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Comparison of low-cost interventions for pain during radial arterial blood gas sampling in the emergency department: a three-arm randomised controlled trial

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Abstract

This study evaluated the efficacy of topical anaesthesia and cryo-analgesia for pain management during radial Arterial Blood Gas (ABG) sampling, compared with standard care. An open-label, randomised controlled trial with blinded statistical analysis in a Thai emergency department (July–September 2024) included 126 adults requiring ABG sampling. Participants were randomised to receive topical anaesthesia (10% lidocaine spray), cryo-analgesia (cold pack), or standard care (2% chlorhexidine) two minutes prior to the procedure. The primary outcome was participant-reported pain, assessed via the Numeric Rating Scale (NRS) during the procedure and 30 seconds post-procedure. ANOVA determined significant differences in pain scores. Statistical significance was set at $p<0.05$. All 126 participants completed the study (42 participants per group). Mean NRS pain scores

did not differ significantly among the groups during the procedure [F(2,123)=0.62, *p*=0.54] or 30 seconds post-procedure [F(2,123)=0.35, *p*=0.71] Cryo-analgesia achieved the highest first-attempt success rate (83.3%, *p*=0.42). No immediate complications occurred within 5 minutes. Neither topical anaesthesia nor cryo-analgesia provided superior pain management compared with standard care during radial ABG sampling. These findings represent an absence of evidence for superiority, rather than evidence of clinical equivalence.

Introduction

Arterial Blood Gas (ABG) sampling is a crucial diagnostic procedure in the Emergency Department (ED); however, it often causes significant pain and patient resistance.[1] While subcutaneous infiltration of local anaesthetics, such as mepivacaine or lidocaine, is established as an effective analgesic method for arterial puncture, its requirement for an additional needle stick can be counter-productive for brief procedures and may contribute to procedure-related anxiety. In the fast-paced environment of a high-volume ED, there is a significant clinical need for non-invasive, rapid-onset alternatives that do not compromise departmental throughput. While topical anaesthesia and cryo-analgesia have shown promising results in minimising pain during invasive procedures,[2] their efficacy for ABG sampling remains controversial, potentially due to variations in coolant modalities, application durations, and temperatures.[1–5] Furthermore, recent systematic reviews emphasise that translating the benefits of topical agents to the rapid workflow constraints of the ED remains a significant clinical challenge.[6]

Effective analgesia is particularly challenging in resource-limited settings. In Thailand, ED visit rates (approximately 500 per 1,000 population) exceed those of high-income regions, including the United States (470), Australia (340), and Europe (305),[7–10] which proportionally increases the frequency of ABG sampling. Despite this demand, published research addressing ABG pain management within Thailand is scarce. To our knowledge, only one study has evaluated needlestick pain relief during blood collection, utilising local anaesthesia

and audiovisual distraction in volunteers.[11] This highlights a critical gap in patient care, underscoring the urgent need for feasible, evidence-based analgesic strategies.

This study aimed to evaluate the efficacy of two low-cost, needle-free interventions—topical anaesthesia (10% lidocaine spray) and cryo-analgesia (cold pack)—compared to standard care (2% chlorhexidine).

Materials and Methods

Study design, setting, and ethics

This open-label, superiority Randomised Controlled Trial (RCT) with blinded statistical analysis was conducted between 15 July and 15 September 2024 in the ED of a Thai semi-tertiary centre. The study adhered to the Declaration of Helsinki and received Institutional Review Board approval (IRB No. 002/2567; registered on ClinicalTrials.gov: NCT06505889). Informed consent was obtained from all participants prior to their involvement in the study.

Participants

Eligible participants were adults (aged ≥18 years) requiring radial ABG sampling. Exclusion criteria included an altered level of consciousness (Glasgow Coma Scale <15), cognitive impairment, local skin lesions, pregnancy, and conditions requiring immediate resuscitation (e.g., cardiac arrest, airway compromise, hemodynamic instability) that precluded the 2-minute intervention pause. Patients with a lidocaine allergy, severe concomitant pain, or those who required more than two sampling attempts were also excluded.

Sample size

Sample size determination utilised G*Power software (version 3.1.9.7)[12] for a one-way analysis of variance (ANOVA, F-test family). The effect size (Cohen's f = 0.28) was based on a prior RCT study by Pagnucci *et al.*[13] We calculated that 126 participants (42 per group) were required to achieve 80% statistical power (1-β) with a significance level (α) of 0.05.

Intervention

Participants received their assigned intervention exactly two minutes prior to the procedure: cryo-analgesia (cold pack, -4°C), topical anaesthesia (0.5 mL of 10% lidocaine spray [Xylocaine pump spray, Aspen, Australia]), or standard care (0.5 mL of 2% chlorhexidine). This 2-minute duration was chosen for pragmatic feasibility within the rapid ED workflow.[2,14] Emergency physicians performed the radial ABG sampling using a 22-gauge, 1-inch heparinised syringe under aseptic conditions, following WHO guidelines.[15]

Outcome measures

The primary outcome was participant-reported pain severity, measured using an 11-point Numeric Rating Scale (NRS, 0–10) at two time points: during needle insertion and 30 seconds post-procedure. Secondary outcomes included first-attempt success rates and factors associated with procedure duration.

Data collection

Baseline demographic and clinical data included age, sex, height, weight, body mass index (BMI), and Emergency Severity Index (ESI). Procedural metrics included the number of attempts and total procedure time. Pain was quantified using a visual, horizontal 0–10 NRS (0 = no pain, 10 = worst imaginable pain).[16] Participants were monitored for 5 minutes post-procedure for immediate complications, including bleeding, swelling, and erythema.[15]

Randomisation, allocation concealment, and blinding

Participants were randomised (1:1:1) using a computer-generated sequence (block size of four) created by an independent physician. Allocation was concealed by an uninvolved research assistant. Due to the visible nature of the interventions, participants and treating physicians were unblinded. This inherent unblinding may introduce performance and detection bias; however, the statistician analysing the data remained strictly blinded to group allocation.

Statistical analysis

Data were analysed using IBM SPSS version 26.0 (IBM Corp., USA). Descriptive analysis characterised the demographic data of each group, including age, sex, weight, height, BMI, and ESI. The Kolmogorov-Smirnov test evaluated data normality. Categorical variables are presented as frequencies and percentages; continuous variables are expressed as means with Standard Deviations (SD) or medians with Interquartile Ranges (IQR), as appropriate. One-way ANOVA (with post-hoc testing) evaluated differences in pain scores across groups. The chi-square test analysed first-attempt success rates, and multivariate linear regression identified factors associated with procedure duration. All analyses followed an intention-to-treat (ITT) principle, with a two-tailed p-value <0.05 indicating statistical significance. There were no missing data.

Results

Between 15 July and 15 September 2024, 261 participants requiring radial ABG sampling were screened. Of these, 135 (51.7%) were excluded, primarily due to altered consciousness (n = 50, 37%) or the need for immediate emergency intervention (n = 49, 36.2%; Figure 1). The final cohort comprised 126 participants (mean age 60.5 ± 18.1 years; 55.6% male), with 67.5% classified as emergencies on the ESI. With the exception of statistically significant difference in participant height, demographic characteristics and pre-procedural pain scores were well-balanced among the groups (Table 1). All participants completed the full 2-minute intervention. No participant required more than two puncture attempts, and no immediate complications were observed within the 5-minute post-procedure period.

Primary outcome

Pain scores did not differ significantly across the groups during the procedure [$F(2, 123)=0.62$, $p=0.54$] or 30 seconds post-procedure [$F(2, 123)=0.35$, $p=0.71$]. During the procedure, mean pain scores were 5.48 ± 2.05 for cryo-analgesia, 5.10 ± 2.62 for topical anaesthesia, and 5.67 ± 2.48 for the control group (Table 2). Compared with the control

group, the mean difference in pain scores was -0.19 (95% CI: -1.18 to 0.80) for cryo-analgesia and -0.57 (95% CI: -1.68 to 0.54) for topical anaesthesia.

Secondary outcomes

Although the cryo-analgesia group achieved the highest first-attempt success rate (83.3%), this difference was not statistically significant [$\chi^2(2)=1.75$, $p=0.42$; Table 3]. Multivariate linear regression (Table 4) indicated that male sex was associated with a significantly shorter procedure duration ($\beta=-14.08$, 95% CI: -26.41 to -1.74, $p=0.03$), whereas increasing age was associated with a prolonged duration ($\beta=0.30$, 95% CI: 0.01 to 0.59, $p=0.04$).

Discussion

The principal finding of this study is that patients experienced similar levels of pain during radial ABG sampling regardless of whether they received topical anesthesia, cryo-analgesia, or standard care. Consequently, our findings did not demonstrate the superiority of the evaluated interventions over standard care for pain management during radial ABG sampling. It is important to contextualise this within our superiority trial design; these results strictly indicate an absence of evidence for superiority, rather than confirming non-inferiority or clinical equivalence. This contrasts with previous studies, such as the systematic review by Gonella *et al*.[2] and trials by Gur and Tekin,[17] which demonstrated the efficacy of these interventions in non-emergency or different procedural contexts.[5,18] Several factors may explain this divergence. First, applying 2% chlorhexidine is an active intervention; the associated tactile stimulation and patient-provider interaction likely generated a contextual placebo effect.[19] This active comparator likely caused an ‘effect dilution’, narrowing the observable contrast between groups, which should be viewed as an expected phenomenon in pragmatic trials rather than a methodological flaw. Second, high inter-individual pain variability and the limited sensitivity of the NRS to brief, sharp procedural pain may have masked subtle differences.[16,20] Finally, while the 2-minute application time is pragmatically justified for the ED setting, it may be pharmacodynamically insufficient.[2,5,21,22] Consequently, a false-negative result under these rapid-use conditions cannot be excluded. This limits our

ability to draw definitive conclusions regarding intrinsic analgesic efficacy when applied for longer, pharmacodynamically optimal durations.

However, while our results differ from those of studies conducted in controlled, non-emergency settings, they align closely with recent literature evaluating procedural analgesia specifically within the rapid-workflow constraints of the ED. A 2024 systematic review and network meta-analysis by Tanaka *et al*.[6] noted that the required pharmacodynamic onset time for topical agents is a primary limiting factor in rapid-workflow environments. Furthermore, a 2025 trial by Altundağ *et al*.[23] evaluating 10% lidocaine spray for radial ABG sampling reported no significant difference in pain reduction compared with a placebo.

Regarding secondary outcomes, cryo-analgesia showed a non-significant trend towards higher first-attempt success, possibly due to cold-induced vasoconstriction stabilising the vessel and reducing soft tissue swelling.[24,25] Procedure times were shorter in males and longer in older patients, aligning with known anatomical and age-related vascular changes.[26–28] Finally, while an isolated baseline difference in participant height was noted, comparable weight and BMI across groups indicate a consistent overall body habitus. This variance lacks biological plausibility to influence radial artery depth or individual pain perception, and therefore did not confound our outcomes.[28]

Strengths and limitations

This study has several key strengths. It represents the first three-arm RCT in Southeast Asia to specifically evaluate low-cost pain management interventions for radial ABG sampling, and it features a pragmatic protocol mirroring high-volume ED constraints. Furthermore, our trial focused specifically on non-invasive modalities to prioritise needle-free interventions that align with the rapid workflow demands of the ED. However, the deliberate exclusion of subcutaneous local anaesthetic infiltration (such as mepivacaine) means our modalities were not directly compared against this standard practice, thereby limiting the scope of our comparative findings. A primary methodological limitation is its design as a superiority trial; the non-significant findings represent an absence of evidence for superiority, not equivalence. An unavoidable limitation is the inability to blind participants and clinicians due to the distinct physical modalities of the interventions. When evaluated against a highly subjective primary outcome like the NRS, this open-label design with blinded data analysis introduces a

substantial risk of performance and detection bias, which may have confounded the true intervention effects. Additionally, the use of chlorhexidine as standard care functioned as an active comparator rather than an inert placebo; the resulting patient-provider interaction may have diluted the observable effect. Finally, the high exclusion rate remains an inherent constraint.

Clinical implications

Systematic evidence[2] confirms that subcutaneous local anaesthetic infiltration provides the greatest pain reduction during arterial puncture and should be considered the standard of care. The findings of this pragmatic trial do not challenge this standard, nor do they justify omitting pre-procedural analgesia to optimize ED throughput. Rather, our results demonstrate that ultra-brief, 2-minute needle-free strategies—such as topical lidocaine spray or a cold pack—offer no added analgesic benefit over standard chlorhexidine preparation alone. These abbreviated, needle-free strategies are insufficient to mitigate procedural pain. If pain reduction is prioritized, clinicians should utilize established local infiltration or allow for significantly extended topical application times.

Conclusions

Under pragmatic ED conditions, neither a 2-minute application of topical anaesthesia nor cryo-analgesia proved superior to standard care for pain management during radial ABG sampling. Despite a non-significant trend towards higher first-attempt success with cryo-analgesia, these results do not imply clinical equivalence; rather, they highlight the need for future research into optimal application durations and non-invasive analgesic strategies.

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Figure 1. Study flow according to CONSORT format.

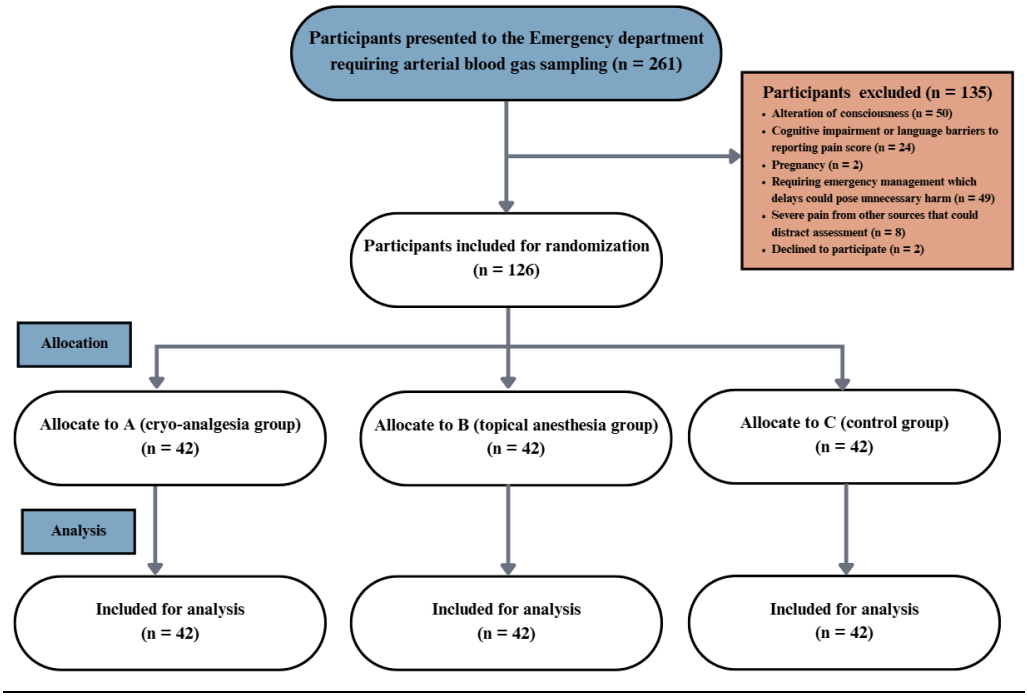

Table 1. Baseline demographic and clinical characteristics of the study cohort.

	Cryo-analgesia (n=42)	Topical anaesthesia (n=42)	Control (n=42)	Total (n=126)
Demographics				

Age (years), mean ± SD	62.40 ± 17.22	57.07 ± 18.99	62.76 ± 16.80	60.75 ± 17.75
Male, n (%)	22 (52.38%)	24 (57.14%)	24 (57.14%)	70 (55.56%)
Weight (kg), mean ± SD	60.64 ± 14.21	66.62 ± 17.32	63.45 ± 17.45	63.57 ± 16.45
Height (cm), mean ± SD	160.40 ± 9.59	164.90 ± 7.49	160.83 ± 7.55	162.05 ± 8.45
BMI, mean ± SD	23.63 ± 5.38	24.42 ± 5.61	24.49 ± 6.36	24.18 ± 5.77
Pulse Quality, n (%)	39 (92.86%)	40 (95.24%)	39 (92.86%)	118 (93.65%)
Clinical Characteristics				
ESI score, n (%)				
Resuscitation	3 (7.14%)	4 (9.52%)	3 (7.14%)	10 (7.94%)
Emergency	30 (71.43%)	27 (64.29%)	28 (66.67%)	85 (67.46%)
Urgency	9 (21.43%)	11 (26.19%)	11 (26.19%)	31 (24.60%)

BMI, body mass index; ESI, Emergency Severity Index; SD, standard deviation.

Table 2. Numeric Rating Scale (NRS) pain scores by intervention group.

Primary outcome	**Mean ± SD**	**95% Confidence interval**
Pain score during procedure (NRS)		
Cryo-analgesia group	5.48 ± 2.05	[4.84, 6.12]

Topical anaesthesia group	5.10 ± 2.62	[4.28, 5.91]
Control group	5.67 ± 2.48	[4.89, 6.44]
Pain score after procedure (NRS)		
Cryo-analgesia group	2.02 ± 2.16	[1.35, 2.70]
Topical anaesthesia group	1.64 ± 1.89	[1.05, 2.23]
Control group	1.81 ± 2.22	[1.12, 2.50]

SD, standard deviation; Pain score during procedure, assessed during needle insertion; Pain score after procedure, assessed 30 seconds post-procedure.

Table 3. First-attempt success rates for radial ABG sampling by intervention group.

Number of attempts	Cryo-analgesia (n=42)	Topical anaesthesia (n=42)	Control (n=42)	Total (n=126)	P-value
One attempt, n (%)	35 (83.33%)	33 (78.57%)	30 (71.43%)	98 (77.78%)	0.42
More than one attempt, n (%)	7 (16.67%)	9 (21.43%)	12 (28.57%)	28 (22.22%)	

ABG, arterial blood gas; Pearson chi-square test ($\chi^2(2) = 1.75$, $p = 0.42$).

Table 4. Multivariate linear regression analysis of factors associated with procedure duration for radial ABG sampling.

Factors associated with procedure duration for radial ABG sampling	Beta-coefficients	95% Confidence Interval	P-value
Male	-14.08	[-26.41, -1.74]	0.03*
Age	0.30	[0.01, 0.59]	0.04*

Weight	0.09	[-0.24, 0.41]	0.60
Height	-0.04	[-0.85, 0.77]	0.93
Cryo-analgesia group	5.58	[-6.36, 17.53]	0.36
Topical anaesthesia group	2.60	[-9.73, 14.93]	0.68
Prior history of radial ABG sampling	5.12	[-4.84, 15.08]	0.31
Pulse quality	2.42	[-18.94, 23.78]	0.82

ABG, arterial blood gas; *Significant differences were established at $p < 0.05$

Contributions

Conceptualization: SV, CT, PS; Data curation: CT, SV, PS; Formal analysis: TL, CT, TS; Funding acquisition: SV, PS; Methodology: CT, TL, PV, PT; Supervision: SV, PS; Writing–original draft: CT, TL, PV, PT; Writing–review & editing: all authors. All authors read and approve the final manuscript.

Competing interest

The authors declare that they have no competing interests.

Ethics approval

The study received approval from the of Queen Savang Vadhana Memorial Hospital (QSMH) ethics committee (IRB No 002/2567) on March 27, 2024 and registered on ClinicalTrials.gov (NCT06505889) on July 1, 2024.

Consent for publication

Not applicable

Availability of data

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

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Use of artificial intelligence (AI)- assisted technologies

The authors used a large language model (Gemini AI assistance, developed by Google) to enhance grammar, and ensure adherence to academic writing standards. The authors reviewed and edited the content as needed and took full responsibility for the content of the published article.

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