



Brief Report

Analgesic pretreatment for antibiotic skin test: vapocoolant spray vs ice cube

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Abstract

Objectives: The objective of this study was to compare the efficacy of ethyl chloride spray and ice cube for the control of pain induced by the antibiotic skin test.

Methods: We performed a prospective, crossover, randomized study in which healthy adult volunteers received an intradermal skin test on both arms after different analgesic pretreatments. We assessed the pretreatment pain and discomfort after the intradermal skin injection using a 100-mm visual analogue scale.

Results: A total of 50 volunteers were enrolled in the study. The mean pain scores after the skin test were 32.4 ± 17.6 and 54.7 ± 22.4 mm, for the ice cube and vapocoolant spray pretreatment, respectively ($P < .0001$). The mean discomfort scores during pretreatment were 20.0 ± 15.2 mm for ice cube and 10.5 ± 11.5 mm for vapocoolant spray ($P < .0001$). Forty-five (90%) subjects preferred the ice cube pretreatment for the intradermal skin test.

Conclusions: The ice cube application was significantly more effective than the vapocoolant spray in reducing the pain of the antibiotic skin test. Hence, the ice cube pretreatment is suggested for easy and fast pain reduction for the antibiotic skin test in the emergency department.

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1. Introduction

When patients presenting to the emergency department (ED) require antibiotic treatment via an intravenous route, an intradermal test is usually performed before administration to evaluate the allergic reaction. According to one study, 14.6% of discharged adult patients and 19.9% of pediatric patients are prescribed antibiotics [1]. Although the intradermal skin test is quite painful, several patients choose to endure the pain and distress without analgesia. This may be because the pain subsides within a brief period or because analgesic administration itself can induce discomfort.

Cryotherapy is the local or systemic use of cold for therapeutic purposes and has been used for thousands of years [2]. A vapocoolant spray with ethyl chloride is often used for the preinjection area or for minor surgical procedures to provide topical analgesia [3]. It immediately cools the sprayed area by lowering the surface temperature through its rapid evaporation. Ice has been also used to control musculoskeletal pain, discomfort from a local anesthetic injection, postoperative pain, and prevention of edema [4-6]. To date, the analgesic efficacies of vapocoolant spray and ice have not been compared when applied to the intradermal skin test. Therefore, the purpose of this study was to evaluate the relative efficacies of these 2 pretreatment methods for control of the pain induced by the antibiotic skin test in healthy adult volunteers.

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2. Subjects and methods

2.1. Study design and subjects

We performed a prospective, crossover, randomized study in healthy adult volunteers with an institutional review board–approved study protocol and written informed consent from each volunteer. Volunteers were recruited from hospital employees. Recruitment was performed through mass mailing of invitational letters to hospital employees. We included healthy adults between the ages of 20 and 55 years, and we excluded pregnant women and individuals with known allergies.

2.2. Study protocol

The order of cryoanalgesia and test arm sidedness was randomly selected with prepared envelopes [7]. After the different cryoanalgesic pretreatments, the subjects received intradermal skin tests on both arms on the anterior aspect of each forearm. Ice pretreatment was performed by putting an ice cube ($2.5 \times 2.5 \times 2.5$ cm) in a latex glove on the forearm for 1 minute. Vapocoolant pretreatment was performed by spraying ethyl chloride (Gebauer, Cleveland, Ohio) on the target area for 5 seconds from a distance of about 15 cm until the skin just began to turn white, according to the manufacturer's instruction. After each pretreatment, an experienced nurse cleansed the target area with an alcohol gauze and injected diluted antibiotics (1:3000) intradermally through a 26-gauge needle. The second-generation cephalosporine, ceftazole, was used for the skin test. The pain assessment was performed 5 minutes after the injection. All pretreatments and skin tests were performed by 1 investigator (WYY) and 1 registered nurse, respectively.

Pain after the intradermal skin injection and discomfort during each pretreatment were assessed using a 100-mm visual analog scale (VAS). We familiarized the subject with the VAS before the assessment. The pain VAS consisted of the question "How much pain did you experience?" followed by the words "no pain" and "most pain imaginable" on either end of a 100-mm line. The discomfort VAS consisted of the question "How much discomfort did you experience during pretreatment?" with the same 100-mm line. After the study was completed, we asked subjects what kind of pretreatment they preferred and if any adverse event occurred during the pretreatment.

2.3. Data analysis

SPSS 12.0 for windows (SPSS Inc, Chicago, Ill) was used for statistical analyses. Sample size was calculated based on our primary outcome variable (pain score). A difference of 13 mm between the mean VAS pain scores of the groups was selected as the minimum clinically significant value [8]. Using this value, we calculated that a sample size of 42

subjects was sufficient to detect an effect size of 0.45 (mean difference/common SD) for pain scores between groups at a significance level of .05 (2-sided) with 80% power [9]. Data are presented as the mean \pm SD. Analysis was performed with the Wilcoxon signed rank test. A *P* value less than .05 was considered statistically significant.

3. Results

A total of 50 volunteers were enrolled in the study. The mean age was 29.9 ± 4.5 years, and 33 (66%) participants were men. Of the 50 volunteers, 24 (48%) received the ice pretreatment first, and 23 (46%) received the first pretreatment in their right arm. Ice pretreatment was perceived as the more efficacious analgesic by 42 (84%) subjects, whereas only 1 (2%) felt that the vapocoolant spray was more efficacious than the ice cube, and 7 (14%) perceived no difference in pain during the skin test. In contrast, 32 (64%) subjects felt that the ice cube was more uncomfortable than the vapocoolant spray, and 16 (32%) subjects perceived no difference in discomfort between the pretreatments. The mean pain scores after ice cube and vapocoolant spray pretreatment for the skin test were 32.4 ± 17.6 and 54.7 ± 22.4 mm, respectively ($P < .0001$). The mean discomfort scores during pretreatment were 20.0 ± 15.2 mm for ice cube and 10.5 ± 11.5 mm for vapocoolant spray ($P < .0001$). Finally, 45 (90%) subjects stated that they preferred the ice cube application for the intradermal skin test. None of the subjects had a positive skin test result, and no one reported an adverse event.

4. Discussion

In 1955, a vapocoolant spray made with the volatile refrigerant liquid, ethyl chloride, was first shown to provide cutaneous anesthesia for injection [10]. Since then, ethyl chloride has been widely used for preinjection anesthesia as well as for pain control in minor surgical procedures, minor sports injuries, and myofascial pain [11,12]. Ethyl chloride applied immediately before skin testing did not adversely affect histamine or standardized aeroallergen wheal and flare responses in adults [9]. Moreover, it is less expensive than EMLA cream (Astra Pharmaceuticals, Westborough, MA), can be rapidly applied, and has an immediate onset of action [2,3]. However, it is controversial with regard to its efficacy in controlling pain from skin tests and injections. Reis and Holubkov [13] reported that vapocoolant spray is more effective than placebo in reducing immunization pain in school-aged children and equally effective as EMLA cream. However, Waibel and Katial [9] reported that although there was a trend toward improved pain scores with ethyl chloride for skin tests, the results were not statistically significant. Furthermore, there are reports that inhalation of or continuous exposure to vapocoolant spray can cause

frostbite, contact dermatitis, and death, although incidences of these are rare [14-16].

On the other hand, humans have used ice for pain relief since the time of Hippocrates [2]. It is readily available, convenient, and fast acting for an anesthetic effect in the ED. Goel et al [5] used ice cubes as a “cryoanalgesic preparation” before local anesthetic injection for lid surgery and found a significant reduction in injection pain with cryopreparation. Kuwahara and Skinner [17] also reported that the distress caused by lidocaine and epinephrine injection was reduced by ice application.

The results of this study showed that ice cube application significantly reduced the pain from the antibiotic skin test compared with vapocoolant spray. Also, the amount of discomfort caused by ice application during pretreatment was significantly higher than that with vapocoolant spray in the statistics. However, the difference in the mean discomfort scores was 9.5 mm, and this difference was not considered clinically significant [8]. Thus, the level of discomfort does not seem to limit the use of ice cube pretreatment. In fact, we found that most subjects preferred ice application.

There were several limitations in this study. Firstly, during an intradermal injection of diluted antibiotics, the amount of pain perceived could vary according to the depth of the needle and the injection technique. To minimize the potential variance in injection depth and technique, only 1 experienced nurse conducted the intradermal injection in this study. Secondly, the discomfort from ice contact is time dependent, and the threshold is very subjective. A 1-minute contact duration of the ice cube used in this study was determined to be optimal based on our preliminary study. Finally, because healthy volunteers with no known allergy history were selected for this study, we were unable to assess the effects of both pretreatments on the allergic reaction to the skin test.

5. Conclusion

To evaluate the efficacies of pretreatment methods in controlling pain from the antibiotic skin test, we compared ice cube and ethyl chloride spray in healthy adult volunteers. Ice cube application reduced the pain from the antibiotic skin

test significantly compared with vapocoolant spray. Hence, the ice cube pretreatment is suggested for easy and fast pain reduction for the antibiotic skin test in the ED.

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