 2.72) increase in pain ($P < 0.001$). Interestingly, although orthopaedic technicians also reported a 1.76 (SD = 2.10) increase in pain, this was significantly less than either the parent or children groups ($P < 0.001$).

**Subgroup Analysis**

No statistically significant differences in pain were found between groups when controlling for mechanism of injury ($P > 0.38$), duration of time that the pins were in situ ($P > 0.42$), or site of pin insertion ($P > 0.42$). Further there was no difference for the length of time between lidocaine application and pin removal ($P > 0.41$). Although there were no differences in pain between groups when comparing by subjects’ age ($P > 0.43$), parents were more likely to rate pain higher in younger children ($P = 0.05$) regardless of group allocation ($P = 0.77$). Furthermore, it appears that the longer time pins are in situ, the higher the child’s reported pain score ($P = 0.02$), regardless of group allocation ($P = 0.52$).

**DISCUSSION**

This study did not demonstrate any reduction in reported pain during PP removal in pediatric subjects in the outpatient setting with the use of liposomal lidocaine as compared with a placebo control. Given that this study was powered as a noninferiority trial, our findings suggest that liposomal lidocaine is not effective as an analgesic during PP removal. Although the pain associated with this procedure is commonly believed to originate from cutaneous sources, these study findings may suggest otherwise. Although bone itself is not innervated, it is possible that periosteal innervation contributes to production of noxious sensations during pin removal. Because of the limited depth of absorption, topical anesthetics are not expected to be effective in reducing pain originating from the periosteum. Interestingly, a previous study did find that liposomal lidocaine was effective in reducing the pain associated with bone marrow aspiration, a procedure that would also affect the periosteum. We hypothesize that perhaps the state of

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**TABLE 1. Baseline Characteristics of Liposomal Lidocaine and Placebo Groups**

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>Liposomal Lidocaine</th>
<th>Placebo</th>
<th>$P$</th>
</tr>
</thead>
<tbody>
<tr>
<td>Demographics</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Age [mean (SD; range) (y)]</td>
<td>7.89 (3.71; 2-6)</td>
<td>7.74 (3.74; 2-16)</td>
<td>0.74</td>
</tr>
<tr>
<td>Sex (male/female) [n (%)]</td>
<td>80 (57.1)/60 (42.9)</td>
<td>78 (55.3)/63 (44.7)</td>
<td>0.76</td>
</tr>
<tr>
<td>Reasons for pin insertion [n (%)]</td>
<td></td>
<td></td>
<td>0.37</td>
</tr>
<tr>
<td>Fracture</td>
<td>132 (95.7)</td>
<td>128 (96.2)</td>
<td></td>
</tr>
<tr>
<td>Fusion</td>
<td>3 (2.2)</td>
<td>2 (1.5)</td>
<td></td>
</tr>
<tr>
<td>Osteotomy</td>
<td>2 (1.4)</td>
<td>0 (0)</td>
<td></td>
</tr>
<tr>
<td>Other</td>
<td>1 (0.7)</td>
<td>3 (2.3)</td>
<td></td>
</tr>
<tr>
<td>Mechanism of injury [n (%)]</td>
<td></td>
<td></td>
<td>0.72</td>
</tr>
<tr>
<td>Falls or accidents</td>
<td>103 (74.6)</td>
<td>107 (76.4)</td>
<td></td>
</tr>
<tr>
<td>Sports</td>
<td>16 (11.6)</td>
<td>17 (12.1)</td>
<td></td>
</tr>
<tr>
<td>Motor vehicle accident</td>
<td>11 (8)</td>
<td>6 (4.3)</td>
<td></td>
</tr>
<tr>
<td>Other</td>
<td>8 (5.8)</td>
<td>9 (6.4)</td>
<td></td>
</tr>
<tr>
<td>Not specified</td>
<td>0 (0)</td>
<td>1 (0.7)</td>
<td></td>
</tr>
<tr>
<td>No. pins</td>
<td></td>
<td></td>
<td>0.18</td>
</tr>
<tr>
<td>Mean (SD; range)</td>
<td>2.17 (0.58; 1-4)</td>
<td>2.08 (0.59; 1-4)</td>
<td></td>
</tr>
<tr>
<td>Time of pins in situ</td>
<td></td>
<td></td>
<td>0.82</td>
</tr>
<tr>
<td>Mean (SD; range) (d)</td>
<td>27.31 (8.07; 14-86)</td>
<td>27.09 (8.13; 10-58)</td>
<td></td>
</tr>
</tbody>
</table>

**FIGURE 2.** Comparison of child, parent, and orthopaedic technician pain assessments of treatment and placebo groups, before, and after percutaneous pin (PP) removal.
the periosteum may partly explain this difference. The periosteum is often displaced during orthopaedic procedures, particularly in the setting of fracture management (the most common reason for stabilization with PPs). As a result, it may be in a more reactive state than one would expect during a bone marrow aspiration.

Many orthopaedic surgeons do not use analgesia during pin removal on the assumption that the procedure is not painful enough to warrant analgesia. However, our findings demonstrate a clinically and statistically significant increase in pain during pin removal. Interestingly, we also note a trend for health care professionals (in this case, the orthopaedic technicians) to underestimate the pain experienced by pediatric subjects during the procedure when compared with the subjects and their parents. This tendency may lead health professionals to undertreat pain in pediatric subjects and warrants some consideration during the management of patients undergoing potentially painful procedures.

The primary limitation to this study is one inherent to many studies examining pain in children: the difficulty in differentiating pain from anxiety. As this was a randomized trial and a standard approach was used in approaching all subjects and their parents before, during, and after the procedure, the confounding effect of anxiety on pain perception would have been mitigated with regards to differences between groups. However, the overall magnitude of pain reported during the procedure in both the groups most certainly may have been increased as the result of anxiety on the part of the subject. It is important in the management of these patients to employ strategies to reduce the anxiety associated with the procedure. To reduce anxiety, a calm and friendly environment should be maintained in the patient’s room and distraction techniques may be employed during the procedure. Parents are also an invaluable resource in decreasing fear and anxiety in their children during the procedure. As such, parents should be educated about the procedure in advance and can help to prepare their children for the pin removal experience before presentation in the clinic. In particular, parents and children should be made aware that the experience will likely involve some pain, but it will be short lived and usually mild.

Obstacles to effective pain management during pin removal in the outpatient setting include the lack of a practical, working solution for pain reduction. On the basis of our findings, we believe that the effective management of pain during pin removal will require a systemic solution. A previous study investigating the effectiveness of the prophylactic use of acetaminophen/NSAIDs for pain management during PP removal found that they were ineffective but this was believed to be due to a lack of adherence such that the parents neglected to administer the analgesic before clinic presentation. We feel that oral administration of an analgesic such as acetaminophen or a NSAID may be appropriate if given in the clinic upon arrival for pin removal. The patient could then be sent for a routine radiograph, giving time for the medication to take effect without causing undue delay in the clinic. Further work is needed to determine if this approach would be efficacious. In exceptional cases where fear and anxiety cannot be effectively mitigated or other factors exist that would be expected to increase procedural pain significantly, general anesthetic may need to be considered.

**CONCLUSIONS**

Topically administered liposomal lidocaine was not effective in reducing pain experienced by children during percutaneous intraosseous pin removal as compared with placebo. Higher pain scores were reported relative to the duration that the pins were in situ; however, no statistically significant differences were found in pain scores relative to the subject’s age, pin location, mechanism of injury and indication for pin insertion, or length of time from topical anesthetic administration to pin removal. Given the large volume of patients who undergo PP removal in the outpatient setting and the long-term consequences of experiencing painful procedures during childhood, it is important to find effective methods to manage pain during this procedure. Future studies may explore the efficacy of oral analgescics or entonox for pain management in these patients.

**ACKNOWLEDGMENT**

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