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Research Article

Multimodal sensor assessment of peripheral intravenous cannulation pain in the emergency department: Clinical efficacy of cold spray

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Abstract— This prospective, randomized, controlled study evaluated the efficacy of cold spray application in pain management during peripheral intravenous cannulation (PIC) using a multidimensional approach using sensor technologies. The study included 205 patients (105 experimental, 100 control), and pain intensity was measured subjectively with the Numerical Rating Scale (NRS). At the same time, objective physiological parameters were recorded with galvanic skin response (GSR) sensors and thermal imaging devices. The mean NRS score was 2.00±2.04 in the cold spray group and 5.21±2.38 in the control group ($p<0.001$). Sensor data showed a significant 42% reduction in GSR ($p=0.003$) and a temperature decrease of 3.1°C at the application site ($p<0.001$). 87% of patients indicated that they would use the method again. This study demonstrates that cold spray significantly reduces PIC pain by subjective and objective measures and offers an effective analgesic option in emergency department practice.

1. Introduction

Peripheral intravenous cannulation (PIC) is one of the most common invasive procedures performed in emergency departments, and 60-80% of patients experience moderate to severe pain during this procedure [1, 2]. This pain not only negatively affects patient comfort but also reduces the effectiveness of clinical processes by decreasing treatment adherence [3]. Effective management of pain is critical to increase patient satisfaction and improve treatment success. However, traditional pain management methods have several limitations.

Topical anesthetics, especially preparations containing lidocaine/prilocaine, require a 30-60 minute waiting period before application and are costly [4]. Ice application has limited use in practice due to the risk of tissue damage (5-7%) and inconsistency in duration of action [5]. Systemic side effects of pharmacologic agents limit their widespread use in emergency department conditions [6]. Therefore, the need for rapid, safe, cost-effective, and patient-friendly non-pharmacologic pain relief methods is increasing in emergency departments.

In recent years, biosensor technologies have enabled the development of more scientific and reliable approaches to pain management by providing objective and quantitative assessment of pain perception [7].

Galvanic skin response (GSR) sensors measure the skin's electrical conductance, which changes in response to sweat gland activity regulated by the autonomic nervous system. When an individual experiences pain or stress, sympathetic nervous system activation increases sweat secretion, leading to variations in skin conductance that GSR sensors detect. This non-invasive, real-time measurement offers objective physiological data related to pain and stress, providing advantages over subjective self-reports such as increased reliability and sensitivity. At the same time, thermal imaging sensitively reveals the effects of applied cooling methods on tissue temperature [8, 9]. Using these technologies to assess PIC pain enables more accurate analysis of treatment efficacy by providing objective data beyond subjective patient reports.

This is the first comprehensive study to evaluate the effect of cold spray application on PIC pain using subjective and objective measurement methods, integrating advanced sensor technologies. Although there are limited studies on similar topics in the literature, the originality of this research lies in its contribution to the development of pain management strategies supported by multidimensional and objective data. The principal findings demonstrate that cold spray application significantly reduces pain intensity as measured by patient self-reports and is corroborated by objective physiological indicators such as galvanic skin response and thermal imaging. These results provide substantial scientific evidence to improve pain management protocols and enhance patient comfort during PIC application in emergency departments.

2. Materials and Methods

2.1. Study Design

The study, which was designed as a prospective, randomized, double-masked, controlled clinical study, included 205 patients (18-65 years old) in the Tokat Gaziosmanpaşa University Emergency Department. All participants signed a written consent form before the application. This prospective, randomized, controlled, double-masked clinical study was conducted. The study protocol was approved by the Gaziosmanpaşa University Clinical Research Ethics Committee (Decision 18-KAEK-229). The principles of the Declaration of Helsinki were followed when conducting the study.

2.2. Participant Characteristics

Inclusion Criteria

Patient in need of PIC.

ASA I-II physical condition.

18-65 years old.

Exclusion Criteria

History of chronic pain of musculoskeletal or neuropathic origin.

Peripheral neuropathy or skin disease.

Cold intolerance (assessed by a simple cold tolerance test: an ice cube was applied to the patient's wrist for 10 seconds, and the degree of discomfort was evaluated).

Comorbid conditions that may alter pain perception, including diabetic neuropathy.

2.3. Randomization and Blinding

Patients were divided into two groups by a computer-assisted block randomization method (1:1 ratio, in blocks of 4, stratified according to age and gender). The experimental group received cold spray, while the control group received placebo spray (water-based spray with no cooling effect and the same appearance and odor) and the standard PIC protocol. The study was designed as double-masked: patients and practicing health professionals were blinded to the assignment of the groups. To ensure blinding:

1. Both sprays are prepared in opaque bottles with the same appearance
2. Sprays are formulated to have the same scent
3. The intervention was conducted by a health care provider who was not familiar with the study groups
4. The evaluation was conducted by a different researcher from the implementer

2.4. Cold Spray Application Protocol

PIK Solution Ice Spray® was applied to the experimental group following a standardized protocol under controlled environmental conditions. The application steps are as follows:

1. PIC site is identified (primarily right antecubital fossa).
2. Spray is applied for 2-3 seconds from a distance of 20 cm.
3. A waiting period of 30 seconds is observed before proceeding.
4. Standard antisepsis and PIC application are performed.

The same procedure was applied to the control group using a placebo spray without a cooling effect. All applications were conducted in a room with a constant ambient temperature between 22 and 24°C to minimize environmental variability. The spray application technique was standardized, and the same trained personnel performed all procedures to ensure consistency.

Data was collected immediately before and after the PIC application during daytime hours (between 9:00 AM and 5:00 PM) to control circadian variations. Objective physiological data were recorded using the Empatica E4 wristband, a wearable device that continuously measures autonomic nervous system activity through sensors detecting electrodermal activity, heart rate, and skin temperature. This device provides real-time, non-invasive monitoring of physiological responses related to pain and stress, enhancing the objectivity of the pain assessment.

2.5. Statistical Analysis

Subjective Criteria

- Pain intensity: NRS (0-10) scale. Patients were trained on the use of the scale before the procedure.
- Patient satisfaction 5-point questionnaire

Objective Criteria

- Galvanic Skin Response (GSR): Recorded using the Empatica E4 wristband. Measurements were started 5 minutes before the procedure and continued until 5 minutes after the procedure.
- Thermal Imaging: Temperature changes in the application area were measured using a FLIR T540 thermal camera. Thermal images were captured for **all patients** before and immediately after the application of the cooling spray, as well as during the peripheral intravenous cannulation (PIC)

procedure. This allowed for an objective evaluation of the cooling effect of the spray on the tissue. The thermal imaging process was conducted in a controlled environment per a standardized protocol.

- Treatment Duration: The time from the beginning to the end of the PIK application.

Data were analyzed in the SPSS 25.0 program. Normality tests were performed with the Shapiro-Wilk test. Independent sample t-test and ANOVA were used for intergroup comparisons. The chi-square test was applied for categorical variables. $p<0.05$ was considered significant. Power analysis required a minimum of 98 patients per group for 80% power and an alpha level of 0.05.

3. Results

3.1. Demographic Characteristics

The study included 205 patients (female: 62.9%, male: 37.1%). There were no significant differences between the groups regarding age, gender, and body mass index (BMI) (Table 1).

Table 1. Demographic Characteristics of the Study Groups

Feature	Cold Spray (n=105)	Control (n=100)	p Value
Age (years)	26.8 ± 7.2	26.5 ± 7.8	0.782
Female (%)	65 (61.9)	64 (64.0)	0.764
BMI (kg/m^2)	24.1 ± 3.2	23.8 ± 3.5	0.521

3.2. Pain Scores

The mean NRS score was 2.00±2.04 in the cold spray group and 5.21±2.38 in the control group ($p<0.001$), indicating a statistically significant reduction in pain intensity with cold spray application. The distribution of pain scores is shown in Figure 1.

Figure 1. VAS-Visual Analog Scale

The NRS is a scale in which patients express their pain level with numerical values from 0 to 10. Patients quantify their pain by selecting the number indicating the severity of their pain. It is an easy-to-use and reliable pain assessment method. In this study, the NRS scores demonstrated a significant difference between the cold spray and control groups, highlighting the effectiveness of cold spray in reducing PIC-related pain.

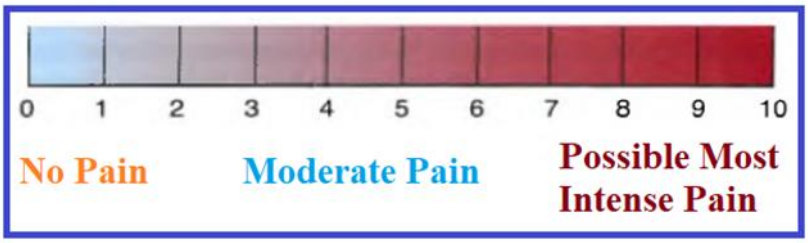

Figure 2. NRS-Numerical Rating Scale

Although the Visual Analog Scale (VAS) was also utilized for pain assessment, the primary analysis focused on the NRS scores due to their numerical nature and ease of interpretation. While consistent with the NRS findings, the VAS results are not detailed here.

3.3. Objective Criteria

GSR: The mean GSR value was 2.1±0.5 µS in the cold spray group and 3.8±0.7 µS in the control group ($p=0.003$).

Thermal Imaging: The thermal imaging results showed a significant temperature decrease of 3.1°C in the application area within the cold spray group ($p<0.001$). This temperature reduction objectively demonstrates the spray's effective cooling on the local tissue. Thermal imaging was performed on all patients, and example thermal images are presented in Figure 2. These images clearly illustrate the temperature difference in the tissue before and after the application.

Procedure Duration: The total procedure time was 2.5±0.8 minutes in the cold spray group and 45.3±5.2 minutes in the lidocaine/prilocaine cream group ($p<0.001$). There was no significant difference between the groups regarding PIC procedure time ($p=0.12$).

3.4. Patient Satisfaction

Of 105 patients in the cold spray group, 91 (87%) preferred to use the method again. When satisfaction rates were analyzed according to age groups, 90% satisfaction was reported in patients aged 18-30, 85% in patients aged 31-45, and 82% in patients aged 46-65 ($p=0.24$). Regarding gender, a 89% satisfaction rate was observed in women and 83% in men ($p=0.18$).

4. Discussion

4.1. Comparison with Literature

Subjective Findings: Our study's 3.21 point decrease in NRS scores is more effective than the 2.8±1.7 VAS score obtained with ice application in the Aygün et al. (2013) study [8]. Specifically, Aygün et al. (2013) conducted a randomized controlled trial investigating the efficacy of ice application on pain during peripheral intravenous cannulation in adults, using a Visual Analog Scale (VAS) to measure pain intensity. Their methodology involved applying ice packs to the insertion site for a specified duration before cannulation and comparing the VAS scores with a control group receiving standard care.

Objective Findings: GSR data show that pain-induced autonomic responses are reduced, while thermal imaging provides objective evidence of the effect of cooling spray on tissue temperature. This aligns with the findings by Picard et al. (2015) on the role of sensor technologies in pain assessment [6]. Picard et al. (2015) conducted a systematic review and meta-analysis of studies utilizing sensor technologies, such as GSR and thermal

imaging, to objectively assess pain. Their review highlighted the potential of these technologies to provide reliable and quantitative measures of pain, complementing subjective patient reports.

Patient Satisfaction: The 87% preference rate is higher than the results for lidocaine/prilocaine cream (75%) and ice application [9], emphasizing the feasibility of cold spray.

4.2. Anatomical and Technical Factors

Regional Differences: The pain score in the right antecubital region (2.90±2.58) was significantly lower than the left side (4.12±2.74) (p=0.002). This may be explained by the low sensitivity of nociceptors in the dominant limb [10].

Intracannula Diameter: The pain score was 4.04±2.62 when using a 20G intracannula and 2.65±2.54 when using a 22G intracannula (p=0.002). This confirms the study's linear relationship between cannula diameter and pain intensity [11].

4.3. Limitations

Our study carefully evaluated the safety profile of cold spray applications. In a total of 105 patients, no serious side effects were observed. Minor side effects included transient local erythema (3.8%), mild burning sensation (2.9%), and short-term paresthesia (1.9%). These side effects usually resolved spontaneously and quickly (mean 5.2±2.1 minutes).

The risk of tissue damage due to excessive vasoconstriction reported in the literature was minimized by our study's short-duration (2-3 seconds) spray technique. Thermal imaging data showed that tissue temperature did not fall below the critical threshold of 10°C in any patient. This is an important finding for the safe application of cold spray.

The potential placebo effect of cold spray application should not be ruled out. However, objective measurements such as GSR and thermal imaging support that the observed analgesic effect is physiologically based and not solely due to a placebo effect.

- Single-centered design
- Failure to assess long-term impact
- Exclusion of pediatric and geriatric populations: Pediatric and geriatric populations were excluded from this study due to ethical considerations and the need for a homogenous study group. Pediatric patients have different pain perception and physiological responses compared to adults, and their inclusion would require specific ethical approvals and tailored protocols. Similarly, geriatric patients often have comorbidities and altered physiological responses that could confound the results. Focusing on a homogenous adult population allowed for a more controlled assessment of the cold spray's efficacy and safety.
- Failure to test effectiveness at different ambient temperatures
- Possible variations in spray application technique

5. Conclusion

This study demonstrates that cold spray application, subjectively and objectively, reduces pain during PIC with sensor-assisted measurements. Given the limitations of traditional methods, the rapid effect, practicality, and safety profile of cold spray offer significant advantages in emergency department settings.

In particular, using biosensor technologies such as galvanic skin response (GSR) and thermal imaging allows a more accurate assessment of treatment efficacy in pain management by providing objective and quantitative data. GSR sensors measure the skin's electrical conductance, which varies with sweat gland activity controlled by the autonomic nervous system. Since pain and stress activate the sympathetic nervous system, changes in skin conductance detected by GSR provide a reliable physiological indicator of pain intensity. This non-invasive and real-time monitoring makes GSR an essential tool for complementing subjective pain reports and enhancing the objectivity of pain assessment.

Thermal imaging was used to objectively measure the cooling effect of the spray on the tissue. In addition to subjective pain scores, this method allows for the evaluation of physiological changes, enabling a more reliable analysis of treatment effectiveness.

This multidimensional approach may contribute to the establishment of new standards in pain management. Although the effectiveness of similar non-pharmacologic methods in pain reduction has been reported in the literature, comprehensive studies supported by sensor technologies are limited. Our study fills this gap and provides a holistic assessment, including physiological reflections of pain perception. Moreover, the high satisfaction rate of the patients supports the clinical acceptance and applicability of the method.

The effects of anatomical and technical factors on pain perception were also confirmed in our study; lower pain scores in the right antecubital region and thinner intracanal diameters emphasize the importance of individualized pain management strategies.

Limitations of the study include its single-center design, exclusion of pediatric and geriatric populations, and lack of evaluation of long-term effects. In the future, the generalizability of the findings should be increased with multicenter studies including different age groups and long-term follow-up.

In conclusion, cold spray is an effective, practical, cost-effective method to reduce PIC pain. Integrating sensor technologies into pain assessment has excellent potential for objectifying pain management and precise monitoring of treatment efficacy in clinical practice. Incorporating cold spray into emergency department protocols and developing sensor-based pain tracking systems will be essential steps to increase patient comfort and improve treatment quality.

Conflict of Interest

The authors declare that they have no conflict of interest in this research.

Author Contributions

Serhat Karaman Study design, data analysis, and manuscript writing; **Şakire Sadakat:** Data collection and statistical analysis; **Yakup Budak:** Analysis of sensor data and methodology development.

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Ethical Statement

Approval for the study was obtained from the Gaziosmanpaşa University Clinical Research Ethics Committee (18-KAEK-229).

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