Original Article

Comparison of the Effectiveness between 5% Eutectic Mixture of Local Anesthetic Cream and Ethyl Chloride Spray Applied on the Skin Prior to Intravenous Cannulation

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Background: Since the patients scheduled for an endoscopic procedure had been unhappy with pain during intravenous cannulation.

Objective: To compare the effectiveness between 5% eutectic mixture of local anesthetic cream and ethyl chloride spray applied on the skin prior to the procedure.

Materials and Methods: One hundred eighty-six patients were randomized equally into three groups, A: 5% eutectic mixture of local anesthetic cream, B: ethyl chloride spray, and C: placebo. Then a nurse used a 22-gauge (22G) needle catheter to administer a cannula. Five minutes after the intravenous cannulation, a co-researcher assessed the patient's pain perception and satisfaction as well as the nurse's difficulty in performance by means of a numeric rating scale.

Results: One hundred seventy-six patients completed the present study. Participants having the anesthetic cream and spray application as well as the placebo expressed their pain scores as 1.7±1.3, 1.6±1.2, and 2.2±1.3, respectively. Therefore, patients applied with local anesthetics had significantly less pain perception than those with the placebo (p=0.039); however, scores were not different between the anesthetic cream and the spray groups.

Conclusion: Patients scheduled for an endoscopic procedure did not showed significant pain relief with either the 5% eutectic mixture of local anesthetic cream or the ethyl chloride spray.

Keywords: 5% eutectic mixture of local anesthetic cream, Ethyl chloride spray, Endoscopic surgery, Intravenous cannulation, Pain

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Intravenous cannulation is a method to open peripheral or central veins with a needle catheter to facilitate the administration of fluid, blood components, medications, and parenteral nutrition. However, it is a painful technique, and most people would like to avoid it if possible. In addition, the perivascular leakage of chemical substances can have a detrimental effect such as edema, hemorrhage, and ischemia.

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Anesthesia personnel work at the forefront of the manipulation of intravenous cannulation, an essential route to handle patients during surgical management. The common sites for intravenous cannulation are the dorsum of the hand, forearm, antecubital fossa, and upper arm[(1)]. Additionally, the fixation of venous sites with adhesive tape is a common cause to concern.

Most patients are unhappy with pain during the maneuver. This somatic reflex conveys sensation via peripheral nerves to the spinal cord and even the central nervous system. Quite a few patients retract their arms from this stimulus, known as a fight-or-flight response. This is not only bothering medical practitioners but also a cumbersome interference with the cannulation process, wasting time and yielding little chance of success on the second trial.

There are many techniques to relieve pain during needle cannulation. Local anesthetics in any forms such as a solution, spray, cream, gel, ointment, lotion, injection, or paste sheet are applied just before the commencement of intravenous cannulation.

Currently, 5% eutectic mixture of local anesthetic cream (EMLA™, Astra Zeneca, södertälje, Sweden) and ethyl chloride spray (Ethyl chloride spray™, Water Ritter GmbH&Co, Alemannia, Germany) are used because of effective outcomes and satisfaction.

EMLA is an amide local anesthetic consisting of 1:1 oil and water emulsion with 2.5% lidocaine and 2.5% prilocaine bases[2,3]. Dose administration is approximately 2 gm per 10 cm^2 with an application time of 45 to 60 minutes prior to intravenous cannulation. Adverse events are skin irritation, discoloration, rash, edema, burning, itching, anaphylactic shock, and methaemoglobinaemia[4].

The ethyl chloride spray is a topical aerosol anesthetic, a mixture of coolants such as ethyl chloride. The product is a skin refrigerant that creates a cooling effect on the surface of the epidermis, followed by immediate evaporation. The cooling effect of the spray decreases nerve conduction, resulting in a delayed physical response to pain[5,6]. Dose administration needs to be applied to a cannulation site continuously for three to seven seconds, from 8 to 23 cm. The effect lasts up to one minute with possibly adverse events such as red skin, swelling, and rash[7].

The primary goal of the present study was to compare the effectiveness between 5% eutectic mixture of local anesthetic cream and ethyl chloride spray applied on the skin prior to intravenous cannulation the patients scheduled for an endoscopic procedure.

Materials and Methods

The present prospective, randomized controlled trial was approved by the Siriraj Institutional Review Board (Si-IRB), Certificate of Approval (COA): Si147/2019 and verified by Thai Clinical Trial Registry (TCTR 20190722004). Written informed consents were obtained from all subjects. The study was conducted at the Siriraj GI Endoscopic Center, Faculty of Medicine Siriraj Hospital, Mahidol University, between April and November 2019.

The population was calculated from a study as follows[8]:

Test significance level, α=0.05

Pain score: anesthetic spray versus placebo

• Difference in means, $\mu_1-\mu_2 = 2.000$

Common standard deviation pain score, σ=3.000

Effect size, $\delta = [\mu_1-\mu_2]/\sigma = 0.667$

Power (%)=90.00

n per group=49

After calculation of the 20% dropouts, 186 outpatients undergoing general anesthesia for an endoscopic procedure aged over 18, male and female, were enrolled. The exclusion criteria were patients having skin inflammation on the site of venous cannulation, hypersensitivity to local anesthetics, atopic dermatitis, and impaired sensory function of hands. The withdrawal or termination criteria were a procedural failure at the first attempt.

All participants were randomized equally (n=62) into three groups using a sealed envelope technique with A receiving 5% eutectic mixture of local anesthesia cream in a 2-ml syringe (0.5 gm) that was applied on the skin dressing with gauze and tegaderm for 60 minutes, and then a mineral solution (placebo) that was sprayed from 10 cm for five seconds, allowing 10 seconds to mimic the absorption of local anesthetics, B receiving ethyl chloride spray, and C receiving a placebo that was sprayed in the same demonstrative manner. The investigator prepared the samples.

After applying the local anesthetic, a nurse with five years of experience in anesthesia used a 22-gauge (22G) needle catheter to apply the intravenous cannulation on the dorsum of a hand in 60 seconds. Five minutes after the intravenous cannulation, a co-researcher assessed the patient's pain perception and satisfaction as well as the nurse's difficulty in performance by means of a numeric rating scale with 0=no pain, 10=severe pain.

Statistical analysis

Data were expressed as the mean ± standard deviation and frequency (percentage). PASW statistics, version 18.0 (SPSS Inc., Chicago, IL, USA) including the one-way analysis of variance F-test, chi-square and Bonferroni post hoc test were used to compare the data among the groups. A p-value of less than 0.05 was considered statistical significance with a 95% confidence interval.

Results

Four patients in group A, four in group B, and two in group C were dropped out due to the procedural failure at the first attempt. Demographic characteristics between the groups showed no significant difference (Table 1).

By using the numeric rating scale of 3 as a cut off point for pain assessment, patients having 5% eutectic mixture of local anesthetic cream, ethyl chloride spray, and placebo expressed their pain scores as 1.7±1.3, 1.6±1.2, and 2.2±1.3, respectively. Patients applied with either local anesthetic cream or spray had

Table 1. Demographic data of patients between the groups

Variable	Group A (n=58); n (%)	Group B (n=58); n (%)	Group C (n=60); n (%)	p-value
Sex				0.861
Male	28 (48.3)	27 (46.6)	26 (43.3)	
Female	30 (51.7)	31 (53.4)	34 (56.7)	
Age (year); mean±SD	60.1±12.7	62.0±13.0	63.0±12.7	0.484
Body weight (kg); mean±SD	62.4±10.8	62.8±13.4	61.2±13.9	0.775
Height (cm); mean±SD	161.2±9.1	162.9±8.6	159.4±8.7	0.177
Body mass index (kg/m^2); mean±SD	24.0±3.5	23.6±3.7	23.9±4.3	0.819
ASA classification				0.966
I	18 (31.0)	12 (20.7)	14 (23.3)	
II	31 (53.4)	40 (69.0)	41 (68.3)	
III	9 (15.5)	6 (10.3)	5 (8.3)	
Experience on intravenous cannulation (times/year)				0.991
<3	38 (65.5)	35 (60.3)	40 (66.7)	
3 to 5	14 (24.1)	15 (25.9)	14 (23.3)	
6 to 10	4 (6.9)	3 (5.2)	2 (3.3)	
11 to 15	0 (0.0)	4 (6.9)	3 (5.0)	
>15	2 (3.4)	1 (1.7)	1 (1.7)	

ASA=American Society of Anesthesiology; SD=standard deviation

Group A: EMLA cream, Group B: Ethyl chloride spray, Group C: Placebo

Table 2. Pain score and satisfaction of patients between the groups

Variable	Group A (n=58); n (%)	Group B (n=58); n (%)	Group C (n=60); n (%)	p-value
Pain score; mean±SD	1.7±1.3	1.6±1.2	2.2±1.3	0.039*
Level of pain score				0.459
<3	50 (86.2)	52 (89.7)	49 (81.7)	
≥3	8 (13.8)	6 (10.3)	11 (18.3)	
Satisfaction score; mean±SD	9.6±0.8	9.8±0.7	9.7±0.9	0.715

SD=standard deviation

* p<0.05 significance, Group A: EMLA cream, Group B: Ethyl chloride spray, Group C: Placebo

significantly less pain perception than those applied with the placebo (p=0.039); however, there were no significant difference between the two anesthetic groups. In addition, they were well-satisfied by the procedural process (Table 2).

Approximately 80% of the nurse anesthetists aged above 40 with at least 15-years of experience in nursing had no difficulty with intravenous cannulation (Table 3).

Discussion

Investigators applied either 5% eutectic mixture of local anesthetic cream or ethyl chloride spray on the skin prior to intravenous cannulation in patients scheduled for an endoscopic procedure.

Studies showed the effectiveness of 5% eutectic mixture of local anesthetic cream[9-14] and an anesthetic mister[10,15,16] for analgesic effects on intravenous cannulation. However, Edwards and Noah, in a randomized, double-blind trial to determine if a vapocoolant in the adult population improved patients' perception of pain with peripheral intravascular access, claimed insignificant effects of the spray[17].

Understandingly, the intravenous line is a cornerstone for patients before commencing surgical or medical treatment. However, the procedure scares most of them[18]. Thus, local anesthetics help to alleviate clinical uneasiness. Though participants expressed marked discomfort during the intravenous cannulation, they showed insignificant pain relief

Table 3. Nurse anesthetists' characteristics

Variable	Group A (n=58); n (%)	Group B (n=58); n (%)	Group C (n=60); n (%)	p-value
Age (year)				0.561
31 to 40	12 (20.7)	11 (19.0)	14 (23.3)	
41 to 50	46 (79.3)	47 (81.0)	46 (76.7)	
Nursing experience (year)				0.498
6 to 10	5 (8.6)	5 (8.6)	7 (11.7)	
11 to 15	3 (5.2)	2 (3.4)	3 (5.0)	
15 to 20	50 (86.2)	51 (88.0)	50 (83.3)	
Experience on intravenous cannulation (cases/year)				0.684
201 to 300	9 (15.5)	9 (15.5)	11 (18.3)	
301 to 400	1 (1.7)	1 (1.7)	1 (1.7)	
401 to 500	48 (82.8)	48 (82.8)	48 (80.0)	

Group A: EMLA cream, Group B: Ethyl chloride spray, Group C: Placebo

with either agent. Possible reasons for the outcomes were the high population age, patients' experience, expectation of more unfavorable pain, pre-emptive focus on procedural instruction-warmth and tender health care, practitioners' skills, site of venous catheterization, and small-bore needles.

Yet, the participants showed indifferent pain response. This might be because the pain threshold increased with age[19]. Lautenbacher et al, in a systematic review and meta-analysis of age effects on pain and tolerance thresholds-age changes in pain perception, stated that aging reduced pain sensitivity for lower pain intensities[20]. However, El Tummi et al in a systemic review with meta-analysis on age-related changes in pain sensitivity in healthy humans, signified that old adults might be more sensitive to mechanically-evoked pain but not heat-evoked pain than young adults[21].

In addition, patients with regular exposure to intravenous cannulation would increase pain tolerance and their ability to handle pain. According to the brain's perception of pain, participants expected more unfavorable pain and paid more attention to ignore it[22]. However, Malmberg et al in a study on preserved acute pain and reduced neuropathic pain in mice, stated that greater exposure to pain would potentiate the cells responsive to pain more vigorously to minor stimulation in the future[23].

Pre-emptive focus on procedural instruction with warmth and tender health care helped patients understand the intravenous cannulation process and in turn lend cooperation to the task. Furthermore, patients who began taking local anesthetics before the maneuver expressed comfort afterward. Thus instruction, health care, and local agents might be good support to venous catheterization. Brown et al, in a study on social support and experimental pain believed that participants in the active and passive support conditions reported less pain than ones in the alone and interaction conditions[24].

An experienced practitioner should manipulate intravenous cannulation swiftly with less pain felt by patients. Nevertheless, it is difficult for beginners to handle a process without help, particularly on patients with distorted venous tributaries, geriatrics, or obese people.

The current study revealed that nurse anesthetists aged above 40 with at least 15 years of experience selected veins on the dorsum of the hand and used a 22G plastic needle for intravenous cannulation without difficulties in less than 60 seconds with satisfied outcomes. However, this seemed to disagree with Goudra et al, in a prospective randomized study on the effects of site selection on the pain of intravenous cannula insertion. They claimed that the antecubital fossa approach was significantly less painful than that of the dorsum of the hand when using a 20-gauge cannula for venous cannulation[25].

Limitation

The effectiveness of the present study was not clarified in detail regarding cost and time of drugs administration.

Some confounding factors such as patients' age, patients' mental state prior to the intravenous cannulation process, the bore size of a needle, and nurse anesthetists involved in the present study were not controlled.

Conclusion

Patients scheduled for an endoscopic procedure expressed significant discomfort during the intravenous cannulation and they showed insignificant pain relief with either a 5% eutectic mixture of local anesthetic cream or a ethyl chloride spray.

What is already known on this topic?

There are many techniques to relieve pain during needle cannulation. Currently, 5% eutectic mixture of local anesthetic cream and ethyl chloride spray are normally used because of the effective outcomes and satisfaction. Nevertheless, the effectiveness of these two local anesthetics has rarely been mentioned in previous studies.

What this study adds?

The present study investigators applied either a 5% eutectic mixture of local anesthetic cream or an ethyl chloride spray on the skin prior to intravenous cannulation in patients scheduled for an endoscopic procedure. Patients expressed significant discomfort during the intravenous cannulation and they showed insignificant pain relief with either a 5% eutectic mixture of local anesthetic cream or an ethyl chloride spray.

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Conflicts of interest

The authors declare no conflict of interest.

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