

## **Effect of Vapocoolant on Pain During Peripheral Intravenous Cannulation**

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### **Methods**

#### **Data Sources**

The Cochrane Central Register of Controlled Trials, MEDLINE, EMBASE, Literatura Latino Americana em Ciencias da Saude, Cumulative Index to Nursing and Allied Health Literature, and ISI Web of Science were searched from inception to May 2015 without language restriction. Trial registries were searched, including [clinicaltrials.gov](http://clinicaltrials.gov), [controlled-trials.com](http://controlled-trials.com), and [trialscentral.org](http://trialscentral.org). Additionally, the authors hand searched the references of retrieved articles and abstracts of the American Society of Anesthesiologists.

#### **Study Selection**

This review included all randomized controlled trials comparing vapocoolant to placebo or no treatment for analgesia associated with intravenous cannulation. Studies of adults, children, and healthy

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volunteers were eligible. Titles and abstracts were reviewed by at least 2 authors, and potentially relevant studies underwent full text review. Discrepancies in study selection were resolved by consensus.

### **Data Extraction and Synthesis**

Three authors independently extracted data, using a standardized data extraction form. Discrepancies in extracted data were resolved by consensus. Studies were assessed as low, unclear, or high risk of bias in each of 6 domains: random sequence generation, allocation concealment, blinding of participants and personnel, blinding of outcome assessors, incomplete outcome data, and selective reporting. Data reported on a 100-point visual analog scale (VAS) were reported as mean difference. When data were measured with different scales, they were combined with standardized mean difference. A fixed-effect model was used when the I<sup>2</sup> statistic was less than 40%; otherwise, a random-effects model was used.

### **Results**

The search identified 2,110 titles, of which 9 met the inclusion criteria and were included in the review. Eight of these (N=848) were included in the meta-analysis. Six studies were conducted in the emergency department (ED), and 3 studies were of children. Four of the studies were blinded, and the overall quality of the evidence was rated as moderate to high. Vapocoolants modestly reduced pain on a 100-point VAS (Table). I<sup>2</sup> was 74%, indicating a high degree of heterogeneity. Sensitivity analyses based on risk of bias, setting (ED versus other), children versus adults, type of vapocoolant, and duration of vapocoolant application did not yield significant differences and did not explain the heterogeneity. Only 2 studies provided dichotomized data by pain relief (yes/no), which suggested that vapocoolant spray had increased odds of relieving pain. The overall summary results based on meta-analysis found that vapocoolants provide pain relief during cannulation (Table); however, pain increased slightly with vapocoolant application. Vapocoolant use did not affect first-attempt success of intravenous cannulation.

### **Commentary**

Intravenous cannulation is one of the most common painful procedures performed in the ED.<sup>1</sup> Needle-related procedures can induce fear and anxiety in both children and adults.<sup>1, 2</sup> Studies have demonstrated that inadequate relief of pain during childhood can lead to negative effects on future pain tolerance and responses.<sup>2</sup> Numerous interventions have been suggested to treat the pain associated with needle insertion, including topical anesthetics,<sup>3</sup> vapocoolants,<sup>4</sup> and nonpharmacologic interventions.<sup>5</sup>

Topical anesthetics have been demonstrated to significantly reduce pain but require 30 to 90 minutes for effect, which may not be feasible for most patients.<sup>3</sup> Nonpharmacologic interventions, such as distraction and cognitive behavioral therapy, have also demonstrated efficacy but require additional resources that may not be available in most EDs.<sup>5</sup> Vapocoolant spray is an ethyl chloride or fluorohydrocarbon-based solution that is sprayed onto the skin before an anticipated painful procedure. The highly volatile solution rapidly evaporates, causing a decrease in skin temperature and temporary decrease in pain sensation. Vapocoolant spray is inexpensive and rapid in onset, which may make it more feasible than the above alternatives.

This study demonstrated a small decrease in procedural pain, with no difference in cannulation success; however, the clinical significance of the difference must be questioned. The often-cited difference in pain measured on a 100-point VAS that is clinically relevant is 13.6.<sup>7</sup> This study demonstrated a decrease in the point estimate of 12.5, which is just below this clinically relevant threshold, and the 95% confidence interval extended down to a difference of only 6.4 points. Additionally, the application of the spray increased pain by a mean of 6.3 on the VAS. Therefore, we cannot say with confidence that the effect is clinically important. The substantial heterogeneity among the trials further decreases confidence in the overall estimate of effect.

There were several additional limitations to this systematic review. Most studies were performed with adults, whereas vapocoolant is more commonly used for children. Half of the included studies did not quantify differences in intravenous cannula size, which can affect the pain of insertion. Four studies did not blind the participants or assessors and only 4 studies used a sham spray, so it is difficult to

determine the magnitude of any placebo effect. There was also no assessment of baseline difficulty of intravenous access. Overall, there was an 83% first attempt success rate for cannulation, suggesting that these patients were not difficult intravenous catheter insertions. Given the potential of cold to induce vasoconstriction, it is unclear whether this treatment will decrease success rates in patients with more difficult intravenous access.

The use of vapocoolants did appear to be safe; reported adverse events were minor and included 4 reports of cold sensitivity, 3 transient reactions of erythema at the site, and 1 report of burning sensation. Although there was a small increase in pain associated with the application of the vapocoolant spray (Table), this also was of questionable clinical significance.<sup>6, 7</sup> Although there were no major complications observed, health care providers should be aware that, rarely, prolonged spraying can cause skin hypopigmentation and atrophic scarring, especially in patients with poor circulation.<sup>8</sup> Finally, one must consider the initial rationale for placing the intravenous catheter. Studies have demonstrated that 50% of intravenous catheters placed in the ED were never used<sup>9</sup>; therefore, the best way to mitigate the pain associated with catheter placement is to not place it when it is unnecessary.

Future studies should compare vapocoolant treatment with and in conjunction with alternative treatments, as well as increase the number of pediatric participants and those with difficult intravenous access.

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Editor's Note: This is a clinical synopsis, a regular feature of the Annals' Systematic Review Snapshot (SRS) series. The source for this systematic review snapshot is: Griffith RJ, Jordan V, Herd D, et al. Vapocoolants (cold spray) for pain treatment during intravenous cannulation. *Cochrane Database Syst Rev.*2016;(4):CD009484.

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**Table. Comparison of outcomes with vapocoolant versus placebo or no treatment.**

<b>Outcome</b>	<b>Number of Studies (Number of Patients)</b>	<b>Mean Difference (95% CI)*</b>	<b>RR (95% CI)</b>	<b><i>I</i><sup>2</sup>, %</b>
Pain during cannulation	8 (848)	-12.5 (-18.7 to -6.4)		74
Pain with application	4 (461)	6.3 (2.2 to 10.3)		49
Dichotomous assessment of "pain relief"	2 (281)		1.67 (1.30 to 2.13)	0
First-attempt success	6 (812)		1.00 (0.94 to 1.06)	48

*CI*, Confidence interval; *RR*, risk reduction.

\*Difference in means as assessed on a 100-point VAS.