Skin disinfection with octenidine dihydrochloride for central venous catheter site care: a double-blind, randomized, controlled trial

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Abstract

To compare the efficacy of two commercially available, alcohol-based antiseptic solutions for preparation and care of central venous catheter (CVC) insertion sites, with and without octenidine dihydrochloride, a double-blind, randomized, controlled trial was undertaken in the haematology units and in one surgical unit of two university hospitals. Adult patients with a non-tunnelled CVC were randomly assigned to two different skin disinfection regimens at the insertion site: 0.1% octenidine with 30% 1-propanol and 45% 2-propanol, and as control 74% ethanol with 10% 2-propanol. Endpoints were (i) skin colonization at the insertion site; (ii) positive culture from the catheter tip (≥15 CFU); and (iii) occurrence of CVC-associated bloodstream infection (defined according to criteria set by the CDC). Four hundred patients with inserted CVC were enrolled from May 2002 through April 2005. Both groups were similar in respect of patient characteristics and co-morbidities. Skin colonization at the CVC insertion site during the first 10 days was significantly reduced by octenidine treatment (relative difference octenidine vs. control: 0.21; 95%CI: 0.11–0.39, p <0.0001). Positive culture of the catheter tip was significantly less frequent in the octenidine group (7.9%) than in the control group (17.8%): OR = 0.39 (95%CI: 0.20–0.80, p 0.009). Patients treated with octenidine had a non-significant reduction in catheter-associated bloodstream infections (4.1% vs. 8.3%; OR = 0.44; 95%CI: 0.18–1.08, p 0.081). Side effects were similar in both groups. This randomized controlled trial supports the results of two observational studies demonstrating octenidine in alcoholic solution to be a better option than alcohol alone for the prevention of CVC-associated infections.

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Introduction

The use of central venous catheters (CVCs) is associated with a high risk of infectious complications [1–3]. In the USA up to 80 000 episodes of nosocomial bloodstream infection associated with CVCs (CA-BSIs) in intensive-care units are reported each year [2,4]. The average rate of CA-BSIs in neutropenic patients in ICUs ranges from 2–10/1000 to 14/11000 catheter days in neutropenic patients [5]. The mortality attributable to these infections may exceed 25%, and the associated increase in morbidity leads to a substantial rise in health care expenditures [6–11].

Suppression of cutaneous colonization is an important strategy for reducing CA-BSI; thus use of skin antiseptics such as chlorhexidine is a CDC category IA recommendation [12]. The bispyridinamine octenidine dihydrochloride (referred to as octenidine) is an antimicrobial effective against most Gram-positive and Gram-negative bacteria [13–15]. At low concentrations (0.1%), it shows excellent

bactericidal and fungicidal, and moderate virucidal, activity [16–18]. It displays minimal absorption (skin, mucous membranes) and no systemic toxicity [19].

An aqueous solution containing octenidine and phenoxyethanol has been shown to be safe for skin disinfection in pre-term newborns [20]. Used for care of CVC insertion sites in patients undergoing bone marrow transplantation, this antiseptic decreased bacterial density at the insertion site over time [21]. In an earlier clinical trial a residual or remnant effect of octenidine combined with propanol in microbial skin decontamination over a 24 h period was shown [22]. The objective of this study was therefore to evaluate further the preventive impact and tolerability of octenidine for the preparation and care of CVC insertion sites.

Methods

Design overview

A double-blind, randomized, controlled trial was conducted to compare the efficacy of two alcohol-based skin disinfectants, one additionally containing the substance octenidine.

Setting and participants

The study was carried out from 2002 through 2005 in the haematology units of University Medical Center Freiburg (FR; Freiburg, Germany) and University Hospital Basel (BS; Basel, Switzerland) and in one surgical unit (BS). Both institutions are tertiary care facilities. The study was approved by both local ethics committees and entered into the clinical trials registry of the University Medical Center Freiburg (UKF000502, http://www.zks.uni-freiburg.de/uklreg/php/show_study.php?STUDIEN_ID=000502&kindOfSearch=frei=DE) [23]. Subsequently the trial was registered at ClinicalTrials.gov (Identifier: NCT00515151).

Adult inpatients scheduled to receive a non-tunnelled CVC for an expected period of 5 or more days were asked for their informed consent. Exclusion criteria were known sensitization to the proposed antiseptics, administration of antimicrobial drugs for therapy (not prophylaxis) <1 week prior to catheterization, pre-existing BSI (i.e. fever and/or other signs of infection and positive blood culture), and existing burns. In addition, patients participating in a clinical trial of other antiseptics within a period of 4 weeks were excluded. Patients who received a new catheter after the follow-up period, i.e. at the earliest 30 days after removal of the first catheter, were permitted to enrol again.

Case report forms and corresponding patient files in 10% of all cases were checked by an independent monitor.

Randomization and interventions

The randomization code was produced by the independent Center for Clinical Studies (FR) using a computerized random-number generator. The study centre was used as a stratification factor and block randomization with randomly varying block length was performed. The randomization was realised using closed envelopes, ensuring that the sequence was concealed before patients entered the trial. The patients, the staff administering the interventions, the microbiology laboratory, and all the investigators assessing the outcomes were blinded to the assignment. Bottles containing the disinfectants were not distinguishable and were coded in random sequence. Both solutions were colourless with a predominantly alcoholic odour.

After obtaining their consent, patients were enrolled and randomly assigned to two different commercially available skin disinfection regimens: 0.1% octenidine with 30% 1-propanol and 45% 2-propanol (referred to as the octenidine group) and 74% ethanol with 10% 2-propanol (referred to as the control group). Before catheterization, the entry site was disinfected with the assigned solution over an area of >200 cm^2 for at least 1 min. After insertion, which was performed under sterile barrier precautions according to a standard protocol, the catheter was dressed with sterile gauze or a semi-permeable transparent dressing. During the change of dressings, the assigned solution was also used for care of the entry site following a standard protocol.

Outcomes and follow-up

The primary outcome variables, as per study protocol, were (i) skin colonization at the insertion site, (ii) positive culture from the catheter tip (≥15 CFU), and (iii) occurrence of CVC-associated bloodstream infection (according to CDC definitions).

1 Quantitative skin cultures were obtained before insertion and at regular intervals (3 ± 1 days) during dressing change from a 6 × 4 cm area of skin around the catheter insertion site using a sterile template [24]. A sterile, moistened cotton applicator was swabbed around the insertion site and across the surrounding 24 cm^2 area. The applicator was placed in a tube containing 1.0 mL of 0.01 M phosphate-buffered saline and taken to the laboratory. After vortex mixing and diluting (1:10), aliquots of 0.1 mL of the suspension and of the dilution and 0.01 mL of the dilution only were plated onto blood agar plates. Colonies were counted after incubation at 35°C for 48 h and the mean value (CFU/24 cm^2) was calculated.
2 After removal, the CVC tip was cultured by the roll-plate technique. Colonization was defined as ≥15 CFU [25].