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EVIDENCE-BASED REVIEW

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Chlorhexidine-based versus non-chlorhexidine dressings to prevent catheter-related bloodstream infections: An evidence-based review

Anthea Azzopardi BSc. (Hons.) in Nursing, Staff Nurse | **Josef Trapani BSc (Nurs.), MSc (Pub. Hlth.), PhD, RN, Senior Lecturer and Deputy Dean**

Department of Nursing, University of Malta, L-Imsida, Malta

Correspondence

Anthea Azzopardi, BSc. (Hons.) in Nursing, Staff Nurse, Department of Nursing, University of Malta, 4, Ayrthea, Triq il-Kavallier Vincenzo Bonello, Mdina, Malta.
Email: anthea.azzopardi.19@um.edu.mt

Abstract

In patients with central venous catheters (CVCs) in situ, the development of catheter-related bloodstream infections (CRBSIs) is often linked with increased morbidity and mortality. Sterile gauze or transparent polyurethane dressings are conventionally used as extraluminal barriers; however, antimicrobial chlorhexidine CVC dressings could potentially reduce infection risk. This short evidence-based review examined the literature comparing the effectiveness of chlorhexidine-based CVC dressings against non-chlorhexidine dressings in reducing CRBSI occurrence. Four systematic reviews with meta-analysis were reviewed, all of which reported a statistically significant reduction in CRBSI occurrence on using chlorhexidine-based dressings. Further research is needed to determine the cost-effectiveness of chlorhexidine-based CVC dressings and their effectiveness in reducing CRBSIs in different catheter types and entry sites because infection risk is not uniform.

KEYWORDS

catheter-related bloodstream infection, central venous catheters, chlorhexidine dressing, CRBSI, CVC dressing

1 | BACKGROUND AND CLINICAL QUESTION

Invasive devices, such as central venous catheters (CVCs), are essential in the critical care setting; however, these often leave patients vulnerable to pathogens. In Europe, over 4 million patients contract hospital-acquired infections (HAIs) annually, with 43% of all bloodstream infections being catheter-related.[1] Such catheter-related bloodstream infections (CRBSI) are associated with prolonged hospitalization, increased morbidity and mortality, and a considerable financial burden on the health care system.[2,3] Conventionally, sterile transparent or gauze CVC dressings are used as extraluminal barriers to reduce CRBSI; however, chlorhexidine-based antimicrobial dressings were introduced as an alternative.[4]

The long-lasting antimicrobial action of chlorhexidine is brought about by its formation of covalent bonds with the proteins in the mucosa and skin.[5] Chlorhexidine disrupts the cytoplasmic membrane of bacteria, consequently eliminating these pathogens. For most bacteria, prolonged exposure to this solution is directly linked to an increased bactericidal effect.[5] Within a clinical setting, this may be achieved by the application of chlorhexidine-based dressings over the CVC insertion site. In contrast with other antimicrobial solutions, such as povidone-iodine, chlorhexidine has very limited systemic absorption, and its effectiveness is not influenced by the presence of body fluids like blood.[5]

This necessitates the question: Are chlorhexidine-based dressings more effective at reducing CRBSI incidence than non-chlorhexidine dressings in critically ill patients with CVCs in situ?

2 | SEARCH STRATEGY

A systematic literature search was conducted for studies comparing CRBSI occurrence rates between chlorhexidine-based and

non-chlorhexidine CVC dressings among critically ill patients. The search was conducted between July and August 2022 using the following health-focused search platforms and databases: EBSCOhost, MEDLINE ProQuest, Google Scholar, PubMed, and Scopus. Through EBSCOhost, multiple databases were searched simultaneously, namely AgeLine, CINAHL Complete, Cochrane Clinical Answers, Cochrane Register of Controlled Trials, Cochrane Methodology Register, Cochrane Database of Systemic Reviews, Academic Search, and MEDLINE Complete. The following keywords were combined using the Boolean operators "AND" or "OR": Central venous catheter(s)/Intravascular catheter(s), Chlorhexidine/Chlorhexidine gluconate, Gauze dressing/Polyurethane dressing/non-antimicrobial, Catheter-related bloodstream infection(s)/CRBSI/bacterial colonization/Central line associated bloodstream infection(s), Health care associated bloodstream infection(s).

Eligibility criteria were applied to better focus the search within the scope of this review. Included studies were limited to those published in the English language and with a publication date within the last 10 years, since CVC practices rapidly changed over time. Moreover, only high quality study designs, as indicated by the hierarchy of evidence, namely systematic reviews, meta-analysis, and randomized control trials (RCTs), were included in the review to reduce the risk of researcher bias and increase the credibility of the review.[6] Studies evaluating the application of chlorhexidine-based dressings on arterial lines were excluded from this review, in order to focus the search on adult patients with CVCs in situ.

The search generated six potentially relevant papers: Four systematic reviews and two RCTs.

On further evaluation of the retrieved articles, both individual RCTs were already included within the retrieved systematic reviews and were subsequently removed from this review to avoid including duplicate data and potentially misleading the conclusion derived.

Therefore, this brief review is based on four systematic reviews with meta-analysis (summarized and appraised in Table 1), which directly address the clinical question.

What is known about the topic

- CRBSIs are associated with increased morbidity and mortality and pose a financial burden on the health care system.
- External CVC dressings are applied at the insertion site to act as extraluminal barriers against infection.
- Various CVC dressings are available (including chlorhexidine-impregnated, highly adhesive, and povidone-iodine-impregnated); however, sterile gauze or transparent polyurethane dressings are commonly used.

What this paper adds

- Current evidence indicates that the application of antimicrobial chlorhexidine-based dressings significantly reduces the incidence of CRBSIs when compared with non-chlorhexidine CVC dressings (sterile gauze or transparent dressings).
- Further research should focus on the cost-effectiveness of the intervention as well as examine a younger study population and different catheter types and insertion sites because infection risk is not uniform.

3 | REVIEW OF THE EVIDENCE

Four systematic reviews with meta-analysis were retrieved, all of which reported statistically significant findings in favour of the chlorhexidine-based dressings' ability to prevent CRBSIs (Table 1).[7–10] The higher ranking of systematic reviews within the hierarchy of evidence when compared with RCTs attributes confidence to the quality and strength of these studies, increasing their value in addressing the review question.[6]

Safdar et al.[7] included nine RCTs in their review, while Wang et al.[8] reviewed 13 RCTs. Considering that only three databases were searched in each review, their searches may have been limited in their ability to discover all potentially relevant articles, possibly leading to the relatively low number of studies retrieved. Nonetheless, the databases utilized are reported to be the most comprehensive in generating health care-related results.[11] Wei et al.[9] yielded a total of 12 RCTs whilst Puig-Asensio et al.[10] gathered 18 RCTs and two quasi-experimental studies. Quasi-experimental studies lack randomization, which can potentially lead to confounding biases and, as such, are not ideal to address questions about effectiveness.[12] Nonetheless, the extensive use of multiple renowned health-focused databases in the latter two reviews attributes confidence to the reliability and sensitivity of the search.[11]

In addition, Safdar et al.,[7] Wei et al.[9] and Puig-Asensio et al.[10] examined the reference lists of the included reviews to help broaden the search and identify additional potentially relevant studies.[14] The latter two[9,10] contacted the respective authors of the included primary studies to obtain additional data when necessary.[13] Puig-Asensio et al.[10] also examined grey literature, which could have greatly contributed to the evidence found because it carries a reduced risk for publication bias; however, these may potentially have undergone less rigorous peer review.

Overall, the eligibility criteria for these four systematic reviews were clearly defined and appropriate to effectively answer the question under review.[7–10] Wang et al. limited their search to the English language, which could have excluded potentially valid studies.[8,13] In contrast, Wei et al.[9] did not limit their search by language, publication status, sample size, or publication year, thus broadening their search.

Safdar et al.[7] and Wang et al.[8] used standard, conventional dressings as the control intervention. Conversely, Wei et al.[9] compared chlorhexidine-based dressings against any other (including povidone-iodine and advanced dressings) or no dressings, whilst Puig-Asensio

TABLE 1 Evidence table displaying studies in chronological order

Authors & type of paper	Design/Setting	Key results	Strengths	Limitations
*Safdar et al. (2014)[7] Systematic Review with Meta-analysis	9 RCTs included in review Sample size: 6067 (11 931 catheters) Publication Bias assessment for CRBSI (Funnel plot and Egger regression test: $p = .15$) Heterogeneity assessment (Cochrane Q statistic and I^2 assessment: $I^2 = 17\%$)	CRBSI occurrence in the chlorhexidine intervention (1.1%) vs. control (2.1%): RR = 0.60 (CI[95%]: 0.41–0.88; $p = .009$) Reduction of catheter colonization: RR = 0.52 (CI [95%]: 0.43–0.64)	Non-significant heterogeneity and publication bias Extensive search on renowned health-related databases Review of reference lists of included studies for the retrieval of additional relevant studies	Small number of databases used
*Wang et al. (2019)[8] Systematic Review with Meta-analysis	13 RCTs included in review Sample size: 7555 (11 931 catheters) Publication Bias assessment for CRBSI (Funnel plot and Egger regression test: $p = .90$) Heterogeneity assessment ($I^2 = 23\%$)	CRBSI occurrence in the chlorhexidine intervention: (1.3%) vs. control (2.5%): RR = 0.55 (CI[95%]: 0.39–0.77, $p = .001$) Reduction of catheter colonization: RR = 0.52 (CI [95%]: 0.40–0.67)	Non-significant heterogeneity and publication bias Extensive search on renowned health-related databases	Small number of databases used Application of language limiter (English articles only) limiting retrieval of studies
*Wei et al. (2019)[9] Systematic Review with Meta-analysis	12 RCTs included in review Sample size: 6208 Publication Bias assessment for CRBSI (Funnel plot and Egger regression test: $p = .071$) Heterogeneity assessment (Chi-square test and I^2 assessment: $I^2 = 24\%$)	CRBSI occurrence in the chlorhexidine intervention vs control: RR = 0.60 (CI [95%]: 0.42–0.85) Reduction of catheter colonization: RR = 0.46 (CI [95%]: 0.36–0.58)	Non-significant heterogeneity and publication bias Extensive search on multiple renowned health-related databases Search not limited by language, publication status, sample size or publication year Review of reference lists of included studies for the retrieval of additional relevant studies	No use of MeSH terms to retrieve alternative terms for index key terms Small sample size presented by retrieved RCTs, limiting accurate statistical evaluation
*Puig-Asensio et al. (2020)[10] Systematic Review with Meta-analysis	20 studies included in review: 18 RCTs and 2 quasi-experimental Sample size: 15590 catheters Publication Bias assessment for CRBSI (Funnel plot: symmetrical plot observed) Heterogeneity assessment (Cochrane Q statistic and I^2 assessment: $I^2 = 0\%$)	CRBSI occurrence in the chlorhexidine intervention vs control: RR = 0.71 (CI [95%]: 0.58–0.87) Reduction of exit-site/tunnel infections: RR: 0.37 (CI [95%]: 0.33–0.80)	Non-significant heterogeneity and publication bias Extensive search on multiple renowned health-related databases Review of grey literature and reference lists of included studies for the retrieval of additional valid studies Respective study authors contacted for additional data when necessary	Inclusion of quasi-experimental study designs risking confounding bias Ambiguous definition of control intervention allowing for the retrieval of more than one type of dressing

Abbreviations: CI, confidence interval; CRBSI, catheter-related bloodstream infection; ICU, intensive care unit; RR, risk ratio.
*Statistically significant findings in favour of the Chlorhexidine intervention.

et al.[10] used non-antimicrobial dressings as the control. Both these reviews remain valuable to address the research question proposed, as the comparator elements are non-chlorhexidine in nature.

No statistically significant publication bias or heterogeneity was identified in any of these four systematic reviews as determined by a combination of tests, including funnel plots, Egger's regression test, the Cochrane Q statistic, the Chi-Square test, and the I^2 assessment.[7–10] This increases the confidence that the respective meta-analyses were not compromised by external bias and allows for adequate comparisons to be made across individual studies to derive pooled results.

A common limitation across all reviews was the challenged generalizability of results because of variations in characteristics (especially, population, setting, and unit protocols); however, heterogeneity was not found to be statistically significant in any of these reviews. Furthermore, the small sample size generated by the RCTs reviewed by

Wei et al.[9] underpowered the Egger's test and limited their statistical evaluation of bias. Despite this, the absence of statistically significant publication bias and heterogeneity in all four reviews underscores their value.

The conclusions reached by these four reviews, as summarized in Table 1, were unanimous. The findings not only support the significant effect of chlorhexidine-based CVC dressings in reducing CRBSIs within the adult critically ill population, but also affirm their superiority over non-chlorhexidine dressings when compared on the basis of this same outcome.

Safdar et al.[7] and Puig-Asensio et al.[10] were the only authors to report on local reactions, as represented by soft tissue and cutaneous abnormalities associated with the chlorhexidine-based dressing. Chlorhexidine caused a low event rate of contact dermatitis as was disclosed by both reviews; however, no systemic reactions were reported.

4 | DISCUSSION

The evidence collected in this review is unanimously in favour of chlorhexidine-based dressings for the reduction of CRBSIs. Future research should further investigate different catheter types and insertion sites, as the risk for infection posed by each is not uniform and, as such, may act as confounding factors.[5] Moreover, the generalisability of the findings to young, critically ill patients is limited because the average age of participants in all reviews ranged between 50 and 70 years. Because age is a potential confounding variable for infection occurrence,[5] further studies focusing on the paediatric and young adult patients having CVCs in situ would be valuable to better evaluate the implications of chlorhexidine-based dressings in critically ill patients across the lifespan. Indeed, current guidelines published by the Centre for Disease Control and Prevention (CDC) recommend the use of chlorhexidine-based dressings only in patients aged 18 or older.[15] The still developing cutaneous membrane of young patients puts them at higher risk for developing dermal reactions. This may cause hypersensitivity to topical agents, with fever, localized erythema, and oedema being a few of the presenting symptoms.[15]

In view of the increasing concern about heightened antibiotic resistance,[16] CRBSIs are becoming increasingly difficult to treat. Consequently, a preventative infection control strategy is ideal to reduce the incidence of CRBSIs. Despite the positive findings gathered in favour of the chlorhexidine dressing intervention, this review cannot fully recommend its use on a routine basis across all critically ill patients. Some studies reported that prolonged exposure to chlorhexidine could likely increase the risk of resistance to certain antibiotic agents.[16] Subsequently, its use should be restricted to patients who would clearly benefit from such an intervention until further research regarding chlorhexidine sensitivity is available.

Merit should be given to the potential value of chlorhexidine as an antimicrobial agent on other vascular access devices. As observed in a trial by Timsit et al. (2012), chlorhexidine-based dressings did not only show significant effects for CRBSI reduction in CVCs but also exhibited a similarly significant effect in reducing bloodstream infections associated with arterial catheters (Hazard Ratio = 0.367; CI [95%] = 0.205–0.656; $p < .001$).[17] This expands the potential for chlorhexidine within the scope of infection prevention and control.

5 | IMPLEMENTATION INTO PRACTICE

Despite this overwhelming evidence, the use of chlorhexidine-based dressings for CVCs in everyday practice may be questioned in view of their higher cost when compared with non-chlorhexidine dressings. Conversely, it may be argued that treating CRBSIs might prove to be more costly with its accompanied complications and increased duration of hospitalization. Moreover, upon taking a holistic approach, longer hospital stays may also pose a substantial negative impact for both patients and their relatives from a financial, emotional, mental, and social perspective.[2] To date, Crawford et al. (2004) and Maunoury et al. (2015) are the only authors to have conducted a cost-effectiveness study regarding this intervention.[18,19] Therefore, further research is required to determine whether chlorhexidine-based dressings are also financially advantageous in the clinical setting. In addition, the relationship between chlorhexidine use and antibiotic resistance needs to be further examined to determine the potential clinical consequences of this intervention.[16]

Critical care staff would need to be properly educated in order to develop competence in the indications for use of chlorhexidine-based dressings and derive the most benefits. This would prevent potential HAIs, which could further compromise patient health. The effectiveness with which the dressing intervention is being applied may be managed through occasional spot checks and audits, identifying areas that need improvement, and thus guiding future educational programmes.[20] It is ultimately within the responsibility of managers and stakeholders involved to procure the most adequate product, centred around current, available evidence.[20] This would encourage evidence-based practice, whereby patient safety is safeguarded and the effectiveness of the intervention is guaranteed.

ORCID

Anthea Azzopardi https://orcid.org/0000-0001-6740-2192
Josef Trapani https://orcid.org/0000-0003-0888-5045

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