

POSTER HIGHLIGHTS

Venous Access Procedures in Children: Strategies for Decreasing Pain and Anxiety

TOPIC HIGHLIGHTS

Lidocaine/Tetracaine Anesthesia Patch: Summaries of Three Clinical Studies

- A Lidocaine/Tetracaine Patch for Local Anesthesia Prior to Vascular Access Procedures in Children: Results From Two Randomized Controlled Studies
- Contribution of a Heating Element to Topical Anesthesia Patch Efficacy: A Randomized, Double-Blind Study
- The Lidocaine/Tetracaine Patch Versus EMLA for Topical Local Anesthesia Before a Vascular Access Procedure: A Randomized Controlled Trial

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Dr Zempsky has received clinical grants from Anesiva, Inc., Sontra Medical Corporation, and Vyteris, Inc. He is a consultant to Anesiva and Endo Pharmaceuticals.

As pediatricians well know, it is common for a child to experience pain and anxiety associated with minor procedures. In particular, procedures that involve “needles” are especially problematic. For example, in a landmark study of a population of school-aged children, Menke¹ reported that injections provoked more anxiety than did major surgery. Today, a quarter of a century after that study was published, perhaps the most often-heard expressions by children in a doctor’s office still center on the fear of “getting a shot.”

Clinicians also are acutely aware of parents’ concerns over their children’s anxieties about injections and venous access procedures. How often do practitioners hear parents say that they had difficulty getting a child to the doctor’s office because the child was “afraid of getting a needle”? This experience is one that many parents would pay out-of-pocket to avoid. In one study, parents said they were willing to spend between \$50 and \$70 to make their children’s immunizations less painful.²

Nonpharmacologic Approaches to Alleviating Procedural Pain in Children

The approach to a child who will undergo a painful procedure must be multidimensional and includes preparation of the child, proper positioning, and distraction maneuvers that provide a child-centered, comfortable, and comforting environment.^{3,4} Distraction techniques that have proved to be helpful are bubble blowers or pinwheels (to concretize an image of “blowing away the pain”)⁵ as well as videos.

The involvement of a parent in the procedure also is important. Parents should understand the approach and should be given

a specific coaching role—perhaps serving as the individual who distracts the child. The parent/coach also must be aware of what is not helpful; for example, statements to children such as “Don’t worry, it’s only going to hurt for a second” actually increase anxiety.



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Consider Topical Anesthetics

In addition to these other measures, topical anesthetics⁶ can be considered a way to provide additional comfort to a child facing painful procedures. Ideally, a topical anesthetic for pediatric use should be safe, effective, with a rapid onset of action, and easy to use.

For a number of years, lidocaine (2.5%)/prilocaine (2.5%) cream has been the gold standard for topical anesthetics. The compound has been well studied and has been shown to be safe and effective for venous access and other minor painful procedures. The main disadvantage is that effective local anesthesia is not achieved for at least 1 hour.

Further, the depth of penetration is limited to about 4 mm in 1 hour, and the intensity of analgesia is adequate, but not excellent. Because an occlusive dressing must be used over a thick layer of cream, careful application of the dressing is necessary to avoid seepage of the cream under the adhesive and subsequent displacement from the desired site.

A compound comparable to lidocaine/prilocaine cream is 4% liposomal lidocaine, also in a cream vehicle. It has not been as extensively studied as the lidocaine/prilocaine product,

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but it has been shown to be safe and effective and has an advantage in that it produces analgesia in about 30 minutes. An occlusive dressing must be used with liposomal lidocaine cream, so the same problems with potential displacement must be considered. Currently, 4% liposomal lidocaine has no US Food and Drug Administration (FDA) indication for venous access procedures.

Pediatric News®

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This supplement is based on a physician interview. It was supported by ENDO Pharmaceuticals.

This supplement was produced by the customized publication department of International Medical News Group. Neither the editor of PEDIATRIC NEWS, the Editorial Advisory Board, nor the reporting staff contributed to its content. The opinions expressed in this supplement are those of the faculty and do not necessarily reflect the views of the supporter or of the Publisher.

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Newer topical anesthesia options include several systems that use a variety of technologies to deliver the anesthetic. One of these systems, lidocaine iontophoresis, involves the transfer of lidocaine under the influence of an electric current. This system provides excellent analgesia and anesthesia in about 10 minutes. The disadvantages of this system include the fact that the required equipment is fairly cumbersome and a sophisticated level of training is needed for its use. In addition, there are several potential safety issues, including tingling, itching, and sometimes burning.

Another system, sonophoresis, uses low-frequency ultrasound (<100 kHz) to facilitate topical drug delivery by enhancing the relative permeability of the skin. The system, used with currently available topical anesthetic creams, greatly enhances the rate at which anesthesia can be achieved—about 5 minutes, instead of 30 to 60 minutes. Here again, the equipment is somewhat cumbersome and its use requires specialized training. Further, the resulting area of anesthesia is relatively small.

Also available is a carbon dioxide injection system that is primarily directed toward patients with diabetes for use with insulin. The device can be used to quickly deliver lidocaine to the skin. Injection of lidocaine under pressure creates a small wheal. Anesthesia is rapidly produced, but only to a very small area, limiting the types of procedures for which this method would be useful. Delivery of lidocaine with this system is not painless and is associated with up to a 27% failure rate secondary to system failure and inability to achieve venous access.

Still under development is a new technology called pressure-assisted lidocaine delivery. With this device, lidocaine is delivered under pressure at a high velocity in an area of the skin the approximate diameter of a quarter. The most attractive feature of this system is that it achieves anesthetic efficacy in about 1 minute.

Lidocaine/Tetracaine Patch

Recently, the FDA approved the use of a new topical anesthetic: a patch containing 70 mg each of lidocaine and tetracaine. The patch is approved for use on intact skin to provide local dermal analgesia for superficial venous access and dermatological procedures in adults and children 3 years of age or older. In addition to the topical anesthetic agents, the peel-and-stick patch incorporates a heating component, a formula containing iron powder, activated carbon, sodium chloride, wood flour, and water, and filter paper. Once the package is opened and the patch is exposed to the air, the heating component provides mild warming of the skin that promotes delivery of the anesthetic compound. Anesthesia for venous access and venipuncture is achieved in about 20 minutes.

The following studies, presented in abstract form at the March 2007 meeting of the National Association of Pediatric Nurse Practitioners, provide additional information about this new option in topical anesthesia, Synera™ (70 mg lidocaine/7 mg tetracaine) topical patch for venous access procedures in children and adults.

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Lidocaine/Tetracaine Anesthesia Patch: Summaries of Three Clinical Studies

A Lidocaine/Tetracaine Patch for Local Anesthesia Prior to Vascular Access Procedures in Children: Results From Two Randomized Controlled Studies

Authors

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Summary

The authors conducted two randomized, double-blind, placebo-controlled studies evaluating a unit-dose patch containing a eutectic mixture of 70 mg of lidocaine and 70 mg of tetracaine for topical local anesthesia for pain relief before a vascular access procedure in children.

Enrolled in the studies were 120 children 7 to 18 years of age who required

a vascular access procedure. In Study 1, 30 patients received an active patch and 30 received a placebo patch for 30 minutes. In Study 2, the distribution of groups was the same, with 30 patients each receiving active and placebo patches; in this study, the patches were left in place for 20 minutes.

In both studies, skin reactions and adverse events were documented following removal of the patches and prior to the performance of the vascular access procedures.

The quality of anesthesia was rated by patients, the investigators, and an independent observer. The Oucher Scale was used for patient pain ratings, ranging from 0 = no pain to 100 = worst pain. (Unlike pain scales commonly used in clinical practice, the Oucher Scale uses photographs rather than drawings to depict degrees of pain.) In both studies, the median Oucher score was 0 among the patients who received the active patch; these ratings were corroborated

by the investigator and independent observer evaluations.

Skin rash occurred in one patient who received the active patch. In Study 1, edema occurred more frequently in patients on the active patch than in those who received the placebo patch (29% vs 10%, respectively; $P=0.033$). In both studies, erythema was significantly more common in the patients who received the active patch (83% vs 27% in Study 1; 90% vs 43% in Study 2; $P<0.001$ for both comparisons).

Comments From Dr Zempsky

This study showed that the lidocaine/tetracaine patch was superior to placebo in producing effective anesthesia. Further, anesthesia was achieved in as little as 20 minutes, a distinct advantage over the 30- to 60-minute delay seen with other topical agents. The most commonly observed skin reaction was erythema, which is expected because of the heating element.

Contribution of a Heating Element to Topical Anesthesia Patch Efficacy: A Randomized, Double-Blind Study

Authors

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Summary

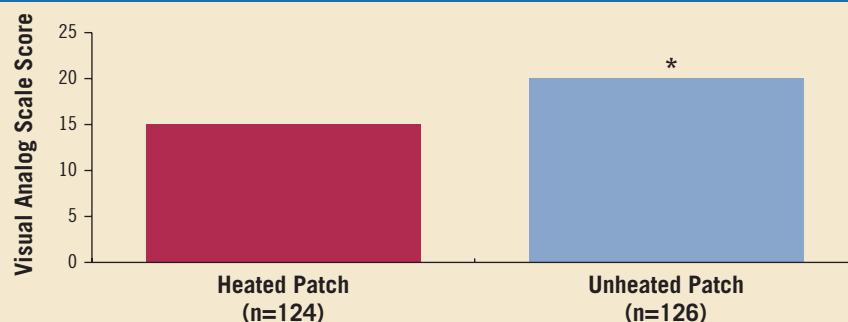
In this double-blind, randomized study, 250 subjects who were to undergo a venous access procedure received a lidocaine/tetracaine patch (70 mg of each

topical anesthetic), either with a heating element ($n=124$) or with the heating element removed ($n=126$). The patches were applied 30 minutes prior to the procedure, which, in this study, was venous insertion of a 16-gauge catheter in the antecubital area of the arm.

Patients used a visual analog scale (VAS) to rate pain intensity during their venous access procedure. Reported pain intensity using VAS was the primary measure of efficacy; patient-reported adequacy of anesthesia was the secondary

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Figure. VAS Score of Subjects Receiving a 20-Minute Application of Heated or Unheated Lidocaine/Tetracaine (Synera) Patch



* $P=0.006$, two sample t-test.

Pain intensity, measured by VAS, was lower in subjects who received the lidocaine/tetracaine patch with heat compared to those who received the patch without heat (14.2 mm vs 20.5 mm, $P=0.006$).

VAS=visual analog scale.

Presented at the 28th Annual National Association of Pediatric Nurse Practitioners Conference, March 21–24, 2007, Lake Buena Vista, Florida.

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efficacy measure. Patients who received the patch with the heating element reported significantly lower pain intensity than did those who received the patch with the heating element removed (VAS, 14.2 vs 20.5 mm, respectively; $P=0.006$). In addition, a higher percentage of patients in the group who received the patch with the heating element said they felt the level of anesthesia provided was adequate (71% vs 53%, respectively; $P=0.004$).

The Lidocaine/Tetracaine Patch Versus EMLA for Topical Local Anesthesia Before a Vascular Access Procedure: A Randomized Controlled Trial

Authors

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Summary

A randomized, double-blind study was conducted in 82 adults who underwent venous access procedures following applications of a lidocaine/tetracaine patch to the antecubital area of one arm and a lidocaine/prilocaine cream (EMLA) to the antecubital area of the other arm in the same patient. The anesthetics were left in place for 10 minutes in 20 patients, 20 minutes in 20 patients, 30 minutes in 22 patients, and 60 minutes in 20 patients.

Skin reactions and adverse events were documented following removal of the

The authors reported that the patches were well tolerated by all subjects.

Comments From Dr Zempsky

This study was conducted to evaluate the effect of the heating element on the delivery of a lidocaine/tetracaine topical anesthetic mixture. The authors demonstrated that the particular topical analgesic patch with a heating element used in this study was superior to the same patch with the heating element

removed. The results reported by these authors also support the findings from studies showing that heat enhances topical analgesic drug absorption through the skin. In addition to enhancing absorption, the incorporation of a heating element into a topical anesthetic patch system causes vasodilation, which has the potential for making venous access easier.

patches and cream and prior to the performance of the vascular access procedures.

The patients used a 100-mm visual analog scale (VAS) to rate pain. In addition, the subjects were asked to evaluate pain relief and whether they would be willing to use the treatment again. The investigators rated the subjects' pain on a four-point scale.

The median VAS scores for the patch versus the cream were, respectively, 16 and 33 in the 10-minute group ($P=0.010$), 15 and 22 in the 20-minute group ($P=0.042$), and 2 and 13 in the 30-minute group ($P=0.001$). (The median VAS scores were the same, 2.0, in the 60-minute group).

In the 10-minute group, the investigators note a trend for the patch—65% of patients reported anesthesia with the patch versus 40% with the cream ($P=0.059$). In the 20-minute group, 90% of patients reported anesthesia with the patch and 60% reported anesthesia

with the cream ($P=0.014$). In the 30-minute group, 95% reported anesthesia with the patch and 64% reported anesthesia with the cream ($P=0.020$). Investigator pain ratings were lower for the patch than for the cream for the 10-minute group ($P=0.046$) but not for the groups with longer treatment durations.

In response to the question of whether patients would be willing to use either of these modalities again in the future, more affirmative answers were given regarding the patch than regarding the cream in each of the groups.

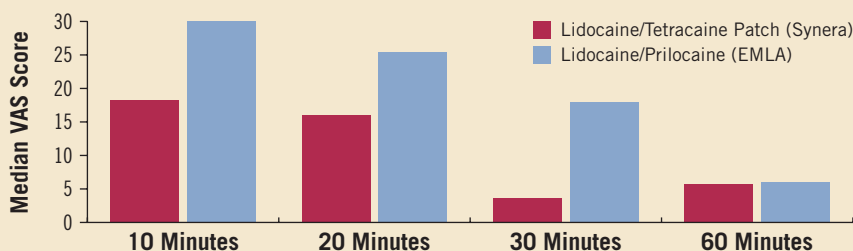
There were no major adverse reactions associated with either the patch or the cream. More erythema was seen with the patch than with the cream at 20, 30, and 60 minutes. The cream was associated with more blanching at 30 and 60 minutes. Two subjects reported nausea and faintness following the venous access procedures; one of the subjects withdrew from the study.

There were no major adverse reactions associated with either the patch or the cream.

Comments From Dr Zempsky

These authors compared the efficacy of a lidocaine/tetracaine patch with the gold-standard topical analgesic compound lidocaine (2.5%)/prilocaine (2.5%). In this comparison, greater percentages of patients in the 10-, 20-, and 30-minute groups reported anesthesia with the patch than with the cream, supporting the findings from the other studies demonstrating the relatively rapid onset of anesthesia achieved with the patch.

Figure. VAS Scores Following Vascular Access Procedures



Significantly less pain was reported for the lidocaine/tetracaine patch compared to EMLA in the 10- ($P=0.01$), 20- ($P=0.042$), and 30-minute ($P=0.001$) groups. VAS=visual analog scale.

Presented at the 28th Annual National Association of Pediatric Nurse Practitioners Conference, March 21–24, 2007, Lake Buena Vista, Florida.