



Canadian Agency for
Drugs and Technologies
in Health

RAPID RESPONSE REPORT: SUMMARY WITH CRITICAL APPRAISAL

TITLE: Use of Chlorhexidine Gluconate with Alcohol for the Prevention of Peripheral Intravenous Device Infections: A Review of Clinical and Cost Effectiveness, and Guidelines

DATE: 03 April 2014

CONTEXT AND POLICY ISSUES

Peripheral intravenous devices are catheters inserted into a small peripheral vein for therapeutic purposes such as administration of medications, fluids, or blood products. Catheter-related infections represent the third leading cause of infections in intensive care units (ICUs) worldwide after pneumonia and abdominal infections.¹ Catheter-related infections increase the length of ICU stay, hospital stay, and mortality, with an additional cost of US\$30,000 per survivor in the US.² Different antiseptic solutions for skin disinfection at the catheter insertion site such as povidone-iodine solution, chlorhexidine gluconate, alcohol, chlorhexidine gluconate in alcohol, and other antiseptics, have been used to help prevent catheter-related blood stream infections.^{3,4} While clinical trials and meta-analyses have been done to compare the efficacy of different antiseptic solutions in patients with central intravenous devices and have shown that the use of chlorhexidine gluconate in alcohol statistically reduced the risk of catheter-related infections compared to povidone-iodine,⁵⁻⁸ it is not clear whether chlorhexidine gluconate in alcohol has the same effect in patients with peripheral intravenous devices.

This Rapid Response report aims to review the comparative clinical effectiveness of chlorhexidine gluconate with alcohol for the prevention of peripheral intravenous device-related infections. Cost-effectiveness of chlorhexidine gluconate with alcohol for the prevention of peripheral intravenous device-related infections, and guidelines associated with its use will also be examined.

RESEARCH QUESTIONS

1. What is the comparative clinical effectiveness and safety of chlorhexidine gluconate with alcohol versus other antiseptics for the prevention of infections associated with peripheral intravenous devices?

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2. What is the cost-effectiveness of chlorhexidine gluconate with alcohol for the prevention of infections associated with peripheral intravenous devices?
3. What are the evidence-based guidelines regarding the use of chlorhexidine gluconate with alcohol as antiseptic for the prevention of infections associated with peripheral intravenous devices?

KEY FINDINGS

The literature search did not find evidence on the clinical effectiveness, safety or cost effectiveness of chlorhexidine gluconate with alcohol compared to other antiseptics for the prevention of infections associated with peripheral intravenous devices. Guidelines recommend decontamination of the skin at the insertion site with 1-2% chlorhexidine gluconate in ≥70% alcohol before inserting a peripheral intravenous catheter.

METHODS

Literature Search Strategy

A limited literature search was conducted on key resources including PubMed, The Cochrane Library (2014, Issue 3), University of York Centre for Reviews and Dissemination (CRD) databases, Canadian and major international health technology agencies, as well as a focused Internet search. No filters were applied to limit the retrieval by study type. Where possible, retrieval was limited to the human population. The search was also limited to documents published between January 1, 2009 and March 5, 2014.

Selection Criteria and Methods

One reviewer screened citations and selected studies. In the first level of screening, titles and abstracts were reviewed for relevance. Full texts of any potentially relevant articles were retrieved, and assessed for inclusion. The final article selection was based on the inclusion criteria presented in Table 1.

Table 1: Selection Criteria

Population	Adults and Children with peripheral intravenous devices
Intervention	Chlorhexidine gluconate with alcohol as topical antiseptic
Comparator	Alcohol alone Povidone iodine Chlorhexidine gluconate without alcohol Other antiseptic
Outcomes	Prevention of infections Adverse events Cost-effectiveness Guidelines
Study Designs	Health technology assessments (HTA), systematic reviews (SRs), meta-analyses (MAs), randomized controlled trials (RCTs), economic evaluations, and guidelines. If few HTA/SR/MA/RCTs were found, non-RCTs will be included.

Exclusion Criteria

Articles were excluded if they did not meet the selection criteria in Table 1, if they were published prior to January 2009, if they were duplicate publications of the same study, or if they were referenced in a selected systematic review.

Critical Appraisal of Individual Studies

The quality of the included guidelines was assessed using the AGREE checklist.⁹ Numeric scores were not calculated. Instead, the strengths and limitations of the study are summarized and presented.

SUMMARY OF EVIDENCE

Quantity of Research Available

The literature search yielded 79 citations. After screening of abstracts from the literature search and from other sources, 10 potentially relevant studies were selected for full-text review. Two guidelines related to the use of chlorhexidine gluconate with alcohol as topical antiseptic for the prevention of infections associated with peripheral intravenous devices were included in the review. The PRISMA flowchart in Appendix 1 details the process of the study selection.

Summary of Study Characteristics

Study design

Two evidence-based clinical guidelines were identified.^{10,11} The NICE clinical guideline, issued in 2012, is a partial update of a guideline entitled “Infection control: prevention of healthcare-associated infection in primary and community care” published in 2003. The guideline stated that new evidence will be checked three years after the publication and that healthcare professionals and patients’ views will be asked, to update the guideline if necessary.¹⁰ The Australian clinical guideline, issued in 2013, was developed as part of the I-CARE intervention bundle for the management of intravascular devices.¹¹

Population

The guidelines provided recommendations for the care of patients receiving treatment for which standard infection-control precautions apply,¹⁰ or patients with a peripheral intravenous catheter.¹¹

Interventions and comparators

The NICE guideline examined the comparative clinical effectiveness of chlorhexidine gluconate with alcohol to povidone iodine in alcohol or to alcohol alone.¹⁰ The Australian guideline considered chlorhexidine gluconate as a skin preparation solution, as well as alternatives for consideration where chlorhexidine or alcohol are contraindicated, but did not report on comparative effectiveness of different solutions.

Outcomes

Recommendations on the use of chlorhexidine gluconate in alcohol for patients with peripheral intravenous catheters were provided in both guidelines. No grading of evidence or recommendations was provided.

Summary of Critical Appraisal

The NICE guideline had specific and unambiguous recommendations, with a systematic and clearly described method of searching for and selecting the evidence, and clearly described methods used to formulate the recommendations. The guideline was piloted among target users, patient view and preferences were sought, and procedures to update the guidelines provided.¹⁰ It is unclear for the Australian guideline whether it was piloted among target users, or whether patients' view and preferences were sought, potential cost implications of applying the recommendations were not included. Methods for identifying and selecting evidence and procedures to update the guideline were not provided.¹¹ Potential cost implications of applying the recommendations were not included in both guidelines, though the NICE guidance did attempt to identify cost-effectiveness evidence (none was identified) and considered the relative costs of different antiseptic solutions.

Details of the strengths and limitations of the included studies are summarized in Appendix 2.

Summary of Findings

Main findings of included studies are summarized in detail in Appendix 3.

1. What is the comparative clinical effectiveness and safety of chlorhexidine gluconate with alcohol versus other antiseptics for the prevention of infections associated with peripheral intravenous devices?

No evidence found on the clinical effectiveness and safety of chlorhexidine gluconate with alcohol compared to other antiseptics for the prevention of infections associated with peripheral intravenous devices.

2. What is the cost-effectiveness of chlorhexidine gluconate with alcohol for the prevention of infections associated with peripheral intravenous devices?

No evidence found on the cost-effectiveness of chlorhexidine gluconate with alcohol for the prevention of infections associated with peripheral intravenous devices.

3. What are the evidence-based guidelines regarding the use of chlorhexidine gluconate with alcohol as antiseptic for the prevention of infections associated with peripheral intravenous devices?

A NICE clinical guideline¹⁰ and a Queensland guideline¹¹ were included in this report.

The NICE clinical guideline "Prevention and Control of Healthcare-associated Infections in Primary and Community care" was developed in 2012 by the National Clinical Guideline centre, UK, with audience as patients receiving treatment for which standard infection-control

precautions apply.¹⁰ The guideline stated under the section “vascular access devices site care” (p. 39):

“Decontaminate the skin at the insertion site with chlorhexidine gluconate in 70% alcohol before inserting a peripheral vascular access device or a peripherally inserted central catheter.”[new 2012] (i.e., the evidence has been reviewed and the recommendation has been updated or added from the 2003 guideline)

The Queensland guideline “Peripheral Intravenous Catheter” was developed in 2013 by the Centre for Healthcare-Related Infection Surveillance and Prevention & Tuberculosis Control, Australia, for patients with peripheral intravenous devices.¹¹ The guideline stated under the section “Skin Preparation: Insertion Site” (p. 4):

“A solution containing 1-2% chlorhexidine gluconate (CHG) in ≥ 70% ethyl or isopropyl alcohol (alcoholic chlorhexidine) should be used by clinicians for preparation of the insertion site”

“If CHG is contraindicated (e.g. sensitivity, allergy) clinicians should use povidone-iodine 10% in 70% ethyl alcohol (ethanol) (povidone-iodine should remain on the skin for at least 2 minutes and until dry before inserting the catheter)”

“If alcohol contraindicated (e.g. allergy, sensitivity, skin condition) clinicians should use aqueous povidone-iodine 10% or sterile normal saline 0.9% (*NB: the drying time for aqueous based antiseptics is longer than alcohol based products).”*

Limitations

Clinical evidence on the use of chlorhexidine gluconate with alcohol as antiseptic for the prevention of infections is largely for central vascular lines, but evidence since 2009 is lacking for peripheral intravenous devices. Studies on cost-effectiveness of chlorhexidine gluconate with alcohol as antiseptic in the prevention of infections, and potential reduction of length of ICU and hospital stay are also lacking. The recommendations related to skin decontamination prior to insertion of a peripheral vascular access device in the NICE guideline was based on what was described as very limited evidence of low and very low quality. The Australian guideline did not describe the nature of the evidence informing the recommendations.

CONCLUSIONS AND IMPLICATIONS FOR DECISION OR POLICY MAKING

The literature search did not find evidence on the clinical effectiveness, safety and cost effectiveness of chlorhexidine gluconate with alcohol compared to other antiseptics for the prevention of infections associated with peripheral intravenous devices. Based on clinical effectiveness review from limited studies published before 2009, guidelines recommend decontamination of the skin at the insertion site with 1-2% chlorhexidine gluconate in ≥70% alcohol before inserting a peripheral intravenous catheter.

Assuming the effectiveness and safety of chlorhexidine gluconate with alcohol as antiseptics for peripheral intravenous catheter is similar to that for a central intravenous catheter, more information will come from a future randomized controlled, assessor-blind trial for which the 2013 protocol indicated that catheter-related infection rates will be measured in adult patients

requiring the insertion of at least one peripheral arterial catheter and/or a non-tunneled central venous catheter and/or a hemodialysis catheter and/or an arterial pulmonary catheter who will be randomly assigned to get one of four skin preparation strategies (2% chlorhexidine/70% isopropyl alcohol or 5% povidone iodine/69% ethanol with or without prior skin scrubbing).¹² Studies on cost-effectiveness of chlorhexidine gluconate with alcohol as antiseptic in the prevention of infections, and potential reduction of length of ICU and hospital stay are also needed.

PREPARED BY:

Canadian Agency for Drugs and Technologies in Health

Tel: 1-866-898-8439

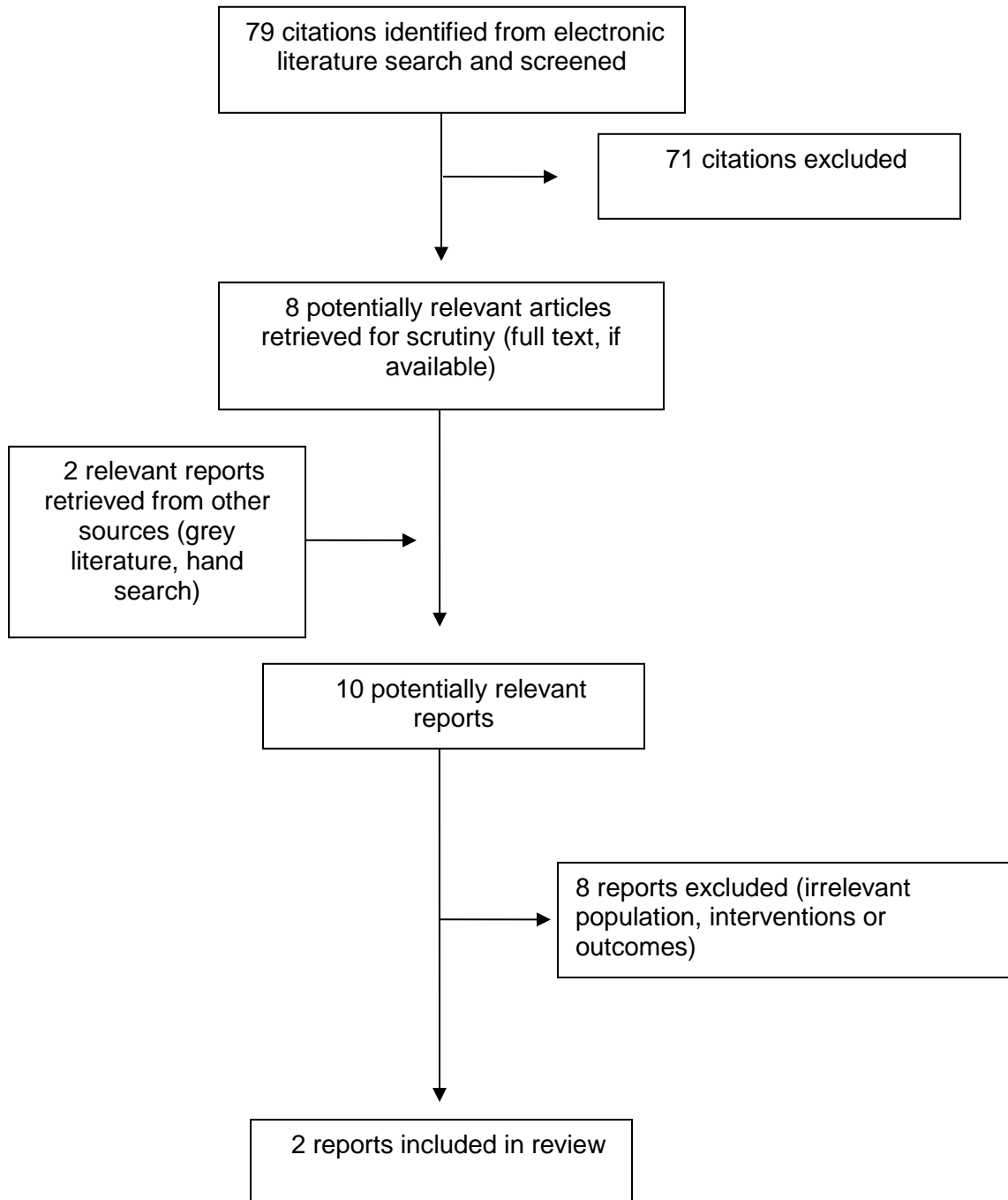
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Appendix 1: Selection of Included Studies



Appendix 2: Summary of Critical Appraisal of Included Study

Table A2: Summary of Critical Appraisal of Included Study		
First Author, Publication Year	Strengths	Limitations
Critical appraisal of included guidelines (AGREE⁹)		
NICE clinical guideline, ¹⁰ 2012, UK	<ul style="list-style-type: none"> scope and purpose of the guidelines are clear the recommendations are specific and unambiguous the method for searching for and selecting the evidence are clear methods used for formulating the recommendations are clearly described health benefits, side effects and risks were stated in the recommendations procedure for updating the guidelines provided target users of the guideline are clearly defined guideline was piloted among target users patients' views and preferences were sought 	<ul style="list-style-type: none"> potential cost implications of applying the recommendation not described, but relative costs of different antiseptic solutions were considered
Queensland guideline, ¹¹ 2013 Australia	<ul style="list-style-type: none"> scope and purpose of the guidelines are clear the recommendations are specific and unambiguous health benefits, side effects and risks were stated in the recommendations target users of the guideline are clearly defined 	<ul style="list-style-type: none"> unclear whether the guideline was piloted among target users unclear whether patients' views and preferences were sought unclear about the method for searching for and selecting the evidence unclear about the methods used for formulating the recommendations. procedure for updating the guidelines not provided potential cost implications of applying the recommendation not included

Appendix 3: Main Study Findings and Authors' Conclusions

Table A3: Main Study Findings and Authors' Conclusions		
First Author, Publication Year	Main Study Findings	Authors' Conclusions
Research question 1 (comparative effectiveness and safety of chlorhexidine gluconate with alcohol versus other antiseptics for the prevention of infections associated with peripheral intravenous devices)		
No evidence found		
Research question 2 (cost-effectiveness of chlorhexidine gluconate with alcohol for the prevention of infections associated with peripheral intravenous devices)		
No evidence found		
Research question 3 (evidence-based guidelines for chlorhexidine gluconate with alcohol use for the prevention of infections associated with peripheral intravenous devices)		
NICE clinical guideline, ¹⁰ 2012	<i>"Decontaminate the skin at the insertion site with chlorhexidine gluconate in 70% alcohol before inserting a peripheral vascular access device or a peripherally inserted central catheter."</i> [new 2012] (p 24)	Not applicable
Queensland guideline, ¹¹ 2013	<i>"A solution containing 1-2% chlorhexidine gluconate (CHG) in ≥ 70% ethyl or isopropyl alcohol (alcoholic chlorhexidine) should be used by clinicians for preparation of the insertion site" "If CHG is contraindicated (e.g. sensitivity, allergy) clinicians should use povidone-iodine 10% in 70% ethyl alcohol (ethanol) (povidone-iodine should remain on the skin for at least 2 minutes and until dry before inserting the catheter)" "If alcohol contraindicated (e.g. allergy, sensitivity, skin condition) clinicians should use aqueous povidone-iodine 10%* or sterile normal saline 0.9% (*NB: the drying time for aqueous based antiseptics is longer than alcohol based products)."</i> (p 4)	Not applicable