



ELSEVIER

Contents lists available at ScienceDirect

International Journal of Antimicrobial Agents

journal homepage: www.elsevier.com/locate/ijantimicag

Review

Systematic review of antimicrobial lock therapy for prevention of central-line-associated bloodstream infections in adult and pediatric cancer patients

LeAnn B. Norris^{a,*}, Farah Kablaoui^b, Maggie K. Brillhart^c, P. Brandon Bookstaver^a^a Department of Clinical Pharmacy and Outcomes Sciences, College of Pharmacy, University of South Carolina, Columbia, SC, USA^b Cleveland Clinic, Abu Dhabi, United Arab Emirates^c Wake Forest Baptist Medical Center, Winston-Salem, NC, USA

ARTICLE INFO

Article history:

Received 8 July 2016

Keywords:

Antimicrobial lock therapy

Central venous catheters

Central-line-associated bloodstream infection

Catheter-related bloodstream infections

ABSTRACT

Background: Central venous catheter (CVC) use is commonplace in cancer patients. Antimicrobial lock therapy (ALT), the instillation of a concentrated antimicrobial solution into the catheter lumen, is one method for preventing infection among CVCs. This systematic review discusses the effectiveness and safety of prophylactic ALT in cancer patients with CVCs.**Methods:** A literature search was performed using the Medline database and Google Scholar from inception until April 2016. The following terms were used: 'antimicrobial lock solution', 'antibiotic lock solution', 'oncology', 'hematology', 'pediatrics', 'prevention', 'cancer', 'catheter related bloodstream infections', 'central-line associated bloodstream infection' (CLABSI) and 'central venous catheter'. Studies evaluating prophylactic ALT in cancer patients alone were eligible for inclusion. Case reports, case series and in-vitro studies were excluded.**Results:** In total, 78 articles were identified. Following all exclusions, 13 articles (three adult and 10 pediatric) were selected for evaluation. The most common agents utilized were vancomycin with heparin; ethanol; taurididine; and minocycline with EDTA. Quality of evidence was moderate to high in adult studies and low to moderate in pediatric studies. Use of ALT decreased the incidence of CLABSI in the majority of studies; however, there were significant differences in definitions of CVC-related infection, dwell times and lock solutions.**Conclusion:** Lock therapy may be an adjunct in high-risk cancer patients for the prevention of CLABSI; higher quality evidence is needed for specific ALT recommendations.

© 2017 Elsevier B.V. and International Society of Chemotherapy. All rights reserved.

1. Introduction

In cancer patients, central venous catheters (CVCs) are utilized for administration of chemotherapy, blood products and total parenteral nutrition. Current guidelines from the Centers for Disease Control and Prevention (CDC) for the prevention of central-line-associated bloodstream infection (CLABSI) include handwashing, aseptic technique, site cleansing and impregnated catheter cuffs [1]. Despite these methods, bloodstream infections (BSIs) secondary to CVCs still occur. Bacterial or fungal colonization can originate at the catheter hub, followed by biofilm formation in the lumen disseminating to the bloodstream. In the general population, the National

Healthcare Safety Network reports a mortality rate as high as 12–25% in patients diagnosed with CLABSI, with approximately 41 000 cases occurring annually [2]. In high-risk populations such as cancer patients, bacteremia rates range from 11% to 38%, and mortality rates of 9.6% have been reported in pediatric oncology patients [3–5]. CLABSIs are associated with excess cost and hospital length of stay, and can delay administration of chemotherapy [6,7]. It is estimated that 10–20% of hematological cancer patients' CVCs will become infected [8]. The CDC considers hospital-acquired CLABSI to be a preventable infection, classified as a 'never event' [9]. This designation limits the reimbursement of such hospital-acquired infections from agencies including the Centers for Medicare and Medicaid Services. The annual burden of cost secondary to CLABSI approximates \$2.68 billion [10].

Skin commensals are often the cause of CVC infections, with 70% of cases involving Gram-positive organisms. Coagulase-negative staphylococci (CoNS) and *Staphylococcus aureus* are the most common pathogens. Gram-negative organisms are identified in 15% of

* Corresponding author. Department of Clinical Pharmacy and Outcomes Sciences, College of Pharmacy, University of South Carolina, 715 Sumter Street, Columbia, SC 29208, USA.

E-mail address: lnorris@cop.sc.edu (L.B. Norris).

infections, with fungi and anaerobes each reported to be the cause in approximately 7% of cases [11]. In cancer patients with febrile neutropenia, Gram-negative infections occur more commonly than in the general population [12].

1.1. Antimicrobial lock therapy

Biofilms, bacteria colonized within the lumen of the catheter, are able to resist antimicrobial therapy at standard concentrations. A method commonly known as antimicrobial lock therapy (ALT) may be an option for both prophylaxis and treatment of CLABSI. ALT involves the instillation of a highly concentrated antimicrobial solution, often in combination with an anticoagulant, into the catheter lumen to dwell while the CVC is not in use [13]. In a prophylactic modality, antimicrobial lock solutions should maintain effective concentrations to prevent bacterial or fungal adherence, have prolonged stability within the lumen, be compatible with desired additives and have limited systemic absorption [14]. Several antimicrobial agents and antiseptic agents have been studied as prophylactic antimicrobial lock solutions.

ALT has been shown to prevent CLABSI, reduce mortality, reduce the burden of healthcare costs, and decrease hospital length of stay in patients with chronic diseases. In a meta-analysis, ALT reduced catheter-related bloodstream infections (CRBSIs) and prolonged catheter survival in hemodialysis-dependent patients [15]. The authors recommended consideration of ALT in routine clinical practice in conjunction with other prevention modalities [15]. Guidelines of the Infectious Diseases Society of America (IDSA) for management of CLABSI do not recommend the routine use of prophylactic ALT, but suggest its use in special circumstances such as patients with a long-term cuffed or tunneled catheter or port that have a history of multiple CLABSIs despite optimal adherence to aseptic technique [16]. The National Comprehensive Cancer Network does not endorse the use of lock solutions in oncology patients due to the potential risk of resistance following widespread use [17]. According to the American Society of Clinical Oncology, data are not sufficient to recommend for or against routine use of ALT, and more research is warranted [18]. To date, the US Food and Drug Administration have not approved any agents or formulations for the use of ALT for CLABSI prevention or treatment.

Cancer patients are at high risk for CLABSI given the need for treatment requiring sustained central venous access. Prophylactic ALT has been shown to reduce CLABSI rates, improve catheter survival, and thus reduce the need for hospitalization. This paper provides a systematic review of the evidence available for the use of prophylactic ALT in pediatric and adult cancer patients. Additional insight into compatibility, stability, optimal dwell times and clinical practice concerns related to ALT are also addressed.

2. Methods

2.1. Search strategy and selection criteria

The Preferred Reporting Items for Systematic Reviews and Meta-Analyses for Protocols was used to facilitate the preparation and reporting of this systematic review [19]. A literature search was performed using the Medline database and all open access journals using Google Scholar from the date of each database's inception until April 2016. The terms 'antibiotic lock solution', 'antimicrobial lock solution', 'oncology', 'hematology', 'prevention', 'cancer', 'ethanol', 'taurolidine', 'central-line associated bloodstream infections', 'catheter related bloodstream infection' and 'central venous catheter' were used. Appropriateness for inclusion in the review was determined by the following criteria: peer-reviewed study that must include hematology/oncology patients; outcomes of interest of either infection rate and/or CVC-free survival rate; and antimicrobial

concentrations used in solution plus any additives. Additional process details including dwell time and administration were included when available. Observational cohorts, case-control studies and other open label studies were evaluated for inclusion.

2.2. Study selection

All articles were reviewed by each of the authors to determine inclusion. In-vitro data, animal models, case reports and studies missing outcomes of interest were excluded. Articles investigating ALT in a treatment modality were also excluded. Review articles were evaluated for cross-referencing.

2.3. Data extraction and outcomes

Two authors extracted relevant data (FK, MB) from included studies on patient population, number of study participants, control and study lock solutions with concentrations, definitions of CVC-associated infections, reported CLABSI rates per patient, and reported rate of infections per 1000 CVC-days. If rates were not provided but could be calculated from available data, these results were included. Two authors independently assessed study quality using the GRADE (Grading of Recommendations Assessment, Development and Evaluation) criteria [20].

2.4. Search results

The literature search revealed 78 possible articles; 34 articles had defined cancer populations but following exclusions, 15 articles were deemed appropriate for inclusion [8,21–32]. Two additional studies were excluded, leaving 13 studies for the final analysis (Fig. 1). One study was excluded as it was based on a smaller subset of a larger study that was included [33]. Another study was excluded due to lack of interpretable data of overall infection rates during the study period [34]. Three studies included adults only [8,21,22] and 10 studies included pediatrics only (>90% of study population) [23–32]. Among the adult-only studies, two studies were considered to be high quality [21,22] and one study was considered to be moderate quality [8]. Among the pediatric studies, two studies were considered to be high quality [23,32], three were considered to be moderate quality [24,29,31], and five were considered to be low quality [25–28,30]. Data were collated and analysed to provide the following summary details and recommendations. The definitions and terminology used to define BSIs secondary to CVCs (e.g. CRBSI, CLABSI) varied between studies, but are reported as reflected in each individual study.

3. Prophylactic studies in adult cancer patients

In adults, CVCs are common and provide convenient delivery of long-term chemotherapy. Recent data have shown infection rates of 2.66 per 1000 line-days in adult hematology/oncology and bone marrow transplant units, and this ranges from 1.3 to 1.9 per 1000 line-days in hematology/oncology units alone [35,36]. This review includes one study that evaluated vancomycin plus heparin (VH) in solution, and two studies that evaluated ethanol, all compared with a standard control solution of heparin or normal saline (Table 1). Case reports of successful use of minocycline plus ethylenediaminetetraacetate (mEDTA) as secondary prophylaxis of CRBSI among adult cancer patients have been reported, but are not included in this review [37].

3.1. Vancomycin-based lock solution

Vancomycin is an antimicrobial with activity against Gram-positive organisms including methicillin-resistant *S. aureus* [24].

Download English Version:

<https://daneshyari.com/en/article/5666783>

Download Persian Version:

<https://daneshyari.com/article/5666783>

[Daneshyari.com](https://daneshyari.com)