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ORIGINAL PAPER

Analgesic effects of ethyl chloride spray in venepuncture – a prospective, randomized, controlled, single-blind study

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ABSTRACT

Introduction and aim. This study evaluated whether ethyl chloride spray had an analgesic effect on pain intensity caused by venepuncture compared to a placebo.

Material and methods. A total of 339 patients were randomly divided into two groups: The group in which ethyl chloride spray was applied (n=212) and the placebo group (n=127). The analgesic efficacy of ethyl chloride spray was compared with the placebo group using the Visual Analog Scale (VAS).

Results. When the analgesic efficacy of ethyl chloride spray was compared with the placebo group, the VAS score was 4 [interquartile range (IQR): 1.0] for the ethyl chloride spray group and 5 (IQR: 2.0) for the placebo group. The efficacy of ethyl chloride spray in reducing pain was statistically significant compared to the placebo ($p<0.001$).

Conclusion. Ethyl chloride spray has analgesic activity in venepuncture. Therefore, this spray can be used at the emergency departments to reduce pain intensity in patients undergoing such interventions.

Keywords. analgesia, anesthesia, ethyl chloride, pain, venepuncture

Introduction

Venepuncture is an intervention that is frequently used in emergency departments. However, due to its invasive nature, patients experience anxiety and fear during this intervention. For some patients, this may be the first negative experience in emergency departments; therefore, it is important for patient comfort to relieve their anxiety before the intervention.[1] To this end, non-pharmacological or pharmacological methods containing pharmacological agents have been used in the literature for pain control in venepuncture.[2] Among these methods are the Valsalva maneuver, eutectic mixture of local anesthetics (EMLA), cytotherapeutic local anesthetic agents, and watching television for pediatric patients.[2-5] These methods are advantageous because they are not invasive, and nurses can use them independently.

Ethyl chloride spray is a non-invasive local anesthetic agent. When sprayed on a body surface, it shows its effects within seconds by numbing nerve endings through cooling tissues up to -20°C. This effect lasts only a short time, 2-3 minutes, and does not disturb the patient as the anesthetic effect wears off.[6] We consider that the use of ethyl chloride spray will contribute to clinical practice as a practical method since it can increase patient comfort through its anesthetic effect without an invasive intervention and can be independently used by nurses.

Aim

This study aimed to evaluate whether ethyl chloride spray had an analgesic effect on pain intensity caused by venepuncture compared to a placebo.

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Material and methods

Study design and setting

This study was conducted with a randomized controlled design from January 1, 2022, through January 30, 2022, at the emergency department of a tertiary hospital. For venous puncture sampling, ethyl chloride spray (Clorethyl Cooling Spray, EBT healthcare services, Bursa, Turkey, Bursa, Turkey) was compared with a placebo (distilled cold water). Written informed consent was obtained from all the patients in the study. The study started after obtaining the Ethical Approval from the Clinical Research Ethics Committee of Erzurum Training and Research Hospital (Number: 37732058-6027, dated: 22/12/2021). This study complied with the principles of Good Clinical Practice of the Declaration of Helsinki and carried out according to the CONSORT directive.

Sample size and patients

G-Power 3.1 software was used to determine the sample size for study. To calculate the sample size, a medium effect size of 0.5, type 1 error of 0.05, and power of 0.80 were used. The sample size for the study was calculated as a minimum of 127 patients in each group (254 patients with a 1:1 allocation ratio) at 10% loss. However, we obtained a larger sample size by including 212 patients in the ethyl chloride spray group and 127 patients in the placebo group.

The study included patients aged older than 18 years and younger than 65 years, who required venepuncture at the emergency department according to the medical criteria. Patients who were allergic to ethyl chloride, pregnant and breastfeeding women, patients who had taken analgesia within 24 hours, those with problems in verbal communication, unconscious patients, patients with peripheral neuropathies, those with a diagnosis of Raynaud's phenomenon, those with skin abrasions, and those with an infection in the region of intervention were excluded from the study. Only the cases in which the first or second access attempt was successful were included in the study. Patients that underwent three or more interventions were excluded.

Randomization and primary outcome

The patients were divided into two groups as ethyl chloride spray and placebo. Ethyl chloride spray and sterile water kept at 4°C were stored separately in the same closed cans numbered 1 and 2, respectively. Only the practitioner knew which drug was in which can. Patient selection was randomly performed according to the preference of the practitioner. The nurse decided on the method to be used in each patient. The patients, on the other hand, did not know the agent applied to them. Ethyl chloride spray kept at 4°C was applied to one group, while sterile water kept at 4°C was applied as a placebo to the other group. It was undertaken by two different nurses with at least six and 10 years of experience in the field. The primary outcome was pain scores evaluated using the 10-point Visual Analog Scale (VAS) in the patients that underwent venous puncture sampling.

Study variables and intervention

The sequential number of patients for the study group was documented in a file. For the placebo group, 127 patients were documented sequentially as a list. The nurse decided on the method to be used in each patient. The patient number of each patient who underwent the procedure was determined, and detailed data about the patients were recorded on the previously prepared forms. The sample size was completed by drawing a line on the sequence number of the patients who underwent the procedure. During the venepuncture procedure, after the patient's vein was palpated; the median vein in the antecubital region was preferred since it provides easier access. This region was first cleaned using cotton wool and 70% alcohol. Then, it was sprayed three times from a distance of 15 cm with the first or second spray can according to the nurse's preference. After waiting for 30 seconds, venous puncture was performed preferably with a pink 20-gauge cannula. All patients were cannulated with a pink 20-gauge. All the interventions at the emergency department were performed by two different nurses with at least six and 10 years of experience in the field. During the procedure, the arm movements of the patients were observed and recorded. After the procedure, the patients were followed up in terms of bleeding, swelling, and redness. Then, the volunteers were asked to mark the degree of pain they felt during the venepuncture intervention from 0 (no pain) to 10 (most severe pain) on a 10-cm horizontal VAS scale. They were also asked to rate their pain character as 0 ('no pain'), 1 ('oppressive pain'), 2 ('dull pain'), and 3 ('sharp pain').[7]

Statistical analysis

Statistical analysis was performed using SPSS software version 25.0 (IBM Corp., Armonk, NY, USA). The distribution of variables was evaluated for normality using the Kolmogorov-Smirnov test. Descriptive statistics were given as frequency (n) and percentage (%) values for categorical variables. The comparison of groups for variables with a normal distribution was made with Student's t-test, and group comparisons for variables that did not have a normal distribution were undertaken with the Mann-Whitney U test. For 2×2 comparisons between categorical variables, the Pearson chi-square test was used if the expected value was >5, the chi-square Yates test if 3-5, and the Fisher's exact test if <3. A p value of <0.05 was considered statistically significant.

Results

Patient populations and characteristics

The study initially included 385 patients; however, 46 patients that did not meet the inclusion criteria were excluded. As a result, a total of 339 patients were included in the sample (Figure 1). Data obtained from the 339 patients were analyzed using SPSS, with no other exclusion.

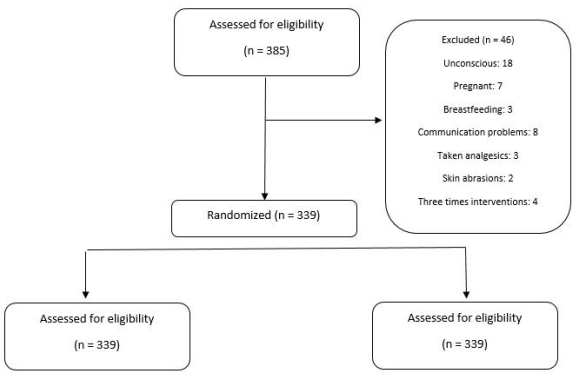

Fig. 1. CONSORT flow diagram of the study

The demographic and characteristic features of the patients are given in Table 1.

Table 1. Patients' demographic and characteristic features of the study groups [a]

Variables		Placebo (n=127)	Ethyl chloride (n=212)	p
Age (years), median (IQR)		61 (34)	42 (35)	<0.001*
Gender				
	Male, n (%)	62 (48.8%)	104 (49.1%)	0.966**
	Female, n (%)	65 (51.2%)	108 (50.9%)	
Attempts number				
	First, n (%)	115 (90.6%)	207 (97.6%)	0.004**
	Second, n (%)	12 (9.4%)	5 (2.4%)	
Wrist movement				
	No, n (%)	115 (90.6%)	194 (91.5%)	0.581**
	Little, n (%)	12 (9.4%)	18 (8.5%)	
Region of intervention				
	Antecubital, n (%)	120 (94.5%)	203 (95.8%)	0.595**
	Hand, n (%)	7 (5.5%)	9 (4.2%)	

[a] * – Mann-Whitney U Test; ** – Chi-square test

The mean age of the placebo group was 61 [interquartile range (IQR: 34)], and the mean age of the ethyl chloride group was 42 (IQR: 35), revealing a significant difference between the groups (p<0.001). The rate of male patients was 48.8% in the placebo group and 49.1% in the ethyl chloride spray group, with no significant difference between the groups (p=0.966). Intravenous access was achieved at the first attempt in 90.6% of the patients in the placebo group and 97.6% of those in the ethyl chloride spray group, and the difference between the groups was statistically significant (p=0.004). The success rate in the first attempt was significantly higher in ethyl chloride spray group. In the placebo group, wrist movement was absent in 90.6% and little in 9.4% of the patients, while in the ethyl chloride group, these rates were 91.5% and 8.5%, respectively, with no statistically significant difference between the groups (p=0.581). The area of intervention was the antecubital region in 94.5% of the patients in the placebo group and 95.8% of those in the ethyl chloride spray group, and the difference was not statistically significant (p=0.595).

Comparison of groups

The median VAS score was 3 (IQR: 2.0) in the ethyl chloride spray group and 5 (IQR: 2.0) in the placebo group. The efficacy of ethyl chloride spray in reducing pain was statistically significant compared to the placebo (p=0.000) (Figure-2). In the evaluation of pain character, 2.4% of the patients in the placebo group and 22.2% of those in the ethyl chloride spray group reported that they did not feel any pain. Thus, the rate of patients feeling no pain was statistically significantly higher in the ethyl chloride group compared to the placebo group (p = 0.000) (Table-2).

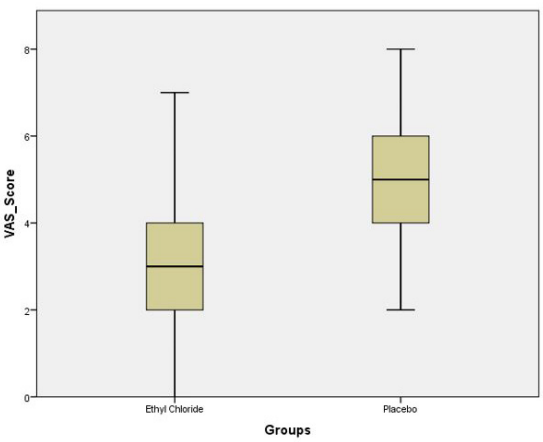

Fig. 2. Primary outcome: pain intensity in ethyl chloride spray and placebo groups

Table 2. Assessment of pain intensity in the study groups

Variables		Placebo (n=127)	Ethyl chloride (n=212)	p
VAS score (median, IQR)		5 (2)	3 (2)	<0.001*
Pain character, n (%)				
	No pain	3 (2.4%)	47 (22.2%)	
	Oppressive	6 (4.7%)	63 (29.7%)	<0.0001**
	Dull	3 (2.4%)	79 (37.3%)	
	Sharp	115 (90.6%)	23 (10.8%)	

[a] * – Mann-Whitney U test; ** – Chi-square test; VAS – Visual Analog Scale; IQR – Interquartile range

Discussion

Pain commonly occurs in intravenous access interventions, but it is actually preventable.[8] For patient comfort, it would be ideal to use a low-cost, easy-to-apply, non-invasive, and short-acting analgesic technique to reduce pain. In this study, we examined the role of ethyl chloride spray in pain reduction during venepuncture by comparing it

with a placebo. Patients treated with ethyl chloride spray reported significantly less pain during this intervention compared to the placebo group. The patients in the placebo group felt significantly more pain.

Pain relief is a human right for all patients undergoing painful interventions. Intravenous venepuncture is also a painful procedure that is applied through the skin. In order to reduce pain during this intervention, in addition to local anesthetic drugs, there are local vapor cooling sprays, such as ethyl chloride and fluorohydrocarbons that provide anesthetic effects on the skin. With the sudden evaporation of the volatile liquid in these cold sprays, there is a rapid drop in skin temperature, the skin becomes temporarily desensitized, and as a result all sensations including pain are interrupted.[9-10] In our study, topically applied ethyl chloride spray was used for analgesia. With the sudden evaporation of the cold spray, there was a significant reduction in pain in the patients that underwent venepuncture.

In the literature, studies evaluating the efficacy of ethyl chloride spray report controversial results.[11] Selby et al. compared EMLA cream, lignocaine, and ethyl chloride spray in relieving pain in venous cannulation; however, they found no significant difference between these agents in terms of pain reduction.[4] In a similar study, ethyl chloride was sprayed continuously for 10 seconds to reduce pain during venepuncture, and it was found to be significantly effective in reducing pain.[12] In another study, Rao et al. compared the efficacy of ethyl chloride sprayed from a distance of 5 cm in reducing pain during venepuncture between once- and twice-sprayed groups. The authors concluded that twice-sprayed ethyl chloride was more effective than a single spray application.[13] In our study, ethyl chloride was sprayed three times from a distance of 15 cm. This group was compared with distilled water as a placebo. Similar to the studies in the literature, we observed a significant decrease in pain experienced by the patients in the ethyl chloride spray group during venepuncture. In light of these findings, we can state that despite the differences in the distance or number of applications used in the literature, the common conclusion is that ethyl chloride spray has an analgesic effect.

Local anesthetic agents can be used to reduce pain, but since most of these agents are administered invasively, they also cause pain. It is also necessary to wait for a while for the analgesia effect to appear, which increases the duration of the whole intervention. In a previous study, the analgesic effect of non-invasive lidocaine spray compared with a placebo in radial artery cannulation, but no significant difference was found.[14] In another study, it was reported that lignocaine spray was more effective than ethyl chloride spray. However, in that study, ethyl chloride spray was sprayed twice from a distance of 10 cm. The reason for different results may be different techniques used in the application of ethyl chloride[11]. Non-invasive analgesic creams applied to the skin have also been used to reduce pain and shown to be effective. However, when these applications are examined, it is noted that creams were applied several times for their analgesic effect, and this took a long time.[15-17] These methods are not practical for use in the emergency department because they have disadvantages related to their application and they are time consuming. In the current study, ethyl chloride spray, which is easy to apply and can be used independently by nurses, was preferred for analgesia. As a result, it significantly reduced pain compared to the placebo.

Study limitations

Since the pain threshold is a relative concept for each person, the VAS score of patients may vary individually. The evaluation of pain with a scale that is dependent on the patient constitutes a limitation of our study. Another limitation is that cannulation in different regions can have different pain intensities.

Conclusion

This study demonstrated the topical analgesic effect of ethyl chloride spray compared to a placebo in patients undergoing venepuncture. Therefore, we consider that the use of ethyl chloride spray during venepuncture in the emergency department will both increase patient comfort and reduce pain.

Declarations

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Author contributions

Conceptualization, A.G. and F.C.; Methodology, A.G.; Software, A.G.; Validation, A.G; Formal Analysis, A.G.; Investigation, F.C.; Resources, F.C.; Data Curation, F.C.; Writing – Original Draft Preparation, A.G.; Writing – Review & Editing, A.G.; Visualization, F.C.; Supervision, F.C.; Project Administration, A.G.; Funding Acquisition, F.C.

Conflicts of interest

No conflict of interest was declared by the authors.

Data availability

The datasets generated during and/or analysed during the current study are available from the corresponding author on reasonable request.

Ethics approval

This study was approved by the local ethics committee (Ethics Committee of Erzurum Training and Research Hospital date: 22.12.2021 decision number: 37732058-6027)

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