KTESCA Protocol

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"*Prevention of pressure ulcers during peripheral catheter maintenance in paediatrics: use of compresses versus standard care*"

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SIGNATURE PAGE

SIGNATURE OF THE PROMOTER

The sponsor undertakes to conduct this study in accordance with all legislative and regulatory provisions applicable to the research and in accordance with the protocol.		
Name and position of the signatory representative: **For the sponsor and by delegation from the Chief Executive Officer, the Director of Medical Affairs and Research**	**Date:**	**Signature:**

INVESTIGATOR'S SIGNATURE S

I have read all the pages of the clinical trial protocol sponsored by CHD Vendée. I confirm that it contains all the information necessary to conduct the trial. I undertake to conduct the trial in accordance with the protocol and the terms and conditions set out therein. I undertake to conduct the trial in accordance with:

- the principles of the "Declaration of Helsinki",
- the rules and recommendations of international (ICH) and French (rules of good clinical practice for biomedical research involving medicinal products for human use) good clinical practice
- European regulations and/or national legislation and regulations relating to clinical trials,

I also undertake to ensure that investigators and other qualified members of my team have access to this protocol and to the documents relating to the conduct of the trial so that they can work in accordance with the provisions contained in these documents.

Coordinating investigator	**Surname:**	**Date:**	**Signature:**
Principal Investigator	**Name and institution:**	**Date:**	**Signature:**

LIST OF ABBREVIATIONS

ANSM	French National Agency for Medicines and Health Products Safety
ARC	Clinical Research Associate (monitor)
GCP	Good Clinical Practice
CHD	Departmental hospital centre
CPP	Committee for the Protection of Individuals
CNIL	National Commission for Information Technology and Civil Liberties
CRF	Case Report Form
DM	Medical Devices
eCRF	Electronic Case Report Form
EPUAP	European Pressure Ulcer Advisory Panel
EvIG	Serious Adverse Event
ICH	International Conference on Harmonisation
IDE	State-registered nurse
MR	Reference Methodology CNIL
NPUAP	National Pressure Ulcer Advisory Panel
TEC	Clinical Research Technician
PIV	Peripheral Venous Access

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INTRODUCTION

Children and adolescents require specific care. Treatments, therapeutic strategies and medical devices cannot always be identical to those used for adults, as they are not always suitable for this population. This leads us to regularly reflect on our professional practices.

Our specific role as nurses or paediatric nurses within a multi-disciplinary paediatric department is to be as responsive as possible to the needs of this population.

The insertion of peripheral venous catheters is a daily practice in the department.

Within the multidisciplinary team, we have observed for several years the appearance of skin lesions similar to bedsores at the junction of the peripheral venous catheter and the extension tube. A practice has spontaneously developed within the department of placing a compress under this junction. The aim is to minimise physical or emotional distress and pain. Pain is a priority in the care of children and adolescents. Pain that is denied or unidentified and not relieved is remembered by the child, which can have consequences on their perception of pain and their subsequent acceptance of care.

To date, through our reading and research, we have found articles mentioning the risk of pressure sores in children associated with medical devices. However, little information is available on pressure sores associated with catheters, particularly on this specific technique for preventing lesions at the catheter-extension junction.

The aim of this study is therefore to compare two peripheral venous catheter fixation devices, with and without compresses, and to analyse the frequency of pressure ulcer occurrence and the severity of this injury.

1. JUSTIFICATION FOR THE STUDY

1.1. POSITIONING OF THE RESEARCH

The insertion of peripheral venous catheters is a daily practice in paediatric and neonatal wards. On average, more than 25 million peripheral venous catheters are inserted annually in France in all healthcare departments combined (1).
These catheters enable the administration of intravenous treatments (isotonic solutions, antibiotics, injectable drugs, etc.) as well as the collection of blood for analysis.

In departments such as paediatrics, these peripheral venous catheters can be difficult to insert due to the small venous capacity associated with the child's age. The difficulty increases when the child is afraid of needles or has had bad experiences, as anxiety activates the sympathetic nervous system, causing local peripheral vasoconstriction (2). Maintaining peripheral venous access (PVA) over time is also difficult due to children's mobility. In fact, 5% of peripheral venous catheters are accidentally removed in children (3).
For all these reasons and in accordance with HAS recommendations, there is no maximum duration for maintaining PIVCs in children (4) and nursing supervision is very important.

The routine use of peripheral venous catheters exposes children to iatrogenic risks such as severe skin damage. Approximately three-quarters of children hospitalised in paediatric wards are fitted with a peripheral or central venous catheter, with a rate of adverse events associated with care reaching up to 80%. However, this rate remains difficult to determine due to variations in the definition of a complication (5).
In 35% of cases, PIVCs are removed due to complications: infiltration (extravasation) 14.4%, occlusion 13.4%, signs of thrombophlebitis 7%, suspected infection 0.3%, wounds and injuries at the puncture site 0.2% (6).

Registered nurses, thanks to their experience and skills, play a fundamental role in the maintenance of peripheral venous catheters. Observation of puncture sites and monitoring of the complications mentioned above are well established in nursing practice.

For several years, we have observed skin changes such as redness and bedsores at the junction of the catheter and the peripheral venous line extender when removing peripheral venous catheters in our paediatric department. This junction between the catheter and the extension tube

is more prominent and is pressed against the skin by the occlusive dressing used to maintain the PIV. Regardless of the type of equipment used and the brand, this junction is always present.
These pressure sores, which can cause pain and scarring on a child's skin, are difficult for a nurse to detect (before removing the PIVC) because they are located under the medical device and the fixation device.
In addition, the specific nature of paediatrics can make pressure sores difficult to detect. One of the main reasons for this is the difficulty of communicating with children about pain and discomfort.

A pressure ulcer is an ischaemic lesion caused by compression of soft tissue between a hard surface and a bony prominence (7). This prolonged compression causes tissue ischaemia.
There are many risk factors for pressure ulcers, which are well described by the EPUAP (European Pressure Ulcer Advisory Panel) and the NPUAP (National Pressure Ulcer Advisory Panel) in their abbreviated reference guide (8).
These include intrinsic factors such as the child's age (level of activity and mobility, skin maturity), nutritional status, peripheral perfusion disorders, certain acute or chronic serious illnesses, and treatments.

Other factors, known as extrinsic or mechanical factors, such as pressure, friction, shear and maceration, are also known to cause pressure ulcers.
In our case, the pressure sores observed at the junction of the catheter and the peripheral venous line extender are mainly related to these extrinsic factors. These are referred to as iatrogenic pressure sores.
Numerous articles mention the fact that children fitted with medical devices are at risk of pressure ulcers. A separate section is devoted to them in the NPUAP's reference guide on the prevention and treatment of pressure ulcers (8).
It also specifies that pressure ulcers associated with medical devices are less studied in children than in adults.

To assess the risk of pressure ulcers in adults, there is a reference assessment scale, the Braden Q scale. This scale is also recommended for children to assess the risk of pressure ulcers related to medical devices. (9)
In a 2017 study, 8% of hospitalised children developed pressure ulcers, 2% of which were related to immobility and 6% to medical devices. (9)
In a 2013 article in the Paediatric Journal (10), various medical devices responsible for pressure ulcers are listed, such as intubation tubes, drains, orthopaedic splints, nasogastric tubes, oxygenation systems and intravenous catheters. Clinicians have identified that MDs positioned in contact with the skin can lead to the development of pressure ulcers. Although the aetiology of

pressure ulcers related to immobility and those related to MDs is different, the mechanism of wound formation is similar.
Few articles specifically discuss pressure ulcers associated with VVP.

These pressure ulcers associated with medical devices are not without consequences for children. In addition to skin damage, there is also psychological trauma related to the care and pain caused by the bedsore, which can make future treatment difficult (10).

An international classification system for pressure ulcer stages was established in 1998 by the National Pressure Ulcer Advisory Panel (8). This scale, which was initially validated on an adult population, is perfectly applicable to the classification of pressure ulcers in children.
Paediatric nurses use it systematically when removing catheters to assess the stage of the pressure ulcer. The pressure ulcers observed in our department and linked to the junction between the catheter and the extension tube are mainly stage I pressure ulcers.

In order to limit the occurrence of these pressure ulcers, specific recommendations are described by the NPUAP (8). These primarily concern the selection and assembly of the medical device. The device must be examined and selected within the institution so that the pressure and shear forces cause as little damage as possible. It must be used correctly in accordance with the manufacturer's specifications.
In addition, the skin and medical device must be inspected at least twice a day.
It is also recommended to keep the skin under the medical devices clean and dry and to use prophylactic dressings to reduce pressure at the skin-device interface.
As soon as medically possible, all medical devices that are a potential source of pressure sores should be removed.

In the Paediatrics Department at CHD Vendée, we try to follow these recommendations as closely as possible.
The equipment is selected by the pharmacy and the medical devices team.
Nurses are trained in pressure ulcer monitoring and ensure that VVP is monitored each time they visit, i.e. more than twice a day. Skin monitoring at the junction is limited because the catheter is held in place by a sterile occlusive dressing that cannot be changed at each monitoring session due to the risk of infection. In addition, the child's lack of cooperation and mobility can make care difficult. PIVCs in children are considered by nurses to be valuable medical devices for the child's recovery.

Following the observation of skin lesions at the catheter-extender junction in the department, a protocol for peripheral venous catheter placement was developed by the team and validated by the hygiene department of the CHD Vendée hospital. It stipulates the placement of a sterile compress cut to size under the hard parts of the medical device (at the catheter/extension junction) covered with a sterile transparent adhesive dressing. The choice of sterile compress is based on the fact that this type of dressing is readily available (a pack of sterile compresses is required for skin disinfection before catheter insertion) and inexpensive. The nurse must cut the compress in advance with sterile scissors to protect the area of contact between the skin and the medical device.

This practice was also recommended at the Pédiadol congress (11). To our knowledge, it is not widely used. We are only aware of practices in the paediatric intensive care unit at Trousseau Hospital, where a compress or thick hydrocolloid dressing is placed under the catheter and under hard areas to prevent pressure sores associated with medical devices. (12)
The application of these prophylactic dressings when inserting a PIVC is not taught to future healthcare professionals during their training at the Institute for the Training of Healthcare Professionals.
The latest SF2H recommendations from May 2019(13) on the placement and maintenance of peripheral venous catheters provide detailed information on infection prevention, but there are no recommendations on pressure ulcer prevention.

To date, no study has been published on this practice, which, if proven effective, would deserve to be more widely disseminated.
We therefore wish to conduct a controlled, randomised study to evaluate the benefits of compresses in the prevention of pressure ulcers associated with peripheral venous catheters.
This single-centre study will be a pilot study that will provide data that can then be used to consider a larger multicentre study if the compress proves to be an effective and safe tool in the prevention of pressure ulcers.

1.2. BENEFITS AND RISKS FOR RESEARCH PARTICIPANTS

1.2.1. Benefits

1.2.1.1. Individual benefit

If the hypothesis proves correct, participating in this study will enable patients in the "PIVC with compress" arm to reduce their risk of developing pressure ulcer-type skin lesions.
Pain and skin damage caused by pressure on this junction can be reduced. This practice would make it easier for children to accept treatment and limit the trauma of infusion.
Patients included in the "VVP without compress" arm will receive standard care in other departments and hospitals.

1.2.1.2. Collective benefit

A collective benefit can be envisaged in terms of harmonising practices within different departments and hospitals. Better prevention of pressure sores associated with the placement and maintenance of VVP would enable compliance with NPUAP recommendations, namely to minimise the risk of pressure sores associated with medical devices. It would also reduce sources of pain.

1.2.2. Risks

1.2.2.1. Individual risk

The placement of VVP exposes patients to a risk related to the presence of medical devices:

- The risk of pressure ulcers exists in both groups;
- A minor risk of infection cannot be ruled out due to the presence of a dressing if it is soiled. Multiple daily monitoring by caregivers greatly minimises this risk.

1.1.2.2 *Collective risk*

Placing a compress under the catheter device does not present any collective risk except for an additional cost (sterile compress and scissors).

1.2.3. Benefit/risk balance

The research manager classifies this research as **minimally risky and minimally restrictive interventional research**, since:

- ✓ All procedures are performed in the usual manner and are defined in the decree of 12 April 2018 issued by the Ministry.

In fact, VVP placement is performed several times a day by registered nurses in the Paediatrics Department of the CHD Vendée hospital in La Roche-sur-Yon.

Furthermore, there are no recommendations regarding the choice of type of pressure ulcer prevention under medical devices.

The research does not focus on techniques or strategies that are either innovative or obsolete.

All patient care will be identical to usual practice. In particular, the discharge date will be decided by the doctor in charge of the patient, independently of the study, but will be recorded in the patient's file and the research CRF.

Consequently, the specific implementation procedures in the research represent negligible constraints for the person participating in the research. (Article R 1121-3 of the Public Health Code (CSP), Decree No. 2006-477 of 26 April 2006)

The research manager shall therefore submit, prior to any implementation of the research, for a favourable opinion and confirmation of the research's eligibility, the study protocol to the Committee for the Protection of Persons in accordance with Article L 1121-1 of the Public Health Code (CSP) as resulting from Laws No. 2004-806 of 9 August 2004 and No. 2006-450 of 18 April 2006 relating to public health policy.

Bibliographical references are listed in section 8 of the document.

2. OBJECTIVES AND ASSESSMENT CRITERIA

2.1. OBJECTIVE AND MAIN ASSESSMENT CRITERION

2.1.1. Primary objective

Compare the incidence of pressure sores during standard fixation versus fixation with a compress at the junction between the catheter and the extension tube in a paediatric population.

2.1.2. Primary assessment criterion

The primary endpoint is the occurrence of pressure ulcers of grade >=1 on the NPUAP scale at the catheter/extender junction. The assessment will be carried out blind by a childcare assistant from the department.

2.2. SECONDARY OBJECTIVES AND EVALUATION CRITERIA

2.2.1. Secondary objective(s)

- Compare the severity of pressure ulcers at the catheter/tube junction.

- Compare the duration of peripheral venous catheter retention between the two groups.

- Compare the rate of nosocomial infections related to peripheral venous catheters between the two groups.

2.2.2. Secondary evaluation criteria

- The severity of pressure ulcers will be assessed using the NPUAP scale

- The duration of catheter retention will be calculated between the time the catheter is inserted and the time it is removed.

- The presence of a nosocomial infection related to the peripheral venous catheter.
This will be defined by a peripheral venous catheter culture >10^3CFU/ml, if the peripheral venous catheter is sent for culture due to suspected infection and in the absence of antibiotic treatment.
In the presence of antibiotic treatment, it will be defined by the presence of pus and/or regression of infectious signs within 48 hours of removal of the peripheral venous catheter.

3. STUDY POPULATION

3.1. DESCRIPTION OF THE POPULATION

The study plans to include 396 patients with the aim of obtaining 360 randomised patients (see section 5.2.1 Description of planned statistical methods).
Inclusions will cease when the potential number of randomised patients has been reached.

Patients will be children aged between 1 month and 18 years, hospitalised in the General Paediatrics Department of the CHD Vendée hospital in La Roche-sur-Yon, or with a high probability of being hospitalised in Paediatrics following a visit to the Paediatric Emergency Department, for whom there is an indication for the insertion of a peripheral venous catheter.

We have chosen the age range of 1 month to 18 years because it appears that the skin is immature before 3-4 weeks of life and therefore at greater risk of iatrogenic skin lesions, according to the French Society of Dermatology (14).

As the patients are minors, prior authorisation will be sought from their parents.

3.2. INCLUSION CRITERIA

Patient:

- Aged between 1 month and 18 years, according to the admission criteria of the paediatric department of the CHD La Roche sur Yon.
- Hospitalised in paediatrics or attending the paediatric emergency department with a high probability of subsequent hospitalisation in paediatrics.
- With an indication for the insertion of a short peripheral venous catheter
- Written consent of the person(s) with parental authority

3.3. EXCLUSION CRITERIA

- Children with pre-existing skin conditions at the time of inclusion and at the puncture site (atopic dermatitis, skin infection, skin wound, chickenpox, epidermolysis bullosa)

- Allergy to fixation devices
- Known immunocompromised children
- Refusal of the patient or legal guardians to participate in the project
- Emergency life-saving treatment
- Patient already included in the study
- Patient without social security coverage

4. DESIGN AND CONDUCT OF THE STUDY

4.1. STUDY SCHEDULE

- Recruitment period: 48 months
- Duration of patient participation in the study: until catheter removal.

a) Inclusion

Information and verbal consent regarding participation in the study will be obtained from the minor patient. Consent will be signed by the person(s) with parental authority (see 7.6.1: special case of the presence of only one parent).

This will be done once the medical prescription for peripheral venous access has been issued, the inclusion and exclusion criteria have been verified, and before randomisation.

The patient will be:

- either in the paediatric emergency department;
- or already hospitalised in paediatrics;

A table tracking patients to whom the study has been proposed will be kept up to date, noting the reasons for non-inclusion and refusals to participate.

b) Randomisation

Once consent to participate has been obtained, randomisation will be carried out via the computerised data base (eCRF):

- VVP placement without compress group: reference strategy group.
- VVP placement with compress group: alternative strategy group.

The peripheral venous line will then be placed according to the group designated by randomisation.
Details of the procedure for each arm are described in 4.4.

c) Follow-up

In both groups, catheter management and maintenance will be carried out by the nursing team responsible for the patient in the paediatric ward in accordance with current institutional procedures (see Appendices 1 and 2, catheter placement protocol with and without compress).

Data will be collected at the time of PPV removal. The peripheral line placed is valuable. In practice, the lines are maintained until the end of treatment unless there is redness and/or discharge at the puncture site.

When the catheter is removed, the nurse in charge of the patient removes the crepe bandage, the compress if there is one, and the catheter.

A childcare assistant from the department who has not been caring for the patient will then be called to assess the condition of the skin and report on the appearance and grade of any bedsores. The nurse will also note the presence or absence of signs of infection according to the Maddox scale. If the index is greater than 3, the paediatrician will prescribe that the catheter be sent for culture.
The microbiological analysis will be carried out by the clinical research biology team at the CHD Vendée.

d) <u>Study design</u>

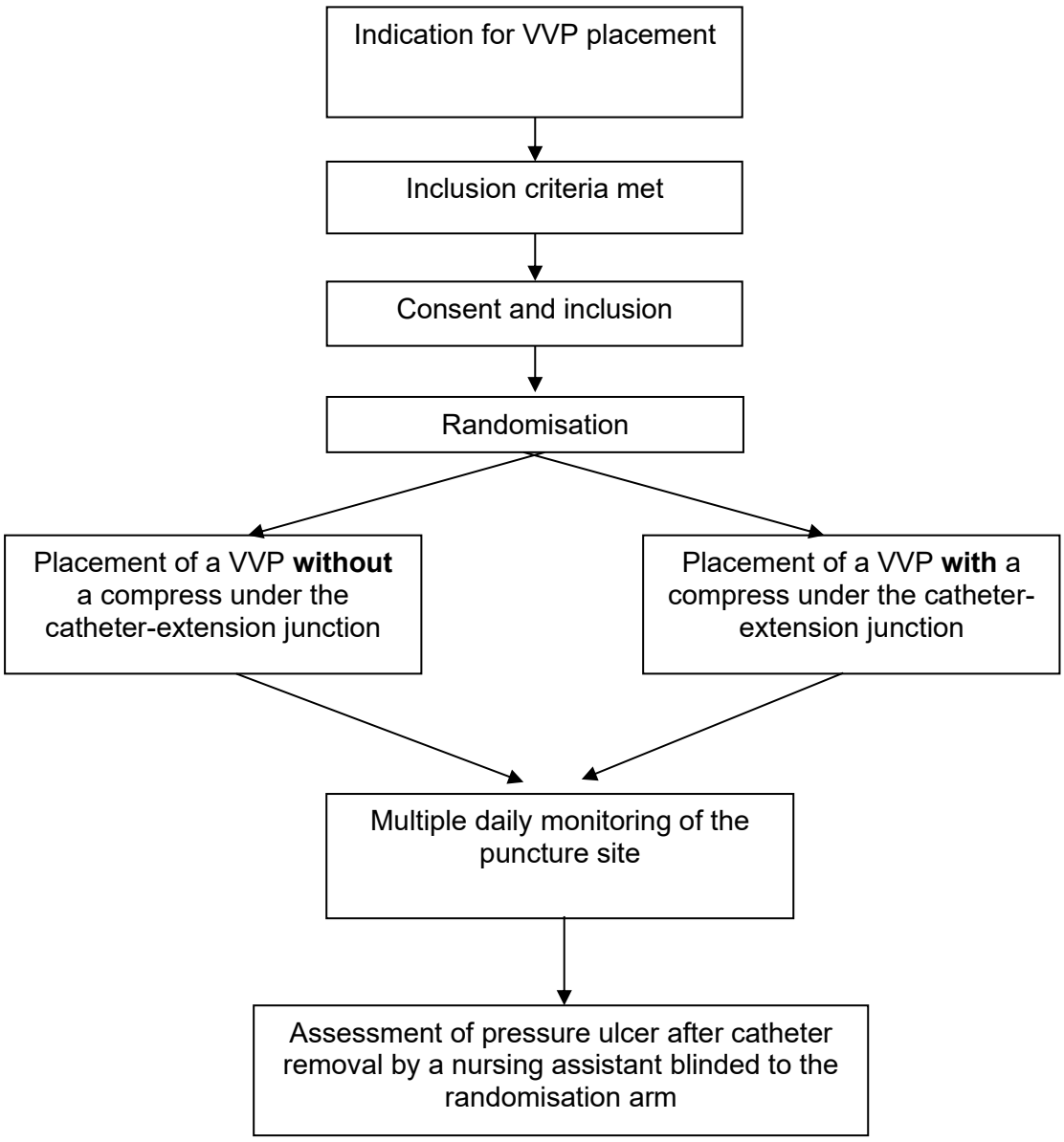
Actions	D0 (Inclusion visit)	Every day	J Withdrawal from the VVP
Patient information	X		
Informed consent from the patient (verbal) + legal guardian (written)	X		
Randomisation	X		
Peripheral venous access	X		
Monitoring of puncture site (catheter sent for culture if local infection)		X	
Assessment of the presence of a lesion + severity of the lesion by a childcare assistant			X

4.2. GENERAL RESEARCH METHODOLOGY

The research has the following characteristics:

- ❖ Single-centre
- ❖ Open
- ❖ With blinded assessment of the primary endpoint
- ❖ Controlled
- ❖ Randomised into 2 parallel groups:
    - Placement of VVP with a compress under the catheter/tubing junction
    - Standard VVP placement, without pad under the tubing

4.3. STUDY DESIGN



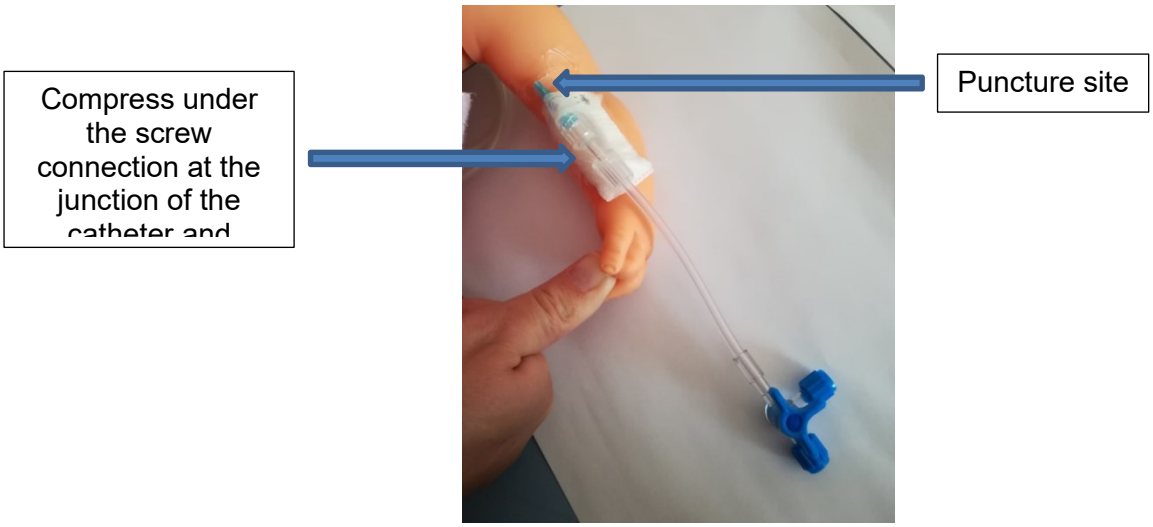
4.4. DESCRIPTION OF THE INTERVENTION STUDIED

The method consists of inserting a BD Insyte® catheter, gauge 20 to 24G, into a peripheral vein located in the crook of the elbow, the back of the hand, the scalp or the top of the foot.
The catheter is inserted after cleansing and disinfecting the skin with appropriate products and in accordance with the procedure in force in the department (see Appendices 1 and 2).
Once venous return has been verified, a 10 cm extension tube with a BECTON-DIC® 3-way stopcock is connected, which has been previously purged with 0.9% sodium chloride.

This catheter will be used as an access route for hydration (Polyionique®, G5% or G10% and NaCl), antibiotic therapy, analgesia, blood products or labile blood products.
Not all vein-toxic products such as chemotherapy drugs will be injected via these catheters, as they are administered via central venous lines.

We currently have 10 cm extension tubes with BECTON-DIC® three-way stopcocks. We are unable to predict future markets during our study.
There will inevitably be an extension catheter junction that will enable us to maintain our monitoring in connection with our study.

For patients with "VPP arm with compress":
A sterile non-woven compress, cut under sterile conditions (3.5 x 1.5 cm), will be inserted under the catheter-extension junction. The assembly will be held in place by a sterile, semi-permeable transparent adhesive dressing such as Tégaderm® (5 x 7 cm) or Oper film 6 x 7 cm.
This area will be secured by applying a crepe bandage (4 m x 7 cm). This will enable the childcare assistant to maintain a blind assessment of the primary endpoint.



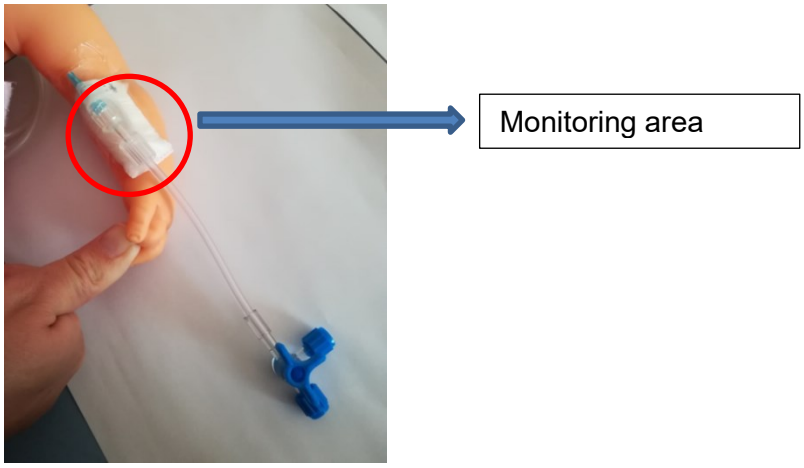
The study will focus on the evaluation of a single catheter placed per patient.

If several catheters are placed, only the first device will be evaluated and monitored until its removal.

With regard to the duration of use, the SF2H recommendations (13) will be applied, i.e. no catheter changes will be made if good patency and asepsis are maintained until the end of treatment.

4.5. DESCRIPTION OF THE EVALUATION AND DATA COLLECTED

The primary endpoint is the development of a pressure ulcer of grade ≥1 on the NPUAP scale at the catheter/tubing junction.

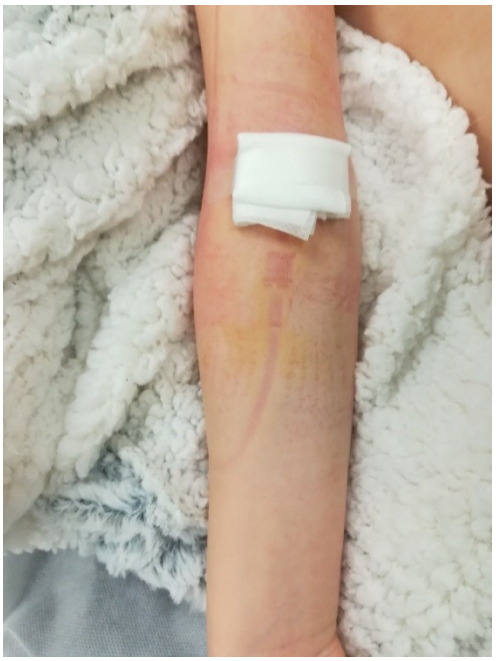


This area is assessed several times a day by nurses, who remove the bandage without removing the fixation device (compress and transparent adhesive dressing). However, if the compress is soiled, the dressing will be changed.

NPUAP scale

The NPUAP pressure ulcer assessment scale, translated from English by ANAES, will be used. This scale allows pressure ulcers to be assessed according to four stages, graded from 1 to 4, with stage 1 being the least severe.

- Stage I: The first stage is an observable change in intact skin, related to pressure and manifested by a change in one or more of the following characteristics compared to the adjacent or contralateral body area: skin temperature (warm or cold), tissue consistency (firm or soft) and/or sensitivity (pain, itching). In people with fair skin, the pressure ulcer appears as persistent localised redness, while in people with pigmented skin, the pressure ulcer may be a persistent red, blue or purplish colour.



Example: Stage 1 pressure ulcer

- Stage II: Loss of part of the skin's thickness; this loss affects the epidermis, the dermis, or both. The pressure ulcer is superficial and clinically presents as an abrasion, blister, or shallow ulceration.

- Stage III: Loss of all skin thickness with alteration or necrosis of the subcutaneous tissue; this may extend to the fascia, but not beyond. The pressure ulcer appears clinically as a deep ulceration with or without invasion of surrounding tissues.

- Stage IV: Loss of the entire thickness of the skin with significant tissue destruction, or involvement of muscles, bones, or supporting structures (e.g., tendons, joints). Invasion and fistulas may be associated with stage IV pressure ulcers.

The catheter will be removed by the nurse in charge of the patient.

In order to allow for a blind assessment of the primary endpoint, this will be performed by a childcare assistant from the department who is on duty 24 hours a day and has not previously cared for the child. The childcare assistant will assess the pressure area and then note their observations in the patient's file (presence or absence of pressure ulcers and NPUAP grade, if applicable).

An assessment based on photographs was initially considered, but given the description of the different stages (particularly stage I, characterised by persistent redness), we believe that a direct assessment by a professional is more appropriate. Furthermore, a 2013 study concluded that assessment based on photographs is not sufficient for an accurate assessment of the stage of pressure ulcers (15).

Maddox Scale

This scale will be used to monitor for any signs of infection at the puncture site.

We have chosen not to include pain assessment as an endpoint criterion, as it is difficult to assess pain specifically related to the medical device in this population.

4.6. IDENTIFICATION OF ALL SOURCE DATA NOT INCLUDED IN THE MEDICAL RECORD

Source data not included in the medical record corresponds to data not routinely collected in the medical and paramedical records.
In this study: The assessment by the childcare assistant of the grade of pressure ulcer reported on a data collection sheet will be considered as the source data.

4.7. RULES FOR DISCONTINUING A PERSON'S PARTICIPATION

4.7.1. Criteria for premature termination of a person's participation in the research

Subjects may withdraw their consent and request to leave the study at any time and for any reason. In the event of premature withdrawal, the investigator must document the reasons as fully as possible.
The investigator may temporarily or permanently discontinue a subject's participation in the study for any reason that is in the best interests of the subject, particularly in the event of serious adverse events.

4.7.2. Procedures for premature termination of a person's participation in research

In the event of withdrawal of consent, data already collected may be analysed unless the patient objects.
Their medical care will be identical to the usual care provided to this type of patient in the department.

The information to be collected is:

- Date of end-of-study visit
- Reason for early withdrawal

For information on how data from individuals who withdrew prematurely from the study will be used, please refer to the statistics section.

4.7.3. Criteria for discontinuing part or all of the research (excluding biostatistical considerations)

The CHD de Vendée reserves the right to interrupt the study at any time if it appears that the inclusion objectives are not being met.

Part or all of the study may be terminated permanently or temporarily by decision of the ANSM, the CPP or the study sponsor.

Written confirmation will be sent to the study coordinator (specifying the reasons for premature termination).

5. DATA MANAGEMENT AND STATISTICS

5.1. COLLECTION AND PROCESSING OF STUDY DATA

5.1.1. Data collection

An electronic case report form (eCRF) will be created for each patient. All information required by the protocol must be provided in the eCRF. It must include the data necessary to confirm compliance with the protocol and all data necessary for statistical analysis; it must allow for the detection of major deviations from the protocol.

The persons responsible for completing the eCRFs (investigator, ARC, etc.) must be defined and identified in the table of delegated responsibilities (kept in the investigator's binder).

5.1.2. Data coding

By signing this protocol, the principal investigator and all co-investigators undertake to keep the identities of the patients who participated in the study confidential.

The transmission of an individual's data for research purposes will therefore only be possible subject to the application of a coding system; the presentation of research results must exclude any direct or indirect identification.

Patients will be identified according to the order of patient inclusion by a number automatically assigned by the Clinsight software (eCRF) and then supplemented by the patients' initials.

This code will be the only information appearing on the eCRF that will allow the eCRF to be linked to the patient at a later date.
The research manager is also required to code patient data on all documents in their possession that may be attached to the CRF.

A correspondence table will be set up at the centre. This table will be kept in a secure location by the centre's principal investigator and will contain the patient code and their personal data , so

that the patient file can be traced in the event of missing or incorrect data. No clinical data will be collected in these correspondence tables.

5.1.3. Data processing

Clinical data will be collected using a database and data entry forms modelled on the observation log, in accordance with the protocol and current regulations.

5.2. STATISTICS

Responsible for statistical analysis:

Lucie Planche
Vendée Departmental Hospital Centre
Clinical Research Unit
lucie.planche@chd-vendee.fr

Software
The analyses will be performed using R software version 3.5.1

5.2.1. Description of planned statistical methods, including the schedule for planned interim analyses

All variables will be described globally and by group. The description will include the numbers and percentages of modalities for qualitative variables and the minimum, maximum, mean, standard deviation and median for quantitative variables.

Primary endpoint

The primary endpoint is defined as the presence of a pressure ulcer at the junction of the catheter with the extension tube or peripheral venous line tubing. The assessment will be performed upon catheter removal and blinded by a nursing assistant from the department.
The percentage of patients will be presented with a 95% confidence interval in the two groups and will be compared using a Chi-square test.

In a second step, the two groups will be compared using logistic regression to take into account the duration of catheter retention.

Secondary criteria

The severity of pressure ulcers will be described between the two groups. At each stage of the NPUAP scale, the number and percentage of patients will be presented. A Mann-Whitney test will be applied to compare the two groups.

The average duration of catheter retention will be described for the two groups with a 95% confidence interval. It will be compared using a Student's t-test.

The number of patients with nosocomial infection will be described in the two groups. No statistical test will be performed.

5.2.2. Statistical justification of the number of subjects

This is a pilot study. To our knowledge, there are currently no data on the assessment of pressure ulcers at the junction of the catheter with the extension tube or peripheral venous line tubing in paediatric hospitalised patients.
This study will therefore provide reliable data on these pressure ulcers in both standard care (without compresses) and will also provide data on the benefits of compresses for pressure ulcer prevention.

With a total of 346 patients, our study will highlight a difference of at least 15% between the two groups (80% power and 5% alpha risk). **In order to guarantee the power of the study, a total of 360 patients will be randomised.**

5.2.3. Expected degree of statistical significance

The alpha risk is set at 5%.

5.2.4. Statistical criteria for stopping the research

NA

5.2.5. Method for handling missing, unused or invalid data

All missing data and the reasons for their absence will be described in each group.

For the analysis of the primary endpoint, in the event of missing data, we will consider the absence of pressure ulcers (regardless of the randomisation group).

5.2.6. Management of changes to the initial strategy analysis plan

NA

5.2.7. Selection of individuals to be included in the analyses

The primary analysis will be performed on the intention-to-treat (ITT) population, i.e. all randomised patients.

A complementary analysis will be performed on the Per Protocol (PP) population, including randomised patients for whom no major deviations from the protocol have been identified.
A data review meeting will be organised to review and define whether each deviation is a major criterion or not.

5.2.8. Randomisation

Randomisation will not be stratified.

It will be carried out according to a 1:1 ratio and will be performed in blocks.

Randomisation will be performed using Ennov Clinical by connecting to the website: https://nantes-lrsy.hugo-online.fr/EnnovClinical/login. Connection will be made using a login, password and study code provided by the data manager of the Clinical Research Unit at La Roche sur Yon Hospital. The following information must be provided:

- First initial of surname,
- First initial of the first name,
- Month and year of birth,
- Compliance with inclusion and exclusion criteria (yes/no),

Randomisation will be carried out after confirmation of the patient's eligibility for inclusion in the study. The inclusion number will be assigned automatically during randomisation.

The randomisation list will be drawn up by the statistician at the Research Unit of La Roche sur Yon Hospital. An explanatory guide to randomisation will be available online at Ennov Clinical.

6. SAFETY EVALUATION

In the context of this Interventional Research with Minimal Risks and Constraints (RIPH Category 2), adverse events (whether serious or not) do not need to be reported to the sponsor. Notification must be made as part of the vigilance system established for the product or practice being researched (pharmacovigilance for a drug, material vigilance for a medical device, etc.) in accordance with the regulations in force.

Only "new developments" and malfunctions that may interfere with the research must be reported to the sponsor without delay after they become known so that corrective measures can be put in place. For these malfunctions, the investigator may use the reporting form provided by the institution's internal vigilance system, which is anonymised (patient inclusion number only).

A new development is any new information that could lead to a reassessment of the benefits and risks of the research or the product being researched, to changes in the use of this product, in the conduct of the research, or in the documents relating to the research, or to the suspension, interruption or modification of the research protocol or similar research.

The sponsor shall immediately inform the competent authority and the human subjects review committee of the new facts and, where applicable, the measures taken, from the day on which they become known.

7. ADMINISTRATIVE AND REGULATORY ASPECTS

7.1. RIGHT OF ACCESS TO SOURCE DATA AND DOCUMENTS

Each patient's medical data will only be disclosed to the sponsor or any person duly authorised by the sponsor and, where applicable, to the competent health authorities, under conditions that guarantee confidentiality.
The sponsor and the supervisory authorities may request direct access to the medical file to verify the procedures and/or data of the clinical trial, within the limits authorised by laws and regulations.

7.2. DATA CONFIDENTIALITY

Persons with direct access shall take all necessary precautions to ensure the confidentiality of information relating to the persons involved, in particular with regard to their identity and the results obtained.
These persons, like the investigators themselves, are subject to professional secrecy (under the conditions defined by Articles 226-13 and 226-14 of the Penal Code).
During or at the end of the research, the data collected on the individuals involved and transmitted by the participants shall be anonymised.
Under no circumstances shall the names or addresses of the persons concerned be disclosed.
Only the first two letters of the subject's surname and the first letter of their first name will be recorded, accompanied by a coded number specific to the study indicating the order of inclusion of the subjects.

7.3. COMPUTERISED DATA AND SUBMISSION TO THE CNIL

This study falls within the scope of the "Reference Methodology" (MR-001) in accordance with the provisions of Article 54, paragraph 5, of Law No. 78-17 of 6 January 1978, revised in June 2018, relating to information technology, files and freedoms. The CHD Vendée de La Roche sur Yon, promoter of the study, has signed a commitment to comply with this "Reference Methodology".

7.4. MONITORING OF THE TRIAL

Monitoring will be carried out by the Promotion Department of the Research Directorate. A Clinical Research Associate (CRA) will visit each site (investigator) regularly to carry out quality control of the data reported in the observation notebooks.

The protocol has been classified according to the estimated level of risk for patients participating in the research. It will be monitored as follows:

Risk A: low or negligible foreseeable risk

On-site monitoring visits will be organised after appointment with the investigator. CRAs must be able to consult the following at each site:
- the data collection notebooks for the patients included,
- the patients' medical and nursing records,
- the investigator's file.

7.5. INSPECTION/AUDIT

An inspection or audit may be conducted as part of this study. The sponsor and/or participating centres must be able to provide inspectors or auditors with access to the data.

7.6. ETHICAL CONSIDERATIONS

7.6.1. Informed consent

The investigator (nurse) undertakes to obtain the patient's free, informed and express consent after providing them with information about the protocol.

Minors who are not emancipated will receive information adapted to their level of understanding, both from the investigator and from their parents or guardians (who will themselves be informed by the investigator).

They will be consulted to the extent that their condition allows. Their personal consent to participate in the research will be sought. Their refusal or revocation of consent cannot be overridden.

As the patients are minors and this is research involving human subjects with minimal risks and constraints in accordance with the decree published on 3 May 2017 establishing the list of such research, express informed consent is required from both parents.
However, in the context of this study, children admitted to paediatric emergency departments are rarely accompanied by both parents. Given that randomisation must be carried out before a peripheral venous line is inserted, which is necessary for the administration of a prescribed treatment that may need to be administered without delay, it will therefore be difficult to obtain the written consent of both parents before it is put in place. Under these circumstances, only the written consent of the parent present will be obtained after verbal consent has been given by the absent parent.

The investigator will provide a copy of the information sheet and a consent form to the person(s) with parental authority. The patient may only be included in the study after having read the information sheet, which will be explained to them in accordance with their level of understanding, and given their verbal consent if they are old enough to understand, and the person(s) with parental authority have given their written consent, after having been given time to consider the matter, if necessary.

The investigator must also sign and date the consent form. Two copies of these two documents will be provided on paper so that the patient (or those with parental authority) and the investigator can each keep a copy. The investigator's original copy will be filed in the investigator's binder. If consent is signed in duplicate, the investigator will keep the original and the duplicate will be given to the patient.
The patient's information and verbal agreement to participate in the research must be noted in their medical file. Written consent will be given by the person(s) with parental authority.

For minors who reach the age of majority during their participation, confirmation of their consent will be required after appropriate information has been provided.

Other requests for exemption from the obligation to obtain the signed consent of both parents may be submitted to the CPP in the following cases:

- if one of the parents is deceased
- if the child is recognised by only one parent

- if only one parent has been designated as the holder of parental authority by court order
- in cases of separated or divorced parents

In these cases, only the signed consent of the parent accompanying the child and holding parental authority will be obtained.

In the case of separated parents, if the second parent (holder of parental authority) who did not sign the initial consent form wishes to withdraw their child from the study, their decision will of course be taken into account.

7.6.2. Committee for the Protection of Persons

The sponsor undertakes to submit the study proposal to a Committee for the Protection of Persons (CPP) for prior authorisation. The information provided relates, on the one hand, to the methods and nature of the research and, on the other hand, to the safeguards provided for patients participating in the trial.

7.7. INFORMATION TO THE COMPETENT AUTHORITIES S

This protocol will be submitted to the ANSM for information.

7.8. AMENDMENTS TO THE PROTOCOL

Requests for substantial amendments shall be submitted by the sponsor to the relevant CPP for its opinion, to the ANSM for information, and to the relevant Committee for the Protection of Persons for authorisation/information, in accordance with the law in force and its implementing decrees.

The amended protocol must be updated and dated.
The patient information and consent forms must be amended if necessary.

7.9. FINANCING AND INSURANCE

The sponsor shall finance the study and take out an insurance policy covering the financial consequences of its civil liability, in accordance with the regulations.

7.10. RULES RELATING TO PUBLICATION

The study will be registered on a freely accessible website (Clinical Trial) before the first patient is included in the study.

Scientific communications and reports relating to this study shall be produced under the responsibility of the study coordinator with the agreement of the principal investigators of the participating centres.

The coordinating investigator shall draw up the list of authors.

A doctor affiliated with the CHD Vendée at the time of publication must be listed as the first or last author.

Publication rules will follow international recommendations (N Engl J Med, 1997; 336:309-315).

A copy of the publication will be sent to the CHD Vendée, the study sponsor, which will necessarily be cited.

7.11. DISPOSAL OF BIOLOGICAL SAMPLES

At the end of the research, biological samples resulting from the catheter being sent for culture in the event of catheter-related infection will be destroyed.

7.12. ARCHIVING OF SOURCE DATA

The investigator must keep all information relating to the study for at least 15 years after the end of the study.
At the end of the study, the investigator will receive a copy of the data for each patient from their centre, sent by the sponsor.

No transfer or destruction may be carried out without the Sponsor's consent. At the end of the 15-year period, the Sponsor will be consulted regarding destruction. All data, documents and reports may be subject to audit or inspection.

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LIST OF APPENDICES

Appendix 1) *Catheter insertion protocol with compress*

Appendix 2) *Catheter placement protocol without compress*

Appendix 3) *Data collected*