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HEALTH TECHNOLOGY INQUIRY SERVICE (HTIS)

TITLE: Use of Topical Anesthetics for Suturing and Circumcisions in Pediatric Patients: A Review of Clinical Effectiveness and Guidelines

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CONTEXT AND POLICY ISSUES:

Topical anesthetics are used in pediatric suturing and may have a role in male circumcision as part of the effort to provide adequate analgesia during these painful procedures.[1-4] With increased research on the management of pediatric pain and recognition of its long term effects, appropriate management of pain has become a standard of clinical practice.[5-7]

In suturing of superficial lacerations, topical anesthetics provide an alternative to local anesthetic injection, thus avoiding the pain of injection and potential distortion of the laceration site.[1] A survey of academic pediatric emergency departments in the US reported use of topical anesthetics for facial lacerations in 84% of centres with significant recent uptake in their use and room for improved use.[5] A survey of emergency departments in the UK regarding medication use for painful pediatric procedures reported use of topical anesthetics for suturing in 41% of centres.[6] The same publication noted use of topical anesthetics in 30% of centres in Australia and New Zealand.[6]

In unanesthetized neonates undergoing circumcision, a rise in adrenal corticoids, skin flushing, vomiting, cyanosis, increased crying, apnea, choking, and pneumothorax have been reported.[7] Inadequate analgesia during neonatal circumcision has resulted in increased heart rate, respiratory rate, and decreased oxygen saturation.[7] It has been suggested that "pain memory" may develop from an early age as seen by increased immunization pain response in circumcised neonates over the following six months.[7]

LET solution is a topical anesthetic that is compounded as a sterile preparation of lidocaine 4%, epinephrine 0.1 to 0.05%, and tetracaine 0.5% in normal saline for a total volume of 3 to 5 millilitres.[1,2] Lidocaine is an amide-type anesthetic agent; tetracaine is an ester-type anesthetic agent, and epinephrine provides local vasoconstriction.[2] Lidocaine's onset of action is rapid while tetracaine has a longer duration of action.[1] The LET solution is swabbed into the wound,

then applied as a LET-soaked sterile gauze or cotton for 20 to 30 minutes and removed before the procedure.[2]

Other topical anesthetic agents are also available. EMLA® is a commercially available combination of lidocaine 2.5% and prilocaine 2.5%.[8] EMLA® is relatively expensive, takes 45 to 60 minutes after application to take effect, and cannot be used on broken skin.[1,8] Methemoglobulemia may occur with high dose local anesthetics and with prilocaine, one of the components of EMLA®.[4,7] Ametop® contains tetracaine 4% and cannot be used on broken skin.[9] Health Canada has recently warned against excessive use of EMLA® and Ametop® in adult and pediatric patients.[4] Another compounded local anesthetic preparation is TAC, which contains tetracaine (0.5% to 1.0%), adrenalin (i.e., epinephrine; 0.025% to 0.05%), and cocaine(4.0% to 11.8%).[1,2] Cocaine-containing products are relatively expensive, require controlled substance recording, and may cause adverse effects (e.g., seizures) with excessive mucosal absorption.[1] A number of other compounded and marketed topical anesthetics have been used in various areas of clinical practice.

This report reviews the evidence for clinical effectiveness and guidelines for use of topical anesthetics, including LET solution, in pediatric patients requiring sutures and undergoing circumcision.

RESEARCH QUESTIONS:

1. What do evidence-based guidelines suggest for topical anesthetics for pediatric patients who require sutures?
2. What do evidence-based guidelines suggest for topical anesthetics for pediatric patients who are undergoing circumcision?
3. What is the clinical effectiveness of using a lidocaine-epinephrine-tetracaine solution as a topical anesthetic for pediatric patients who require sutures?
4. What is the clinical effectiveness of using a lidocaine-epinephrine-tetracaine solution as a topical anesthetic for pediatric patients who are undergoing circumcision?

METHODS:

A limited literature search was conducted on key health technology assessment resources, including PubMed, The Cochrane Library (Issue 1, 2009), University of York Centre for Reviews and Dissemination (CRD) databases, ECRI, EuroScan, international health technology agencies, and a focused Internet search. Results include English language articles published between 2004 and February 2009. Articles dealing with topical anesthetics for sutures and circumcision in pediatrics were included without limiting to study type. Broader results dealing with topical anesthetics in pediatrics are limited to the following study types: health technology assessments, systematic reviews, meta-analyses, randomized controlled trials, controlled clinical trials, observational studies, and guidelines.

SUMMARY OF FINDINGS:

The literature search identified one systematic review of topical anesthetics in suturing and one observational study of anesthetics in digital lacerations with limited applicability to the research questions within the research time frame. For pediatric circumcision, two systematic reviews on pain relief in male circumcision were identified. No other systematic reviews, health technology assessments, meta-analyses, guidelines, randomized controlled trials (RCTs), or observational studies were found.

Health technology assessments, systematic reviews, and meta-analyses

Topical anesthetics in suturing

A systematic review comparing topical anesthetics for dermal laceration repair in 22 RCTs including 3190 patients was published in 2004.[1] The RCTs were published between 1980 and 1998. Patients were at least 3 years of age in all studies. The majority of trials included pediatric patients, defined as up to 18 years of age. Lacerations were superficial, did not involve mucous membranes and were not infected. A total of seventeen different topical anesthetic preparations were utilized as active treatment. Patients in the control groups received lidocaine injection (i.e., infiltration), TAC solution or gel, placebo, or LET gel. The primary outcomes were analgesic efficacy as reported by patients. Secondary outcomes included surrogate pain scores when patient-reported analgesia was not reported, anesthetic failures, supplemental analgesic requirement, and patient behavioural responses. Due to differences in outcome measures between trials, meta-analysis was not possible. Lacerations were primarily located on the face, scalp, and extremities, and laceration length was 1.5 to 10 centimeters. Five of the 22 trials included LET solution or LET gel as active treatment. Of these, two involved pediatric patients and the other three involved adult patients. The results are described below, followed by the author's conclusions regarding the remaining studies.

Four trials included patient groups receiving LET solution and one study compared LET gel to lidocaine infiltration. The first was a double-blinded trial which compared LET solution to TAC, applied for 15 minutes, in pediatric patients. Results of this trial, which included 78 children (1 year to 17 years of age), showed physician-assessed adequate analgesia by needle probe before suturing in 79.5% of the TAC group and 74.4% of the LET group (p=ns). A second physician-assessment of analgesia after suturing indicated complete anesthesia in 75% of the TAC group and 82.4% of the LET group (p=ns). Complete anesthesia was defined as no requirement of supplemental lidocaine infiltration and absence of pain 30 minutes after application of the topical anesthetic. In the second study, which included 194 pediatric patients (ages not reported), LET solution was compared to LET gel with physician-assessment of analgesic efficacy. LET gel and solution, applied for 20 minutes, were found to be equally effective with complete anesthesia in 76% of the LET solution group and 85% of the LET gel group (p=0.017). As in the previous study, complete analgesia was defined as no supplemental lidocaine infiltration requirement and absence of pain for 30 minutes after topical anesthetic application. The results of the third study suggested that LET solution, applied for 20 to 30 minutes, was more effective than placebo in suturing in 60 adults. The fourth study included 95 adults and found no significant difference in pain during suturing between LET and TAC solution patient groups. In the fifth study, LET gel was compared to lidocaine infiltration in 66 patients, 5 years to adult, with comparable pain ratings reported.

The authors of the review noted that topical anesthetics appear to provide equivalent or superior analgesic efficacy compared with lidocaine infiltration. They found no difference in analgesic efficacy of cocaine-containing versus cocaine-free topical anesthetics, including LET solution and others. It should be noted that these studies were published over 10 years ago, included small numbers of adult and pediatric patients, exhibited poor randomization and blinding techniques, and reported pain outcomes in different ways or did not report outcomes.

Topical anesthetics in circumcision

A systematic review, published in 2004, reviewed pain relief in neonatal circumcision.[10] Thirty-five randomized trials from 1983 to 2001 compared treatment with placebo, no treatment, or another active treatment. A total of 1997 patients, primarily full term neonates, were included in these trials. No treatment completely eliminated the pain response to circumcision. Dorsal penile nerve block (DPNB) was more effective than placebo, no treatment, oral sucrose, or EMLA®. DPNB was also the most frequently studied treatment. Ring block was more effective than placebo. EMLA® was more effective than placebo. Topical lidocaine cream was more effective than placebo or no treatment. Both EMLA® and topical lidocaine were noted to require difficult and time-consuming application. Ten of the trials reported adverse events. In untreated patient groups, gagging, choking, and emesis were reported, while DPNB groups had minor bleeding, swelling, and hematomas at the nerve block injection site. EMLA® patient groups exhibited erythema and minor skin pallor, and two patients receiving EMLA® had redness and blistering of the foreskin. Sixteen of 35 trials did not report outcome data or the pain outcomes were difficult to compare.

While further study is necessary, the authors suggested that placebo or no active treatment groups are not acceptable. The authors also noted survey results suggesting that significant numbers of physicians do not use analgesia or anesthesia for neonatal circumcision due to concerns about adverse drug effects or the belief that pain management is not required. The interpretation of these studies is limited due to small sample size, differing patient characteristics, uncertain blinding methods, varied circumcision procedures, and varied application of treatments for analgesia.

A second systematic review in 2008 compared caudal epidural block with other methods of post-operative pain relief for elective male circumcision in boys aged 28 days to 16 years.[3] Ten randomized and quasi-randomized trials published between 1979 and 2005 were included. No difference was found between DPNB and caudal block in the need for supplemental analgesia or nausea and vomiting. Caudal block resulted in motor block with leg weakness. No difference was found between caudal block and analgesia by injection. No topical anesthetics were used in these trials. The authors suggested DPNB for day surgery procedures since leg weakness can be associated with caudal epidural block in children old enough to walk. The studies in this review included small patient numbers, had weak methodology, and many were completed over 10 years ago. The authors suggested that more data is needed to evaluate the optimal clinical use of nerve block techniques with other pain-reducing modalities like topical anesthetics.

Randomized controlled trials

No RCTs were identified using topical anesthetics in pediatric suturing or male pediatric circumcision.

Observational studies

White *et al.* published a prospective case series of 67 pediatric patients, ages 5 to 18 years, with simple finger lacerations of up to 3 cm in length.[11] The study took place in an academic pediatric emergency department investigating the efficacy of LET gel for finger lacerations and risk of digital ischemia. LET gel (lidocaine 4%, epinephrine 0.05%, tetracaine 0.5%) was applied for 45 minutes with occlusive dressing, followed by removal before suturing. Success or failure with LET gel was defined as whether or not the patient reported any sharp sensation before or during suturing. Patients reporting any sharp sensation before or during suturing were

considered failures and were given supplemental lidocaine infiltration. Evaluation of pain on a 0 to 10 visual analog scale (VAS) with markings for 0 of “no pain”, 5 of “moderate pain”, and 10 of “worst pain” was made for all patients. Digital ischemia was defined as capillary refill greater than 3 seconds or white to pale colouring of the distal digit. Examination of the digit was performed after LET gel removal before suturing, and 30 minutes later. Patient and parental satisfaction with LET treatment was ascertained before discharge. Follow-up phone survey enquiring about infection and ischemia was completed within 3 to 5 days after discharge. Overall, LET gel was successful for anesthesia in 53.7% of patients with higher success for patients with lacerations of the dorsal surface of the finger (68.6%) than those of the ventral surface (37.5%). No signs of digital ischemia were noted on discharge or in follow-up. In the success group, 93.9% of parents and 94.3% of patients responded that they would use LET gel again. In the failure group, 44.4% of parents and 50.0% of patients responded that they would use LET gel again. Pain scores by VAS were a mean of 2.7 in the success group and 6.7 in the failure group. The authors noted that previous studies using TAC for extremity lacerations reported success in 43% to 55% of patients. The current study was not randomized, included patients with a mean age of 12 years, and used LET gel. It is unknown if these results could be extrapolated to the use of LET solution in younger children. The authors suggested that a larger study may have detected digital ischemia which may be of concern with epinephrine.

Guidelines

No clinical guidelines regarding topical anesthetics in pediatric suturing or pediatric male circumcision were identified.

Limitations

The literature search resulted in very limited, and somewhat dated, evidence of low quality assessing the effectiveness of topical anesthetics in pediatric suturing and circumcision. The systematic review identified LET solution as an option in suturing, while no mention of LET solution was made in the literature for circumcision.[1,3,10] Variability in patient groups and ages, lack of pain assessment and varied methods of pain assessment, varied suturing and circumcision techniques, and multiple analgesia therapies were evident in the studies. The studies in the systematic reviews included small patient numbers. The observational study using LET gel in pediatric suturing was a prospective case series without a control group for comparison and may be subject to bias. No other RCTs or observational studies of topical anesthetics or LET solution for suturing or pediatric circumcision were identified. No evidence-based guidelines for either indication were identified.

CONCLUSIONS AND IMPLICATIONS FOR DECISION OR POLICY MAKING:

Suturing of simple lacerations in pediatric patients and pediatric circumcision are frequent painful procedures. There was little evidence identified to ascertain optimal agent or combination of agents for these procedures. The included studies suggested topical anesthetic use for suturing instead of, or preceding, anesthetic infiltration.[1,11] The literature reports that LET solution is a choice that is effective, rapid-acting, and practical to use in suturing of simple lacerations of the face and scalp.[2] Considering the limited available information, selection of a specific topical anesthetic product for pediatric suturing is difficult. No literature was identified related to the role of topical anesthetics or LET solution in neonatal or pediatric circumcision. No evidence-based guidelines about the use of topical anesthetics in pediatric patients for suturing or circumcision were identified.

Topical anesthetics may not be universally available or used in either clinical setting, and room for improved pain control in both procedures is apparent.[3,5-7] Concerns about appropriate pain management in pediatric patients may be addressed with published evidence in the future. The limited information should be considered in decisions about the use of topical anesthetics in pediatric patients.

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