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Effect of topical alkane vapocoolant spray on pain with intravenous cannulation in patients in emergency departments: randomised double blind placebo controlled trial

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ABSTRACT

Objective To assess the efficacy, acceptability, and safety of a topical alkane vapocoolant in reducing pain during intravenous cannulation in adults.

Design Randomised double blind placebo controlled trial.

Setting Emergency department of a metropolitan teaching hospital.

Participants 201 adult patients (54% male), mean (SD) age 58.2 (19.5) years, who required intravenous cannulation.

Interventions Less than 15 seconds before cannulation, the skin area was sprayed with either water (control, n=98) or vapocoolant (intervention, n=103), from a distance of 12 cm for 2 seconds. The intervention spray was a blend of propane, butane, and pentane.

Main outcome measures Pain with cannulation and discomfort with spray, measured with a 100 mm visual analogue scale.

Results Groups did not differ significantly in age, sex, indication for or site of cannulation, cannula size, or who cannulated the patient (P>0.05). Median (interquartile range) pain scores for cannulation in the control and intervention groups were 36 (19-51) and 12 (5-40) mm, respectively (P<0.001), and 59 (60%) and 33 (32%) reported pain scores ≥30 mm (P<0.001). Scores for spray discomfort also differed significantly (P<0.001) because of skewing to the right within the intervention group. The median discomfort scores, however, were 0 mm in both groups. Success rates for first cannulation attempt did not differ between groups (P=0.39). Thirty four (39%) and 62 (62%) patients said they would choose the spray they received for analgesia in the future (P=0.002). At follow-up at five days, two patients in the intervention group reported transient skin redness.

Conclusions Topical alkane vapocoolant spray is effective, acceptable, and safe in reducing pain with peripheral intravenous cannulation in adults in the emergency department.

Trial registration Australian Clinical Trials ACTRN12607000470493.

INTRODUCTION

As about half of patients report moderate to severe pain with cannulation and anxiety before the procedure, administration of local anaesthetic might be justified.[1] On a 100 mm visual analogue scale pain scores in untreated adults ranged from 24 mm to 38 mm.[1-3] Intradermal injection of lidocaine is commonly used for analgesia.[4] This effectively reduces pain[2 3] by clinically important amounts.[5] The injection itself, however, is painful,[3] and, theoretically, there is an increased risk of needle stick injury. Additionally, reports are divided on whether local tissue distortion, caused by the injection, increases[3] or has no effect on[1 2] the rate of cannulation failure.

Another strategy is the application of topical local anaesthetic. These agents must penetrate the stratum corneum barrier,[6 7] which necessitates application times of at least 45 minutes for Emla (lidocaine 2.5% and prilocaine 2.5%)[8] and 30 minutes for Ametop (4% tetracaine).[9] In emergency departments, such application times are often unacceptable as immediate cannulation is often required.

Less than half of medical and surgical doctors use local anaesthetic for insertion of large bore intravenous cannulas.[10] Furthermore, for the most commonly used cannula (size 20 gauge), less than 20% of all doctors used any local anaesthetic.[10] Another study reported that 35% of junior doctors had previously used local anaesthetic for cannulation but their current rate of use was only 6%.[4]

Topical vapocoolant sprays can produce immediate skin anaesthesia. Commonly used vapocoolants include ethyl chloride, fluorohydrocarbon, and alkane mixtures (butane, propane, and pentane). Alkane vapocoolant sprays are primarily used to provide rapid pain relief from acute muscular injuries. Rapid evaporation of the volatile liquid spray from the skin surface causes a drop in temperature and results in temporary interruption of pain sensation, possibly through desensitisation of pain receptors or activation of ion channels involved in pain transmission.[11]

Topical vapocoolant spray therefore offers a potentially convenient and effective anaesthetic for intravenous cannulation.

Previous studies of vapocoolant sprays for reducing pain with intravenous cannulation in adults have shown inconsistent results. Four randomised controlled trials have been reported. Two showed ethyl chloride to be effective,[2 3] while two others found ethyl chloride[1] and fluorohydrocarbon,[1 2] respectively, to be ineffective. Methods in these studies varied, including variation in cannula size, duration and distance of spray, small sample sizes, and lack of blinding.

We assessed the efficacy, acceptability, and safety of a topical alkane vapocoolant spray for reducing pain with intravenous cannulation in adults by comparing its effects with a control (water) spray.

METHODS

Study design

The trial took place from November 2007 to May 2008. It was a randomised double blind placebo controlled clinical trial set in a mixed (adult and paediatric) emergency department that treated about 55 000 patients a year.

Patients were included if they were aged ≥18 and needed intravenous cannulation. Exclusion criteria were refusal to participate, inability to provide informed consent (non-English speaking, altered mental state, severe illness, urgent need for cannulation), moderate to severe discomfort or pain, skin disease associated with cold intolerance (such as Raynaud's phenomenon), known allergy to spray contents, peripheral neuropathy or numbness, parenteral analgesia within the previous four hours, and the use of other local anaesthesia.

Recruitment

We enrolled a convenience sample comprising consecutive patients who met the entrance criteria during periods when the principal investigator was present in the emergency department (mainly 9 am to 5 pm on weekdays). The emergency department staff notified the principal investigator of patients who required cannulation. Patients who met the entrance criteria received a verbal and written explanation of the study and gave written consent to participate.

Randomisation

Each enrolled patient was then assigned the next sequentially ordered study pack. These contained all the documents for data collection and a sealed envelope containing a note that advised the group to which the patient had been randomised. Patients were block randomised (blocks of six) by an independent pharmacist using a computerised random number generator. Until after informed consent had been obtained, only the pharmacist knew the randomisation status. At that time, the principal investigator opened the sealed envelope and prepared to administer the assigned spray. The patients, their carers in the emergency department, and independent emergency department staff who collected outcome data were all blinded to the randomisation status.

Intervention and control sprays

The vapocoolant (intervention) spray was CO LD Spray, manufactured by DIFA Chemical Industries for Alpha First Aid Supplies. It is a propane, butane, and pentane blend, with an added fragrance, and is supplied in a standard (about 20 cm long, 250 g in weight) handheld pressurised spray can. It is registered with the Therapeutic Goods Administration, Australia, for the first aid treatment of muscular pain and other injuries. One 250 g can costs $A13.90 (£6, €7) and contains about 70 administrations.

The control (placebo) spray was Evian Eau Minerale Naturelle, a pure water spray with hydrocarbon propellant. This product is used to provide a cooling mist for comfort during hot weather. It is also packed in a handheld pressurised spray can of about the same size as the intervention spray.

Spray application

The intervention and control spray cans were masked in white paper and labelled A and B. Because of the slight differences in the two sprays (variable transient skin blanching, jet force, and trajectory) the principal investigator (spray administrator) could not be blinded.

Table 1 | Baseline characteristics of patients undergoing cannulation according to allocation to control (water spray) or intervention (vapocoolant spray) group. Figures are numbers (percentages) of patients unless specified otherwise

	Control (n=98)	Intervention (n=103)
Mean (SD) age (years)	56.3 (20.0)	59.9 (19.0)
Men	52 (53)	57 (55)
Main reason for cannulation:		
Blood test	68 (69)	65 (63)
Drug administration	19 (19)	24 (23)
Fluid administration	7 (7)	9 (9)
Blood transfusion	1 (1)	4 (4)
Unspecified	3 (3)	1 (1)
Cannulation site:		
Cubital fossa	45 (46)	56 (54)
Dorsum of hand	29 (30)	24 (23)
Radial side of wrist	10 (10)	4 (4)
Radial side of forearm	7 (7)	11 (11)
Other	7 (7)	8 (8)
Cannula size:		
18 gauge	13 (13)	12 (12)
20 gauge	77 (79)	84 (82)
22 gauge	8 (8)	7 (7)
Who cannulated patient:		
Nurse	76 (78)	79 (77)
Resident	6 (6)	11 (11)
Medical student	8 (8)	4 (4)
Registrar	5 (5)	3 (3)
Consultant	3 (3)	4 (4)
Intern	0 (0)	2 (2)

The intervention spray had a slight fragrance that might have precluded effective blinding. A simultaneous one second spray from both cans, directed away from staff, was undertaken about 30 seconds before the allocated spray administration thus a slight fragrance was generated regardless of the nature of the spray administered.

A blinded member of emergency department staff identified a suitable vein for cannulation. The overlying skin was wiped with an alcohol swab and allowed to dry, as per standard operating procedures. The principal investigator then administered the allocated spray from a distance of about 12 cm for two seconds. This technique avoided "frosting up" of vapocoolant on the skin. Liquid spray on the skin was allowed to evaporate for up to 10 seconds. The area was again wiped with an alcohol swab and cannulation proceeded immediately. Cannulation had to be carried out within 15 seconds of administration of the spray.

Outcome measures

Our primary outcome measure was pain with cannulation. Secondary measures were discomfort with the spray on administration, success rate of cannulation, willingness of the patient to choose the allocated spray in the future, the patients' guess at randomisation status, and unexpected events.

We used separate visual analogue scales to assess pain with cannulation and discomfort with the spray. Each comprised a 100 mm horizontal line labelled "no pain" at the left end and "worst pain imaginable" at the right. About one minute after cannulation, the patient marked their perceived level of pain with cannulation, followed by level of initial discomfort with the spray. Compared with verbal descriptor scales and numerical rating scales[13] the visual analogue scale is validated as a highly discriminant method of assessing pain and has a high test-retest repeatability.[14] After we collected data on pain and discomfort, we asked the patient about their willingness to choose the allocated spray in the future and to guess at their randomisation status.

A blinded assistant (emergency department physician or nurse) not involved with the patient's care collected all outcome data, independent of the principal investigator. The principal investigator recorded only patients' demographics, reasons for cannulation, site and success of cannulation, size of cannula, and who cannulated the patient.

The principal investigator attempted to follow-up all patients five days after cannulation, either by visiting the ward or by telephone at home. Patients were asked to provide a description of any unexpected events they experienced at the cannulation site. The investigator also asked specific closed questions (presence and timing of any pain, redness, swelling, and itching). At least three attempts were made to contact each patient.

Statistical analysis

The mean pain score with cannulation has been reported as 30 mm (SD 25).[1] Reports of clinically important reductions in pain scores range from 9-18 mm.[5 15-17] Our study was conservatively powered to detect a 10 mm difference between mean pain scores in the groups (30 mm *v* 20 mm, respectively). At least 98 patients were required in each group (power 0.8, level of significance 0.05).

We compared the scores for cannulation pain and spray discomfort using the Mann-Whitney U test as neither variable was normally distributed (Kolmogorov-Smirnov test P=0.011 and P<0.001, respectively). We used the Kolmogorov-Smirnov test to compare age distributions and χ^2 (with Yates's correction) to compare categorical data. Unexpected events are reported descriptively. All data were analysed with the intention to treat principle and SPSS statistical software (SPSS, Chicago, IL) (level of significance 0.05).

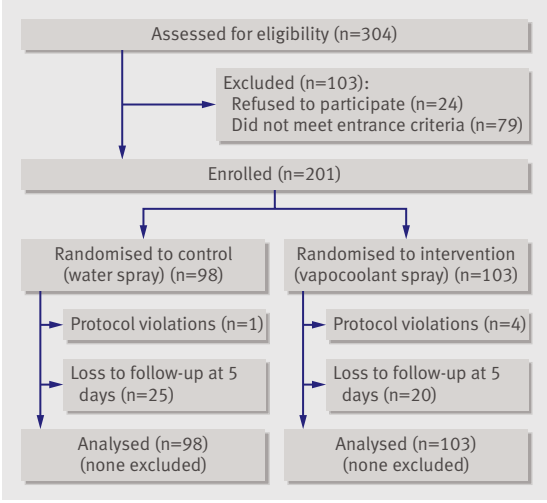

Fig 1 | Recruitment and flow of participants though trial

RESULTS

Study population

Of 304 patients assessed for enrolment, 201 were randomised: 98 to the control group and 103 to the intervention group (fig 1). The groups did not differ significantly (P>0.05) in age, sex, reason for cannulation, cannulation site, cannula size, or who cannulated the patients (table 1). There were, however, five protocol violations. For one patient in the control group and two in the intervention group, the cannulation site was slightly away from the site sprayed. Also, for two patients in the intervention group, incomplete preparation resulted in a delay of more than 15 seconds between spraying and cannulation.

Study outcomes

Table 2 shows the main outcome measures. Patients in the intervention group reported significantly lower pain scores with cannulation; their median pain score was one third that of the control group. There were also significantly fewer patients in the intervention group who reported a pain score of ≥30 mm. Figure 2 presents the pain score distributions graphically.

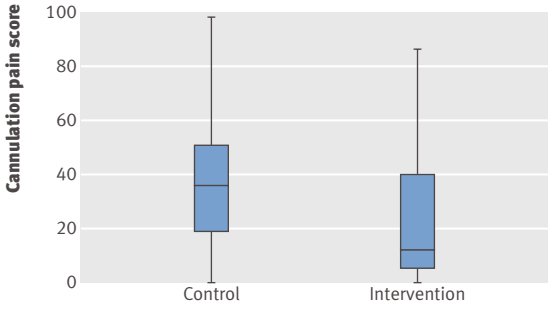

Fig 2 | Distribution of pain scores with cannulation

Discomfort from both sprays was generally slight, with median discomfort scores of zero in both groups. However, 23 (24%) and 50 (49%) patients in the control and intervention groups, respectively, reported a discomfort score of more than zero. Hence, skewing of the scores to the right in the intervention group resulted in a significant difference between the groups. Significantly more patients in the intervention group reported that they would choose the spray they received if they had a choice in the future. The nature of the spray did not affect success rates of cannulation.

Significantly more patients in the control group correctly guessed the nature of the spray they received. Despite this, almost a third and a half of patients in the control and intervention groups, respectively, did not correctly guess which spray they received. This suggests a considerable level of blinding in both groups.

At five days after cannulation, 73 (75%) and 83 (81%) patients in the control and intervention groups, respectively, were followed up. Of these, two patients in the intervention group reported transient redness at the site sprayed. No other unexpected events were reported.

DISCUSSION

Anecdotally, alkane vapocoolant sprays are used in some UK and Irish emergency departments to decrease pain with intravenous cannulation. There are few reports, however, regarding the use of these agents for this indication. We have shown that, compared with control patients, those who received alkane vapocoolant had a 24 mm lower median pain score (18 mm lower mean) and significantly fewer had pain scores ≥30 mm. Alkane vapocoolant spray before intravenous cannulation does, therefore, result in a meaningful decrease in the pain experienced.

There was a significant difference between the discomfort of placebo and vapocoolant application. The median discomfort score in both groups, however, was zero, and the absolute amount of discomfort from the vapocoolant was small. Furthermore, almost two thirds of patients who received the vapocoolant spray would choose this treatment in the future to reduce cannulation pain compared with about one third of patients who received the placebo. This difference probably reflects patients' satisfaction with the spray administered.

Unexpected events with the vapocoolant spray were minor and seen in only two patients. It is not known whether these events were attributable to the vapocoolant itself, and the difference between groups might have been attributable to the higher rate of follow-up within the vapocoolant group. Notably, our event rate was low compared with those reported for tetracaine (erythema 34%, pruritus 6%),[18] Emla (erythema 6%),[18] and lidocaine (erythema 13%, swelling 53%).[1]

Other risks associated with vapocoolant are likely to be minimal. Like many other vapocoolants, the one we examined is flammable and its use around heat or ignition sources is not recommended.[11] The short duration of spray (two seconds) and the lack of heat or ignition sources in the immediate vicinity, however, is likely to ensure its safety. The manufacturer recommends a spray time of no longer than five seconds and a distance of at least 12 cm to avoid frostbite.[11] We had trialled a range of spray times (while spraying from 12 cm) and frosting, with the chance of frostbite, did not occur with a duration of two seconds. The risk of local atmospheric pollution is also likely to be minimal given the short and focused administration.

Though vasoconstriction from cooling might increase the difficulty of cannulation, we found no significant difference in success rates of cannulation between the two groups. Lidocaine has been reported to increase the failure of cannulation because of tissue distortion,[3] and Emla can cause vasoconstriction,[18 19] which can increase difficulties with cannulation.[18]

Strengths and limitations

Selection bias might have occurred if patients who refused or were excluded differed from those enrolled. The periods when the principal investigator was available for enrolment were limited. While this extended the length of the study, enrolment of consecutive patients during enrolment periods probably minimised selection bias. Only 24 patients refused to take part, and there is no reason to believe that excluded patients differed substantially. Harris et al reported that the perception of cannulation pain is unaffected by the presence or absence of other painful conditions.[20] Hence, selection bias is unlikely to have affected the results. Although the baseline characteristics of the two groups were similar, we did not

Table 2 | Outcome measures in patients undergoing cannulation according to allocation to control (water spray) or intervention (vapocoolant spray). Figures are numbers (percentages) of patients unless specified otherwise

	Control (n=98)	Intervention (n=103)	P value
Median (IQR) pain with cannulation	36 (19-51)	12 (5-40)	<0.001
Cannulation pain ≥30 mm	59 (60)	33 (32)	<0.001
Median (IQR) discomfort with spray	0 (0-0)	0 (0-11)	<0.001
Successful cannulation	73 (75)	83 (81)	0.390
Future choice of same spray*	34 (39)	62 (62)	0.002
Correct guess at nature of spray	68 (69)	56 (54)	0.001

IQR=interquartile range.
*Data missing for 10 in control group and three in intervention group.

WHAT IS ALREADY KNOWN ON THIS TOPIC

There have been conflicting reports from small unblinded studies on the efficacy of vapocoolant sprays to reduce pain with intravenous cannulation

Some clinicians use these agents for this indication

WHAT THIS STUDY ADDS

Alkane vapocoolant spray results in significant reductions in pain with cannulation and is safe and acceptable to patients

measure other potential confounders, such as pain threshold and needle anxiety. The large sample size and the randomisation used, however, probably distributed these confounders evenly between the groups. We took considerable effort to ensure blinding of patients, though about two thirds of patients in the control group guessed their randomisation status, which might have resulted in measurement bias. This is unlikely to have resulted from the lack of blinding of the sprayers, as we used an independent blinded assessor to collect pain scores and all other outcome data. Ideally, all assessments would have been made by the same blinded assessor to ensure consistency. However, all assessors were familiar in the use of the visual analogue scale, and any bias in variation between them is likely to have been balanced between the two groups. As the telephone follow-up provided limited data, it is difficult to compare these data with those of others. Its purpose, however, was to screen for a range of unexpected events rather than to determine their exact nature. As unexpected events were rare, minor, and transient, a more detailed examination would not have been useful.

Comparison with other studies

Although methods differed, our findings are consistent with those of two studies that examined ethyl chloride for the same indication.[2 3] In contrast, other vapocoolant trials of ethyl chloride[1] and fluorohydrocarbon[12] did not show significant pain relief. The ethyl chloride study, however, was not blinded, used a larger sized cannula (18 gauge rather than 20 gauge), sprayed the vapocoolant from 25 cm until a layer of frosting was seen,[1] and had a vapocoolant group comprising only 30 patients. The fluorohydrocarbon study, which was also undertaken in an emergency department setting, was not blinded and was probably underpowered as the standard deviation used in the sample size calculation was considerably smaller than that observed in the data collected.[12] Small sample sizes probably limited the findings of earlier vapocoolant studies. Indeed, the largest group analysed in any of these studies was 47 patients.[12] Hence, strengths of our study are the use of blinding and the considerably larger sample size.

Recommendations

Notwithstanding these limitations, our findings indicate that vapocoolant spray might be useful for decreasing pain with cannulation. If further trials confirm our findings, consideration should be given for its routine use. Trials comparing vapocoolant spray with intradermal lidocaine are recommended and should include the additional outcomes of cost, application time (preparation, administration, onset of effect), and convenience.

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Competing interests: None declared.
Ethical approval: The Austin Health human research and ethics committee approved the study. All patients gave written informed consent.

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