Vapocoolant Spray Is Equally Effective as EMLA Cream in Reducing Immunization Pain in School-aged Children

Evelyn Cohen Reis, MD*, and Richard Holubkov, PhD‡

ABSTRACT. Background. Untreated immunization pain causes undue distress and contributes to underimmunization through physician, and possibly parental, resistance to multiple simultaneous injections.

Objective. To compare the efficacies of two pain management methods in reducing immediate immunization injection pain and distress in school-aged children.

Design. A randomized, controlled clinical trial of eutectic mixture of local anesthetics (EMLA) cream and vapocoolant spray.

Patients. Children aged 4 to 6 years and scheduled to receive diphtheria and tetanus toxoids and acellular pertussis vaccine (DTaP) during health supervision visits.

Interventions. Enrolled children were randomized to one of three treatment groups: 1) EMLA cream + distraction; 2) vapocoolant spray + distraction; or 3) distraction alone (control). The specific pharmacologic pain control interventions consisted of EMLA cream (2.5% lidocaine, 2.5% prilocaine [Astra Pharmaceutical Products, Inc, Westborough, MA] $15.00/patient; applied 60 minutes before injection) and vapocoolant spray (Fluori-Methane [Gebauer Company, Cleveland, OH] $0.50/patient; applied via spray-saturated cotton ball for 15 seconds immediately before injection).

Main Outcome Measures. The blinded investigator (Bl) measured (by edited videotape) cry duration and the number of pain behaviors using the Observational Scale of Behavioral Distress. Pain visual analog scales (linear and faces scales) were completed by the child, parent, nurse, and the Bl.

Results. Sixty-two children, aged 4.5 ± 0.4 years (mean ± SD) were randomized. The three treatment groups had similar subject characteristics. All pain measures and cry duration were similar for EMLA and vapocoolant spray. Both EMLA and spray were significantly better than control. Results for spray vs control: cry duration (seconds): 8.5 ± 21.0 vs 38.6 ± 50.5; number of pain behaviors: 1.2 ± 1.9 vs. 3.1 ± 2.1; child-scored faces scale: 2.0 ± 2.4 vs. 4.1 ± 2.3; parent-scored faces scale: 1.6 ± 1.6 vs. 3.0 ± 1.7; nurse-scored faces scale: 1.6 ± 1.2 vs. 3.1 ± 1.4; and BI-scored faces scale: 1.0 ± 1.5 vs. 2.4 ± 1.4.

Conclusions. When combined with distraction, vapocoolant spray significantly reduces immediate injection pain compared with distraction alone, and is equally effective as, less expensive, and faster-acting than EMLA cream. As an effective, inexpensive, and convenient pain control method, vapocoolant spray may help overcome physician and parent resistance to multiple injections that leads to missed opportunities to immunize. Pediatrics 1997;100(6). URL: http://www.pediatrics.org/cgi/content/full/100/6/e5; pain control, EMLA cream, vapocoolant spray, immunization.

ABBREVIATIONS. AHCPR, Agency for Health Care Policy and Research; EMLA, eutectic mixture of local anesthetics; DTaP, diphtheria and tetanus toxoids and acellular pertussis vaccine; VAS, visual analog scales.

Despite recent advances in the assessment and management of acute pediatric pain, outlined in the clinical practice guideline of the Agency for Health Care Policy and Research (AHCPR),1 children continue to be subjected to the pain and distress of immunization injections.2-6 Parents, as well as their children, experience distress related to untreated immunization pain.6 In addition to undue pain and distress, lack of pain control for injections is a barrier to immunization. Many physicians withhold scheduled vaccines out of concern for the excessive pain of simultaneous immunizations.7-11 We recently showed that children scheduled for three immunization injections were significantly more likely to miss a vaccine than children scheduled for fewer than three.12 This finding suggests that the number of scheduled injections during well-care visits is independently associated with missed opportunities to immunize. Parents’ concerns about injection pain may also contribute to underimmunization through their poor compliance with preventive health care visits.10,13,14 Missed opportunities by physicians combined with appointments not kept account for nearly the total underimmunization rate,15 which far exceeds the target levels set by Healthy People 2000,16 especially among disadvantaged youth.17,18

Reasons for inadequate pain control for immunization are unclear. One possible explanation is that physicians may have negative attitudes toward the applicability of available pain control methods. A topical anesthetic cream, EMLA, or eutectic mixture of local anesthetics, (2.5% lidocaine, 2.5% prilocaine, [Astra Pharmaceutical Products, Inc, Westborough, MA]), is approved for use in reducing the pain of pediatric procedures, including injection. Despite its proven efficacy,19-22 EMLA cream has not been widely accepted for control of immunization pain possibly due to its delayed onset of anesthesia (60
minutes) and expense (approximately $15.00 per 2-dose tube). Another pain management intervention offers promise. In 1955, a vapocoolant spray of a volatile refrigerant liquid (ethyl chloride) was shown to provide cutaneous anesthesia in seconds at a fraction of EMLA’s cost (current cost $0.50 per patient). To date, these interventions have not been compared with regard to their efficacy in controlling pediatric immunization pain and distress. Therefore, the present study was designed to assess the relative efficacies of two methods of pain control, EMLA cream and vapocoolant spray, in reducing immediate immunization injection pain and distress among school-aged children.

METHODS

This randomized, controlled trial of immunization pain control interventions was approved by the Human Rights Committee of the Children’s Hospital of Pittsburgh.

Subjects

Children aged 4 to 6 years and scheduled to receive diphtheria and tetanus toxoids and acellular pertussis vaccine (DTaP) at the Children’s Hospital of Pittsburgh Primary Care Center were eligible for the study. Parents of these children were approached in the registration area. After the study was explained, interested parents gave written informed consent for their children to participate and children gave assent. Children for whom the use of EMLA cream or Fluori-Methane (Gebauer Company, Cleveland, OH) was contraindicated were excluded. Contraindications to EMLA cream consisted of: known history of sensitivity to amide anesthetics (lidocaine, prilocaine); glucose-6-phosphate deficiency; congenital or idiopathic methemoglobinemia; severe hepatic or renal disease, or use of Class I antiarrhythmic drugs. Contraindications to Fluori-Methane consisted of: known history of sensitivity to dichlorodifluoromethane and/or trichloromonomfluoromethane.

Pain Control Treatments

Subjects were randomly assigned to one of the three treatment groups: EMLA cream + distraction; vapocoolant spray + distraction; or distraction alone (control). For subjects scheduled for multiple injections, the same pain control intervention was used for all injections. However, measurements were limited to the target immunization (DTaP), which was administered first.

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<tr>
<th>Outcome Domains</th>
<th>Measure</th>
<th>Assessment Period</th>
<th>Informant</th>
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<tr>
<td>Anticipatory distress-Child</td>
<td>Prior experience VAS</td>
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<td>Pain-Child</td>
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<td>Pain VAS:</td>
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VAS indicates visual analog scale.

Key for assessment period information is as follows: E, Enrollment in waiting room; −1 m, 1 minute before immunization administration; 0, during immunization administration; +1 m, 1 minute after immunization administration; +5 m, 5 minutes after immunization administration.

Key for informant information is as follows: C, Child; I, Investigator, blinded; I*, Investigator, nonblinded; N, Nurse; P, Parent.
used to test for differences between two groups (ie, EMLA vs spray). The $\chi^2$ test was used to test for differences in nominal level data.

Assessment of the statistical significance of the findings necessitates consideration of the multiple between-group comparisons for each outcome. By conservative Bonferroni correction, $P$ values <.016 would be considered significant.

RESULTS

Subject Characteristics

Sixty-two children, aged 4.5 ± 0.4 years (mean ± SD) were randomized. As shown in Table 2, subject characteristics for the three treatment groups were comparable. Of note, patients in the three groups had similar prior experience with injections and similar levels of distress noted at enrollment. In addition, most patients received more than the one target injection, most commonly the measles, mumps, and rubella vaccine.

Child Pain and Distress

Nonblinded Informants

Using the linear and faces VAS scales, parents and nurses rated both EMLA + distraction and vapocoolant spray + distraction as significantly better than distraction alone (control) in reducing children’s immunization-related pain (Table 3). Scores for the control group were approximately twofold higher than for the other two groups. Furthermore, mean scores for the EMLA and spray groups were equivalent. Notably, the children self-reported that vapocoolant spray significantly reduced injection pain relative to control; however, self-reported pain scores for EMLA cream were not significantly different from the control group.

Of note, as most of these significant differences reached the .01 level of significance, our findings are not substantially affected by the consideration of multiple comparisons.

Blinded Observer

The blinded investigator also scored both EMLA and vapocoolant spray as significantly better than control in reducing pain, using the linear and faces VAS scales (Table 4).

The more objective measures scored by the blinded investigator, Observational Scale of Behav-
The children in the control group exhibited twice as many pain behaviors and cried nearly 30 seconds longer than the children in the vapocoolant spray group. Although average cry duration for the EMLA group was shorter than for the control group, this difference did not reach statistical significance ($P = .10$). Of note, although EMLA and spray were both significantly more effective than control in reducing many pain behaviors and cried nearly 30 seconds longer than the children in the vapocoolant spray group, this difference did not persist at 5 minutes postinjection.

**Parent Distress and Satisfaction**

As shown in Table 5, parents reported that children who received EMLA or spray had significantly less pain during the study visit compared with previous immunizations, whereas children in the control group had a mean “comparison VAS” score approaching 50 (“the same pain as previous shots”). This finding is consistent with the other pain outcome measures. Levels of parental distress were not significantly different among treatment groups, although there was a trend toward less distress among parents whose children received EMLA or spray. Of interest, parents of all three groups had similarly strong preferences for their children to receive the same pain treatment again for future injections. This may be due to parental perception that all treatment methods, including distraction, were preferable to standard practice (ie, no attention to pain control).

Parents of children in the EMLA and spray groups were asked about the monetary value of the pain treatment received. On average, parents responded that they would be willing to pay $11.90 for EMLA and $8.40 for vapocoolant spray for future injections.

**DISCUSSION**

Pediatricians are responsible for recognizing and relieving children’s pain in all medical settings, including pain related to procedures. As directed in the AHCPR clinical practice guideline on acute pain management, appropriate relief for pediatric procedures should address both pain and anxiety, using pharmacologic and nonpharmacologic methods.

Our current study of pain control for DTaP injections used both pharmacologic and nonpharmacologic interventions. Although cognitive-behavioral approaches, such as distraction, are effective in treating procedure-related pain and distress, we found that adding EMLA cream or vapocoolant spray to the distraction technique was superior to using distraction alone.

As pain is a subjective experience, individual self-report is the gold standard. We obtained self-report using a child-scored faces scale, which has demonstrated test-retest reliability among 6-year-old children. Given the young age of our patients, we also obtained pain assessments by adult observers, including parents, nurses, and an investigator blinded to treatment group. Of interest, these adult observers rated EMLA and vapocoolant spray as equivalent; however, the children rated the spray as superior to EMLA.

To date, injection pain has received little attention by guest on September 23, 2017http://pediatrics.aappublications.org/Downloaded from
prove vaccine coverage, achieving full second year coverage of 30% of underimmunized children. Second, if parents do bring their children back to receive the postponed vaccines, these additional visits lead to increased health care costs. In addition, untreated injection pain often leads to children’s fear of pediatric visits and time-consuming struggles between patients and office staff.

Many reasons have been proposed to explain the lack of attention to injection-related pain. These include: 1) the myth that children do not experience or remember the pain of injections; 2) lack of assessment of children’s and parents’ distress; 3) physicians’ and nurses’ personal beliefs about the meaning and value of pain in the development of the child (eg, pain builds character); 4) lack of knowledge about possible pain treatments; and 5) negative attitudes toward the feasibility of applying pain control methods in practice. In hopes of addressing this last concern, we designed our current clinical trial to identify an effective and practical pain control method for immunization injections. We found that vapocoolant spray is equally effective as EMLA cream in reducing immediate injection pain, yet it is faster-acting and much less expensive.

With the newly revised immunization schedule, including inactivated poliovirus vaccine and DTaP for infants, the likelihood of multiple, simultaneous injections, and therefore the need for improved pain control, is considerably increased. As an effective, safe, convenient, and inexpensive pain control method, vapocoolant spray may help overcome the barrier of physician and parent resistance to multiple injections that leads to missed opportunities to immunize.

Although generalization of our findings is limited by our study of the DTaP vaccine in 4- to 6-year-old children, these results suggest that the use of vapocoolant spray may help overcome resistance to multiple immunization injections for infants. We are currently conducting a randomized clinical trial of vapocoolant spray versus control in young children, 2 to 24 months old.

**SUMMARY**

Sixty-two children, aged 4 to 6 years, were randomized to one of three pain treatment groups for administration of DTaP: EMLA cream + distraction; vapocoolant spray + distraction; or distraction alone (control). When combined with distraction, vapocoolant spray significantly reduces immediate injection pain compared with distraction alone, and is equally effective as, faster-acting, and less expensive than EMLA cream. As an effective, convenient, and inexpensive pain control method, vapocoolant spray may help overcome the barrier of physician and parent resistance to multiple injections that leads to missed opportunities to immunize.

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