Intraurethral Lidocaine for Urethral Catheterization in Children: A Randomized Controlled Trial

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OBJECTIVES: To determine whether lidocaine is superior to nonanesthetic lubricant (NAL) for relieving pain in children undergoing urethral catheterization (UC).

METHODS: Children 0 to 24 months requiring UC were randomized to NAL or topical and intraurethral 2% lidocaine gel. Primary outcome was facial grimacing in the pre to during drug administration and catheterization phases. Secondary outcome was caregiver satisfaction by using a Visual Analog Scale.

RESULTS: There were 133 participants (n = 68 lidocaine, n = 65 NAL). There were no significant differences in mean (SD) scores during UC between lidocaine and NAL (86.4% [121.5%] vs 85.2% [126.6%]), respectively (Δ [confidence interval (CI)] = −1.2 [−21.0 to 49.0], P = .4). There was a significantly greater difference in mean (SD) scores during instillation of lidocaine versus NAL (61.8% [105.6%] vs 3.2% [84.9%]), respectively (Δ [CI] = −58.6 [−95.0 to −32.0], P < .001). There were no significant differences in mean (SD) parental satisfaction scores between lidocaine and NAL (4.8 [3.2] vs 5.9 [2.9]), respectively (CI = 0.1 to 2.2; P = .06). In the subgroup analysis, age, gender, and positive urine culture did not significantly influence between-group differences in facial grimacing.

CONCLUSIONS: Compared with NAL, topical and intraurethral lidocaine is not associated with significant pain reduction during UC, but significantly greater pain during instillation. Therefore, clinicians may consider using noninvasive pain-reducing strategies for young children who require UC.

WHAT'S KNOWN ON THIS SUBJECT: Urethral catheterization is a painful, yet common procedure to obtain a sterile urine sample in young children. There are conflicting results regarding the effectiveness of lidocaine to reduce pain, and it is unclear if it should be routinely used.

WHAT THIS STUDY ADDS: In young children, combined topical and intraurethral lidocaine does not reduce pain during urethral catheterization and is associated with more pain than nonanesthetic lubricant during instillation. Clinicians should use noninvasive methods of analgesia during this painful procedure.
Suspected urinary tract infections (UTI) account for up to 14% of pediatric emergency department (ED) visits yearly.1 Among febrile infants, the prevalence of UTI is as high as 7% and definitive confirmation requires either urethral catheterization (UC) or suprapubic aspiration.2–4 As such, UC is one of the most frequently performed ED procedures.5,6

There is ample evidence that analgesia is underused in the ED setting.7–10 Furthermore, untreated pain in childhood has been reported to lead to slower healing11–14 and long-term issues, such as anxiety, needle phobia,15 hyperesthesia,13 and fear of medical care.16 Despite general acceptance that children experience significant pain-related urethral procedures,17–19 suboptimal analgesia is particularly prevalent in children undergoing UC, with analgesic rates ranging from 0%6 to 2%.20 A more recent survey found that 44% of EDs did not offer any analgesia for UC in children.9 This wide range suggests a great deal of uncertainty regarding the best analgesic options for children undergoing UC. This uncertainty may be explained by the conflicting results of pediatric trials of topical analgesia. These inconsistencies could be due to suboptimal application times, restraining the infant, small sample sizes,21,22 or exclusively topical administration.23

The importance of providing optimal pain treatment is echoed by both the World Health Organization24 and the American Academy of Pediatrics,25 who recently reaffirmed its advocacy for adequate analgesia for painful procedures in children. Our objective was to determine if a combination of topical and intraurethral lidocaine with a longer application time relieved the pain of UC in unrestrained children aged 0 to 24 months without a concomitant increase in instillation-associated pain.

METHODS
Study Design and Setting
We conducted a randomized, blinded, placebo-controlled, superiority trial designed to test the hypothesis that a combination of intraurethral and topical 2% lidocaine gel was superior to nonanesthetic lubricant (NAL), the standard of care, in reducing pain associated with UC. Participants were recruited between April 2012 and October 2014 from the pediatric ED of the Children’s Hospital, London Health Sciences Centre. The study was approved by Western University’s Health Sciences Research Ethics Board and the intervention protocol received approval from Health Canada. The study was registered on www.clinicaltrials.gov (NCT01690767).

Participants
We included children 0 to 24 months who presented to the ED and required a UC to obtain a urine sample. We excluded children with known hypersensitivity to lidocaine, previous UC, or analgesia within 24 hours of study enrollment, external genitourinary anomalies, and previous participation in the study.

A trained research assistant assessed eligibility, obtained informed consent, and enrolled and performed all correspondence with participants. Participants were screened consecutively for eligibility for 10 hours per week between 1200 and 1700 hours when both the research nurse and research assistant were available. Written informed consent was obtained from caregivers.

Blinding
Parties blinded to the intervention included the nurse performing UC, outcome assessors, and caregivers who agreed to leave the room during the intervention phase.

Interventions
Randomization and allocation concealment were pharmacy-controlled using computer-based randomization (www.randomization.com). Eligible participants were randomized in a 1:1 allocation, with a block size of 6 to 2% lidocaine gel (Lidocaine hydrochloride; AstraZeneca, Toronto, Canada) or a water-based NAL (Lubricating jelly; Health Care Plus, Toronto, Canada). Concealment of allocation was performed using sequentially numbered, opaque, sealed envelopes. The interventions were kept in their original packaging at room temperature. A volume of 1 mL of 2% lidocaine gel was applied topically to the external meatus using sterile gauze for 5 minutes before intraurethral 2% lidocaine administration. The latter was delivered by a trained research nurse by using a 3-mL plastic syringe attached to a 25-gauge angiocatheter and inserted 5 mm into the distal urethra. As previously described,22 children <7 kg and ≥7 kg received 1 mL and 1.5 mL of intraurethral lidocaine, respectively. Five minutes were allowed to elapse from the time of intraurethral lidocaine administration to UC. In the NAL group, the participant’s diaper was removed during the time segment corresponding to topical lidocaine administration. During the time segment corresponding to intraurethral lidocaine administration, participants in the NAL group received a topical application of 1 mL NAL to the external meatus for 5 minutes by using sterile gauze (Fig 1). Topical and intraurethral interventions and UC were performed using aseptic technique. The child was placed in the lithotomy position with the legs abducted just enough to clean the perineum and visualize the urethral meatus. Apart from the intervention phase and UC, the child was allowed to assume either a supine or lateral decubitus position to prevent displacement of the intervention. Participants did not receive any analgesic agents (cointerventions)
before or during any of the study phases.

A trained research assistant videotaped the infant’s face and thoroughly reviewed the nursing record for adverse events associated with the procedure. Urine culture results were followed for 5 days postcatheterization. Video segments commenced 30 seconds before intervention administration and ended 30 seconds after UC. For the purposes of analysis, the videos were segmented into 4 phases: pre and during lidocaine/NAL application; pre and during UC. Each 30-second video segment was assigned a randomization number. Caregivers who agreed to leave the room during the intervention phase and return during the catheterization phase were asked to rate their level of satisfaction with their child’s comfort during UC.

**Outcome Measures**

The primary outcome was the pre-during difference in pain associated with both instillation and UC. This was assessed by the percentage of time children displayed facial grimacing, specifically brow bulging (BB), nasolabial furrowing (NLF), and eye squeeze (ES), during the first 30 seconds of each phase of the procedure. We used facial grimacing as the primary outcome because it has been described as “the most reliably specific indicator of pain” in infants and it permitted the outcome assessor to remain blinded because only the participant’s face needed to be recorded. The 3 facial indicators included in the assessment of pain were derived from the Neonatal Facial Coding System (NFCS), a 10-item behavioral pain scale validated in preterm, full-term, and older infants with excellent construct validity and high interobserver reliability at the bedside. The rating of all 10 items of the NFCS is very labor intensive. To reduce complexity, we measured the 3 most common facial actions (BB, ES, NLF), similar to that reported in other studies. These 3 actions have been found to be most frequently associated with tissue damage and exhibit high interobserver reliability, contribute most heavily to the pain experience, and are associated with improved specificity without compromising sensitivity or validity.

Using a previously described approach, the presence or absence of a facial action was scored for 2-second intervals for each video segment by 2 independent outcome assessors blinded to study hypothesis and group assignment. The percentage of time the facial action was present was calculated for each 30-second segment by dividing the sum of the number of times the facial action was observed in each 2-second interval by the total number of intervals observed, and multiplying by 100. Comparisons were made on the pre-during difference score between groups for the sum of scores for all 3 indicators (ie, BB, ES, NLF). The score ranged from 0% to 300%. To maintain blinding of outcome assessors, only participants’ faces were recorded. To minimize order bias, video segments were sent to 2 independent outcome assessors as individual digital files identified by a unique identification number generated by a computerized random number generator. Outcome assessors were trained by an expert in the NFCS (AT). Exploratory outcomes included an a priori subgroup analysis of the primary
outcome based on age (>180 or ≥180 days), gender, and positive urine culture as covariates.

Secondary outcomes included caregiver satisfaction with their child’s comfort during UC using a 100-mm Visual Analog Scale and frequency of adverse events including the possibility of introducing a pathogenic organism into the urine. The latter was defined as the presence of at least 50,000 colonies per mL of a single uropathogenic organism.4

Statistical Analysis
The intention-to-treat population was defined as all participants who underwent UC and in whom video segments were of sufficient quality for analysis. Means and SDs or frequencies and percentages, as appropriate, were used to summarize baseline characteristics. To facilitate making inferences at a participant rather than a time segment level, the primary outcome was assessed using an arcsine (square root) transformation of an analysis of covariance. A prespecified subgroup analysis by gender, age, and UTI on the pre-during difference between groups during UC was performed by using a test of interaction between the subgroup factor and the treatment group. Differences in parental satisfaction were compared by using the Student’s t test and frequencies of adverse outcomes between groups were compared using the Pearson χ². Interrater agreement between outcome assessors was determined by using an intraclass correlation. We considered a between-group difference of 20% in facial grimacing scores to be a minimal clinically important difference.37 Assuming an SD of 35%, 65 participants per group were required to detect a 20% between-group difference at the 5% 2-sided level of significance with 90% power.38 Data were analyzed by using the SPSS statistical software package (version 21; IBM SPSS Statistics, IBM Corporation, Chicago, IL). P < .05 was considered statistically significant.

RESULTS
Participants
Flow of participants through the trial can be found in Fig 2. Of 157 randomized participants, 133 were included in the analysis (68 in the lidocaine group and 65 in the NAL group). Demographic features of participants are summarized in Table 1. All participants who were included in the analysis were successfully catheterized on the first attempt.

Primary Outcome
There was significantly greater pain associated with instillation of intraurethral lidocaine compared with NAL as measured by facial grimacing (Table 2). However, there were no significant differences in pain associated with UC among participants who received lidocaine versus NAL (Table 3). In the subgroup analysis, tests of interaction were nonsignificant for the instillation phase (group × age, P = .13; group × gender, P = .76; group × positive urine culture, P = .77), and UC (group × age, P = .72; group × gender, P = .89; group × positive urine culture, P = .39). Given baseline heterogeneity in weight, and therefore dose of lidocaine, between groups, a post hoc analysis was performed to explore whether between-group differences in pain were associated with weight (<7 vs ≥7 kg). The test of interaction was nonsignificant for both the instillation phase (P = .22) and UC (P = .87).

The interrater agreement between outcome assessors for all variables was 0.89 (95% confidence interval [CI] 0.88 to 0.90).

Secondary Outcomes
There were no significant differences in mean (SD) parental satisfaction scores between lidocaine (n = 64) and NAL (n = 57) groups (4.8 [3.2] versus 5.9 [2.9]), respectively (95% CI ~0.1
to 2.2; \( P = .06 \). There were no significant differences in the proportion of positive urine cultures between participants in the lidocaine (15/65) and NAL (11/68) groups (\( P = .3 \)). There were 3 cases of a falsely positive urine culture in the NAL group and 1 case in the lidocaine group. There were no adverse events (hypersensitivity, bacteremia, sepsis, gross urethral injury, cardiovascular or respiratory decompensation, or death) observed.

**DISCUSSION**

In this randomized controlled trial of unrestrained children 0 to 24 months, we demonstrated that topical and intraurethral lidocaine gel was not effective in reducing the pain of UC. Our findings suggest that intraurethral lidocaine should not be routinely recommended for UC in young children, as its instillation is associated with significantly greater pain than NAL.

It is widely held that UC is painful for both children and adults. The suggested practice to reduce UC-related discomfort in children has typically included instillation of an anesthetic gel. Although evidence supporting the use of lidocaine gel in adults is clear, pediatric studies have yielded conflicting results.

Our finding that lidocaine did not significantly alleviate distress associated with UC contradicts evidence of the efficacy of lidocaine in older children. In children aged 4 to 11 years, Gerard et al\(^{21} \) found that 3, 2-minute instillations of topical and intraurethral lidocaine gel were associated with significantly less pain. Similarly, adult studies have found lidocaine to be effective in reducing pain associated with UC.\(^{41,42} \)

Studies in younger children, however, are consistent with our findings. Mularoni et al\(^{22} \) found no significant differences on a global measure of distress in children aged 2 to 24 months undergoing UC. The authors concluded that the administration time of 2 minutes might not have been sufficient for optimal analgesia. In addition, restraining patients in the lithotomy position may have contributed to distress.\(^{22} \) Vaughan et al\(^{23} \) studied the effectiveness of a 2-minute application of lidocaine to the urethral meatus in children <2 months of age and found no significant benefit. The authors stated that the short application time and exclusively topical administration may have mitigated optimal analgesia, particularly in boys.\(^{23} \)

Age-related differences in response to painful procedures are well described.\(^{43,44} \) It has been postulated that older children are better able to differentiate “pain” from “fear,”\(^{45} \) and may be more capable of appearing stoic.\(^{46} \) We restricted our investigation to children <2 years of age to ensure our results could be extrapolated to the demographic most likely to receive a UC for sterile urine collection.\(^{3,4} \) The mean age of participants in the lidocaine group was ~3 months greater than the NAL group and calls into question whether this could have affected the final results. The fact that the subgroup analysis showed that age was not associated with responses in facial grimacing between groups suggests that this was not the case. Alternatively, developmental differences underlying the response to painful stimuli may not have been distinct enough between the age groupings we prespecified (eg, <180 days and ≥180 days).

Our study sought to overcome limitations of previous work demonstrating lidocaine to be ineffective for UC. We used an application time of 5 minutes because topical lidocaine requires an administration time of at least 4 minutes for effective analgesia.\(^{47,48} \) We also chose not to restrain the participants in the lithotomy position. Although restraint has been used in previous protocols,\(^{22,23} \) it was described as distressing.\(^{22} \) We felt that by allowing the child to move and be comforted after the instillation phase, it would reduce overall anxiety during UC and enhance the generalizability of our findings.

Previous authors also have reported that intraurethral instillation of lidocaine is distressing to infants.\(^{22,23} \) In an effort to minimize pain, we applied lidocaine to the external meatus for 5 minutes before intraurethral instillation. The fact that these strategies did not alleviate pain suggests several possibilities. First, the instillation phase may have caused some tissue damage or may have been emotionally distressing, thereby sensitizing the child to UC. Second, the child’s pain experience

**TABLE 1 Demographic Features of Participants**

<table>
<thead>
<tr>
<th>Demographic Feature</th>
<th>Lidocaine, ( n = 68 )</th>
<th>NAL, ( n = 65 )</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, d</td>
<td>234.5 (196.1)</td>
<td>141.2 (144.1)</td>
</tr>
<tr>
<td>No. of boys (%)</td>
<td>30 (44)</td>
<td>37 (57)</td>
</tr>
<tr>
<td>Weight, kg</td>
<td>8 (3.1)</td>
<td>6.3 (2.2)</td>
</tr>
<tr>
<td>No. with previous urethral catheterization (%)</td>
<td>17 (25)</td>
<td>18 (28)</td>
</tr>
</tbody>
</table>

Data are presented as mean (SD) unless otherwise noted.

**TABLE 2 Facial Grimacing Pre-During Difference Between Groups During the Instillation Phase**

<table>
<thead>
<tr>
<th>Facial Grimacing Parameter</th>
<th>Lidocaine, ( n = 68 )</th>
<th>NAL, ( n = 65 )</th>
<th>( \Delta ) (95% CI)</th>
<th>( P )</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total</td>
<td>61.8 (105.6)</td>
<td>3.2 (84.9)</td>
<td>−58.6 (−85.0 to −32.0)</td>
<td>&lt; .001</td>
</tr>
<tr>
<td>BB</td>
<td>21.5 (37.1)</td>
<td>0.2 (54)</td>
<td>−21.3 (−33.6 to −9.2)</td>
<td>&lt; .001</td>
</tr>
<tr>
<td>ES</td>
<td>19.4 (33.5)</td>
<td>0.6 (26.1)</td>
<td>−18.8 (−29 to −8.4)</td>
<td>&lt; .001</td>
</tr>
<tr>
<td>NLF</td>
<td>21 (37.9)</td>
<td>2.4 (29.5)</td>
<td>−18.6 (−30.2 to −6.9)</td>
<td>&lt; .001</td>
</tr>
</tbody>
</table>

Data are presented as mean (SD). Facial grimacing scores represent the number of 2-second time segments in which the action was seen divided by the total number of 2-second time segments multiplied by 100.
TABLE 3  Facial Grimacing Pre-During Difference Between Groups During Catheterization Phase

<table>
<thead>
<tr>
<th>Facial Grimacing Parameter</th>
<th>Lidocaine, n = 68</th>
<th>NAL, n = 65</th>
<th>Δ (95% CI)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total</td>
<td>86.4 (121.5)</td>
<td>85.2 (126.6)</td>
<td>−1.2 (−21.0 to 19.0)</td>
<td>.4</td>
</tr>
<tr>
<td>BB</td>
<td>27.6 (40.7)</td>
<td>26 (42.7)</td>
<td>−1.6 (−15.8 to 12.7)</td>
<td>.6</td>
</tr>
<tr>
<td>ES</td>
<td>29.2 (41.7)</td>
<td>30.8 (42.6)</td>
<td>1.6 (−12.9 to 16.1)</td>
<td>.4</td>
</tr>
<tr>
<td>NLF</td>
<td>29.5 (42.1)</td>
<td>28.3 (46.7)</td>
<td>−1.2 (−16.4 to 14.1)</td>
<td>.5</td>
</tr>
</tbody>
</table>

Data are presented as mean (SD). Facial grimacing scores represent the number of 2-second time segments in which the action was seen divided by the total number of 2-second time segments multiplied by 100.

may have included an anxiety component fueled by parental separation, cold exposure, and other factors that could not be lessened with an anesthetic. Although we cannot be sure that handling to facilitate the instillation of lidocaine rather than the installation itself was not the source of distress, participants in both groups received a similar degree of handling.

Despite contradictory evidence for benefit in children, clinicians use lidocaine to alleviate pain associated with UC. Our findings provide evidence that intraurethral lidocaine is ineffective at alleviating pain in young children undergoing UC. Societal recommendations have made UC one of the most commonly performed procedures to obtain a sterile urine specimen in young children. However, it is also one of the most painful. Therefore, it is imperative that future studies explore the effectiveness of noninvasive strategies, such as sucrose, distraction, and positioning, which have been found to be effective in other painful procedures. Until future studies can explore the utility of these strategies, we believe that noninvasive approaches to reduce pain should be used in children undergoing UC.

The main limitation of our study was the lack of binding of the research assistant filming the video segments. Our study design favored the pragmatic end of the Pragmatic-Explanatory Continuum Indicator Summary. As such, our decision not to restrain participants made it difficult to obscure the lower half of the participant’s body and therefore blind the research assistant. However, given that no video segments were deemed uninterpretable, we believe the possibility of bias introduced by the research assistant was minimal. We were also not able to blind the research nurse performing the instillation, as the use of an intraurethral placebo was deemed unethical. However, we attempted to minimize bias by blinding the outcome assessors. In addition, the research nurse performing UC was not involved in collecting data or assessing outcomes. Another limitation was our decision not to measure physiologic parameters. However, evidence suggests that in infants, facial grimacing is more specific to tissue damage during an invasive procedure than is heart rate. Finally, UC was performed by nursing staff with varied clinical experience. Although there is a possibility that this may have introduced variability, all nurses in our department are trained to use a standardized protocol for UC. Inclusion of multiple operators improves generalizability of the findings.

CONCLUSIONS

UC is a commonly performed but painful procedure, particularly in young children. We have shown that despite a 5-minute application time without a restraint, the combination of topical and intraurethral lidocaine is not associated with significant pain reduction during UC and is associated with significantly more pain during instillation. Our results suggest that intraurethral lidocaine should not be administered to young children undergoing UC. Future work should explore the effectiveness of noninvasive analgesic strategies for young children who require this common, painful procedure.

ABBREVIATIONS

BB: brow bulging
CI: confidence interval
ED: emergency department
ES: eye squeeze
NAL: nonanesthetic lubricant
NFCs: neonatal faces coding system
NLF: nasolabial furrowing
UC: urethral catheterization
UTI: urinary tract infection
REFERENCES


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