Evaluation of Eutectic Lidocaine/Prilocaine Cream (EMLA®) for Steroid Joint Injection in Children with Juvenile Rheumatoid Arthritis: A Double Blind, Randomized, Placebo Controlled Trial

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ABSTRACT. ***Objective.*** To evaluate the efficacy of eutectic lidocaine/prilocaine cream (EMLA®) in reducing the pain associated with steroid joint injection in children with juvenile arthritis.

Methods. A randomized, double blind, placebo controlled parallel group trial. Thirty-one children (ages 8–18 yrs) scheduled for steroid injection into a knee were randomized into groups having either 2.5 g lidocaine/prilocaine cream or placebo cream applied to the injection site 60–90 min before the procedure. Patients assessed the pain associated with initial needle insertion and subsequent steroid injection using a 10 cm visual analog scale.

Results. No significant difference was found in the pain reported after needle insertion or steroid injection between the lidocaine/prilocaine cream group (n = 17) and the placebo group (n = 14). There was a trend toward an association of lower median scores with the pain of steroid injection in the lidocaine/prilocaine group (6 mm) compared with the placebo group (22 mm).

Conclusion. Application of 2.5 g lidocaine/prilocaine cream for 60–90 min had no statistically significant analgesic effect on pain associated with injections of steroids into the knees of children with juvenile arthritis. (J Rheumatol 2003;30:594–6)

Key Indexing Terms:
EMLA® INTRAARTICULAR STEROID INJECTIONS JUVENILE ARTHRITIS

Intraarticular corticosteroid therapy has become widely used to control joint inflammation in children with juvenile rheumatoid arthritis (JRA)[1,2]. However, the insertion of the needle and subsequent steroid injection into the joint may be both painful and stressful, especially in young children. Since patients with JRA may require repeated injections, a pain-free procedure would facilitate patient care. To lessen the anxiety and pain associated with the procedure, young patients frequently have arthrocentesis performed under general anesthesia or are sedated with agents such as propofol or midazolam. Older children not thought to require deep anesthesia may or may not be given a local anesthetic before needle insertion.

The eutectic mixture of lidocaine/prilocaine cream 5% (EMLA®) containing 2.5% of each drug has been proven to induce surface anesthesia when applied topically under occlusion. EMLA® has been used successfully for pain relief in adults and children in numerous procedures, including venipuncture[3], lumbar puncture[4], intramuscular injection vaccinations[5,6], and various superficial skin procedures[7,8].

To our knowledge, the analgesic effect of EMLA® in joint injections in children has only been briefly addressed in one uncontrolled study[9]. We assessed the efficacy of EMLA® in reducing the pain associated with both needle insertion and subsequent steroid injection into the knees of children with JRA.

MATERIALS AND METHODS

Patients. Patients with JRA who attended the pediatric rheumatology clinic at the Hospital for Sick Children were recruited into the study. Eligibility was restricted to patients between the ages of 5 and 18 years who were scheduled for steroid injection into inflamed knee joints, and whom the investigators

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considered able to evaluate the pain associated with the procedure, using a visual analog scale (VAS). The hospital's research ethics committee approved the study, and informed consent was obtained from patients and parents.

Procedures. The study was a randomized, double blind, placebo controlled parallel group trial. A thick layer of EMLA® or placebo cream, roughly 2.5 g or one-half of a 5 g tube, was applied to the injection site under occlusion with a Tegaderm® dressing. No analgesic or sedative other than the patient's usual arthritis therapy was allowed during the 12 h before the procedure. After at least 60 but no longer than 90 min, the cream was removed, ensuring that at least 50% Tegaderm® adhesion remained in contact with the skin. The skin was prepared with betadine and alcohol solutions. A 21 gauge needle on an empty syringe was used to enter the knee joint, and when applicable, synovial fluid was aspirated. The syringe was then replaced with one containing corticosteroid, which was then injected into the knee. Immediately after the procedure, the patients completed 2 self-assessments on a horizontal 100 mm VAS to quantify the degree of pain caused, first by insertion of the needle and second by the steroid injection.

Data analysis. The treatment and placebo groups were compared using the Wilcoxon rank sum test. All patients were included in the analysis.

RESULTS

Thirty-one patients, 20 girls and 11 boys, were enrolled during the 22 months of the study. Their characteristics are presented in Table 1. There were 17 patients in the EMLA® treatment group, 14 in the placebo group. The groups were similar in age, sex, and previous experience of joint injection. Twenty-two patients (11 in each group) had had previous joint injection, but EMLA® cream was not used for any of these prior injections.

Pain scores recorded by the patients are presented in Table 2. No significant differences were found between the EMLA® and placebo group for either pain assessment ($p > 0.3$). No adverse effects occurred, other than mild itching or burning sensations, and transient skin blanching in some patients.

Table 1. Characteristics of patients.

Variable	EMLA® Group	Placebo Group
Number	17	14
Male	6	5
Female	11	9
Mean age ± SD, yrs	13.4 ± 2.9	13.5 ± 2.8
Age range, yrs	8–17	9–18
Previous injections	11	11

Table 2. Patient pain scores on 100/mm visual analog scale.

Variable	EMLA® Group	Placebo Group
Needle insertion pain, mm		
Median (min, max)	45 (2, 98)	46 (3, 97)
Mean ± SD	47.6 ± 32.1	47.1 ± 31.2
Steroid injection pain, mm		
Median (min, max)	6 (0, 95)	22 (0, 98)
Mean ± SD	21.6 ± 29.7	34.6 ± 35.4

There was a trend toward a slightly lower VAS score in the EMLA® versus the placebo group in association with the steroid injection. No differences in VAS scores were seen between the patients who had previously experienced joint injections and those who had not.

DISCUSSION

Intraarticular corticosteroid injection is the fastest and most effective treatment for the pain and swelling associated with an acute flare of JRA[1,2]. Many rheumatologists use it as first-line therapy in children with pauciarticular JRA. However, the pain associated with the injection (or the anticipated pain) may affect the child's cooperation, which is important for successful placement of the steroid within the joint. General anesthesia or conscious sedation is used but both need specific preparation and assistance. An effective local analgesic would be much easier to use and less expensive.

EMLA® cream is used widely in young children for pain related procedures[10]. Only one report (in abstract form) has addressed the use of EMLA® cream for arthrocentesis in children, comparing its cost-effectiveness with oral midazolam[9]. The authors suggested that EMLA® was more cost-effective and marginally shortened the hospital stay. However, the analgesic effect of EMLA® compared to placebo has not been studied. Our objective was to evaluate the analgesic effect of EMLA® 5% cream applied to children's skin before needle insertion and steroid injection for arthritis of the knee. We found no statistically significant differences for either phase of the procedure. There was a slight trend toward a decrease (median difference, 16 mm) in the pain associated with the second phase of steroid injection in the EMLA® group, perhaps because analgesia of superficial skin structures might affect nociceptive stimuli influencing the pain perception from deeper structures[5,6]. The depth of EMLA® analgesia has been shown to be approximately 3 mm after 60 min of application on intact skin and up to 5 mm after 120 min of application[11]. The synovial membrane is heavily vascularized as part of the inflammatory process, and is usually deeper than 5 mm. The pain of arthrocentesis probably results both from capsular and synovial penetration as well as from the needle penetrating the skin. VAS pain scores may therefore be higher for procedures that involve deep tissue than for other local skin procedures[10]. EMLA® may be more effective if it were applied for 2 h or longer before the injection, allowing deeper penetration. It may also be effective for injections of superficial joints, such as small joints of the hands or feet or tendon sheaths. Topical amethocaine (Ametop®), a lipophilic anesthetic, may have deeper penetrating properties and may therefore deserve further study. It has been shown to be effective in reducing pain in a variety of pediatric procedures[12,13].

Seventy-one percent of our subjects had a previous joint injection, the memory of which might have affected their interpretation of the pain associated with the current procedure. However, there was no difference in VAS scores

between the patients who had received injections and those who had not. In one study, patients who had placebo cream applied and were told that it might help had lower pain scores[14]. Therefore a large placebo effect might have reduced the measured treatment effect size.

We detected no analgesic effect of EMLA® on knee injections in patients with JRA. The topical cream was safe and well tolerated. The number of children studied was small and therefore the statistical power to detect a treatment effect, if present, was low. We were not able to recruit the number of patients required to meet our desired sample size of 32 patients per group (based on probability of ß error of 0.10, i.e., study power of 0.90, and α error of 0.05) during the time of our study. Thus, we cannot exclude a type II error. While larger studies using EMLA® cream for a longer time would be required to definitively assess efficacy, our results do not support its effectiveness in reducing the pain associated with knee injections.

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