American Journal of Emergency Medicine 34 (2016) 798–804

Contents lists available at ScienceDirect

American Journal of Emergency Medicine

journal homepage: www.elsevier.com/locate/ajem

Original Contribution

Prospective, randomized, double-blind controlled trial comparing vapocoolant spray vs placebo spray in adults undergoing venipuncture☆,☆☆,★,★★

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ARTICLE INFO

Article history:
Received 19 October 2015
Received in revised form 5 January 2016
Accepted 6 January 2016

ABSTRACT

Introduction: Topical anesthetics are used to decrease procedural pain such as venipuncture. Advantages of vapocoolants include rapid onset, ease of application, low cost, and lack of associated pain of injection and other needlestick-related risks. We hypothesized that the pain of venipuncture would be reduced by at least 1.8 points on a 10-point numerical rating scale after application of a vapocoolant compared with placebo.
Methods: We conducted a prospective, randomized, double-blind controlled trial of vapocoolant vs placebo spray in 100 adults (ages 18-80) requiring venipuncture in a hospital emergency department or observation unit. The primary efficacy outcome was the difference in pain scores immediately after venipuncture, measured on a 10-point verbal numeric rating scale from 0 (none) to worst (10). Safety outcomes included local adverse effects (edema, erythema, blanching) and changes in vital signs (VS).
Results: Patient characteristics and venipuncture procedure were not significantly different for the 2 groups. The median (interquartile range) pain of venipuncture was 3 (1.2-5) in the placebo group and 1 (0-3) in the vapocoolant group, $P < .001$. Skin checklist revealed the following: vapocoolant—minimal blanching 4%, minimal erythema 18% which resolved within 5 minutes; placebo—no visible skin changes. Photographs at 5 to 10 minutes revealed no visible skin changes in any patient. There were 2 complaints: "very wet and cold on skin" (placebo) and "felt burning on skin" (vapocoolant).
Conclusion: The vapocoolant significantly decreased venipuncture pain in adults compared with placebo and was well tolerated with minor adverse effects that resolved quickly. There were no significant differences in VS and no visible skin changes documented at the site by photographs taken within 5 to 10 minutes postspray/venipuncture.

1. Introduction

1.1. Background

Painful medical procedures, including needlestick procedures, are frequently done in the emergency department (ED) [1–4]. Pain is the most common reason for ED visits, and oligoanesthesia is common, with practitioners frequently failing to provide adequate analgesia for patients with painful medical conditions [5]. Oligoanesthesia also applies to painful medical procedures, with health care providers failing to use anesthetics before performing painful procedures even though patients indicate that they would like to receive analgesia before a painful procedure [6–9].

Local anesthetics including topical anesthetics are a method of decreasing the pain of procedures [7–11]. The vapocoolant sprays offer many potential advantages over other topical or local infiltrative anesthetics including avoidance of painful injections, local tissue distortion, and health care provider risks of a needlestick. Vapocoolants are also low cost and result in more rapid onset, less administration time, greater staff convenience, and decreases in ED length of stay [4,7,10–17].

The objective of the study is to evaluate the efficacy and safety of a vapocoolant spray in adults in the ED undergoing venipuncture. We hypothesized that the pain of venipuncture would be at least 1.8 points lower after vapocoolant vs placebo spray and that there would be no permanent skin changes associated with the use of a vapocoolant spray [12,18,19].

☆ Presentations: American Society of Regional Anesthesia and Pain, November 2012, Miami, FL; Society of Academic Emergency Medicine, May 2012, Atlanta, GA; American College of Emergency Physicians Scientific Assembly, October 2011, San Francisco, CA.
☆☆ Supported by a grant from the Gebauer Company.
★ The funding source had no involvement in study design; collection, analysis, and interpretation of the data; writing of the report; and the decision to submit the article for publication.
★★ The trial is registered at ClinicalTrials.gov NCT01712776.

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http://dx.doi.org/10.1016/j.ajem.2016.01.002
0735-6757/

2. Methods

2.1. Study design and setting

This is a prospective, double-blind, randomized, placebo-controlled efficacy and safety trial conducted at an urban, academic, tertiary care referral hospital conducted from June 2011 to 2012. The study was approved by the institutional review board, and all patients gave written informed consent.

2.2. Study population

Adults (ages 18-80 years) undergoing venipuncture in the ED or ED observation unit (OU) were eligible for enrollment in the study. Inclusion criteria were as follows: patient undergoing venipuncture, mentally competent patient able to understand the consent form, and clinically stable. Patients were excluded from the study if any of the following criteria were met: allergy to the spray components (eg, 1,1,1,3,3-pentafluoropropane or 1,1,1,2-tetrafluoroethane), critically ill or unstable, extremes of age (pediatric <18 years or elderly geriatric >80 years), pregnant, previous experience with any vapocoolant spray, venipuncture site located in area of compromised blood supply, venipuncture site located in area of insensate skin, patient intolerant of cold or with hypersensitivity to cold, and patient unwilling to give consent. Examples of venipuncture sites located in areas of compromised blood supply would include patients with peripheral vascular disease, gangrene, Raynaud disease or Buerger disease. Examples of patients with insensate or abnormal sensation of the skin would include patients with a peripheral neuropathy. None of the patients recently received an analgesic (such as an opioid) before the venipuncture. Informed written consent was obtained from all subjects.

This was a convenience sample because patients were enrolled when the ED research staff was available, eg, day and evening shifts on weekdays and weekends. The ED research staff members conducting the study were not involved in the care of the patient or in the actual blood draw. The primary researcher was not present and not involved in patient enrollment or data analysis.

The medical history including comorbidities, current medications, and characteristics of the venipuncture itself was listed to determine if the patient populations for the 2 groups were well matched at baseline because comorbidity and medication use, and the venipuncture itself (eg, needle size, location) could possibility affect the difficulty of the venipuncture procedure and the response to the pain of the venipuncture.

Patients were randomized to either sterile water placebo spray (Nature's Tears) or to vapocoolant spray (1,1,1,3,3-pentafluoropropane and 1,1,1,2-tetrafluoroethane) (Gebauer's Pain Ease Medium Stream). The application of the spray in all patients was completed by 1 of 2 trained research assistants whose job was to enroll patients and to standardize administration of the topical spray. After prepping and cleansing the venipuncture site per protocol, the spray was applied in the same manner for all patients, both control and vapocoolant subjects, as recommended by the manufacturer. The specific technique of spray application for both the placebo spray and the vapocoolant spray was as follows: hold the can 3 to 7 in from the venipuncture site; spray onto the venipuncture site steadily for 4 to 10 seconds or until the skin begins turning white, whichever comes first (the anesthetic effect is complete at this time); then immediately perform the venipuncture. There is about a 1-minute time frame to complete the venipuncture because the topical anesthetic lasts only about 1 minute.

The spray cans were not identified as to whether they were the placebo spray or the vapocoolant spray and thus were blinded to the subjects, the research assistants applying the spray, and the health care providers performing the venipuncture. The actual blood draw was done by the ED staff and not by the 2 research associates. All the blood draws were obtained using a Vacutainer with a size 21-gauge needle.

Randomization was accomplished using a computer random number generator with block randomization using randomly varied block sizes of 20 or 30. The spray cans were supplied from outside the ED in varied block sizes such that the randomization was not done by or knowledgeable to the ED research staff performing the actual patient enrollment and data collection to maintain allocation concealment.

2.3. Data collection and processing

All data were collected by trained research associates who had no patient care duties. Their research duties included patient enrollment, data recording, and application of the spray. They recorded on standardized case report forms the demographic data, vital signs (completed by ED nursing staff), clinical variables (from the electronic medical record), all adverse effects/complications, and pain scales (eg, numeric rating scale [NRS]) as reported verbally by the patients: NRS immediately postspray/prevenipuncture and NRS for the pain of venipuncture. They completed the standardized checklist and took before-and-after photographs of the venipuncture site to document any visible skin changes.

All data were entered into a REDCap database and then analyzed using R software (version 2.15.0) by a biostatistician. Continuous variables were summarized using means with variability assessed using standard deviations. Categorical variables were summarized as counts and percentages. Tests for differences of continuous variables were done using Welch 2-sample t tests or Wilcoxon rank sum tests. Tests on categorical variables were done using either Pearson χ^2 tests with Yates continuity correction or Fisher exact test for count data. Significance was at $P < .05$, and the results of testing were given by P values and/or confidence intervals (CIs).

2.4. Outcome measures

The primary outcome was the pain of venipuncture on a 10-point NRS scale ranging from 0 (none) to 10 (worst). The primary safety measures were the documentation of any and all adverse effects/complications and vital signs. Secondary safety measures included a checklist for any changes of the skin: redness, blanching or pallor, itching, edema, or changes in skin pigmentation done immediately post spray/postvenipuncture, NRS postspray/prevenipuncture, and photographs of the venipuncture site done preapplication and 5-10 minutes postapplication of the spray/postprocedure for any visible skin changes.

According to previous studies, a change in NRS of 1.3 or greater is deemed clinically significant [18,19]. A pediatric study found a decrease of 19 mm for the pain of intravenous (IV) cannulation on a 0-100 VAS scale with the use of a vapocoolant spray [12]. Therefore, we decided to use a decrease of ≥1.8 on the NRS because this would include the meaningful difference and was similar to the earlier pediatric study findings. To detect a clinically important decrease of 1.8 on the NRS [18,19], a sample size of 90 adults (45 per treatment group) was chosen, assuming a 2-tailed test, power of 90%, and type I error rate of 0.05. The sample size was increased to 100 (50 per group) to compensate for potential dropouts or protocol deviations.

3. Results

3.1. Study subjects

Of the 136 patients screened for the study, 100 were randomized and received their allocated treatment: 50 patients received sterile water spray (placebo arm), and 50 patients received vapocoolant spray (treatment arm) (Fig. 1). For all 100 study subjects, the mean age (± SD) was 52. 2 (± 12.4) years (range, 19-75 years), with 46 men and 54 women and 62 African Americans and 38 Caucasians. The patients in the 2 study arms had similar baseline characteristics with no significant differences in any of the demographic variables (age, sex, race) or clinical