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Original Investigation

Prevention of Tunneled Cuffed Hemodialysis Catheter–Related Dysfunction and Bacteremia by a Neutral-Valve Closed-System Connector: A Single-Center Randomized Controlled Trial

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Background: Hemodialysis (HD) tunneled cuffed catheters may be fitted with neutral-valve closed-system connectors. Such connectors, which are flushed with saline solution and used for 3 consecutive HD sessions, provide a mechanically closed positive-pressure barrier and potentially may be useful to prevent catheter-related bacteremia and dysfunction.

Study Design: Single-center randomized controlled trial.

Setting & Participants: 66 adult HD patients with a tunneled cuffed catheter.

Intervention: Neutral-valve closed-system connector (Tego Needlefree Hemodialysis Connector) versus trisodium citrate, 46.7%, locking solution (Citra-Lock; control group).

Outcomes: Primary composite outcome was the incidence rate of catheter-related dysfunction or bacteremia. Secondary outcomes were the separate incidence rates of catheter-related dysfunction and bacteremia and the cost of both procedures.

Measurements: Catheter dysfunction was defined as the requirement of urokinase and/or a mean blood flow ≤250 mL/min during 2 consecutive HD sessions. Catheter-related bacteremia was defined as ≥2 positive blood cultures. Time of catheter use was calculated and the incidence rate of complications was expressed per 100 person-years.

Results: 66 patients were followed up for a median of 86 (IQR, 29-200) days. The composite primary outcome was not significantly reduced in the closed-system-connector intervention group versus the citrate-locking-solution control group (63.56 vs 71.51 per 100 person-years; $P = 0.3$). Catheter dysfunction in the intervention group was not decreased versus controls (59.59 vs 51.64 per 100-person-years; $P = 0.9$). Only 6 catheter-related bacteremia events were identified, one in the intervention group (3.97 vs 19.86 per 100 person-years; $P = 0.06$).

Limitations: Small size of the patient population and single-center study.

Conclusions: Superiority of the closed-system connector in terms of prevention of the primary efficacy end point compared to the standard locking solution was not observed. Further evaluation in a larger study is suggested.

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INDEX WORDS: Tunneled cuffed hemodialysis catheter; Tego connector; bacteremia; thrombosis.

The planning and care of an efficient vascular access for long-term hemodialysis (HD) remains a challenge for nephrology teams worldwide. Besides specific complications related to a native arteriovenous fistula (AVF), it is well established that the use of tunneled cuffed catheters has a significant impact on the morbidity and mortality of HD patients.[1,2] However, despite recommendations of the National Kidney Foundation,[3] dependence on tunneled cuffed catheters remains too high in some countries, especially in Belgium.[4] The factors contributing to this are numerous: patients' late referral to a nephrologist, severe cardiovascular comorbid conditions prohibiting AVF creation, and patients' refusal of an AVF. In addition, local medical practices can explain important heterogeneity in vascular access modalities.[5]

In order to reduce the risk of tunneled cuffed catheter–related dysfunction and bacteremia, many strategies have been developed with variable success: anticoagulant,[6] fibrinolytic,[7] and/or antibiotic locking solutions.[8] These procedures have a significant cost and also impact on the nursing procedures to be applied before and after each HD session. For prophylactic use of antibiotics, questions remain about

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whether this practice can induce antibiotic resistance in bacteria.[9]

Trisodium citrate is known to have antimicrobial and antithrombotic properties when used as a catheter lock. It is proved in vitro that inhibition of biofilm synthesis is dependent on the citrate concentration (from 4%-46.7%).[10]

Another alternative is a closed positive-pressure system, flushed with 0.9% sodium chloride (saline) solution and attached on the hubs of the tunneled cuffed catheter. According to the manufacturer's recommendations, the connector remains in place during 3 consecutive HD sessions and thus is changed every week. By constituting a mechanical barrier, it could be an attractive alternative for reducing intraluminal contamination and the risk of bacteremia.

Because the impact of the closed-system connector on tunneled cuffed catheter–related dysfunction and bacteremia to our knowledge has not been studied, we conducted a randomized controlled study in our center by comparing the antithrombotic and anti-infectious efficacy of this connector to trisodium citrate, 46.7%. The global cost of both procedures also was evaluated.

METHODS

Study Design

This is a prospective, single-center, randomized (allocation ratio 1:1), and controlled study performed in our in-hospital HD center and our outpatient clinic from Erasme University Hospital (Brussels, Belgium). The objective was to assess in long-term HD patients whether use of the closed-system connector (Tego Needle-free Hemodialysis Connector; ICU Medical Inc) was able to reduce the incidence of a composite end point of catheter-related bacteremia or dysfunction versus controls receiving trisodium citrate, 46.7% (Citra-Lock; Dirinco) as an interdialytic locking solution. There was no blinding of interventions to either patients or investigators. This clinical study received the approval of the Ethics Committee of Erasme Hospital and was conducted from December 1, 2009, to March 30, 2011.

Patient Populations

All adult HD patients, prevalent or incident, were included in our study after having signed an informed consent. The standard HD weekly frequency was at least 3 sessions per week, and use of a functional tunneled cuffed catheter (defined as mean blood flow >250 mL/min) was required. The efficiency of the HD procedure was assessed by measuring once a month the individual urea Kt/V by the single-pool method. The target was at least 1.2-1.3 per dialysis session. Patients with a mature AVF or who presented with an episode of catheter-related bacteremia 1 week before randomization were excluded.

Patients were randomly allocated to receive the closed-system connector with saline solution as locking solution (the intervention) or trisodium citrate, 46.7%, locking solution (the control group). Patients were allocated to the intervention or control group using block randomization with permuted blocks of 4 allocations. Allocations were placed into sealed envelopes by a person unrelated to the conduct of the study. A number was attributed to the 6 possible combinations and the sequence of blocks was determined randomly by using a random number table. The envelopes with treatment allocation were opened in this sequence after eligible patients had signed the informed consent document.

Outcomes and Definitions

The primary composite outcome was the incidence rate of tunneled cuffed catheter–related dysfunction or bacteremia. Catheter dysfunction was defined as the requirement of fibrinolytic therapy or a mean blood flow ≤250 mL/min during 2 consecutive HD sessions. The indication and procedure for fibrinolysis with urokinase (Actosolv; Eumedica) was defined per protocol (see Item S1, provided as online supplementary material). The use of urokinase was noted in the patient record book as an outcome.

Catheter-related bacteremia was defined as the presence of the same microorganism (ie, identical in terms of species and antimicrobial susceptibility profile) in at least 2 qualitative blood cultures sampled through the catheter during the dialysis session (BD BACTEC FX Blood Culture System; BD).[11] Qualitative cultures were completed with a quantitative blood culture (ISOLATOR 1.5 Tube; Oxoid) on request of the consulting microbiologist. An infection of the hemocatheter was suspected when other sources of infection were excluded. Any HD patient presenting with hyperthermia (temperature >38°C) and/or shivering underwent physical examination by the nephrologist in search of an infectious source. According to a standardized protocol, a chest radiograph was obtained, as well as bacteriologic analysis of a urine sample (if the patient had residual diuresis). Other complementary diagnostic approaches (computed tomography, echocardiography, and positron emission tomography) were considered according to the clinical situation.

No blood samples were systematically obtained for bacteriologic analyses during the study. Only patients with fever, chills, and/or biological inflammatory syndrome were investigated by blood sample cultures. All bacteremia episodes were directly registered by our microbiologists and bacteremia events related to another origin than the catheter were excluded from the analysis. Secondary outcomes were the separate incidence rates of catheter dysfunction and catheter-related bacteremia.

Cost Comparison

We also attempted to evaluate the cost of both procedures per patient and per year. The cost of the citrate locking solution and catheter caps versus the cost of the closed-system connector and prefilled saline solution syringe were taken into account and compared.

Standard Nursing Procedures of Catheter Care

A strict multidisciplinary approach has been established for years in our hospital. All tunneled cuffed catheters are inserted under strict aseptic conditions by a vascular radiologist in the left (default) or right jugular vein. Subclavian access is prohibited.

Two types of tunneled cuffed dual-lumen catheters are used in our HD unit: those provided with a staggered tip (Hickman Dialysis Catheter; Bard Access Systems Inc) and a more recent type provided with a split tip (Cannon II Plus; Arrow International, Inc). Standardized sterility procedures have been revised previously and approved by our Nursing and Medical Central Committee. Catheters were manipulated by only experienced HD nurses or HD medical staff using sterile gloves and masks. They were never used for parenteral alimentation or other perfusion. Dressings (Opercat; Iberhospitex SA) were inspected and changed at every dialysis session. The exit site and catheter hub surface were disinfected with a chlorhexidine solution (0.5%); no topical antibiotic was used.

After dialysis, the dead space of all catheters of the control group was filled with trisodium citrate, 46.7%. For the intervention