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Infrared illumination for difficult peripheral venous catheterisation in critically ill adult patients: the prospective, randomised, multicentre ICARE trial

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ABSTRACT

Introduction The insertion of a peripheral venous line is of paramount importance in the stabilisation of critically ill patients. It is a preferred method of venous access over more invasive techniques due to its immediacy and fewer complications. Difficulties of catheterisation can result in delays to treatment, increased complication risks and pain, and a waste of valuable time and healthcare resources. Our hypothesis is that infrared vein illumination could improve the success rate of peripheral venous catheterisation in critically ill patients at risk of difficult catheterisation.

Methods and analysis This is a prospective, multicentre, randomised, open-label controlled trial. It will be conducted in France and will involve critically ill patients at risk of difficult peripheral catheterisation. Patients will be randomly assigned to usual care or infrared vein illumination. The primary outcome is the rate of successful peripheral venous catheterisation at first puncture. Secondary outcomes include time to placement, overall rate of successful peripheral venous catheterisation, number of punctures, quality (calibre of the catheter), replacement rate, need for central line and local complications (dysfunction, diffusion, haematoma and lymphangitis).

Ethics and dissemination The study has been granted ethical approval (CPP Ile de France 1). Following the provision of informed consent, patients will be included in the study. The results will be submitted for publication in peer-reviewed journals.

Trial registration number NCT03932214.

STRENGTHS AND LIMITATIONS OF THIS STUDY

⇒ The trial is being conducted in intensive care units under conditions of urgent care.
⇒ A clinically relevant endpoint, namely the primary success rate, will be employed to assess the efficacy of the intervention.
⇒ It is not possible to blind patients and investigators to the interventions during the study.

INTRODUCTION

It is crucial to insert a peripheral venous line for initial stabilisation of critically ill patients.[1] Peripheral venous catheterisation is the preferred method over more invasive routes due to its immediate applicability by nurses and reduced complication rates.[2] Several factors can contribute to a challenging peripheral catheterisation, and risk scores have been established for children (difficult intravenous access, DIVA) and adults (A-DIVA).[3] These difficulties can result in the wastage of nursing time, cause pain and delay treatment, sometimes leading to the use of unconventional insertion sites or more invasive accesses, which increases the risk of complications.

Imaging tools such as ultrasound and infrared illumination may improve catheterisation practices. However, practical limitations of ultrasound include preparation time, the risk of cross-contamination, and the need for permanent ultrasound equipment and trained staff. Infrared illumination maps the peripheral venous network, is intuitive, easy to use without special training, does not require direct skin contact and poses

no risk to patients.[4] It has been shown to benefit certain patient groups, such as haemophiliacs and young children, by improving vein localisation and reducing puncture pain.[5–7] However, some studies showed no benefit in unselected patients. No trial has been specifically conducted in critically ill patients, despite the high risk of difficult peripheral catheterisation in these patients.[8] Some infrared devices, such as AccuVein (AccuVein, New York, USA) and Veinviewer (B. Braun Medical, Pennsylvania, USA), have been shown to offer superior vein visualisation compared with others.[4]

Our hypothesis is that infrared vein illumination could facilitate peripheral venous catheterisation in the upper limbs of critically ill patients at risk of difficult catheterisation.

OBJECTIVES

Primary objective

The primary objective is to evaluate the effectiveness of infrared illumination (AccuVein) for the primary success (from the first puncture) of peripheral venous catheterisation of the upper limbs in critically ill patients at risk of difficult venous catheterisation.

Secondary objectives

The secondary objectives are to assess the benefits of infrared illumination on the success of peripheral venous catheterisation, including time to placement, number of punctures, failure rate, quality (calibre of the catheter), replacement rate, need for central venous line and local complications (dysfunction, diffusion, haematoma and lymphangitis).

Ancillary studies

Not applicable.

METHODS AND ANALYSIS

Trial design

ICARE (Infrared illumination for difficult peripheral venous CAtheterization in intensive caRE) This is a comparative, superiority, prospective, multicentre, randomised, controlled, open-label, phase III trial. Subjects will be allocated to the groups in a 1:1 ratio. Prior to the study commencing, nurses at the participating centres will be trained in the use of the device. The device is intuitive to use. A training session is provided by the principal investigator to local investigators through a train-the-trainer approach. Subsequently, brief training sessions are conducted by each local investigator for nurses in their respective centres. The decision to conduct an open trial rather than a blind trial is based on the nature of the device being tested (illumination) and the procedure being evaluated (catheterisation). The randomisation process will be carried out at the patient level, rather than in clusters, for the following reasons:

- The intervention is applied individually to each patient, rather than to the entire intensive care unit (ICU).
- The risks of intergroup contamination or mimicry effects are minimal.
- This approach avoids the hierarchical structure of the data (correlation of participants nested in clusters) and the selection bias associated with clusters.

Study setting

The trial will be conducted at 11 trial sites across France. A sufficient number of patients will be randomly assigned to ensure that at least 460 evaluable patients are included in the entire trial programme (refer to the section on sample size and its justification).

As part of this study involving minimal risk and constraints, adverse events will be reported through the standard materiovigilance procedure.

Eligibility criteria

Inclusion criteria

All consecutive patients aged 18 years or older admitted to the ICU will be enrolled if they meet the following criteria:

- Peripheral venous access is required.
- There is a risk of difficult peripheral venous catheterisation. In practice, this risk will be considered to be present if it is impossible to palpate and/or visualise the upper end of the target vein and/or if the diameter of the vein is estimated to be no more than 2 mm. This definition is derived from the A-DIVA difficult catheterisation risk score.[3]
- Informed consent was obtained in accordance with local regulations.

Non-inclusion criteria

The following exclusions apply:

- Patient has already participated in the ICARE study during the current hospitalisation.
- Patient declines participation.
- Patient is not affiliated with the social security system (as per French law).

Study interventions

The nurse in charge of the patient will perform the puncture to place the peripheral venous access in accordance with the randomisation group. In the control group, the nurse will perform the procedure as usual (visual identification under room light and palpation). In the interventional group, the nurse will use the Accuvein device to locate the veins prior to each puncture and then proceed as usual under the illumination of the device. The Accuvein device is used with the hands-free accessory, allowing the nurse to perform the procedure with both hands free. The rest of the care is left to the discretion of the care team. Accessories such as heated pads or nitroglycerin paste to dilate the veins are not used in the participating centres.

Endpoints

Primary endpoint

The primary endpoint is the percentage of primary successful placements of peripheral venous catheters in the upper extremities, defined as the success of a single puncture. The successful placement of the peripheral venous catheter will be confirmed by the appearance of venous reflux when the perfusion bag is lifted.

This criterion will also be analysed in subgroups defined by the experience of the nurse (at least 2 years in the ICU).[9]

Secondary endpoints

- Number of venipunctures required to place the peripheral catheter.
- Procedure failure rate (failure to place a peripheral venous line by the end of the procedure). The end of the procedure is defined as either the actual placement of the peripheral venous catheter, defined as the achievement of venous reflux, or the decision to consider an alternative to the peripheral venous catheter, after a minimum of three puncture attempts by two different nurses. Alternatively, the end of the procedure is defined as the patient's refusal of any further attempts at venipuncture.
- Total procedure time, measured by a third operator using a stopwatch. In the event that venous sampling for blood tests is conducted prior to the connection of the infusion tubing, the sampling time will be deducted from the total time.
- The size of the peripheral venous catheter in gauge and how it compares to what the carer wanted to use.
- The frequency of peripheral venous catheter replacement within 72 hours of randomisation due to malfunction.
- The frequency of placement or maintenance in place of a central venous catheter due to failure of peripheral venous catheterisation alone.
- Local complications of peripheral venous catheterisation within 72 hours of randomisation: diffusion (extravenous perfusion), haematoma at the puncture site or lymphangitis (thrombophlebitis).

Sample size and its justification

The sample size calculation is based on the results of a previous randomised trial in paediatrics with a similar device, which demonstrated an increase of more than 30% in the primary success rate in the subgroup at risk of difficult catheterisation.[10] Given the limited sample size of the previous study (n=44 at risk of difficult catheterisation), the present project will use a more conservative difference to be detected of 15% between the two groups. This equates to an expected success rate of 47% (control)[3] versus 62% (intervention). Based on these assumptions and a two-sided alpha risk of 5%, the inclusion of 230 patients per group (total 460) is required to detect a significant difference with a power of 90%.

Recruitment

Patients will be enrolled for 54 months starting in December 2019. The study timeline is as follows: (1) January 2021: winning grant award; (2) June 2019: approval by an independent ethics committee; (3) December 2019–2024: inclusion of patients; (5) 2024–2025: the investigators will review the data and check for protocol violations; (6) 2024–2025: the investigators will analyse the data, write the manuscript and submit it for publication.

Allocation of intervention and data collection

Centralised block randomisation using a 1:1 ratio will be prepared by the Clinical Research Unit before the start of the trial. Randomisation will be carried out using permuted blocks of varying size and stratified according to the centre and the experience of the operator in the ICU (≥2 vs < 2 years) because of the likely impact of experience on the success of catheterisation. There is no need to stratify by patient characteristics, as patients are already selected based on a risk score for difficult catheterisation. Patients will be randomised electronically via a website. A computer-generated randomization list will be prepared prior to enrolment of the first patient into the trial. No patient can be enrolled twice. Investigators or research assistants at each centre will enter data into the e-CRF (CleanWeb) via a web browser. The centres can access the e-CRF forms via a web-based data collection system.

Statistical methods

All analyses will be conducted in accordance with a predefined statistical analysis plan, using R V.4+ (R Foundation for Statistical Computing, Vienna, Austria). A two-tailed p value of less than 0.05 will be considered statistically significant. A flow diagram will describe the progress of the two groups of patients throughout the different phases of the trial (enrolment, allocation, receipt of interventional strategies, follow-up, and data analysis). The primary endpoint analysis will be performed on an intention-to-treat (ITT) basis. In the event of a premature interruption or withdrawal from the study, patients will not be substituted. Any missing values will be described and, according to their nature and frequency, missing data imputation methods will be applied, including, but not limited to, multiple imputation by chained equations algorithm. A per-protocol (PP) analysis will be conducted as a supportive sensitivity analysis to investigate PP-excluded patients and check the robustness of the results in those patients without substantial protocol deviation. All secondary endpoints analyses will be conducted on both ITT and PP populations.

A prespecified interim analysis of efficacy will be carried out when 50% of patients have been included in the study, according to an O'Brien-Fleming design.[11] The significance threshold for this interim analysis is 0.0054, with a threshold of 0.0492 for the final analysis in the event of non-significance at the interim analysis.

Descriptive analyses

A descriptive statistical analysis will be conducted on the trial groups in terms of demographics, history and baseline characteristics. Quantitative variables will be presented as mean (±SD) or median (25–75th percentiles) in accordance with the normality of their distribution. Qualitative variables will be presented as numbers (%). Comparisons between randomised groups will be conducted using the χ^2 test or Fisher's exact test, as appropriate, for categorical variables. Quantitative variables will be analysed using t-tests or non-parametric Mann-Whitney tests (pairwise comparisons), as required.

Data monitoring

The trial steering committee will oversee the progression and monitoring of the study. Study monitors will conduct regular on-site inspections to verify protocol compliance and the accuracy of recorded data. It is the responsibility of the investigator or research technician at each centre to perform daily patient screening, patient enrolment, adherence to protocol and completion of the eCRF.

Patient and public involvement

This study was not developed with the input of patients or the public. However, we plan to conduct focused group discussions with patient survivors, hospital and trial staff at the end of the study.

ETHICS AND DISSEMINATION

Ethical approval

The study has been approved by an independent ethics committee (Comite de Protection des Personnes Ile De France 1) under the registration number CPPIDF1-2019-ND49 cat.2.

Consent to participate

Patients will be included after they have signed a written informed consent form (see online supplemental file). In the event that the patient is unable to comprehend the information provided in the consent form, they may be included in the study if a next of kin consents. Patients who are eligible for inclusion but unable to receive information and for whom a substitute decision-maker is not present can still be included through a process of deferred consent. Once the patient has recovered, or their next of kin has been contacted, whichever occurs first, permission to keep the patient in the study will be sought.

Dissemination policy

The findings will be published in peer-reviewed journals and presented at national and international meetings. The principal investigator, senior principal investigator and steering committee will be responsible for the communication, reports and publication of the results of the study. All reports will adhere to the Consolidated Standards of Reporting Trials reporting guidelines. Publication rules will follow the international recommendations as set out in The Uniform Requirements for Manuscripts (ICMJE, April 2010).

Confidentiality

All data collected about the study participants and sent to the sponsor by the investigators (or any other specialised collaborators) during and after the clinical study will be anonymised.

Access to data

Investigators will make the documents and individual data required for monitoring, quality control and audit of the study available to designated personnel in accordance with the relevant legislation.

Data statement

The trial steering committee will facilitate the availability of study data in response to legitimate requests, in accordance with applicable regulations.

DISCUSSION

We herein present the first prospective multicentre study on the use of infrared illumination in critically ill patients at risk of difficult peripheral venous catheterisation of the upper limbs.

The rationale for selecting this population is that any delay or failure in peripheral catheterisation is highly detrimental in the critical care setting, as it may delay or prevent appropriate management of life-threatening emergencies. Furthermore, the quality of the catheterisation (good calibre and absence of malfunction) is crucial for the management of life-threatening complications. Selecting patients who are at higher risk of failure of peripheral venous catheterisation provides a prognostic enrichment strategy for our trial. To select these patients, we will use criteria for difficult catheterisation derived from a validated score (A-DIVA).[3]

The study focuses on peripheral venous catheterisation of the upper limbs, as this is the reference site for this type of catheterisation. The lower limbs are not recommended in standard practice. This is a high-grade recommendation from the French Health Authorities.[12]

The infrared vein illumination system provides real-time mapping of superficial venous vascularisation, enabling users to visualise veins with greater accuracy, check vein patency and avoid catheterisation at bifurcations. Furthermore, it can be used to visualise the entire peripheral venous network of the upper arm (particularly the cephalic veins), which is generally very rarely catheterised by nurses. Many devices are available on the market or in development.[13] We selected AccuVein because it offered several superior features compared with other vein illumination devices. These include laser-based projection technology, which provides highly accurate and real-time vein visualisation; ease of use, as it is handheld, lightweight, portable and requires no calibration; and standard and

inverse modes with adjustable brightness, making it adaptable to various skin tones and lighting conditions.

Infrared technology may have several limitations for vein catheterisation: (1) its penetration depth is limited to 5–10 mm, making it less suitable for deeper veins or patients with obesity; (2) skin pigmentation, tattoos and scars can interfere with light absorption, reducing image clarity; (3) motion sensitivity can cause blurring, especially in agitated patients.

We did not include a safety margin for potential early withdrawals or loss to follow-up. However, given the short duration of the study (3 days) and the straightforward implementation of the protocol, we considered the risk of such occurrences to be minimal.

If the efficacy of infrared illumination is demonstrated in critically ill patients, the device could reduce the nurses' stress involved in infusing patients, freeing up time and availability for other care. It may also reduce the use of more invasive catheterisation routes such as intraosseous and central venous.

In conclusion, the ICARE study will provide meaningful information on the usefulness of infrared illumination for the care of critically ill adult patients at risk of difficult catheterisation.

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Competing interests None declared.

Patient and public involvement Patients and/or the public were not involved in the design, or conduct, or reporting, or dissemination plans of this research.

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