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Original Contribution

Topical ethyl chloride to reduce pain associated with venous catheterization: a randomized crossover trial☆,☆☆

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ABSTRACT

Objective: To compare pain associated with venous catheterization after administration of topical ethyl chloride vs placebo among emergency department health care providers.
Methods: We conducted a randomized, double-blind, placebo-controlled, crossover trial among a convenience sample of health care provider volunteers in a tertiary care urban emergency department. We randomly allocated subjects to initial treatment (ethyl chloride vs sterile water aerosol spray) and catheterization site (left or right antecubital fossa). After venous catheterization placement and discontinuation, subjects underwent a 5-minute washout period. All subjects then underwent venous catheterization in the contralateral antecubital fossa after administration of the alternative agent. We measured all outcomes after discontinuation of the second catheter. The primary outcome was difference in pain verbal numeric rating scale score (0-10) between the 2 agents. Secondary outcomes included preferred agent (binary) and future willingness to use agent on patients (5-point Likert scale).
Results: Thirty-eight health care providers were recruited; all completed the study. Median pain verbal numeric rating scale scores were 4 (interquartile range, 2-5) for placebo vs 2 (1-4) for ethyl chloride. The effect size for pain reduction with ethyl chloride compared with placebo was 2 (95% confidence interval, 0.5-2; $P = .001$). Most subjects (68.4%) preferred ethyl chloride to placebo. Five-point Likert scale scores measuring willingness to use preferred product on future patients were higher by 2 (95% confidence interval, 1-3) among subjects preferring ethyl chloride vs placebo.
Conclusions: We found that topical ethyl chloride yields a greater reduction in pain associated with venous catheterization compared with topical placebo.

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1. Introduction

Intravenous catheter insertion is a frequent cause of pain for patients [1,2]. Venous catheterization is a common procedure, with one study reporting approximately 15% of all emergency department (ED) patients undergoing intravenous access [3]. Interventions reducing the discomfort associated with intravenous cannulation may significantly alleviate the discomfort associated with ED visits. Several options exist to reduce pain associated with venous catheterization. Analgesic creams are one possibility but may take up to an hour to achieve clinically significant pain relief [4]. Intradermal anesthetics offer another alternative but are invasive and painful [5]. A third option is topical skin refrigerant, or vapocoolant, which potentially provides fast-acting noninvasive analgesia.

Several studies that examine the use of topical skin refrigerants exist. The agents in these studies include fluorohydrocarbon [6] and alkane vapocoolants [7,8]. Prior studies of ethyl chloride yield conflicting results. One unblinded randomized study of patients undergoing intravenous catheterization prior to elective surgery demonstrated no significant analgesia with ethyl chloride vs no intervention [9]. Conversely, 3 unblinded randomized studies of patients undergoing venipuncture demonstrated superior analgesia with ethyl chloride vs no intervention [5,10,11]. An unblinded randomized crossover trial of hemodialysis patients demonstrated superior analgesia with ethyl chloride spray vs placebo [12]. To our knowledge, there are no prior blinded studies comparing ethyl chloride to placebo. A blinded study would provide a useful contribution to the literature. Given the subjectivity of pain, such an investigation would benefit from a randomized crossover trial design in which patients serve as their own controls [13].

This study seeks to determine the effectiveness of topical skin refrigerant compared with placebo in alleviating the pain associated with venipuncture. It is a randomized, double-blind, placebo-controlled, crossover trial of health care provider volunteers. Through double-

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blinding and a crossover design, it seeks to achieve an optimal measure of the effect of ethyl chloride on subjective pain experienced due to venipuncture. Our hypothesis is that topical ethyl chloride spray will lead to a greater reduction in pain associated with intravenous cannulation when compared with placebo.

2. Methods

2.1. Study design and setting

We conducted a single-center randomized, double-blind, placebo-controlled, crossover trial at an urban tertiary care hospital. The annual ED census is approximately 80 000 patients. The institutional review board approved the study. The ClinicalTrials.gov registration number is NCT02499965.

2.2. Study population

We recruited a convenience sample of ED health care providers to participate in the study. Eligible subjects included health care workers (residents, nurses, or medics) 18 years or older who routinely either order or perform venous catheterization on patients. Exclusion criteria included history of hypersensitivity to ethyl chloride, upper extremity amputation or neurologic deficits, or recent injury to or infection of the antecubital fossae. Study investigators confirmed eligibility by physical examination. Participation was voluntary and investigators did not record any demographics or other identifying information.

We publicized the study for 1 month prior to data collection via department-wide e-mails and announcements at weekly grand rounds. On the day of the study, research assistants approached health care providers in the ED patient care areas and invited them to participate. Consent forms disclosed that the subjects would undergo experimental topical therapies prior to antecubital intravenous catheterization in both arms. Subjects understood that they would undergo random allocation to initial receipt of their right vs left arm and 1 of 2 interventions and that by study end, both arms would undergo cannulation and they would receive both therapies. Subjects received no additional details regarding the topical treatments. Study investigators obtained written informed consent from all subjects. Research assistants (nurses or medics) blinded to the study interventions applied the topical treatments, inserted the intravenous catheters, solicited subject responses to study outcomes, and recorded all outcomes on data collection forms. We documented subject intervention and arm allocation in accordance with the CONSORT statement (Fig. 1) [14].

2.3. Study protocol

All study subjects underwent antecubital intravenous catheterization with both topical skin refrigerant and placebo. Research assistants (nurses or medics) not acting as study subjects performed all venous catheterizations using 20-gauge needles. A single research assistant performed both cannulations for each subject. We did not collect detailed information regarding each research assistant's prior background and experience. Similarly, we did not collect any data allowing us to link any subject to the research assistant administering his or her venous catheterizations.

When undergoing the study intervention, subjects received sprays from aerosol containers filled with ethyl chloride (Gebauer's Ethyl Chloride; Gebauer Company, Cleveland, OH). When undergoing placebo administration, subjects received sprays from identical aerosol containers filled with sterile water (Nature's Tears EyeMist; Bio-Logic Aqua Research Technologies Incorporated, Grants Pass, OR) stored at 36°F to better simulate a topical refrigerant sensation. Pharmacy personnel prepared all aerosol containers to obscure contents to blind study investigators, subjects, and research assistants to contents. Research assistants sprayed the antecubital fossa with the aerosol

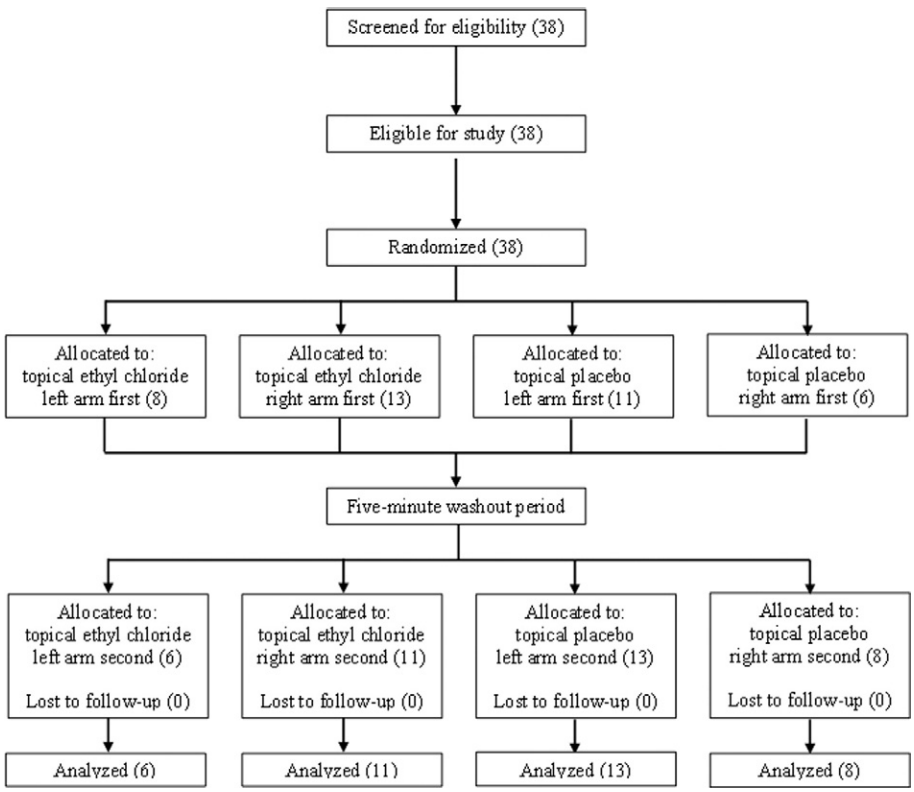

Fig. 1. Flow diagram of patient enrollment, allocation, follow-up, and analysis.