



Centre for

CLINICAL EFFECTIVENESS

EVIDENCE CENTRE REPORT

REQUEST:

To assess the efficacy of various cutaneous antiseptics in the prevention of peripheral intravenous catheter related infection, including povidone iodine, 70% alcohol and chlorhexidine.

REQUEST MADE BY:

Ms. Melissa Aberline, infection control consultant at Monash Medical Centre, approached the Centre in October 1998 requesting a review of the evidence concerning the efficacy of various cutaneous antiseptics in preventing infection related to peripheral intravenous catheters.

DATE OF REPORT:

26 October 1998.

DISCLAIMER

The information in this report summarises the best available current evidence. It is primarily designed to give readers a starting point to consider the currently available research evidence. Readers should not use the comments made in isolation and should have read the literature suggested. Readers should also be aware that more appropriate research might have become available since the request was dealt with.

SUMMARY

On the basis of this review:

- Extensive guidelines on the prevention of intravascular device related infections were identified, published by the Centers for Disease Control and Prevention(CDC) in 1996. Only these and studies published since have been included in this report.
- The guidelines published by the CDC in 1996 report that skin cleansing/antiseptics of the insertion site is regarded as one of the most important measures for preventing catheter related infection. The CDC recommend the use of any of the following antiseptics; 70% alcohol, 10% povidone iodine, or 2% tincture of iodine.
- Some evidence exists to suggest that some antiseptics are more effective than others. The CDC guidelines state that one study showed that 2% aqueous chlorhexidine was superior to either 10% povidone iodine or 10% alcohol in preventing infection, however chlorhexidine was not included in the guidelines because it was not commercially available in the United States. One further study since then has shown that a new antiseptic solution containing 0.25% chlorhexidine gluconate in combination with 0.025% benzalkonium chloride and 4% benzyl alcohol was more effective than povidone iodine.
- Comparison between studies is limited by the wide variety of different antiseptic solutions used.

INTRODUCTION

Centre for Clinical Effectiveness

The Centre for Clinical Effectiveness exists to enhance patient outcomes through the clinical application of evidence-based research. The Public Health Division, Department of Human Services, Victoria, and the Southern Health Care Network fund the Centre. Amongst other programs, the Centre operates the Evidence Centre which accepts requests to identify and critically appraise the available evidence on particular clinical topics. The service operates for staff of the Southern Health Care Network, especially Program Directors, who will use the information provided to influence medical planning and decision-making.

SEARCH STRATEGY

Search terms

Procedure terms:	Catheterisation
Intervention terms:	Anti-Infective Agents, Local, Disinfectants, Chlorhexidine, Povidone Iodine, Alcohol, Propyl
Other terms:	Infection Control, Phlebitis, Catheter-Related Infection

REPORTING CONSTRAINTS

We have included only those reports whose full text, or English language abstract or translation, published since 1992 was available to us before 26 October 1998. There were no articles excluded because of arrival after this date. The search was limited to humans, and inpatients only. Material relating to letters to editors and short (<2 page length) reviews have not been included since these were assessed as offering no additional relevant information.

SEARCH RATIONALE

The Centre for Clinical Effectiveness Evidence Centre searches for best available evidence by a strategy that incorporates two factors:

1. A hierarchy that reflects methodological quality, that is the likelihood of systematic bias affecting the research results reported.
2. A desire to limit the amount material obtained if adequate, sound, research summaries already exist.

The Evidence Centre goes first to databases that enable us to identify systematic reviews, then evidence-based clinical practice guidelines or health technology assessments, then individual randomised controlled trials. If adequate, sound, summaries of the best evidence available are found in this way then individual research trials are not included in the report. If adequate summaries are not found our search strategy becomes considerably broader and may incorporate individual studies that may be more prone to bias, less generalisable, or have other difficulties identified through our critical appraisal of their methodology. For this reason, when citing research, we define the NHMRC Level of Evidence appropriate for each study.

LEVELS OF EVIDENCE

The quality of the evidence presented in this report was systematically assessed and classified according to the NHMRC's *Guidelines for the Development and Implementation of Clinical Practice Guidelines* (1995):

Level I	Evidence obtained from a systematic review or a meta-analysis of at least two relevant randomised controlled trials
Level II	Evidence obtained from at least one properly designed randomised controlled trial
Level III	Evidence from well designed controlled trials without randomisation, well-designed cohort or case-control analytic studies preferably from more than one centre or research group, or multiple time series with or without the intervention
Level IV	Opinions of respected authorities, based on clinical experience, descriptive studies or reports of expert committees

DATABASES

We searched the following databases and websites in this order:

Cochrane Library CD-ROM
 Best Evidence CD-ROM
 OVID Medline
 CINAHL
 NHS Centre for Reviews and Dissemination (NHS CRD)
 NHS Office for Health Technology Assessment
 International Network of Agencies for Health Technology Assessment (INAHTA)
 National Institutes of Health (NIH)

RESULTS

From these sources we identified, and appraised:

Evidence-based clinical practice guidelines	0
Non-evidence-based clinical development and use guidelines	1
Systematic reviews or meta-analyses	0
Randomised controlled trials	1
Well-designed controlled trials, cohort or case-control analytic studies	3
Concurrent comparisons	0
Descriptive case series	0
Consensus reports, narrative reviews	0

We are reasonably confident these figures represent the most important findings published to date by those considered experts in the field.

EVIDENCE SUMMARIES

FORMAT

Evidence Summaries are in the form of a one page spreadsheet. Each spreadsheet contains the article citation, the level of evidence available according to NHMRC guidelines (NHMRC, 1995), patient description, validity of the article, results and pertinent remarks from the authors and Centre for Clinical Effectiveness reviewer.

FINDINGS

The commentary below combines data from the Evidence Report Summary Tables to provide an integrated view of the selected best evidence relating to the use of cutaneous antisepsis in the prevention of intravascular device related infection.

Overall results

The CDC guidelines and the other articles included state that cutaneous antisepsis is important prior to insertion of peripheral intravenous catheters. It is difficult to definitely say which, if any, of the available antiseptics is most effective. The CDC guidelines recommend using either 70% alcohol, 10% povidone iodine, or 2% tincture of iodine. The guidelines state that 2% aqueous chlorhexidine has been shown to be superior to 10% povidone iodine or 10% alcohol in preventing central venous and arterial catheter related infection. It seems reasonable to assume that these results translate into prevention of peripheral catheter related infection. A small study of povidone iodine versus chlorhexidine gluconate solution and alcohol wipes in precannulation disinfection in haemodialysis patients (Wellard *et al.* 1996) found that there were no infections in either treatment group during the trial. Another small study (de Vries *et al.* 1997) compared skin disinfection by 70% alcohol with 2% iodine dissolved in 70% alcohol. Although the phlebitis rate was higher in the alcohol alone group, this did not reach statistical significance. A larger study (Mimoz *et al.* 1996) which concerned infections in central venous and arterial catheters, compared a new antiseptic solution 'Biseptine' (0.25% chlorhexidine, 0.025% benzalkonium chloride and 4% benzyl alcohol) with 10% povidone iodine. The 'Biseptine' group had less catheter colonisation and catheter related sepsis, which was related mainly to a decrease in gram positive infection. The final study was concerned with skin disinfection methods prior to blood donation and therefore does not relate specifically to intravenous catheters. The study showed that isopropyl alcohol in combination with tincture of iodine resulted in less bacterial

growth than povidone iodine. A combination of chlorhexidine and isopropyl alcohol resulted in similar amounts of bacterial growth.

Levels of evidence

Included in the report are five articles. The guidelines from the CDC are detailed and have extensive references to support the recommendations, however no details are provided on the search strategy, or on assessment of validity of the included articles. This means they must be classified as non-evidence based clinical practice guidelines which are NHMRC level IV evidence. The other studies include a randomised controlled trial (level II evidence) and three controlled trials (level III evidence).

Study numbers

The study numbers are small overall. No comment on study numbers was made in the CDC guidelines. The other studies add to a total of 484 patients.

Selection criteria

The selection criteria were generally broad. Most studies were concerned with all patients admitted to a certain ward over a certain time period. The study of haemodialysis patients excluded those with prosthetic arterio-venous fistulas, while the larger study of patients in intensive care (Mimoz *et al.* 1996) excluded those patients who had central lines inserted for long term total parenteral nutrition.

Research methodology

The CDC guidelines are extensive, and contain a large bibliography with over 400 references, however the methods used to search for the literature and appraise it are not described which means the guidelines represent level IV evidence. The study of ICU patients (Mimoz *et al.* 1996) was a well performed randomised controlled trial. There were some significant differences in the study populations, however these tended to favour the povidone iodine group and therefore the results which suggest that the other treatment was better are not affected. The study of haemodialysis patients (Wellard *et al.* 1996) was a 'reversal' type controlled trial, which means that both treatments were used on the same patients at different times. This increased the numbers in the treatment and control groups. The trial by de Vries *et al.* was a small randomised trial which had very limited power. The clinical assessment of phlebitis rate only may not be as accurate as colonisation/infection rates. The evaluation of blood donor skin disinfection methods (Goldman *et al.* 1997) was a non-randomised trial, with all subjects receiving standard disinfection of one cubital fossa and a study disinfection method on the other cubital fossa.

REFERENCES

Anonymous. Guideline for the prevention of intravascular device-related infections. Part I-II. *American Journal of Infection Control*. 1996; 24(4):262-293.

De Vries JH, van Dorp WT, van Barneveld PWC. A randomised trial of alcohol 70% versus alcoholic iodine 2% in skin disinfection before insertion of peripheral infusion catheters. *Journal of Hospital Infection*. 1997; 36(4):317-320.

Wellard S, Palaster L. An evaluation of two methods of pre-cannulation skin disinfection. *Australian Journal of Advanced Nursing*. 1996;14(1):3-7.

Mimoz O et al. Prospective, randomised trial of two antiseptic solutions for prevention of central venous or arterial catheter colonization and infection in intensive care unit patients. *Critical Care Medicine*. 1996.;24:1818-1823.

Goldman M, Roy G, Frechette N, Decary F, Massicotte L, Delage G. Evaluation of donor skin disinfection methods. *Transfusion*. 1997;37(3):309-312.

REFERENCES NOT INCLUDED (No new information)

Van Wijngaerden E, Bobbaers H. Intravascular catheter related bloodstream infection: epidemiology, pathogenesis and prevention. *Acta Clinica Belgica*. 1997; 52(1):9-18.

Anonymous. Management of peripheral intravascular devices. *Best Practice*. 1998; 2(1):1-6.

EVIDENCE REPORT SUMMARY TABLE	STUDY DESIGN & NHMRC LEVEL OF EVIDENCE	DESCRIPTION: Patients, Interventions, Comparisons, Outcomes. Inclusion & exclusion criteria.	VALIDITY: Methodology, rigour, selection, opportunities for bias.	RESULTS: Generally favourable or unfavourable, specific outcomes of interest, estimate of experimental effect and precision if appropriate	AUTHORS' COMMENTS: Risk/benefit; limitations	REVIEWERS' COMMENTS: Risk/benefit; methodology, conclusions
Wellard S., Palater L. An evaluation of two methods of pre-cannulation skin disinfection. <i>Aust.J.of Advanced Nursing</i> . 1996. 14(1);3-7.	Reversal design' controlled trial. Level III evidence.	<p>Patients: n=17, however this was reduced to 9. Patients were on haemodialysis and had an arm arterio-venous fistula. The total number of skin disinfection episodes was 971 for povidone iodine and 840 for chlorhexidine and alcohol wipes.</p> <p>Intervention: Pre AVF cannulation skin disinfection with povidone iodine vs. chlorhexidine gluconate solution and alcohol wipes. All patients received both treatments for two 3 month periods.</p> <p>Outcome: Skin inflammation, infection.</p> <p>Exclusions: Patients with prosthetic AVF's were excluded.</p>	<p>Randomisation: No-reversal design where all patients received both treatments at different times.</p> <p>Follow up: No details.</p> <p>Blinding: No.</p> <p>Similar groups: N/A</p> <p>Potential for bias: Small study, non-randomized.</p>	No skin inflammation/infection with either treatment regimen.	Neither method was shown to be a more effective skin disinfectant. Treatment with chlorhexidine gluconate was more acceptable to patients than with povidone iodine. The former method also produced less waste and was less expensive.	Small study which shows no difference between the treatment options.
de Vries JH. <i>et al.</i> A randomized trial of alcohol 70% versus alcoholic iodine 2% in skin disinfection before insertion of peripheral infusion catheters. <i>Journal of Hospital Infection</i> . 1997. 36(4);317-320.	Randomized trial. Level III evidence.	<p>Patients: n=109 patients admitted to the pulmonary ward of a teaching hospital for parenteral corticosteroid after exacerbation of asthma or COAD.</p> <p>Intervention: Skin disinfection with 70% alcohol (n=55) or 2% iodine dissolved in 70% alcohol (n=54) prior to insertion of a peripheral venous catheter.</p> <p>Outcome: Phlebitis.</p> <p>Exclusions: Previous skin reaction to one of the disinfectants.</p>	<p>Randomisation: Yes-using tables of random numbers.</p> <p>Follow up: 16 patients excluded from the study, because of accidental removal of the catheter or mechanical problems, dressings that did not fit the study criteria, or removal of catheter before an end point was reached. Followup for 96hrs..</p> <p>Blinding: Investigators were blinded.</p> <p>Similar groups: Yes</p> <p>Potential for bias: Assessment of phlebitis rate only. No assessment of infection/culture results. Small study with limited power.</p>	Absolute phlebitis rate was 6 in the alcohol group and 12 in the iodine group (not significant). This was described as a nonsignificant 53% RR reduction when using alcohol cf. alcoholic iodine.	The power of the study was only 0.55, meaning there was a 45% chance of missing a true difference. A larger trial seems warranted.	A number of different criteria were used to diagnose phlebitis. The major finding is that further study is required.

<p>Mimoz O. <i>et al.</i> Prospective, randomized trial of two antiseptic solutions for prevention of central venous or arterial catheter colonisation and infection in intensive care patients. <i>Crit. Care Med.</i> 1996. 24;1818-1823.</p>	<p>Randomised controlled trial. Level II evidence.</p>	<p>Patients: n=162 patients admitted to ICU over a 16 month period. The total number of catheters inserted in the study was 315. Intervention: Pre catheterization skin disinfection; 0.25% chlorhexidine gluconate, 0.025% benzalkonium chloride, 4% benzyl alcohol (Biseptine) vs. 10% povidone iodine. Outcome: Catheter colonization, catheter infection, and catheter related sepsis. Exclusions: Catheters inserted for long term TPN. Insertion prior to ICU admission. reinsertion over a guidewire.</p>	<p>Randomisation: Yes, into 2 groups Follow up: Until catheter removal, which was when they were no longer required, or if evidence of infection, or routinely after 7 days for arterial catheters and 15 days for CVC's. Blinding: No. Similar groups: No - the iodine group had less patients post abdominal surgery, but more trauma. The average length of hospitalization prior to catheter insertion was shorter for the iodine group.. Potential for bias: Differences in study populations, although they tended to favour the iodine group.</p>	<p>For catheter colonization (per 1000 catheter days); 'Biseptine' 12, povidone iodine 31 (95%CI 0.1-0.9). For catheter related sepsis (per 1000 catheter days); 'Biseptine' 6, povidone iodine 16 (95%CI 0.1-1). For bacteraemic catheter related sepsis (per 1000 catheter days); 'Biseptine' 3, povidone iodine 4 (95%CI 0.1-2.2). The increased efficacy of the chlorhexidine solution was mainly related to a decrease in gram +ve bacteria.</p>	<p>Our study shows that 'Biseptine' was more effective than 10% povidone iodine in preventing short term central venous and arterial catheter related sepsis and colonization.</p>	<p>The differences in the two groups probably favoured the iodine group, thereby not affecting the overall result.</p>
<p>Goldman M. <i>et al.</i> Evaluation of donor skin disinfection methods. <i>Transfusion.</i> 1997. 37(2);309-312.</p>	<p>Non-randomised controlled trial. Level III evidence.</p>	<p>Patients: n=196, blood donors and red cross personnel, divided into 3 groups. Intervention: Skin cultures were taken from both antecubital fossa of all patients. One antecubital fossa of all patients was disinfected with standard disinfection (pov.iodine swab stick with 0.75% iodine followed by swabstick with 1.0% iodine), the other with one of 3 other disinfection methods; 70% isopropyl alcohol scrub + 2% iodine tincture (n=126), green soap sponge + 70% isopropyl alcohol swab (n=30), 0.5% chlorhex. gluconate + 70% isopropyl alcohol sponge followed by 0.5% chlorhexidine gluconate and 70% isopropyl alcohol (n=40). Outcome: Antecubital fossa skin culture rates. Exclusions: None.</p>	<p>Randomisation: No. Follow up: N/A. Blinding: No. Similar groups: Yes Potential for bias: Not randomized, blinded. Possible inaccuracy of contact plate method.</p>	<p>Compared to the standard povidone iodine method, isopropyl alcohol and tincture of iodine resulted in less bacterial growth ($p < 0.001$), the green soap and isopropyl alcohol resulted in significantly more bacterial growth ($p < 0.001$), and the chlorhexidine and isopropyl alcohol resulted in similar amounts of bacterial growth.</p>	<p>Isopropyl alcohol scrub followed by tincture of iodine is more efficacious than povidone iodine as measured by contact plate cultures.</p>	<p>Small non-randomized study, however does suggest a difference in disinfection methods.</p>

EVIDENCE REPORT SUMMARY	STUDY DESIGN & NHMRC LEVEL OF EVIDENCE	DESCRIPTION: Patients, Interventions, Comparisons, Outcomes. Inclusion & exclusion criteria.	VALIDITY: Methodology, rigour, selection, opportunities for bias.	RESULTS: Generally favourable or unfavourable, specific outcomes of interest, estimate of experimental effect and precision if appropriate	AUTHORS' COMMENTS: Risk/benefit, limitations	REVIEWERS' COMMENTS: Risk/benefit, methodology, conclusions
<p>Anonymous. Guidelines for the prevention of intravascular device-related infection, parts I-II. <i>Am J of Infection Control</i> 1996. 24(4);262-293.</p>	<p>Consensus guidelines. Level IV evidence.</p>	<p>Patients with intravascular devices. Comparison of infection rate with the use of different cutaneous antiseptics, including 2% aqueous chlorhexidine, 10% povidone iodine, tincture of iodine and 70% alcohol.</p>	<p>Consensus guidelines from the Centers for Disease Control. Extensive bibliography with references to support most conclusions, but there is no description of searching strategy, or inclusion, exclusion criteria. There is no assessment of validity of the original studies. These are both significant potential biases and are the reason that these guidelines are only level IV evidence.</p>	<p>One trial showed that 2% aqueous chlorhexidine is superior to either 10% povidone iodine or 10% alcohol in preventing central venous or arterial catheter related infection, with an 84% lower catheter related blood stream infection rate. The guidelines stipulate the use of 70% alcohol, 10% povidone iodine, or 2% tincture of iodine prior to catheter insertion. The reason for lack of inclusion of 2% aqueous chlorhexidine in the guidelines was because it was not available in the US.</p>	<p>Skin cleansing/anti sepsis of the insertion site is regarded as one of the most important measures for preventing catheter related infection.</p>	<p>Extensive guidelines produced by the CDC, but the lack of study inclusion criteria and the lack of assessment of study validity mean that the evidence is only level IV. 2% chlorhexidine was described in the text as more effective than the other options, but in the guidelines there was no comment about this.</p>