

STUDY PROTOCOL

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OFFICIAL TITLE

Efficacy of the MOLI Technique and Virtual Reality Versus Conventional Venipuncture for Pain and Anxiety in Paediatric Patients: A Three-Arm Randomised Controlled Trial

BRIEF TITLE / ACRONYM

MOLIVeR Trial

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SPONSOR

Hospital Universitario Marqués de Valdecilla, Santander, Spain

PRINCIPAL INVESTIGATORS

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ETHICS APPROVAL

Research Ethics Committee for Medicinal Products of Cantabria (CEIm Cantabria), reference 2024.249

Document History

Version / event	Date	Description
Protocol v1.0	21 June 2024	Initial approval by CEIm Cantabria (reference 2024.249).
Protocol v1.1	December 2024	Amended protocol: age range 4–12 years; recruitment extended to the Paediatric Short-Stay Unit (UCEP) and the Paediatric Inpatient Ward; recruitment procedure detailed.
Amendment approval	24 January 2025	Protocol v1.1 approved by CEIm Cantabria (amendment 2/2025).
English version	September 2026	English translation of protocol v1.1, prepared for the retrospective registration of the trial on ClinicalTrials.gov.

1. General Information

1.1 Title

Efficacy of the MOLI Technique and Virtual Reality Versus Conventional Venipuncture for Pain and Anxiety in Paediatric Patients: A Three-Arm Randomised Controlled Trial.

Original (Spanish) title: Eficacia de la técnica MOLI y realidad virtual frente al método convencional de venopunción en el dolor y la ansiedad de pacientes pediátricos: ensayo clínico aleatorizado.

1.2 Sponsor and Site

Hospital Universitario Marqués de Valdecilla (HUMV), Santander, Cantabria, Spain.

1.3 Funding

This research was funded by the Marqués de Valdecilla Research Institute (IDIVAL), Spain, 26th National Call for Research Projects “Enfermería Valdecilla”, grant number ENFVAL24/26.

1.4 Investigators

Principal Investigators: Rocío Contreras-Martín, Abraham Corchero-Gata and María Martín-García (paediatric nursing residents, HUMV).

Collaborating investigators / units: Paediatric Emergency Unit of HUMV; Sonia Mateo-Sota, Carolina Lechosa-Muñiz, Soraya Sañudo-Martínez and José Luis Cobo-Sánchez (Hospital Universitario Marqués de Valdecilla).

1.5 Ethics Approval

Research Ethics Committee for Medicinal Products of Cantabria (CEIm Cantabria), code 2024.249, and Hospital Management of HUMV.

2. Summary

Background: venipuncture is considered one of the most traumatic and painful procedures for paediatric patients and their families, generating fear before and during the intervention. Health professionals face the challenge not only of relieving pain but also of preventing it or reducing its perception through pharmacological and non-pharmacological methods. Distraction techniques include breathing exercises and virtual reality through interactive games, which can divert the child's attention from painful external stimuli.

Objective: to compare pain perception during peripheral venous catheter (PVC) insertion between the MOLI technique and virtual reality versus the conventional technique in children attended at HUMV.

Methods: randomised clinical trial applying three low-risk interventions (MOLI technique, virtual reality and conventional technique) in paediatric patients attended in the Paediatric Emergency Department, the Paediatric Short-Stay Unit (UCEP) and the Paediatric Inpatient Ward of HUMV. The target population comprises children aged 4 to 12 years with triage priority III–V (SET-MAT triage system) and an indication for venipuncture, able to collaborate in the technique together with a family member, after signature of informed consent.

Keywords: Pain, Procedural; Anxiety; Phlebotomy; Virtual Reality Exposure Therapy; Child, Preschool; Child.

3. Background and Rationale

Venipuncture is the most frequent technique in paediatric emergency departments, whether for blood sampling or for venous cannulation to administer drugs, intravenous fluids or contrast-enhanced tests. It is considered one of the most traumatic and painful procedures for children and their families. According to a 2018 study by the Analgesia and Sedation Working Group of the Spanish Society of Paediatric Emergencies (GTAS-SEUP), the prevalence of pain among children attending a paediatric emergency department is approximately 53%, with moderate–severe pain in about 74% of them. Factors associated with ineffective pain management include a lack of protocols, insufficient knowledge and awareness, delays in assessment, misconceptions about paediatric pain, fear of drug adverse effects and a lack of pain-management skills.

Non-pharmacological methods aim to address the anxiety caused by pain without the use of drugs. Evidence supports distraction methods such as interactive videos, games, music and breathing exercises, as well as physical methods such as cold and vibration. Reviews confirm that distraction, combined cognitive-behavioural therapy, hypnosis, breathing interventions and procedural information reduce pain and distress during needle-related procedures in children.

Deep breathing with forced inspirations and expirations has been described as an active distraction method that may reduce pain during venipuncture. Techniques such as balloon inflation increase intrathoracic pressure, which may activate cardiopulmonary and sino-aortic baroreceptor reflex arcs with an antinociceptive effect. Breathing-based distraction combines two psychological strategies: distraction through the blowing game and relaxation through deep expiration. An observational study using soap bubbles during removal of a peripheral line dressing also showed usefulness for pain management.

Virtual reality (VR) is one of the most attractive and promising distraction techniques for children, who become actively immersed in a virtual game and may ignore aversive external stimuli. VR has reduced pain and anxiety during port needle insertion in paediatric oncology patients, and a randomised trial in children aged 4 to 12 years undergoing venipuncture in Hong Kong showed significant improvements in pain and anxiety compared with a control group. Despite this evidence, a 2021-2022 survey of Spanish paediatricians found that only physical methods such as cold (10.2%) or vibration (5.7%) were reported, and not distraction techniques.

Justification: although the literature on VR is extensive, there is no consensus on standardised applicability criteria. For breathing techniques, the available evidence is limited by unclear reporting, high risk of bias, heterogeneity and small sample sizes. This project therefore evaluates different techniques during PVC insertion to test their efficacy in paediatric patients.

4. Hypothesis and Objectives

4.1 Hypothesis

The MOLI technique and the use of virtual reality reduce the perception of pain and anxiety compared with the conventional technique in paediatric patients undergoing PVC insertion at HUMV.

4.2 Primary Objective

To compare the perception of pain and anxiety during PVC insertion between the MOLI technique and virtual reality versus the conventional technique in children attended at HUMV.

4.3 Secondary Objectives

- To compare the satisfaction of the responsible family member among the three techniques.
- To compare the success rate of PVC insertion among the three techniques.
- To evaluate nurse satisfaction when applying the three techniques.
- To compare procedure duration among the three techniques.

5. Methods

The project was designed following the CONSORT statement for randomised clinical trials.

5.1 Study Design

Randomised clinical trial (1:1:1) applying three low-risk nursing interventions (MOLI technique, virtual reality and conventional technique) during PVC insertion in paediatric patients aged 4 to 12 years attended in the Paediatric Emergency Department, the Paediatric Short-Stay Unit (UCEP) and the Paediatric Inpatient Ward of HUMV. Given the characteristics of the trial, participants and intervention providers are not masked (open-label). To limit assessment bias, the primary outcomes are recorded by an observer external to the procedure.

5.2 Study Population

Paediatric population attending the Paediatric Emergency Department, UCEP and Paediatric Inpatient Ward of HUMV requiring PVC insertion.

Inclusion criteria:

- Age between 4 and 12 years.
- Need for PVC insertion.
- Triage priority III to V (SET-MAT triage system). Priority III: patients requiring urgent care within a maximum of 60 minutes who are haemodynamically stable; priority IV: minor urgency with a maximum waiting time of 120 minutes; priority V: non-urgent, waiting time of 240 minutes. For patients admitted to the Inpatient Ward, the triage level of the emergency episode leading to admission is considered.

Exclusion criteria:

- Inability of the patient or family member to collaborate owing to a language barrier or a disabling physical condition.
- A pathological process preventing application of the technique, such as severe respiratory distress or neurological impairment with a Glasgow Coma Scale score ≤ 14 .
- Sensory impairment to pain (e.g., spina bifida).
- History of seizures or dizziness.
- Psychomotor or neurocognitive delay, owing to the difficulty of assessing anxiety.
- Visual impairment preventing viewing of the virtual screen, or incompatibility of the child's own glasses with the VR headset.
- Hearing impairment preventing interaction between the professional and the child for correct performance of the procedure.

5.3 Sample Size

The sample size was calculated with the GRANMO sample size calculator, version 7.11 (March 2011). To detect a difference in pain intensity score of 1 point or more, with a standard deviation of 0.5 points after the use of virtual reality (Koç Özkan & Polat, 2020), a total sample of 201 participants is required (67 in each of the three arms: MOLI, virtual reality and control), accepting an alpha risk of 0.05 and a beta risk of 0.2 in a two-sided test, with an anticipated loss-to-follow-up rate of 5%.

5.4 Randomisation

Eligible participants are randomly allocated in a 1:1:1 ratio to the MOLI, virtual reality or control group. An independent statistician prepares in advance a sequence of group identifiers (M = MOLI group; RV = virtual reality group; C = control group) using a computer-generated randomisation list produced with the statistical package Epidat 4.2, in permuted blocks of variable size (6 and 9).

Group identifiers are placed in sealed, opaque, serially numbered envelopes according to the random sequence list generated by the statistician. Allocation follows the order of enrolment and the identifier contained in the corresponding numbered envelope. Group allocation is concealed from the child and parents until informed consent and baseline data have been obtained. The characteristics of the trial prevent blinding; this is not expected to be a major source of bias, as children are unlikely to change their behaviour even when aware of receiving a particular intervention.

5.5 Study Interventions

Before the start of the study, healthcare professionals (nurses and nursing care assistants, TCAE) of the Paediatric Emergency Department of HUMV are trained in an information session explaining the project, its methodology and the three interventions. A practical pilot is performed before the study, and videos demonstrating each technique are recorded. A contact phone number and corporate e-mail are provided for queries, and a leaflet with the procedure is distributed as a support resource.

MOLI technique (experimental arm 1).

Children up to 10 years of age sit on the lap of the family member/guardian, who sits on a chair placed perpendicular to the trolley, with one arm hugging the family member and the other extended on the trolley; children aged 11 and 12 years sit directly on the trolley with the backrest raised to 30°. The nurse stands on the opposite side of the trolley, while the TCAE immobilises the limb from the family member's side, blocking the child's view of the procedure. Before cannulation, the companion holds a pinwheel 20-30 cm from the child's mouth and, at the moment of puncture, the patient is encouraged to blow on it as a distraction method.

A story is told: the nurse enters with the tourniquet, the pulse oximeter and the pinwheel and explains that this “bracelet” (tourniquet) measures the child's “super strength” while blowing the pinwheel, and that a “sticker with a red light” (pulse oximeter) will be placed. The child is then placed in position and the TCAE brings in the venipuncture material out of the child's sight. During cannulation the child is encouraged to blow as hard as possible.

Virtual reality (experimental arm 2).

Positioning of the child (on the family member's lap up to 10 years; on the trolley with the backrest at 30° at 11-12 years), family member, nurse and TCAE is identical to the MOLI technique. The child uses the controller with the arm contralateral to the puncture site. At the moment of venipuncture, the patient is encouraged to interact with the game in the Meta Quest 3 virtual reality headset, using the video game “Fruit Ninja VR” (Halfbrick Studios), “Classic” mode, which can be played with one hand. The nurse enters with the tourniquet, pulse oximeter and VR headset and explains that the tourniquet is a bracelet that squeezes a little and is needed for the headset to work, and that a “sticker with a red light” (pulse oximeter) will be placed. The child is placed in position, the TCAE brings in the venipuncture material out of the child's sight, and during cannulation the child is encouraged to interact with the virtual game.

Conventional venipuncture technique (control arm).

The patient lies on the trolley while the TCAE immobilises the upper and lower limbs so that the procedure can be performed, and a family member/legal guardian stands on the side opposite the nurse together with the TCAE. Before the intervention, a pulse oximeter is placed to measure heart rate.

5.6 Study Variables

Dependent variables:

- Pain perception, measured with the Faces Pain Scale-Revised (FPS-R): self-report scale of pain intensity for children, adapted by the International Association for the Study of Pain (2001), scored from 0 (“no pain”) to 10 (“very much pain”), valid for ages 4 to 16 years. The child is asked to point to the face that best matches the perceived pain, immediately after PVC insertion

(approximately 1 minute after catheter fixation); the score is recorded by an observer external to the procedure.

- Anxiety, measured with the Groningen Distress Scale (Humphrey et al., 1992): observational scale for short procedures, based on crying and muscle tension, with five grades: 1 (calm, no crying), 2 (tension without crying), 3 (tension and some crying), 4 (tension and continuous crying), 5 (aggression/screaming/physical resistance). Rated by an observer external to the procedure immediately after PVC insertion.
- Heart rate (before and after the intervention).
- Success of the technique: insertion of a patent PVC at the first attempt (yes/no).
- Procedure duration, in minutes, from skin disinfection (start) to placement of the semi-transparent dressing over the puncture site (end).
- Satisfaction of the nurse performing the procedure, 5-point Likert scale: 1 (not at all satisfied), 2 (slightly satisfied), 3 (neutral), 4 (very satisfied), 5 (totally satisfied).
- Satisfaction of the family member/legal guardian, 5-point Likert scale (same categories).

Independent variables:

- Patient sex (female/male) and age (4-12 years).
- Difficulty of cannulation measured with the paediatric Difficult Intravenous Access (DIVA) score (0-10 points; items: vein visible after tourniquet, vein palpable after tourniquet, age, history of prematurity); DIVA $\geq$ 4 points (yes/no).
- Puncture site (antecubital fossa, dorsum of the hand, other: specify).
- Catheter gauge (22 G or 24 G).
- Triage priority (III, IV or V).
- Age of the nurse performing the intervention (years) and clinical experience in paediatrics (years).
- Technique-related variables: number of punctures required until success; PVC allowing blood sample collection (yes/no).
- Adverse events (free text), including:
 - MOLI technique: respiratory distress or vasovagal syncope during forced expiration when blowing the pinwheel.
 - Virtual reality: seizures, headache, dizziness due to the proximity of the screen, visual symptoms such as irritation and blurred vision.
 - Conventional technique: erythema and skin lesions, joint pain derived from the force applied when immobilising the joints.

5.7 Procedures

Preparation:

- Approval of the study by the nursing residency tutor, the head of the medical service and the nursing supervisor of the Paediatric Emergency Department.
- Approval by the CEIm and by HUMV.
- Practical pilot before the study and information session for paediatric emergency professionals, with leaflet, videos, phone contact and corporate e-mail.

- Information to the family member/legal guardian, verification of eligibility criteria and informed consent.
- Randomisation, intervention delivery according to allocation, data collection, analysis, discussion and conclusions.

Data collection:

The nurse identifies children requiring venipuncture. If they meet the inclusion criteria, the nurse meets the patient and family member/legal guardian in a suitable place (consultation box, or patient room in the Inpatient Unit), provides an information sheet and explains the study. If they agree to participate, written informed consent is obtained from the accompanying family member/guardian, and the child, who receives an age-adapted information sheet, gives assent when appropriate. Before randomisation, the patient's data and clinical characteristics are recorded. The intervention is then allocated according to the randomisation sequence generated with Epidat 4.2: children in the control group receive standard care with the conventional technique, and children in the intervention groups receive the MOLI technique (M) or virtual reality (RV).

Participants are assessed before the procedure, during the procedure (catheter insertion) and after the procedure. The nurse records heart rate before and after, procedure duration and nurse satisfaction; pain and anxiety are recorded after the procedure by an observer external to the procedure. The accompanying family member completes the satisfaction scale after the procedure.

Variable	Before venipuncture	During venipuncture	After venipuncture
Patient data	✓		
Heart rate	✓		✓
Procedure duration		✓	
Pain (FPS-R)			✓
Anxiety (Groningen)			✓
Parent satisfaction			✓
Nurse satisfaction			✓

5.8 Statistical Analysis

A database will be built from the data collected. Statistical analysis will be performed with IBM SPSS Statistics version 26. Two-sided tests will be used, with a 95% confidence level and 80% power. Point estimates and confidence intervals will be provided. Parametric techniques will be used when their assumptions are met; otherwise they will be replaced by non-parametric techniques. Normality will be assessed with the Kolmogorov–Smirnov test, homogeneity of variances with Levene's test and sphericity with Mauchly's W test.

The presence of outliers will be explored and, if detected, sensitivity analyses will be performed to explore their effect on the results. Quantitative variables will be described with mean and standard deviation, with histograms and box plots for the most relevant results. Qualitative variables will be

summarised with absolute and relative frequencies (percentages), with pie and bar charts for the most relevant data. Bivariate analyses will use parametric or non-parametric tests as appropriate.

A subgroup analysis by age (4-6, 7-9 and 10-12 years) is planned for the primary outcomes (pain and anxiety), and the secondary outcomes will be compared among the three arms according to the secondary objectives.

The intention-to-treat principle will be adopted for comparisons between the intervention and control arms. Parametric tests: Student's t test, ANOVA and Pearson's correlation. Non-parametric tests: Wilcoxon test, Mann–Whitney U test, Kruskal–Wallis test and Spearman's correlation; chi-square test for categorical variables. All analyses will be two-sided with a significance level of 0.05.

A Statistical Analysis Plan describing the analyses actually performed is provided as a separate document.

5.9 Ethical Considerations

Participation is voluntary. Before participating, the family receives verbal and written information about the research team, the purpose of the study, the advantages and disadvantages of participating, where and for how long data are stored, and their authorisation to participate; signed informed consent from the parent or legal guardian and assent of the child when appropriate are required. Participants may withdraw at any time without explanation and without any effect on the child's care. Data are identified by a code so that the patient cannot be identified.

The study is conducted in accordance with Spanish Organic Law 3/2018 of 5 December on the Protection of Personal Data and Guarantee of Digital Rights, Regulation (EU) 2016/679 (GDPR) and the principles of the Declaration of Helsinki. The project was approved by the Research Ethics Committee for Medicinal Products (CEIm) of Cantabria (code 2024.249) and by the Hospital Management of HUMV.

5.10 Timeline

Phase	Planned period
Pilot	Month 1
Data collection	Months 2-7
Database construction, statistical analysis and interpretation	Months 8-10
Detailed study report	Month 11
Dissemination of results	Month 12

Note added for registration: actual recruitment took place from 1 November 2024 to 31 August 2025.

6. Selected References

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