

Efficacy of topical local anesthetic, topical cooling spray, and audiovisual distraction on relief of needle-related pain during blood collection: A randomized controlled trial

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Conflict of interest

None declared

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Abstract

Background. Venipuncture is one of the most common invasive procedures in healthcare, often resulting in the experience of pain. While audiovisual distraction, topical anesthesia and cold spray application have been reported as methods to reduce pain, there is a lack of studies that focus on comparing their efficacy and safety.

Objectives. We aimed to compare the efficacy and safety of pain reduction during venipuncture using audiovisual distraction, topical anesthesia and cold spray application.

Materials and methods. A randomized controlled study was conducted at Walailak University (Nakhon Si Thammarat, Thailand) from April 2023 to July 2023. Eligible adult participants voluntarily enrolled in the study and were randomly assigned to 1 of 4 groups: group 1 (control), group 2 (topical anesthetic), group 3 (cooling spray), and group 4 (audiovisual distraction). Pain scores and satisfaction levels were assessed following the venipuncture procedure on the upper extremities.

Results. Forty-seven participants were included in the final analysis. The participants had a mean age of 42.3 years (standard deviation ($\pm$ SD): 13.1), with the majority being female (66.0%). The participants in the intervention groups reported lower pain scores than those in group 1. The mean differences were 2.67 points in group 2 (95% confidence interval (95% CI): 1.49–3.84; $p < 0.001$), 1.56 points in group 3 (95% CI: 0.15–2.98; $p = 0.077$), and 1.67 points in group 4 (95% CI: 0.37–2.96; $p = 0.042$). However, the pain reduction did not reach statistical significance when comparing these 3 interventions. All groups reported a median satisfaction level of 3, with no significant difference among them ($H(3) = 6.050$, $p = 0.109$).

Conclusions. Pain reduction interventions, including topical anesthetic, cooling spray and audiovisual distraction, are effective methods for alleviating pain during venipuncture. Participants who received a topical anesthetic reported the lowest pain scores and highest levels of satisfaction.

Key words: pain, venipuncture, topical anesthetic, cooling spray, audiovisual distraction

Background

Pain is defined as an unpleasant sensory and emotional experience associated with, or similar to, actual or potential tissue damage.¹ The perceived intensity varies depending on biological, psychological and social factors. The nociceptive signal emanating from an injury undergoes modulation through endogenous mechanisms that can amplify or diminish both the signal and the perceived pain.² Failing to alleviate acute pain can lead to physiological and psychological effects. These effects include stress and inflammation, as well as a range of impacts on the cardiovascular, gastrointestinal and respiratory systems.³ Also, this can result in increased anxiety, sleep disturbances, and a diminished quality of life across biological, psychological and social aspects of health.⁴

Venipuncture involves the process of drawing blood and remains one of the most prevalent invasive procedures in healthcare, often leading to the experience of pain.⁵ The pain score varies across studies, ranging approx. from 3 to 7 out of 10.^{6–9} Although our comprehension of the intricacies surrounding pain remains partial,² the existing theories serve as guiding principles for interventions aimed at pain reduction. At present, methods for pain reduction encompass both pharmacological and non-pharmacological interventions. Common interventions include audiovisual distraction, topical anesthesia and the use of cold spray.^{10–14} The reduction of perceived pain through audiovisual distraction occurs due to the inherent limitations of human attention capacity. When a person's attention is diverted from the stimulus, the perception of pain diminishes.^{15,16} Topical anesthetics reversibly block nerve conduction by targeting free nerve endings and competing with calcium-binding sites that control sodium permeability. This results in decreased permeability, depolarization and an increased excitability threshold.^{17,18} The utilization of cold spray for pain reduction was elucidated by its ability to induce vasoconstriction and alter nerve conduction patterns.¹⁹ Based on the gate control theory, the perception of cool sensations is primarily detected by A-delta fibers, which in turn exert inhibitory effects on the active C fibers.²⁰ Additionally, pain signal transmission is decelerated at lower tissue temperatures.^{14,21}

However, there is still a lack of randomized controlled trials that compare the efficacy and safety of these interventions. This study was conducted to determine the extent of pain alleviation through the use of common methods during venipuncture. The findings can provide valuable insights to establish optimal clinical practices in the context of venipuncture procedures.

Objectives

We aimed to compare the efficacy of pain reduction during venipuncture using audiovisual distraction, topical anesthesia and cold spray application.

Methods

Participants

This randomized controlled study was conducted from April 2023 to July 2023 at the Walailak University (Nakhon Si Thammarat, Thailand). We posted online announcements about this study and asked for volunteers on our academic websites. To minimize undue influence, we had our co-investigators organize the registration and withdrawal processes. The inclusion criteria included: (1) being 18–40 years old; (2) willing to participate in the study; and (3) being able to read, write and understand Thai and English as well as the capacity to provide informed consent. The exclusion criteria included: (1) mental restriction or being unable to rate pain scores; (2) needle insertion with more than 2 attempts; (3) body mass index (BMI) >30 kg/m²; (4) being unable to collect blood from the antecubital area; (5) history of allergy to topical anesthesia; (6) audiovisual impairment with a decreased quality of life; (7) psychiatric disorders; (8) peripheral neuropathy; (9) cold intolerance; (10) peripheral arterial disease affecting the antecubital areas; and (11) history of taking non-steroidal anti-inflammatory drugs within 1 week of the intervention.

This prospective study was approved by the Walailak Ethics Committee (No. WUEC-23-070-01). Written informed consent was obtained from all participants after a full explanation of the study. This study complied with the principles of the Declaration of Helsinki and the International Conference on Harmonization of Good Clinical Practice. Participants were permitted to withdraw from the study at any time for any reason without consequence.

This clinical trial was registered in the Thai Clinical Trials Registry (No. TCTR20230324007). The ethics committee took into account and complied with the laws of Thailand, including the Personal Data Protection Act. All data files and sensitive personal information were encrypted, password-protected, and saved to a secure computer that was only accessible to the study coordinators to ensure confidentiality. Participants could access their own data by directly contacting study coordinators. No information that could link an individual to the data was revealed. Twelve months after completion of the study, all data were deleted.

Intervention and study design

After eligible participants were voluntarily recruited, they were randomly assigned to 1 of 4 groups using Excel 2019 (Microsoft Corp., Armonk, USA) with allocation concealment using sealed envelopes: group 1 (control), group 2 (topical anesthetic), group 3 (cooling spray), and group 4 (audiovisual distraction). To anesthetize the skin at the needle insertion area of 10 cm², 1 g of EMLA cream (5% emulsion containing 2.5% each of lidocaine and prilocaine; Recipharm Karlskoga AB, Karlskoga, Sweden)

was applied in the topical anesthetic group for 1 h before venipuncture. In the cooling spray group, the needle insertion site was sprayed with Perskindol cool spray (0.5% Menthol; IGS Aerosols GmbH, Wehr, Germany). The spray was administered for 5 s at a distance of 15 cm and a 90° angle from the skin. After allowing the spray to evaporate from the skin for 10 s, vascular access was performed after skin disinfection. In the audiovisual distraction group, participants were instructed to watch a 1.22-min video clip (<https://youtu.be/vJG698U2Mvo>) while doing venipuncture. This intervention, the selective attention test, consisted of 6 players playing with 2 basketballs. Participants were asked to count and answer how many times the players wearing white passed the basketball. In the control group, participants underwent venipuncture after skin disinfection without additional intervention.

A blood pressure cuff was placed 5 cm proximal to the antecubital fossa and was then inflated to 40–60 mm Hg. The needle insertion sites were sterilized with 70% alcohol patches and allowed to dry. The venipuncture was performed using a 21-gauge needle by 1 medical staff member. The total blood volume collected was 5–15 mL, with the specific vein selected depending on the number of laboratory tests requested by the attending physicians. Baseline characteristics were collected through structured questionnaires and medical records, including age, gender, height, weight, and vital signs. Pain scores, satisfaction levels and adverse events resulting from the intervention were accessed and recorded by a blinded investigator. Pain scores ranged from 0 (indicating no pain) to 10 (indicating extreme pain), while satisfaction levels ranged from 0 (representing extreme dissatisfaction) to 3 (representing extreme satisfaction).

Sample size and power

To estimate sample size, the effect sizes were based on outcomes from a previous study.²² A sample size of 9 in each group was initially planned, which had a 90% power to detect an effect size of 2.1, comparing each intervention arm and the control arm using a 2-sample t-test. All t-tests were 2-sided with a 0.01 significance level. Assuming an approx. 25% loss to follow-up, we proposed to recruit and randomize 12 participants per intervention group to give a total sample size of 48 participants.

Statistical analyses

For descriptive statistics, means and standard deviations (SDs) were used to describe normally distributed continuous data, while medians and interquartile ranges (IQRs) were applied for continuous data that were not normally distributed. Additionally, 95% confidence intervals (95% CIs) were calculated to estimate the precision of the mean values. Frequency and percentages were utilized for analyzing categorical data. For inferential statistics, the study incorporated a variety of tests. Normally

distributed variables were evaluated, as shown in Supplementary Table 1. We verified the equality of variances across the groups prior to conducting the statistical tests to assess differences in pain scores among the groups. The results of this analysis are provided in Supplementary Table 3. Following this verification, a one-way analysis of variance (ANOVA) was conducted to assess the significance of differences in age and BMI among the different groups. Due to the limited sample size, a Fisher's exact test was utilized to assess proportion comparisons among independent groups. According to pain scores and satisfaction levels, as non-parametric data, differences among the 4 groups were tested using the Kruskal–Wallis test, and Dunn's test was used for the post hoc analysis for pairwise comparisons. A multiple comparisons correction was performed to adjust the significance level (α) for comparing pain scores between the groups. To address the issue of the family-wise error rate, the Bonferroni correction method was applied. This approach involves dividing α by the number of comparisons to control the family-wise error rate, with α specifically divided by 6 for our 6 pairwise comparisons. For comparisons of pain across different factors between the 2 groups, the Mann–Whitney U test or independent t-test was selected depending on the normality of the data. Additionally, Spearman's rho was utilized to measure the strength and direction of association between 2 ranked variables in the context of non-normal data. To investigate the link between BMI and pain, we created scatter plots with locally estimated scatterplot smoothing (LOESS) curves for an initial visual analysis. We then applied a range of regression models (Linear, Logarithmic, Inverse, Quadratic, and Cubic) to precisely examine this relationship, aiming to capture the complex dynamics between BMI and pain experiences. In this study, all the statistical tests, including the Fisher's exact test, one-way ANOVA, Mann–Whitney U test, independent t-test, and Kruskal–Wallis test, were conducted as two-tailed tests. For each of these two-tailed tests, a p-value of < 0.05 was required to indicate statistical significance. All statistical analyses were conducted using SPSS software v. 15 (SPSS Inc., Chicago, USA) and the R programming environment (R Foundation for Statistical Computing, Vienna, Austria). This comprehensive analysis included a range of model fittings (Linear, Logarithmic, Inverse, Quadratic, Cubic, and LOESS) to assess the association between BMI and pain. The utilization of both SPSS and R enabled a thorough investigation of the data through various statistical lenses, ensuring a robust examination of the underlying relationships.

Results

Forty-eight eligible volunteers were recruited for the study; however, 1 participant had to be excluded due to extreme, intolerable pain. As a result, 47 participants

Table 1. Baseline characteristics (n = 47)

Characteristics		Group 1 (n = 12)	Group 2 (n = 12)	Group 3 (n = 11)	Group 4 (n = 12)	Test name and p-value
Sex, n (%)	male	4 (33.3)	1 (8.3)	4 (36.4)	7 (58.3)	p = 0.080 ^a
	female	8 (66.7)	11 (91.7)	7 (63.6)	5 (41.7)	
Age [years] $\pm$ SD		43.5 ($\pm$ 13.0)	36.8 ($\pm$ 13.9)	45.3 ($\pm$ 14.0)	43.8 ($\pm$ 11.5)	F(3) = 0.993, p = 0.405 ^b
BMI [kg/m ²] $\pm$ SD		23.0 ($\pm$ 2.2)	22.5 ($\pm$ 3.3)	24.9 ($\pm$ 4.5)	21.6 ($\pm$ 2.6)	F(3) = 2.165, p = 0.106 ^b
Education, n (%)	secondary education	3 (25.0)	1 (8.3)	5 (45.5)	2 (16.7)	p = 0.209 ^a
	higher education	9 (75.0)	11 (91.7)	6 (54.5)	10 (83.3)	
Dominant hand, n (%)	right	7 (58.3)	11 (91.7)	11 (100.0)	12 (100.0)	p = 0.010 ^a
	left	5 (41.7)	1 (8.3)	0 (0.0)	0 (0.0)	
Correlation between punctured site and dominant hand, n (%)	same side	7 (58.3)	3 (25.0)	4 (36.4)	4 (33.3)	p = 0.429 ^a
	different side	5 (41.7)	9 (75.0)	7 (63.6)	8 (66.7)	
Punctured vessel, n (%)	median vein	11 (91.7)	9 (75.0)	11 (100.0)	8 (66.7)	p = 0.038 ^a
	cephalic vein	1 (8.3)	2 (16.7)	0 (0.0)	0 (0.0)	
	basilic vein	0 (0.0)	1 (8.3)	0 (0.0)	4 (33.3)	
History of blood sampling, number of times (%)	0	1 (8.3)	5 (41.7)	2 (18.2)	2 (16.7)	p = 0.756 ^a
	1–3	2 (16.7)	2 (16.7)	3 (27.3)	2 (16.7)	
	4–6	2 (16.7)	1 (8.3)	1 (9.1)	1 (8.3)	
	7–10	0 (0.0)	1 (8.3)	0 (0.0)	0 (0.0)	
	>10	7 (58.3)	3 (25.0)	5 (45.5)	7 (58.3)	

BMI – body mass index; SD – standard deviation. Group 1 – control group; group 2 – topical anesthetic group; group 3 – cooling spray group; group 4 – audiovisual distraction group. Statistical test notations: ^a Fisher's exact test; ^b one-way analysis of variance (ANOVA).

Table 2. Comparison of pain scores and satisfaction levels across the 4 participant groups (n = 47)

Group	n	Pain score		Satisfaction level	
		median	IQR	median	IQR
Group 1	12	4.00	2.00	3.00	1.00
Group 2	12	1.00	2.00	3.00	0.00
Group 3	11	2.00	3.00	3.00	1.00
Group 4	12	2.00	2.00	3.00	0.00
All	47	2.00	3.00	3.00	0.00

Group 1 – control; group 2 – topical anesthetic; group 3 – cooling spray; group 4 – audiovisual distraction; IQR – interquartile range. Pain scores were measured on a scale from 0 to 10, with 0 indicating no pain and 10 indicating extreme pain. Satisfaction levels were gauged on a scale from 0 to 3, where 0 represented extreme dissatisfaction and 3 represented extreme satisfaction.

remained for the final analysis. The mean age of the participants was 42.3 years (SD $\pm$ 13.1). The majority of participants were female (66.0%), held higher education qualifications (76.6%) and exhibited right-hand dominance (87.2%). Common comorbidities included essential hypertension (33.0%), hypothyroidism (27.0%), dyslipidemia (20.0%), type 2 diabetes mellitus (13.0%), and others (33.0%), such as coronary artery disease, allergic rhinitis, and hepatitis B infections. Table 1 displays the baseline characteristics of the participants in each group.

Comparison of pain scores and satisfaction levels across the four intervention groups are demonstrated in Table 2 and Fig. 1,2. The participants in the intervention groups reported lower pain scores than those in group 1. The mean

differences were 2.67 points in group 2 (95% CI: 1.49–3.84; $p < 0.001$), 1.56 points in group 3 (95% CI: 0.15–2.98; $p = 0.077$), and 1.67 points in group 4 (95% CI: 0.37–2.96; $p = 0.042$), as shown in Table 3. Multiple t-tests using Dunn's test with Bonferroni correction revealed a statistically significant difference in pain between group 1 and group 2 (test statistic = 3.716, $p < 0.001$). The median satisfaction level in all groups was 3.00 (interquartile range (IQR) 0.00), and the Kruskal–Wallis test indicated no significant difference in satisfaction levels across all groups ($H(3) = 6.050$, $p = 0.109$). The study revealed no statistically significant differences in pain scores based on sex, educational level, hand dominance, puncture side, type of vessel, or history of blood sampling, as shown in Supplementary

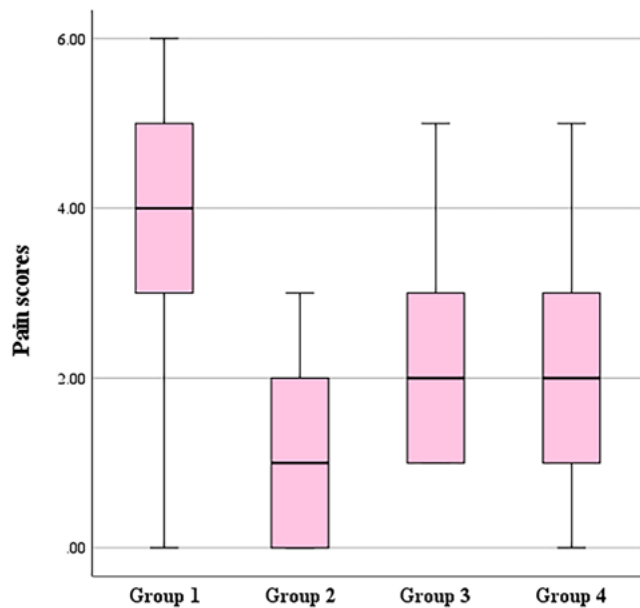


Fig. 1. Pain scores across the 4 participant groups (n = 47)

The midline of the box represents the median of the data. The bottom and top of the box depict the 25th and 75th percentiles, respectively. The whiskers extend to show the range of the data, from the minimum to the maximum values.

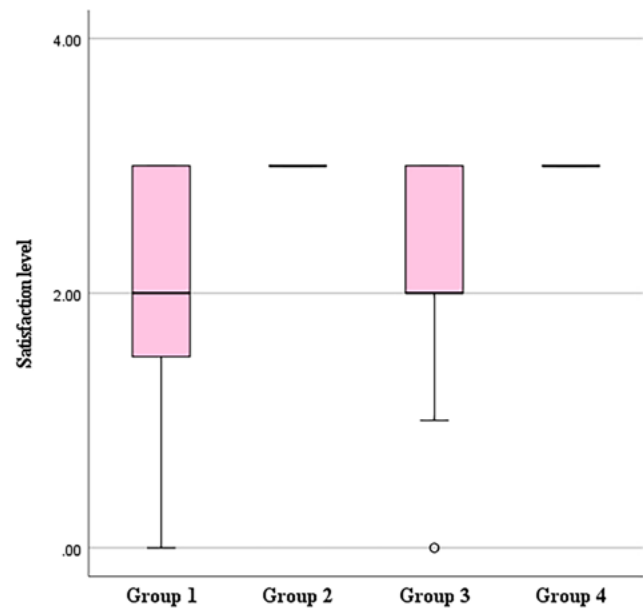


Fig. 2. Satisfaction levels across the 4 participant groups (n = 47)

The midline of the box represents the median of the data. The bottom and top of the box depict the 25th and 75th percentiles, respectively. The whiskers extend to show the range of the data, from the minimum to the maximum values.

Table 3. Comparison of pain scores and satisfaction levels across different groups (n = 47)

Comparisons	Mean differences (95% CI)	Test value and p-value*
Pain scores		
Among 4 groups	N/A	H(3) = 14.020, p = 0.003 ^a
Group 1 and 2	2.67 (1.49, 3.84)	test statistic = 3.716, p < 0.001 ^{b*}
Group 1 and 3	1.56, (0.15, 2.98)	test statistic = 2.143, p = 0.096 ^{b*}
Group 1 and 4	1.67 (0.37, 2.96)	test statistic = 2.177, p = 0.089 ^{b*}
Group 2 and 3	−1.11 (−2.31, 0.10)	test statistic = −1.492, p = 0.407 ^{b*}
Group 2 and 4	−1.00 (−2.05, 0.05)	test statistic = −1.540, p = 0.371 ^{b*}
Group 3 and 4	0.11 (−1.22, 1.43)	test statistic = −0.014, p = 1.000 ^{b*}
Satisfaction levels		
Among 4 groups	N/A	H(3) = 6.050, p = 0.109 ^a

95% CI – 95% confidence interval; N/A – not applicable. Statistical test notations: ^a Kruskal–Wallis test; ^b Dunn's test. * To adjust the significance level (α) for multiple comparisons of pain scores among groups, multiple Dunn's tests were used. The family-wise error rate was controlled by applying the Bonferroni correction, which involved dividing α by the number of comparisons (e.g., α/6 for 6 comparisons).

Table 2. However, the Kruskal–Wallis test indicated significant differences among weight categories (H(3) = 8.368, p = 0.039). Compared with participants having a BMI over 27.5 kg/m², those with a BMI of 18.5–22.9 kg/m² and

Table 4. Correlation between each factor and pain

Variables	Correlation coefficient and p-value
Age	r = 0.243, p = 0.100
Weight	r = −0.197, p = 0.184
Height	r = −0.083, p = 0.578
BMI	r = −0.200, p = 0.178

BMI – body mass index. Spearman's rho was employed as the statistical method for analyzing the correlations presented in the data set.

those with a BMI of 23.0–27.5 kg/m² reported significantly higher pain scores, with test statistics of 2.593 (p = 0.029) and 2.490 (p = 0.038), respectively. The Spearman's rho correlation analysis was conducted due to the non-normal distribution of the data, aiming to identify any monotonic component in the association between pain and other factors, including age (r = 0.243, p = 0.100), weight (r = −0.197, p = 0.184), height (r = −0.083, p = 0.578), and BMI (r = −0.200, p = 0.178). The results, detailed in Table 4, indicate the absence of a significant monotonic component in these associations. However, this does not preclude the existence of non-monotonic components between these variables.

No immediate serious adverse reactions were noted across all groups. In group 3, a notable observation involved 3 participants (27.3%) reporting minor side effects associated with the use of vapocoolant sprays, which manifested as transient erythema at the application site. This erythema typically resolved spontaneously within 5–10 min.

Discussion

Pain is a common adverse effect of the venipuncture procedure. While most people experience mild pain, failing to alleviate acute pain can lead to both physiological and psychological effects.³ To date, several methods have been proposed to alleviate pain during the procedure. However, there is still a lack of randomized controlled trials that compare the efficacy and safety of these interventions. To the best of our knowledge, our study was the first to compare the efficacy of pain reduction during venipuncture using audiovisual distraction, topical anesthesia and cold spray application. Our findings revealed that participants in each intervention group reported lower pain scores compared to those in the control group. Participants who received the topical anesthetic reported the lowest pain scores, and this difference was statistically significant. Additionally, they expressed high levels of satisfaction.

Consistent with our findings, previous research has demonstrated a significant reduction in pain scores with 3 specific interventions. First, local anesthetics have shown a substantial and statistically significant effect in reducing pain during venipuncture procedures (mean = 1.04, 95% CI: 0.92–1.34) and intravenous insertions (mean = 1.05, 95% CI: 0.84–1.46).¹⁰ Second, the application of vapocoolants has been associated with a significant decrease in pain scores (median = 1, range: 0–3) compared to a control group (median = 3, range: 1.2–5) during venipuncture ($p = 0.001$).⁹ Third, audiovisual distraction techniques have been effective in significantly reducing needle-related pain. Gandhar et al. found that the mean pain score for a group watching cartoons during venipuncture was significantly lower (mean 4.6, SD ± 1.5) than that of the control group (mean 7.7, SD ± 0.8 , $p < 0.001$).⁸ Similarly, Orhan and Gozen demonstrated that the post-venipuncture pain score for a group engaged in virtual reality was significantly lower (mean 1.46, SD ± 1.49) than that of a control group (mean 4.44, SD ± 2.26 , $p = 0.001$).¹¹

Our findings emphasize that all 3 interventions (topical anesthetic application, cooling spray and audiovisual distraction techniques) successfully lowered pain scores associated with venipuncture procedures. However, the pain reduction did not reach statistical significance when comparing these 3 interventions. The ideal anesthetic intervention should be effective, quick, painless, inexpensive, and side-effect-free. The audiovisual distraction, therefore, appears to be a practical choice in real-world applications in the venipuncture procedure due to its advantages, including time efficiency, non-invasiveness and the absence of disposable materials. Prior to venipuncture, the patients need to wait for the topical anesthetic to reach its peak effects. The cream needs time to be absorbed and the pain to be relieved. The average insertion depths with acceptable pain following 60 min and 120 min of lidocaine and prilocaine local anesthetic application were 2.9 mm and 4.5 mm, respectively.²³ The average depths of the basilic, median cubital, and cephalic veins after applying

a tourniquet are 2.9 mm (SD ± 1.7), 1.7 mm (SD ± 0.8) and 1.7 mm (SD ± 0.6), respectively.²⁴ Therefore, if blood needs to be collected from the deeper parts of these veins, it may take longer than 1 h to achieve the desired effect.

Adverse effects related to EMLA cream are exceedingly rare and mostly limited to localized, temporary reactions, such as blanching, redness, altered temperature sensation, edema, pruritus, burning, purpura, and contact hypersensitivity.²⁵ The major concern for systemic toxicity is the development of methemoglobinemia. Thus, caution is advised when administering EMLA cream to patients with glucose-6-phosphate deficiency, those concurrently using methemoglobin-inducing medications, and infants below 3 months of age.²⁶ Correspondingly, no local or systemic side effects were observed in our findings. Previous studies reported a total of 8 adverse events out of 279 participants (2.9%). All of the reactions were minor, including cold sensations, 3 temporary instances of erythema at the spray site and 1 case of a burning sensation.²⁷ We also observed that 3 participants developed temporary erythema, with no further consequences or concerns.

Individuals show substantial differences in their perception of pain. Distinctive individual variations result from biological, psychological and social factors. Nevertheless, these factors do not directly influence pain themselves; instead, they signify the various processes that modify pain.²⁸ Kivrak et al.²⁹ revealed that anxiety may predict pain, but other factors like sex, depression, somatosensory amplification, age, and weight do not seem to influence the perception of pain during the venipuncture procedure. Pain tolerance thresholds in the upper extremity veins can vary. Yoshida et al.³⁰ found that the superficial dorsal vein had a significantly higher pain tolerance threshold at 250 Hz in response to pinprick sensations compared to the median cubital, basilic and cephalic veins at the wrist. There was no significant difference between the pain tolerance thresholds of the cephalic vein at the cubitus and the superficial dorsal vein. Previous studies have provided support for the impact of hand laterality on pain perception, revealing that the non-dominant hand tends to be more sensitive to pain than the dominant hand.^{31,32} Our findings, in relation to pain and obesity, align with those of Emerson et al.,³³ who suggested that obesity had a limited effect on pain sensitivity. This indicates that obesity alone may not significantly increase the risk of developing chronic pain by intensifying nociceptive mechanisms. In contrast, Mendonça et al.³⁴ reported significant prevalences of musculoskeletal and severe pain among severely obese individuals. They identified the factors contributing to pain in adults with severe obesity, including clinical conditions, a sedentary lifestyle, the extent of obesity, and overall body fat. Additionally, Majchrzak et al.³⁵ found that obese lung cancer patients undergoing thoracic surgery experienced more intense and longer-lasting pain than their non-obese counterparts. The reasons behind the varying pain thresholds observed between obese and non-obese patients remain unclear.

Possible explanations for this phenomenon could include chronic inflammation associated with obesity, the release of inflammatory mediators by macrophages, genetic variations, and nocturnal hypoxemia.^{36–39} Our study found a non-significant trend suggesting an inverse relationship between obesity and pain sensitivity. This observation might be explained by various factors, including differences in participant characteristics, psychological influences, biological mechanisms, and the limitations of a small sample size.¹ Future research, potentially involving larger sample sizes or incorporating a broader range of variables, including comprehensive biological, psychological and social factors, might, therefore, provide clearer insights into the nuanced relationship between BMI and the experience of pain.

Limitations

We acknowledge several limitations of this study. First, our study is limited to a single center, which may restrict its applicability to a broader population. To enhance the external validity of our findings, it is essential to conduct multicenter randomized controlled trials involving larger and more diverse populations and settings. Second, psychological factors such as anxiety and depression, as well as social factors, were not comprehensively assessed. These factors can influence the perceived intensity of pain. Nevertheless, we screened for them through history-taking and physical examinations and excluded individuals with psychiatric disorders. Third, certain baseline characteristics across the 4 groups, including the participant's dominant hand and the correlation between the punctured site and punctured vessels, differed significantly. Further studies are needed to control for these differences to confirm the pain reduction findings across interventions. Lastly, the combined interventions were not evaluated or compared with single interventions. Further studies should be conducted to assess the additional effects of combining interventions.

Conclusions

The intervention for pain reduction, which includes topical anesthetic, cooling spray and audiovisual distraction, is an effective method for alleviating pain during venipuncture. Participants who received a topical anesthetic reported the lowest pain scores and high levels of satisfaction. When selecting the intervention, consideration should be given to the availability of resources, patient preferences and time constraints.

Supplementary data

The Supplementary materials are available at <https://doi.org/10.5281/zenodo.11079400>. The package includes the following files:

Supplementary Table 1. Evaluating normal distribution in each variable group.

Supplementary Table 2. Comparison of pain across different factors.

Supplementary Table 3. The assessment of equal variances.

Supplementary Table 4. The numbers of expected observations.

Supplementary Fig. 1. Correlation between age and pain scores (n = 47).

Supplementary Fig. 2. Correlation between weight and pain scores (n = 47).

Supplementary Fig. 3. Correlation between height and pain scores (n = 47).

Supplementary Fig. 4. Correlation between body mass index (BMI) and pain scores (n = 47).

Supplementary Fig. 5. Correlation between body mass index (BMI) and pain scores (n = 47) using Locally Weighted Scatterplot Smoothing (LOESS) curves.

Data availability

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

Consent for publication

Not applicable.

ORCID IDs

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