Lidocaine Gel for Urethral Catheterization in Children: A Meta-Analysis

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Objective To compare the efficacy and safety of lidocaine gel vs nonanesthetic gel (NAG) in reducing transurethral bladder catheterization (TUBC) procedural pain in children.

Study design A systematic literature search was done using electronic medical databases and trial registries up to September 2016 with no language restrictions. Randomized controlled trials (RCTs) that assessed the efficacy and safety of lidocaine gel vs NAG in reducing TUBC-associated pain in children were screened, identified, and appraised. Risks of bias and study quality of the eligible trials were assessed according to the Cochrane Collaboration recommendations. Various pain assessment scales from the included studies were extracted as mean differences and standard deviations for each treatment group. Standardized mean differences (SMDs) were generated with 95% CIs for between-group difference estimation. Effect estimates were pooled using the inverse variance method with a random-effects model. Subgroup analysis was performed for different age groups.

Results Five RCTs (with a total of 369 children) were included. Overall pooled effect estimates showed that compared with NAG, lidocaine gel has no significant benefit in decreasing TUBC-associated pain in children (SMD, −0.22; 95% CI, −0.65 to 0.21). Effect estimates from 4 studies revealed no difference in pain reduction between the lidocaine gel and NAG in children aged <4 years (SMD, 0.01; 95% CI, −0.22 to 0.24). No serious adverse events from the lidocaine gel use were reported in any of the studies.

Conclusions Lidocaine gel does not appear to reduce TUBC pain compared with NAG, specifically in children aged <4 years. *(J Pediatr 2017;■■:■■-■■).*

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Urinary tract infection is one of the most common reasons for healthcare visits in a general pediatric practice, accounting for an estimated overall prevalence of 5%-7% in young children with unexplained fever.[1-3] According to the latest guidelines from the American Association of Pediatrics, transurethral bladder catheterization (TUBC) is a preferred method for urine collection owing to its high success rate and comparable diagnostic accuracy with suprapubic aspiration.[3,4] However, because of parental perception of the pain caused by catheterization, TUBC is often refused, and instead suboptimal bagged samples are acquired.[5,6]

Lidocaine is a commonly used local anesthetic compound that acts on the voltage-operated sodium channels of nociceptive receptors to block the transmission of pain sensory impulses to the brain.[7,8] Lidocaine-containing lubricant gel is commonly used to reduce the procedural pain associated with TUBC, specifically recommended in adults.[8] Its use in children is inconsistent, mainly owing to conflicting results reported in the literature.[9,10] We identified an opportunity to clarify the clinical utility of lidocaine anesthetic gel in reducing the pain associated with TUBC in children. Our aim was to assess the efficacy and safety of lidocaine gel vs nonanesthetic gel (NAG) in reducing the pain associated with urethral catheterization in children by performing a meta-analysis of randomized controlled trials (RCTs).

Materials and Methods

The study protocol for this meta-analysis was registered in PROSPERO (CRD42016050018). The meta-analysis was performed following the recommendations from the Cochrane Handbook for Systematic Reviews of Interventions[11]; likewise, it is reported according to the PRISMA statement.[12]

Two physician reviewers independently identified any published human literature studying the use of lidocaine gel as a local anesthetic before TUBC. The systematic literature search was carried out with no language restriction in September 2016

GRADE	Grades of Recommendation, Assessment, Development, and Evaluation
NAG	Nonanesthetic gel
RCT	Randomized control trial
SMD	Standardized mean difference
TUBC	Transurethral bladder catheterization

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using the following electronic databases: Ovid MEDLINE and MEDLINE in process, Embase, SCOPUS, and the Cochrane Library. The reviewers also searched the websites of clinicaltrials.gov and WHO-International Clinical Trials Registry Platform for any possible unpublished trials. Additional inquiries were sent to the authors and trial investigators regarding incomplete data. A search strategy was done using both Medline Subheading terms and free text, as follows: ((lidocaine) AND (("urinary catheters") OR ("urinary" AND "catheters") OR ("urethral" AND "catheter") OR ("urethral catheter" OR urethral catheterization)). For non-Ovid platforms, the search strategy applied was (Lidocaine AND urethral catheterization). We then individually reviewed the relevant articles and cross-referenced the reference lists that met our inclusion criteria to search for more potentially relevant titles. A comprehensive literature search for eligible studies was carried out to minimize reporting bias, publication bias, and their potential impacts on the process. In addition, external peer reviewers were asked to identify additional pertinent studies not included in the initial draft.

Inclusion criteria predetermined for this meta-analysis considered randomized control trials that compared the efficacy of lidocaine-containing gel vs NAG in reducing procedural pain or distress among pediatric patients (aged <18 years) undergoing TUBC. We excluded trials that involved adults, compared different methods of obtaining urine samples, did not assess procedural pain, did not compare a nonanesthetic gel control group, or were non-RCTs.

The primary outcome measure for this meta-analysis was the pain intensity associated with urethral catheterization, as determined by a validated scale used in the individual studies. The procedural pain score was defined as the mean difference score between the baseline and actual pain score reported in the study. We also assessed the adverse events associated with lidocaine gel and summarized the reported incidence. If any incomplete data were encountered, the trial investigator was contacted for additional results. A subgroup analysis was performed according to age group of age <4 years vs ≥4 years, based on reports that the majority of children achieve daytime continence at age 4 years.[13,14]

Two reviewers independently evaluated the citations and abstracts. The reviewers flagged article titles that were relevant to the study and narrowed down the list to studies that included only children. Articles that either reviewer flagged, as well as articles in which the abstract or title relevance could not be determined, were further assessed independently. Two physician reviewers then independently reviewed each full-text article and determined whether all the inclusion criteria were met. The reviewers were knowledgeable in the principles of critical appraisal and performed the assessment according to the Cochrane Handbook for Review of Intervention.[11] The RCT risk of bias assessment tool adopted from the Cochrane Collaboration was used to specifically assess the study domains: randomization sequence generation, allocation concealment, blinding of participants, providers and outcome assessors, completeness of outcome data, selective outcome reporting, and other potential sources of bias. Each study domain was rated according to the following: "low" if the risk of bias was very unlikely, "high" if the bias was strongly suggestive, or "unclear" when insufficient information was described for risk determination. Any discrepancies were resolved through consensus and any further differences encountered were reviewed by senior physician researchers.

Study characteristics (ie, source of study, patient characteristics, procedural setting, catheterization technique, lidocaine dosage, concomitant pain management, comparator control, and pain assessment scale used) and primary outcome assessment data (ie, procedural pain assessment score and adverse events) from the included studies were extracted and tabulated by 1 reviewer and counterchecked by another.

Using the RevMan5 calculator (The Nordic Cochrane Center, Copenhagen, Denmark), the procedural pain score mean and SD or median and 95% CI were extrapolated as the mean difference between baseline and procedural pain scores for each treatment group. Whenever a study was not able to provide any data for this extrapolation, the reported mean procedural pain score and SD was used. The standardized mean difference (SMD) was generated with 95% CI for between-group treatment effect estimation. The SMD expresses the effect size of the intervention for each study relative to the variability observed within each individual study; thus, it is the more generalizable and appropriate summary statistic to standardize the results of different studies that assess the same outcome, but measured on different validated scales.[11,15] Taking into consideration the methodological diversity, after standardization of effect estimates using the SMD and corresponding 95% CI, data were pooled using the inverse variance method with a random-effects model to determine the average treatment effect.[16]

The χ^2 statistical test was used to assess the heterogeneity of treatment effects among studies. A low P value (or a large χ^2 statistic relative to its degrees of freedom) suggests evidence of treatment effects heterogeneity. A P value of .10 rather than .05 was used in this meta-analysis to show heterogeneity, because only a small number of trials with small sample sizes were included. Furthermore, the I^2 statistic was used to quantify the variations between the studies when heterogeneity was strongly suspected. If a value >40% was found, then significant heterogeneity was assumed, and the source of heterogeneity was identified by considering the clinical and methodological characteristics among the studies included in the meta-analysis. A preplanned subgroup analysis was performed to verify the identified study variation. A funnel plot was generated to explore the possibility of publication bias.[11] The RevMan program, downloaded from www.cochrane.org, was used for data synthesis, data analysis, forest plot construction, and funnel plot construction.[17]

Results

A total of 102 articles were retrieved from the systematic literature search, of which 79 were excluded based on title and abstract assessment. Twenty-three full text articles were further assessed for eligibility, of which 18 were excluded based on the

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