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A Randomized Clinical Trial of Vapocoolant for Pediatric Immunization Pain Relief

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### Abstract

**OBJECTIVES:** The purpose of the current study was to evaluate the effectiveness of vapocoolant for preschoolers' immunization injection pain relief.

**STUDY DESIGN:** 57 4- to 6-year-old children were randomized to vapocoolant alone or typical care conditions. Pain was measured at baseline and at injection via self-report, caregiver-report, nurse-report, and an observational scale.

**RESULTS:** Self-report suggested that children in the vapocoolant alone condition demonstrated stronger increases in pain from baseline to injection than typical care. All other measures showed significant increases in pain from baseline to injection, but none indicted treatment effects.

**CONCLUSIONS:** Consistent with prior studies, vapocoolant might not be an effective pain-management intervention for children's intramuscular injections.

**KEY WORDS:** Pain control, vapocoolant, immunization, children, pain

## A Randomized Clinical Trial of Vapocoolant for Pediatric Immunization Pain

### Introduction

Children exhibit and report high levels of distress during painful medical procedures, which can lead to heightened anxiety and pain during subsequent procedures (1, 2). Furthermore, early pain has been associated with increased sensitivity to later medical insults (3) and poorer future health care attitudes and behaviors (4). Given the potential negative impacts of pediatric procedural distress, the development and evaluation of interventions in this area are important endeavors.

Optimal pain management interventions should be effective, safe, and require minimal resources (e.g., staff time, cost). One treatment that appears to meet these demands and is becoming used regularly in some medical centers is ethyl chloride, often referred to as vapocoolant cold spray. Vapocoolant is relatively inexpensive (e.g., approximately \$0.50 per patient), requires little time to take effect (e.g., approximately 20 seconds), and is easy to use (e.g., spray or apply directly to tissue). There is a fair amount of evidence supporting the pain management efficacy of vapocoolant for medical procedures in adults (e.g., (5)), but results in children have been mixed. For example, two investigations of vapocoolant and placebo spray for children revealed no differences between conditions (6, 7). Alternatively, Reis and Holubkov (1997) (8) found vapocoolant combined with distraction was superior to distraction alone. Unfortunately, this study did not include a vapocoolant alone condition, thus it remains unclear whether vapocoolant without distraction is an effective pain management invention for children.

The purpose of this study was to evaluate the effectiveness of vapocoolant alone for pediatric immunization pain. A multi-informant, multi-modal assessment was conducted, which employed children's self-report, caregiver- and nurse-report, and an observational measure of

children's pain. Consistent with Reis and Holubkov, it was hypothesized that children in the vapocoolant alone condition would demonstrate lower levels of pain across measures.

## Materials and Methods

### *Participants*

This study was designed in accord with, and adheres to the guidelines detailed in, the Consolidated Standards of Reporting Trials (CONSORT) statement (9, 10, 11) (see Figure 1 for the CONSORT Flowchart). Appropriate institutional approval was obtained prior to study initiation. All participants were recruited from a University-based outpatient primary care clinic. Eligible participants were children 4 to 6 years of age receiving routine immunizations in the pediatric clinic over a three month period. A power analysis with .80 power and using the large effect size of .90 found across a number of measures in a prior study (8) revealed that 15 participants per condition would be necessary. However, given the null findings in other studies (6, 7), it was determined that a larger sample might be appropriate. Thus, approximately 30 participants per condition were projected. Sixty-nine caregivers were approached to participate in this study. The caregivers of 7 children receiving immunizations declined participation. Four of these stated that they were not interested and three reported that they did not have enough time to participate. Five of the recruited participants were not included in analyses (four did not receive injections and one failed to complete the post-immunization ratings). The final sample consisted of 57 children and their caregivers. Children were on average about 5 years of age ( $M = 5.17$ ,  $SD = 0.52$ ). Thirty-two children were female (56%). Thirty-eight children were Caucasian (66.7%), six were Asian American (10.5%), three were Native American (5.3%), two were African American (3.5%), two were Hispanic (3.5%), and six were reported as Other by their caregiver (10.5%).

Caregivers ranged in age from 18 to 56 years ( $M = 32.92$ ,  $SD = 8.24$ ), 41 (71.9%) were Caucasian, six were Asian American (10.5%), four were Native American (7.0%), three were Hispanic (5.3%), one was African American (1.8%), and two reported Other (3.5%). Caregivers' annual income was approximately \$42,353.49 ( $SD = \$30,134.77$ ) and they had completed on average one year of college education (mean years of education = 13.41,  $SD = 2.64$  years). In addition, most caregivers were married (75.4% married, 10.6% separated or divorced, 1.8% widowed, 10.5% single, and 1.8% not reported).

### *Measures*

*Observational instrument.* The Child-Adult Medical Procedure Interaction Scale (CAMPIS; (12)) served as an observational measure of child injection distress. The subcodes of cry, scream, verbal resistance, verbal pain, negative emotion, physical restraint, and flail were intercorrelated and combined as a Child Distress composite.

Research assistants who coded with the CAMPIS were kept blind to study hypotheses (e.g., vapocoolant alone hypothesized to be more effective) but not to participant's group assignment given the nature of the intervention utilized. Research assistants were trained according to CAMPIS protocol using similar videotaped data from a prior study. A CAMPIS code was recorded if it began, occurred, and/or ended at any time during a five-second interval, and coding spanned from three minutes prior to cleaning the child's arm for the immunization until the child left the room or three minutes had passed, whichever came first. The codes were summed and divided by the total number of five-second intervals in the procedure to obtain a percentage score.

To establish interrater agreement, raters coded the same non-study data until at least 80% agreement was found for occurrence of behavior. Once raters reached these criteria, coding of

study data began. Twenty percent of the data was randomly selected to check interrater agreement with Cohen's Kappa, a conservative statistic that corrects for chance agreement (13, 14). Kappa for Child Distress subcodes ranged from .55 (physical restraint) to 1.0 (flail) with the average Kappa being .76, which reflects a very good level of agreement (15).

*Child self-report.* The Faces Pain Scale-Revised (FPS-R; (16)) was utilized to assess children's self-reported pain at baseline before the immunization and after to assess the pain associated with the immunization. The FPS-R consists of six faces exhibiting increasing levels of pain intensity. Scores on the FPS-R range from 0 to 10, with 0 representing no pain and 10 presenting very much pain. The FPS-R has demonstrated adequate reliability and validity (16), (17).

*Caregiver- and nurse-report.* Prior to the immunization, caregivers and nurses rated child baseline distress using a 100mm visual analog scales (VASs) anchored by Not Distressed to Very Distressed. Following the immunization, caregivers and nurses used similar VASs to indicate child immunization distress. VASs are widely used in pediatric pain studies, they have good reliability and validity, and they do not result in the clustering of scores as is common with likert-type scales (18, 19).

### *Procedure*

Potential participants were approached by a research assistant in the waiting room of the pediatric clinic. All pre-procedure measures were completed before the caregivers and participants had contact with the medical staff, and before they were assigned to a condition. After completing the baseline measures, participants were then randomly assigned to one of two conditions (Vapocoolant Alone or Typical Care). A randomization schedule was determined before the initiation of data collection and assignments were listed on a form kept in a binder at

the site. Therefore, the randomization list was not fully concealed from research assistants. After a participant was enrolled, researcher assistants assigned conditions based on the next condition listed (i.e., Vapocoolant Alone or Typical Care). Thirty-one participants were randomized to Vapocoolant Alone condition and 26 to the Typical Care condition. Consistent with the procedure of Reis and Holubkov (1997) (8), children assigned to the Vapocoolant Alone condition received the vapocoolant solution via the nurse placing a cotton ball saturated with vapocoolant on the immunization site for approximately 20 seconds immediately prior to the injection. No other intervention was implemented in this condition. Nurses were instructed to follow their normal routine. Typical Care involved the usual routine used by nurses in this setting. In both conditions, a camcorder in the treatment room was used to record the procedure for later behavioral coding. Participants, nurses, and research assistants were not kept blind to participant group assignment given the nature of the vapocoolant intervention.

## Results

### *Preliminary Analyses*

Due to technical difficulties with video equipment 3 participants did not have video data and therefore could not be evaluated for any observational measures of child distress. These data were left as missing points in analyses and other compensatory actions (e.g., inserting a mean value) were not taken.

Preliminary analyses were conducted to determine whether there were any significant between-group differences on demographic variables. Chi-square analyses (see Table 1) indicated no differences between groups on caregiver and child race and gender. T-tests revealed no significant differences between conditions on caregiver educational level, caregiver-report of child prior distress during immunizations, and caregiver-report of the amount of pre-procedure

child distress (Table 1). Results indicated a significant difference between groups on family income with families in the Control group reporting higher incomes than those in the Vapocoolant Alone condition,  $t(41) = 1.95, p = 0.05$ . Income was not related to any of the dependent variables and was thus not used as a covariate in subsequent analyses.

### *Treatment Effects*

*Observational.* CAMPIS Child Distress composite was analyzed using a repeated measures analyses of variance (ANOVA) with one within subjects variable (Time: baseline-immunization) and one between subjects variable (Group: vapocoolant-control). Results revealed a significant main effect for Time,  $F(1, 53) = 119.86, p < .001$ , but no significant main effect of Group or interaction of Time and Group.

*Caregiver and nurse report.* Similar to observational measures, there was a significant main effect of time for caregiver-report,  $F(1, 54) = 89.10, p < .001$ , and nurse-report of child distress,  $F(1, 53) = 25.21, p < .001$ , but no significant main effect of Group or Time x Group interaction.

*Self-report.* Analyses involving children's self-report revealed a significant main effect for Time,  $F(1, 49) = 71.15, p < .001$ , but no main effect for Treatment on children's self-report (see Table 2). Contrary to observational and report by others findings, children's self-reported distress showed a significant Group x Time interaction,  $F(1, 49) = 6.76, p < .05$ . Follow-up analyses indicated that children in the vapocoolant alone group had a more significant increase in self-reported pain from baseline to injection than children in the control condition, .

### Discussion

The purpose of the study was to provide a thorough evaluation of the effectiveness of vapocoolant for children's immunization pain. This evaluation compared vapocoolant alone to

typical care. In short, the results do not support vapocoolant alone for reducing children's intramuscular injection pain. This is consistent with prior results (6, 7). The most parsimonious explanation is that vapocoolant does not provide effective pain management for children's intramuscular injections. If this is the case, it is important to disseminate the information to avoid spending time and money on interventions that are not helpful.

However, there are other explanations for the lack of treatment effects. It could be that the cold sensation after the application of the chemical to the skin was an irritant that offset the benefit of any pain relief. This might help explain why children's self-report reflected heightened pain for vapocoolant in this study. Yet, no adverse events were reported to study personnel by nurses who administered the vapocoolant. Related, data exist suggesting that children are more sensitive to water temperatures than adults (20, 21). Another explanation might be that children expected greater pain relief from vapocoolant, and when any pain sensation was experienced, children's anxiety and pain reports were elevated.

Some discussion of the lack of consistency in results between this study and the one by Reis and Holubkov (1997) (8) is in order. First, in the prior study, vapocoolant was not evaluated in isolation – it was combined with distraction. There might be some synergistic benefit to this combination that resulted in effective anxiety and pain management. It could be that the distraction decreased the pain from the cold sensation, which may have eliminated that aversive aspect of vapocoolant.

Another explanation for the lack of findings could be that the sample size did not provide sufficient power. Using the effect sizes from the current study, post-hoc analyses revealed that sample sizes of 98 (self-report), 212 (observational), 406 (caregiver-report), or 880 (nurse-report) would have been needed to find group differences with .80 power. This begs the question as to

whether statistical differences in scores with larger samples would truly be clinically meaningful. Thus, it is not likely that the results found in this study are the result of Type II error. It could also be that the anxiety associated with the injections was sufficiently high which may have masked differences in pain scores. Had an anxiety management intervention been employed, such as distraction, differences in pain might have been revealed.

In sum, these results are consistent with those found by Abbot and Fowler-Kerry (1995) (6) and Ramsook et al. (2001) (7), and suggest that vapocoolant does not provide effective pain management for preschoolers' immunizations when used alone. Additional evaluations are in order, especially for participants of different ages and patients undergoing different procedures. In addition, continuing to evaluate vapocoolant paired with additional pain management interventions seems warranted.

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