# Study protocol

## Comparative study of two hemodialysis catheter exit site dressing regimens: chlorhexidine gluconate dressing vs chlorhexidine 2% solution.

**Identifier:** NCT05855616 Unique Protocol ID: HUMV-PIE2020-02

**Date**: 20 september 2021

**Hypothesis**

**Primary**:

Curing the exit site of the indwelling hemodialysis catheter with 2% self-adhesive chlorhexidine gluconate semi-permeable polyurethane dressings (AGC) will correlate with a lower incidence of catheter-related infections (bacteremia, exit site infection, and tunnelitis), than healing with chlorhexidine in 2% aqueous solution and covered with a dressing of self-adhesive semi-permeable polyurethane dressings.

**Secondary:**

- The degree of comorbidity, previous infections, time on renal replacement therapy, and catheter duration will correlate with a higher rate of catheter-related infections.
- Hemodialysis catheter exit site dressing with AGC dressings will correlate with higher patient satisfaction than dressing with 2% chlorhexidine solution and covered with a self-adhesive semi-permeable polyurethane dressing.

**Objectives**

**Main**:

To compare the rate of catheter-related infections (bacteremia, exit site infection and tunnelitis) between hemodialysis catheter exit site dressing with self-adhesive ACG dressings and dressing with 2% chlorhexidine solution and covered with self-adhesive semi-permeable polyurethane dressing.

**Secondary**:

- To evaluate factors related to the incidence of hemodialysis catheter-related infections.

- To evaluate the incidence of dressing-related skin alterations.

- To assess patient satisfaction with regard to the type of hemodialysis catheter exit site dressing.

**Methodology**

**Design**: Experimental, controlled and randomized study. Patients will be randomized from sealed envelopes. These envelopes will contain the outflow orifice treatment group to which each patient will be assigned. The envelopes will be numbered and the patients will be included consecutively. The contents of the envelopes will be made by a person outside the research team. A member of the research team will invite the patient to participate in the study, informing him/her of the details of the study orally and in writing (see patient information sheet), after his/her acceptance and signature of the informed consent, the patient will be randomized. Duration: November 2020 to December 2022.

**Intervention**:

- Cure guideline control group- cleansing exit orifice with physiological saline (0.9%), drying with sterile gauze, disinfection with 2% water-based chlorhexidine solution, environmental drying for 30 seconds and covering with self-adhesive semi-permeable polyurethane dressing.
- Cure guideline experimental group - cleaning of the exit orifice with physiological saline (0.9%), drying with sterile gauze, application of a semi-permeable polyurethane dressing with 2% self-adhesive chlorhexidine gluconate, centering the chlorhexidine gluconate band well in the exit orifice.

Outflow orifice curettage will be performed by experienced nurses from our hemodialysis unit, after a briefing on the study methodology. In both cases the treatment will be performed weekly (first day of the week), or whenever there is exudate from the exit site or detachment of the dressing; before connecting the catheter to the hemodialysis monitor. In both cases, the treatment will be carried out under maximum aseptic measures: previous hand hygiene, sterile material and treatment, and use of masks by the patient, nurse and nursing assistant. The connection to the hemodialysis monitor will be performed under these aseptic measures, covering the connection between the lines and the catheter with gauze impregnated with 2% water-based chlorhexidine solution and a sterile cloth. In addition, a bioconnector is used for hemodialysis catheters.

**Population**: patients on renal replacement therapy with hemodialysis whose vascular access is an indwelling catheter. Fifty patients will be included (25 patients in the control group - chlorhexidine 2% solution and covered with self-adhesive transparent polyurethane dressing - and 25 patients in the experimental group - with self-adhesive ACG dressings). The sample size calculation was performed with the GRANMO program version 7.12, accepting an alpha risk of 0.05 and a beta risk of 0.2 in a bilateral contrast, to detect as statistically significant the difference between two proportions, which for the control group is expected to be 25% and the experimental group 5%. A loss-to-follow-up rate of 10% has been estimated.

**Inclusion criteria:**

- Be included in hemodialysis program in our unit.
- Be a carrier of a catheter as vascular access, inserted 1 month prior to inclusion in the study.
- Remain on hemodialysis treatment for at least 3 months at the dialysis center
- Consent to participate in the study.

**Exclusion criteria:**

- Allergy or hypersensitivity to chlorhexidine or polyurethane dressing
- Use of a non-tunneled venous catheter as vascular access.
- Active catheter-related infection at the time of inclusion in the study.

**Causes of patient loss:**

- Exitus.
- Renal transplantation
- Use of arteriovenous fistula as vascular access.
- Transfer to peritoneal dialysis program.
- Hypersensitivity reaction to chlorhexidine gluconate.
- Exit from hemodialysis program due to other clinical situations.

**Follow-up period**: Patients carrying an indwelling catheter: 3 months.

**Variables:**

a) **Patient clinical variables**- age, sex, etiology of renal disease according to ERA/EDTA code, degree of comorbidity according to the modified Charlson Index for patients with renal disease, time on renal replacement therapy with hemodialysis.
b) **Catheter affiliation variables** - design (twin or single), material (carbonate or polyurethane), date of insertion, date of removal, vein of insertion, previous catheter-related infections (bacteremia, tunnelitis, exit site infection).

c) **Catheter-related infections** during the follow-up period- will be defined as:

- *Bacteremia*- presence of fever (body temperature ≥38°C) along with a positive blood culture, with no other focus of infection.
- *Exit site infection*- positive culture of pericatheter smear together with presence of inflammatory signs limited to 2 cm around the cutaneous exit site, with no upper extension to the catheter cuff if tunneled.
- *Tunnelitis*- appearance of inflammatory signs extending beyond 2 cm from the cutaneous exit site and in the subcutaneous tract of the catheter (tunnelitis). It may or may not be associated with fever and bacteremia, and may be accompanied by purulent exudate through the cutaneous exit site.

In case of clinical suspicion of bacteremia due to fever (body temperature ≥38ºC), 2 blood cultures will be taken 30 minutes apart, from aerobic and anaerobic germs, directly from the arterial branch of the catheter.

The exit orifice will be inspected at each dressing, and the nurse in charge will take a photograph of it before performing the dressing, to check for the presence of signs of infection by the investigating team. In the presence of signs of infection, a culture of the pericatheter smear will be taken before the exit site is cured.

d) **Patient satisfaction** with the treatment regimen. - Patients will be surveyed after the follow-up period of the study about discomfort related to the type of treatment: pain on withdrawal, presence of pruritus, loss of adherence, alteration of body image, degree of comfort. To assess these aspects, SCALE 18 Degree of perception of positive expectations, of the NOC taxonomy (5-point Likert-type scale where 1- Not at all satisfied, 2- Somewhat satisfied, 3- Moderately satisfied, 4- Very satisfied, 5- Completely satisfied) will be used.

e) Incidence of dressing-related skin alterations. - will be assessed at each hemodialysis session, using the following NOCs:
   - [110115] Skin lesions
   - 110121] Erythema

SCALE 14 Degree of a negative or adverse condition or response (Severe - Substantial - Moderate - Mild – None)

**Data collection and analysis**: An Excel-type data collection sheet will be created with the variables to be studied. The variables will be introduced by a member of the research team and will be extracted from the patients' clinical records (clinical reports, dialysis evolution sheets, catheter evolution sheets and analytical results). The survey of satisfaction with the treatment will be carried out by a member of the research team at the end of the follow-up period.

A descriptive analysis of the variables under study will be performed: in the case of quantitative variables, measures of central tendency and dispersion appropriate to the distribution and their 95% confidence intervals will be calculated; in the case of categorical variables, the frequency and percentage will be calculated. The catheter-related infection rate (bacteremia, exit site infection and tunnelitis) will be calculated using the following formula: number of catheter-related infections/ days of follow-up x 1000; both for the total number and by intervention group and type of catheter. In the case of comparisons between categorical variables, the chi-square test or Fisher's exact test will be used when necessary. Continuous variables will be compared using Student's t-test or Mann Whitney U-test, depending on their distribution. For the study of variables associated with the presence of catheter-related infections, a multiple logistic regression analysis will be performed including as independent variables age, sex, etiology of renal disease, degree of comorbidity, time on renal replacement therapy with hemodialysis,

type and model of catheter, duration of the catheter, location, and presence of previous catheter-related infections. The results will be considered significant if the critical level observed is less than 5% ($p<0.05$). Statistical analysis will be performed with the PSPP statistical package.

**Limitations of the study**

The main limitation of the study is the follow-up period of the tunneled catheters, which is limited to three months, due to the lack of resources for the acquisition of a greater number of self-adhesive chlorhexidine gluconate dressings.

**Ethical considerations**

Approval of the project will be requested from the Cantabria Drug Research Ethics Committee (CEIm de Cantabria). The research team declares that it has no conflict of interest with respect to the products used in the study.

All patients will be passed the Information and Informed Consent Sheet prior to their inclusion in the study, such consent will be made based on the provisions of Regulation (EU) 2016/679 of the European Parliament and of the Council of 27 April 2016 on Data Protection (RGPD); and the Organic Law 3/2018, of December 5, on the Protection of Personal Data and guarantee of digital rights.

The research will be conducted on the basis of the Declaration of Helsinki, complying with the standards of Good Clinical Practice (GCP) as applicable.

Those patients who wish to receive the intervention but not participate in the project will be provided with the same intervention as the experimental group.

The custody of all documentation related to the project will be carried out by the principal investigator of the project, for a period of 5 years, after which it will be destroyed following the standardized procedure.

**Institutional Authorizations**

The study has the authorization of the Chief of the Nephrology Service of the Marqués de Valdecilla University Hospital. Once the project has been authorized by the CEIm of Cantabria, authorization will be requested from the Management of the Marqués de Valdecilla University Hospital to carry it out.

**Informed consent**

The participant will be informed what the study consists of (verbally and in writing) and will be invited to participate by signing the informed consent.

All data will be treated with strict confidentiality in accordance with the Organic Law 3/2018, of December 5, on Personal Data Protection and guarantee of digital rights. In accordance with the provisions of the aforementioned legislation, the patient may exercise the rights of access, modification, opposition and cancellation of data, for which he/she should contact the principal investigator of the study.