The Journal of Emergency Medicine, Vol. 47, No. 6, pp. 736–749, 2014

0736-4679/$ - see front matter

http://dx.doi.org/10.1016/j.jemermed.2014.06.028

Clinical Reviews

A SYSTEMATIC REVIEW OF VAPOCOOLANTS FOR REDUCING PAIN FROM VENIPUNCTURE AND VENOUS CANNULATION IN CHILDREN AND ADULTS

Mary-Ellen Hogan, BSCPHM, PHARMD, MSC,* Sarah Smart, BSC, MSC,* Vibhuti Shah, MD, MSC,† and Anna Taddio, BSCPHM, MSC, PHD*‡

*Graduate Department of Pharmaceutical Sciences, Leslie Dan Faculty of Pharmacy, University of Toronto, Toronto, Ontario, Canada, †Department of Paediatrics, Mount Sinai Hospital and Institute of Health Policy, Management and Evaluation, University of Toronto, Toronto, Ontario, Canada, and ‡Department of Child Health Evaluative Sciences, The Hospital for Sick Children, Toronto, Ontario, Canada
Reprint Address: Anna Taddio, BSCPHM, MSC, PHD, Graduate Department of Pharmaceutical Sciences, Leslie Dan Faculty of Pharmacy, University of Toronto, 144 College Street, Toronto, Ontario, Canada M5S 3M2

☐ **Abstract—Background: Studies of vapocoolants for pain reduction from venipuncture have demonstrated conflicting results. Objective: Our aim was to systematically review the literature regarding the analgesic effectiveness of vapocoolants in children and adults. Methods: We searched MEDLINE, EMBASE, CINAHL (Cumulative Index to Nursing and Allied Health Literature), and Cochrane Central Register of Trials using key words: *vapocoolant*, *pain*, *venipuncture*, and *cannulation*. We included randomized or quasi-randomized studies comparing vapocoolants to placebo or no treatment. Two authors reviewed titles and abstracts and extracted data. Quality was assessed by consensus using the Cochrane risk of bias tool. The primary outcome was self-reported pain using a 100-mm visual analog scale, a 0- to 10-point numerical scale, or observational scale for preverbal children. Data were pooled using a random effects model. Results: Twelve studies including 1266 patients (509 children, 757 adults) were identified. No significant pain reduction was found in children receiving vapocoolants vs. placebo or no treatment (mean difference −10 mm; 95% confidence interval [CI] −26 to 6). In adults, less pain was reported when vapocoolants were compared with no treatment: −10 mm on a 100-mm scale (95% CI −17 to −4); but not when compared to placebo (−12 mm; 95% CI −26 to 2). Pain from application of vapocoolants was greater than placebo (8 mm; 95% CI 4 to 2). Conclusions: Vapocoolants were ineffective in children and adults when compared to placebo, and effective in adults only when compared to no treatment. The magnitude of effect was low and was offset by increased pain from application. They cannot be recommended for routine use in children or adults.** © 2014 Elsevier Inc.

☐ **Keywords—vapocoolant; analgesia; pain; procedural pain; pediatrics; venipuncture; intravenous cannulation; systematic review; meta-analysis**

INTRODUCTION

Venipuncture for blood sampling and peripheral intravenous (i.v.) cannulation are routine procedures experienced by children and adults who require treatment in health care facilities. They are an important source of iatrogenic discomfort due to the accompanying pain they induce. Pain management during medical care, in addition to being recognized as a basic human right, impacts a patient's satisfaction (1,2). Steps should be taken whenever possible to prevent iatrogenic pain. An ideal

Sarah Smart was supported by a Canadian Institutes of Health Research Pain in Child Health training award and Mary-Ellen Hogan was supported by a Hospital for Sick Children Clinician Scientist Training Award while this project was underway.

Anna Taddio has received research grants from Pfizer Canada Inc. and study supplies from Natus and Ferndale.

RECEIVED: 18 October 2013; FINAL SUBMISSION RECEIVED: 4 March 2014;
ACCEPTED: 30 June 2014

analgesic for venipuncture or i.v. cannulation would be effective, pain-free, and require little to no preparation time, and vapocoolants could be suitable for that role.

Vapocoolants, or skin refrigerants, are volatile liquids applied on the skin that immediately lower the surface temperature of the skin while they evaporate. Several commercial products exist and availability varies by country. In the United States, two licensed vapocoolants are ethyl chloride (Gebauer's Ethyl Chloride®; Gebauer, Cleveland, OH) and 1,1,1,3,3-pentafluoropropane/1,1,1,2-tetrafluoroethane (Painease®, Spray and Stretch®, and Instant Ice®; Gebauer, Cleveland, OH). The manufacturer states that these products can be used to reduce pain for a number of conditions, including minor surgical procedures, injections, venipuncture, i.v. cannulation, myofascial pain, muscle spasm, minor sports injuries, bruises, contusions, swelling, and minor sprains (3).

Two theories have been postulated regarding how they might work to decrease pain. One is that the cold sensation might reduce pain by gating pain signals so that the cold sensation is felt rather than pain (4,5). Another theory is that they decrease the velocity of nerve impulse transmission across nerve fibers (5,6).

Many studies have investigated the use of vapocoolants to reduce pain from venipuncture or i.v. cannulation in children and adults and have demonstrated conflicting results. At present, it is not clear whether vapocoolants are effective and there has been little consideration of the potential discomfort from their use (due to the cold sensation). In addition, it has been suggested that children might perceive the cold effect of vapocoolants more intensely than adults and so might respond differently (7). We therefore carried out a systematic review and separate meta-analyses of the analgesic effectiveness and safety of vapocoolants in children and adults for venipuncture or i.v. cannulation.

METHODS

The Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines for reporting meta-analyses of randomized controlled trials were used in this study (8). A protocol was planned in advance and any post-hoc analyses are indicated in this section and the Results sections.

Studies selected for the review were required to have the following characteristics: randomized or quasi-randomized* design in adults or children; healthy volunteers or patients requiring venipuncture or peripheral i.v. cannulation for therapeutic reasons; treatment group included application of a vapocoolant; control group included placebo or no treatment; pain was self-reported on a visual analog scale, numerical rating scale, or validated pictorial scale, or for preverbal children, a validated observer-reported tool. No language restrictions were applied. Studies were excluded from the analysis if they included an additional analgesic or sedative in the intervention group and not in the control group (e.g., vapocoolant and another analgesic vs. placebo or usual care) or if they included both children and adults and did not report outcomes separately. Unpublished studies or those published as abstracts or letters were excluded.

The following databases were searched: MEDLINE (1946–July 2013), EMBASE (1980–July 2013), CINAHL (Cumulative Index to Nursing and Allied Health Literature) (1982–July 2013), and Cochrane Central Register of Trials (June 2013) using key words *vapocoolant*, *pain*, *venipuncture*, appropriate to each database (see Appendix for search strategy). References from the identified studies and reviews of the topic were hand-searched for additional articles. Titles and abstracts identified in the search were reviewed independently by two authors.

Quality was assessed using the risk of bias tool by the Cochrane Collaboration and further developed by the StaR Child Health Group (9,10). Bias is a systematic deviation from the truth and can operate to either overestimate or underestimate the effect of an intervention. Certain aspects of study design have demonstrated that they contribute to bias, but it is not possible to know the magnitude of an effect (if any) from a particular bias in a study; therefore, it is more appropriate to consider the risk of bias in a study (9). The risk of bias tool assessed each study for sequence generation, allocation concealment, blinding of participants, personnel and outcome assessors, incomplete reporting of outcome data, selective outcome reporting, and other sources of bias. Three authors assessed each domain according to preset criteria and judged it as low, high, or unclear risk of bias. Judgements were compared and differences were discussed until consensus was achieved. When more than one comparison within the study was relevant to the meta-analysis (eg, vapocoolant vs. placebo, vapocoolant vs. no treatment), relevant domains were assessed separately for each comparison and reported separately if different. Reviewers were not blinded to the study authors, locations of the studies, author funding, or study acknowledgments.

Data were extracted by two authors using a structured data form. Content included author, citation, type of procedure, age of participants, diagnosis, study design, type of vapocoolant and comparator(s), sample size for treatment and control groups, pain assessment tool(s), and outcome data (efficacy and adverse effects). Discrepancies were discussed until consensus was reached.

*Quasi-random designs use a nonrandom sequence generation, such as alternating days of the week or odd/even medical record numbers, to allocate patients to treatment groups.