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Prevention of central venous catheter-associated bloodstream infections in paediatric oncology patients using 70% ethanol locks: A randomised controlled multi-centre trial

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Abstract ***Background:*** The prevention of central venous catheter (CVC) associated bloodstream infections (CABSIs) in paediatric oncology patients is essential. Ethanol locks can eliminate pathogens colonising CVCs and microbial resistance is rare. Aim of this study was to determine whether two hour 70% ethanol locks can reduce CABSI in paediatric oncology patients.

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Methods: We conducted a randomised, double blind, multi-centre trial in paediatric oncology patients (1–18 years) with newly inserted CVCs. Patients were randomly assigned to receive two hour ethanol locks (1.5 or 3 ml 70%) or heparin locks (1.5 or 3 ml 100 IU/ml), whenever it was needed to use the CVC, maximum frequency once weekly. Primary outcomes were time to CABSI or death due to CABSI.

Results: We recruited 307 patients (ethanol, $n = 153$; heparin, $n = 154$). In the ethanol group, 16/153 (10%) patients developed a CABSI versus 29/154 (19%) in the heparin group. The incidence of CABSI was 0.77/1000 and 1.46/1000 catheter days respectively ($p = 0.039$). The number-needed-to-treat was 13. No patients died of CABSI. In particular, Gram-positive CABSIs were reduced (ethanol, $n = 8$; heparin, $n = 21$; $p = 0.012$). Fewer CVCs were removed because of CABSI in the ethanol group ($p = 0.077$). The ethanol lock patients experienced significantly more transient symptoms compared to the heparin lock patients (maximum grade 2) (nausea, $p = 0.030$; taste alteration, $p < 0.001$; dizziness, $p = 0.001$; blushing, $p < 0.001$), no suspected unexpected serious adverse reactions (SUSAR) occurred.

Conclusions: This is the first randomised controlled trial to show that ethanol locks can prevent CABSI in paediatric oncology patients, in particular CABSI caused by Gram-positive bacteria. Implementation of ethanol locks in clinical practice should be considered.

1. Introduction

The use of central venous catheters (CVC) is indispensable in the modern-day treatment of children with cancer. Despite improved international guidelines on CVC placement and catheter care, CVC colonisation is still an important problem in such patients [1]. Colonised CVCs can cause CVC-associated bloodstream infections (CABSI), with reported infection rates between 0.1 and 2.3 CABSIs per 1000 catheter days [2]. CABSIs are often difficult to treat. Pathogens become embedded in a self-made polymeric matrix, a biofilm and are difficult to eradicate with systemic antimicrobials: only 24–66% of CVCs are salvaged [2,3]. Therefore CABSIs require prolonged treatment with extended hospital admissions, leading to increased healthcare costs [1]. The prophylactic flushing of CVCs with vancomycin/heparin locks has been reported to result in a significant reduction of Gram-positive CABSIs [4]. Nevertheless, such antibiotic locks may contribute to microbial resistance, and therefore alternative solutions need to be sought. Ethanol is a promising agent; it is easily available, cheap and bacterial resistance to ethanol is rare. Several studies in paediatric patients receiving parenteral nutrition have presented promising results with ethanol locks for the prevention of CABSI [5]. This is the first randomised controlled trial (RCT) investigating prophylactic ethanol locks in paediatric oncology patients. The primary aim of the study was to investigate the use of 70% ethanol locks for preventing CABSI. A secondary aim was to register (a)symptomatic thrombosis in paediatric oncology patients with tunnelled CVCs. These results will be published in a separate manuscript.

2. Patients and methods

2.1. Setting

Five paediatric oncology centres in The Netherlands participated in this study and the protocol was approved by their respective institutional boards. The trial was registered in the Dutch trial register (http://www.trialregister.nl): NTR 1275. Written informed assent or consent was obtained from all parents and patients >12 years. The study medication was manufactured by a central pharmacy. The placement and care of the CVCs were performed in accordance with international guidelines [1]. In the Netherlands, all CVCs in children with cancer are made of silicone. The data were collected prospectively, encoded and stored centrally in the DCOG database PRoMISe. The protocol was also made available on the DCOG website (www.skion.nl).

2.2. Patients

All paediatric oncology patients (1–18 years) with a newly inserted, tunnelled CVC, placed between October 2007 and December 2012, were eligible. Within four weeks after CVC placement, the first study lock was inserted. Catheter days were counted from the day of randomisation. Patients with any of the following criteria were excluded: ⩽1 year at diagnosis, a primary immunological disorder, an ethanol allergy or a CVC inserted in a vessel with previously confirmed thrombosis. In October 2010 the protocol was amended to include patients whose previous CVC had been removed for more than 12 months.

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