

Use of chlorhexidine-impregnated dressing to prevent vascular and epidural catheter colonization and infection: a meta-analysis

Kwok M. Ho* and Edward Litton

Department of Intensive Care, Royal Perth Hospital, Perth 6000, Western Australia, Australia

Received 3 February 2006; returned 20 April 2006; revised 2 May 2006; accepted 12 May 2006

Objectives: Vascular and epidural catheter-related infections cause significant morbidities and mortality in hospitalized patients. This meta-analysis assessed the effect of chlorhexidine-impregnated dressing on the risk of vascular and epidural catheter bacterial colonization and infection.

Methods: Literature search was based on MEDLINE (1966 to 1 November 2005), EMBASE and Cochrane Controlled Trials Register (2005 issue 3) databases. Only randomized controlled clinical trials comparing chlorhexidine-impregnated dressing with placebo or povidine-iodine dressing were included in this meta-analysis. Two reviewers reviewed and extracted the data independently.

Results: Eight studies assessing a single type of chlorhexidine-impregnated dressing were identified and subjected to meta-analysis. The chlorhexidine-impregnated dressing reduced the risk of epidural [3.6% versus 35%, odds ratio (OR) 0.07, 95% CI: 0.02–0.31, $P = 0.0005$] and intravascular catheter or exit-site bacterial colonization (14.8% versus 26.9%, OR 0.47, 95% CI: 0.34–0.65, $P < 0.00001$) (overall 14.3% versus 27.2%, OR 0.40, 95% CI: 0.26–0.61; $P < 0.0001$). The use of chlorhexidine-impregnated dressing was associated with a trend towards reduction in catheter-related bloodstream or CNS infections (2.2% versus 3.8%, OR 0.58, 95% CI: 0.29–1.14, $P = 0.11$). Local cutaneous reactions to chlorhexidine-impregnated dressing were reported in 5.6% of the patients in three studies (OR 8.17, 95% CI: 1.19–56.14, $P = 0.04$), and 96% of these reactions occurred in neonatal patients. The number needed to prevent one episode of intravascular catheter-related bloodstream infection was 142 for an average period of catheter *in situ* of 10 days and a change of dressing every 5 days. The cost of preventing one vascular catheter-related bloodstream infection was estimated to be £298 (US\$532.5).

Conclusions: Chlorhexidine-impregnated dressing is effective in reducing vascular and epidural catheter bacterial colonization and is also associated with a trend towards reduction in catheter-related bloodstream or CNS infections. A large randomized controlled trial is needed to confirm whether chlorhexidine-impregnated dressing is cost-effective in preventing bacterial infection related to vascular and epidural catheters.

Keywords: infection control, antiseptics, disinfecting agents

Introduction

Intravascular and epidural catheters are commonly used in patients requiring anaesthesia. However, the devices used for vascular access or epidural analgesia can lead to serious infectious complications. Central vascular catheters (CVCs) are the most frequent source of nosocomial bloodstream infection, and between 250 000 and 500 000 episodes occur in the United States annually.^{1,2} Each of these episodes is associated with a 20–25% attributable mortality.¹ Infections related to epidural catheters are

less common than those related to vascular catheters.³ Nevertheless, serious consequences including permanent neurological deficits can occur if an epidural catheter is complicated by an epidural abscess.⁴

Chlorhexidine gluconate solution is an antimicrobial agent used for disinfecting skin surfaces and has been used widely as a surgical scrub, hand wash and skin disinfectant with good safety profile.⁵ Most catheter-related bloodstream infections with short-term percutaneously inserted, non-cuffed CVCs are extraluminally acquired and derived from the cutaneous microflora such

*Correspondence address. Intensive Care Unit, Royal Perth Hospital, Perth, WA 6000, Australia. Tel: +61-8-92241056; E-mail: kwok.ho@health.wa.gov.au

as coagulase-negative staphylococcus.⁶ Chlorhexidine gluconate has a strong activity against this organism and using chlorhexidine gluconate to disinfect the insertion site before vascular catheterization is more effective than povidine-iodine solutions in reducing catheter-related bloodstream infections.⁷ A novel dressing device consisting of hydrophilic polyurethane absorptive foam impregnated with chlorhexidine gluconate (Biopatch™, Antimicrobial Dressing, Johnson & Johnson Wound Management, Ethicon, Inc., Somerville, NJ, USA) has been shown to release chlorhexidine gluconate onto the underlying skin surface over a 10 day period when placed over the catheter exit-site.⁵ Biopatch™ is the only chlorhexidine-impregnated dressing available and *in vitro* assessment showed that this device has significant antimicrobial effect against antibiotic-resistant *Staphylococcus*, *Enterococcus* species and *Candida* species.⁸ However, the use of chlorhexidine-impregnated dressing device is not a standard practice to prevent vascular and epidural catheter colonization and infection in many institutions. Whether this device should be routinely used in the care of short-term vascular catheters remained unresolved in the latest issue of Centers for Disease Control and Prevention Guidelines for the prevention of intravascular catheter-related infections.⁹ As CVCs remain a major cause of nosocomial bloodstream infection in most institutions, we assessed whether the use of chlorhexidine-impregnated dressing could reduce the risk of vascular and epidural catheter colonization and infection in this meta-analysis.

Materials and methods

Literature search was based on MEDLINE (1966 to 1 November 2005), EMBASE and Cochrane Controlled Trials Register (2005 issue 3) databases. Only randomized controlled clinical trials comparing chlorhexidine-impregnated dressing with either placebo or povidine-iodine dressing were included in this meta-analysis. Animal and volunteer studies were excluded in this meta-analysis. During the electronic database search, the following exploded MeSH terms were used: 'biopatch', 'chlorhexidine', 'disinfectant', or 'antiseptic' with 'dressing*', and 'sponge' with 'catheter'. The reference lists of related reviews and identified original articles were checked for relevant trials. Finally, the web sites of International Network of Agencies of Health Technology Assessment and International Society of Technology Assessment in Health Care and the manufacturer of chlorhexidine-impregnated dressings (<http://www.jnj.com>) were searched. The manufacturer (<http://www.jnj.com>) was also contacted to obtain more unpublished data that evaluated chlorhexidine-impregnated dressings but the manufacturer did not reply to our request. The authors of one of the pooled studies gave additional unpublished data that were important in the data analysis.¹⁰ No studies published in languages other than English were identified in this meta-analysis. Two independent reviewers examined the titles and the abstracts of all identified trials to confirm they had fulfilled the above defined inclusion criteria. They examined and recorded the trial characteristics and outcomes independently, using a pre-designed article abstraction form. This abstraction form was used to record information regarding the quality of the trial such as allocation concealment, randomization method, blinding of treatment, and inclusion and exclusion criteria. The quality of the study was assessed by the individual component that constitutes the quality of the study. The grading of allocation concealment was based on the Cochrane approach, i.e. adequate or uncertain or clearly inadequate. Articles that fulfilled the inclusion criteria were analysed further for data extraction. Two reviewers extracted the data

independently and the results were checked for consistency. Any duplicated publications were combined to represent one single trial. Data were checked and entered into Review Manager (version 4.1 for Windows, Oxford, England: The Cochrane Collaboration, 2003) database by two independent reviewers.

Statistical analysis

The two main outcomes of this meta-analysis were the proportion of patients with either exit-site or catheter colonized with bacteria and systemic infections such as bloodstream and CNS infection related to a vascular catheter and an epidural catheter, respectively. Systemic infection related to either vascular or epidural catheters is more specific but less sensitive than colonization of the catheter.¹¹ Local inflammation at the insertion site was not chosen as an end point because the majority of catheter-related infections are caused by coagulase-negative staphylococci, a pathogen that incites little local or systemic inflammation.¹ Local and systemic adverse reactions to chlorhexidine-impregnated dressing were recorded if available. All categorical end points were reported as odds ratio (OR) with 95% confidence interval, using a random effect model. The effect of chlorhexidine-impregnated dressing on the proportion of patients with catheter colonized with bacteria and catheter-related systemic infections were further stratified into studies assessing epidural or vascular catheters and the interaction was tested by ratio of the ORs.¹² The presence of heterogeneity between trials was assessed by the χ^2 statistics and the extent of inconsistency¹³ was assessed by I^2 . A P value <0.05 was regarded as significant and a P value <0.15 was regarded as a trend in the present study.

Sensitivity analyses were conducted by excluding one study that compared two different methods of catheter exit-site care (weekly chlorhexidine gluconate-impregnated dressing change versus twice weekly povidine-iodine dressing change) and also by excluding one study that evaluated the effectiveness of chlorhexidine-impregnated dressing on long-term tunnelled intravascular catheters. Publication bias was assessed by funnel plot using catheter-related systemic infections as an end point.

Results

We identified 10 potentially eligible studies of which 8 studies^{5,9,14–19} fulfilled the inclusion criteria and were subjected to meta-analysis (Figure 1). All the pooled studies assessed a single type of chlorhexidine-impregnated dressing (Biopatch™, Antimicrobial Dressing, Johnson & Johnson Wound Management, Ethicon, Inc., Somerville, NJ, USA). Two studies were excluded because they were based on the results of another study that was pooled in this meta-analysis,¹⁹ one study was a subgroup analysis²⁰ and the other one was a cost-benefit analysis.²¹ Seven studies compared chlorhexidine-impregnated dressing with placebo, and weekly chlorhexidine-impregnated dressing change was compared with twice weekly povidine-iodine dressing change in one study.¹⁵ The duration of the intravascular or epidural catheters *in situ* varied between studies but was similar between the treatment and controlled arm in all the included studies. There was significant heterogeneity between the participants of the studies. Three studies evaluated elective surgical patients and one study included only haematological patients. Two studies included critically ill paediatric or neonatal patients and one study included only critically ill adult patients. Three studies reported the number of catheters colonized with bacteria and the episodes of catheter-related bloodstream infection

Systematic review

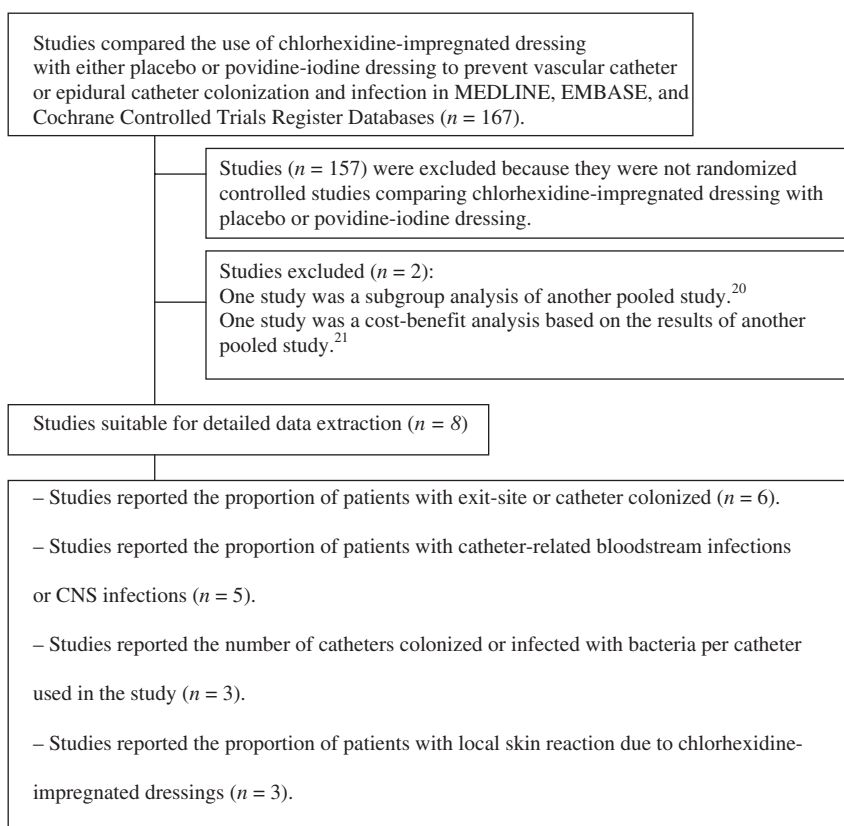


Figure 1. Flow chart showing study inclusion and exclusion in this meta-analysis.

per catheter used, and the data of these three studies were pooled with other studies that assessed the number of catheters colonized and episodes of catheter-related bloodstream infection *per patient* in the forest plots. Allocation concealment was adequate in five studies but none of the studies was double blinded. There was no disagreement between two reviewers to be resolved by consensus. Four studies were funded by the company that manufactures the chlorhexidine-impregnated device.^{14,15,18,19} The details of the included studies are described in Table 1.

Chlorhexidine-impregnated dressing reduced the risk of epidural [3.6% versus 35%, OR 0.07, 95% CI: 0.02–0.31, $P = 0.0005$] and intravascular catheter or exit-site bacterial colonization (14.8% versus 26.9%, OR 0.47, 95% CI: 0.34–0.65, $P < 0.00001$) (overall 14.3% versus 27.2%, OR 0.40, 95% CI: 0.26–0.61; $P < 0.0001$) (Figure 2). The protective effect of chlorhexidine-impregnated dressing against bacterial colonization was stronger for epidural catheter than vascular catheter (ratio of ORs 0.17, 95% CI: 0.06–0.50, $P = 0.001$). Chlorhexidine-impregnated dressing was associated with a trend towards reduction in catheter-related bloodstream or CNS infections (overall 2.2% versus 3.8%, OR 0.58, 95% CI: 0.29–1.14, $P = 0.11$, $I^2 = 30.2\%$) (Figure 3) when the results of both epidural (OR 0.17, 95% CI: 0.01–3.63, $P = 0.25$) and vascular catheters (OR 0.61, 95% CI: 0.30–1.26, $P = 0.19$, $I^2 = 38.3$) were pooled. Local cutaneous reactions to chlorhexidine-impregnated dressing were reported in 5.6% of the patients in three studies (OR 8.17, 95% CI: 1.19–56.14, $P = 0.04$), and 96% of these reactions occurred in the neonatal patients. No significant systemic adverse events were reported in the pooled studies.

Sensitivity analyses

After excluding the study that compared twice weekly povidine-iodine dressing change with weekly chlorhexidine-impregnated dressing change,¹⁵ the use of chlorhexidine-impregnated dressing was associated with a significant reduction in catheter-related bloodstream infection when compared with placebo (OR 0.40, 95% CI: 0.21–0.75, $P = 0.004$). Excluding the data of the largest study¹⁹ did not change the effect of chlorhexidine-impregnated dressing on the risk of catheter colonization (OR 0.30, 95% CI: 0.15–0.62, $P = 0.001$) but reduced the magnitude of its protective effect on catheter-related bloodstream infections (OR 0.74, 95% CI: 0.34–1.61, $P = 0.45$). Similarly, excluding the only study that evaluated tunnelled intravascular catheters did not change the magnitude and direction of the results.¹⁷

Discussion

The present meta-analysis demonstrated that chlorhexidine-impregnated dressing is effective in reducing the bacterial colonization of vascular and epidural catheters. Its use is also associated with a trend towards reduction in systemic infections related to these catheters. Furthermore, this protective effect becomes statistically significant if the study comparing chlorhexidine-impregnated dressing with twice weekly povidine-iodine exit-site dressing is excluded. Local cutaneous reactions due to chlorhexidine-impregnated dressing are very uncommon and occur mainly in the neonatal patients.

This meta-analysis showed that chlorhexidine-impregnated dressing was effective in reducing infective complications of

Table 1. Characteristics of the included studies

Study	Participants	Comparison group	Outcome assessment	Allocation concealment, blinding, loss to follow-up, intention to treat analysis
Shapiro <i>et al.</i> , 1990	57 patients who required an epidural catheter for surgery, mean duration of the catheter <i>in situ</i> was 3.7 days	sterile support pad without chlorhexidine-impregnated dressing underneath it	number of colonized epidural catheters when they were removed	adequate allocation concealment, unclear blinding, unclear per cent loss to follow-up, intention to treat (unclear)
Hanazaki <i>et al.</i> , 1999	50 patients who required a central venous catheter for abdominal surgery, duration of catheter <i>in situ</i> not available	transparent film dressing without the chlorhexidine-impregnated dressing	number of patients with the exit-site colonized with bacteria (swabs taken on a weekly basis)	adequate allocation concealment, no blinding, no loss to follow-up, intention to treat (yes)
Mann <i>et al.</i> , 2001	74 patients who required an epidural for gynaecological surgery, mean duration of the catheter <i>in situ</i> was 3.5 days	transparent film dressing without the chlorhexidine-impregnated dressing	number of patients with exit-site colonized with bacteria when the epidural catheter was removed and the number of patients with signs and symptoms of CNS infection requiring antibiotic treatment	adequate allocation concealment, no blinding, 26% loss to follow-up (catheter removed without exit-site swab taken), intention to treat (no)
Garland <i>et al.</i> , 2001	705 neonates from 6 neonatal intensive care units, mean duration of the catheter <i>in situ</i> was 17 days	twice weekly povidine-iodine dressing change as compared with weekly change of chlorhexidine-impregnated dressing change	number of patients with the central venous catheter colonized (≥ 15 cfu) and number of patients with catheter-related bloodstream infection (catheter and blood culture with the same organism)	adequate allocation concealment, no blinding, 2% loss to follow-up (catheter not cultured), intention to treat (yes)
Levy <i>et al.</i> , 2005	166 infants and children (0–18 years old) from a paediatric cardiac intensive care unit, mean duration of the catheter <i>in situ</i> was 4.5 days	transparent film dressing without the chlorhexidine-impregnated dressing	number of patients with at least one segment of the central venous catheter colonized (>15 cfu) and number of patients with catheter-related bloodstream infections (same organism isolated from blood and the catheter)	adequate allocation concealment, no blinding, 12.7% loss to follow-up (catheter removed without cultured), intention to treat (no)
Chambers <i>et al.</i> , 2005	95 patients who required tunnelled intravascular catheter for chemotherapy in a haematology unit, median duration of the catheter <i>in situ</i> was 67 days	sterile gauze and porous adhesive dressing till dry and free from ooze and then received no dressing	number of patients with the exit-site infection with positive culture of the exit-site and the number of patients with catheter-related bloodstream infections (same organism isolated from the catheter and the blood)	unclear allocation concealment, no blinding, 1.8% loss to follow-up (transferred to another hospital), intention to treat (no)
Roberts <i>et al.</i> , 1998	40 critically ill patients who had a central venous catheter, mean duration of the catheter <i>in situ</i> was 7.5 days	sterile dressing and cleaning the insertion site with 0.5% chlorhexidine in 70% alcohol every 5 days	number of patients with exit-site colonization and catheter-related bloodstream infection (same organism isolated from exit-site and blood culture)	unclear allocation concealment, no blinding, 17.5% loss in follow-up, intention to treat (no)
Maki <i>et al.</i> , 2000	unknown exact number of patients but 1401 catheters (central venous, pulmonary artery or peripheral arterial catheters) were recruited, mean duration of the catheter <i>in situ</i> not reported	transparent film dressing	number of catheters colonized (≥ 15 cfu) and number of episodes of catheter-related bloodstream infections per catheter used	unclear allocation concealment, probably not blinded, loss to follow-up not reported, intention to treat (not clear)

Systematic review

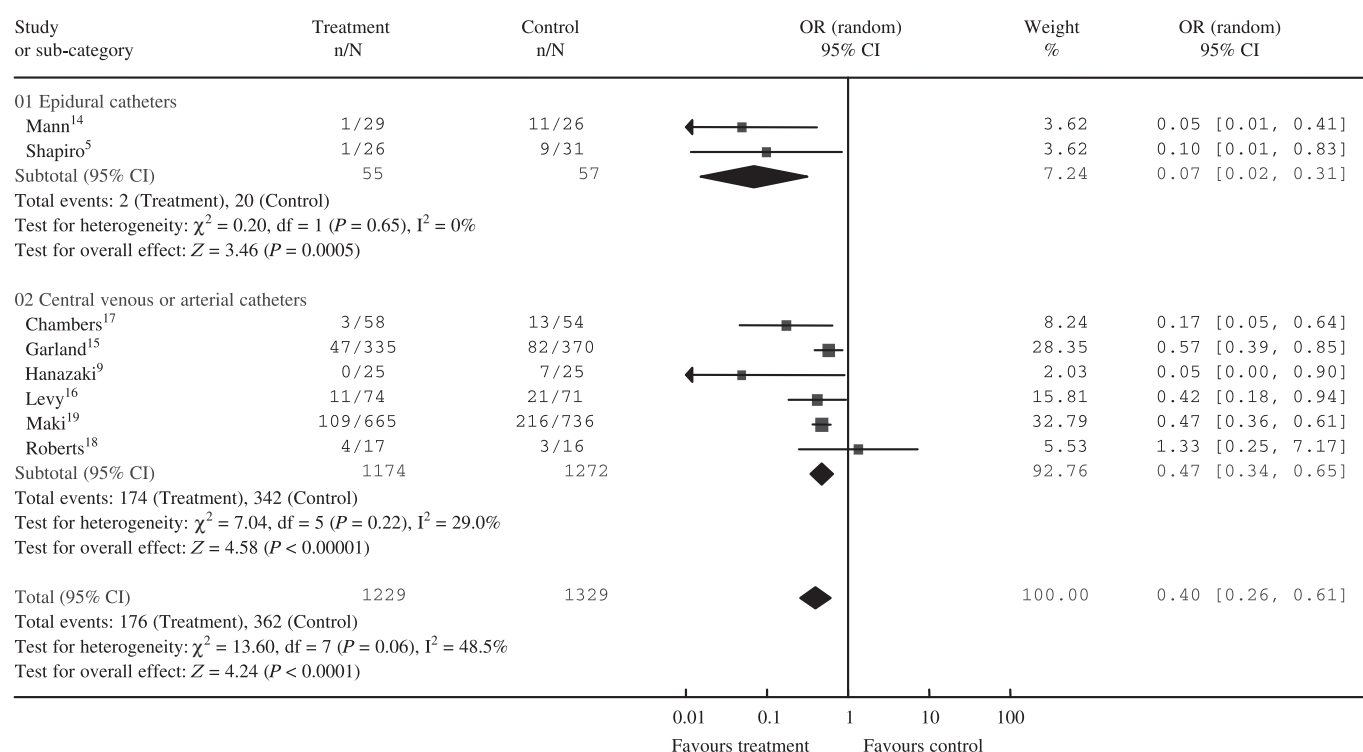


Figure 2. Forest plot showing the effect of chlorhexidine-impregnated dressing on bacterial colonization of the catheter or exit-site on skin.

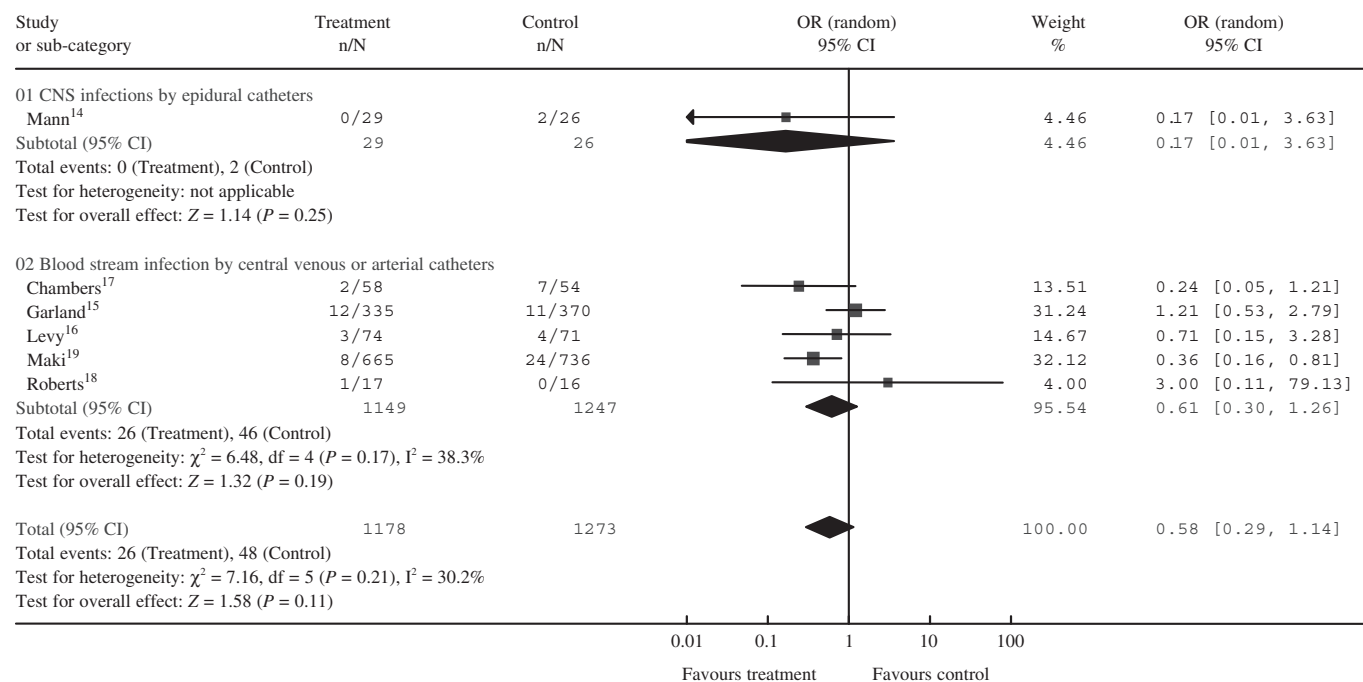


Figure 3. Forest plot showing the effect of chlorhexidine-impregnated dressing on bacteraemia and CNS infection related to vascular and epidural catheter, respectively.

the vascular and epidural catheters. Although there was significant heterogeneity in the magnitude of protective effect across the included studies and also between epidural or vascular catheters, the positive protective effect of chlorhexidine-impregnated

dressing was largely consistent in most studies. Previous studies showed that colonization of vascular catheters is strongly associated with subsequent bloodstream infection,¹¹ and such colonization of the catheter may represent an important intermediate

Systematic review

step towards subsequent bloodstream infections if the catheter is left *in situ* after being colonized.⁶ The stronger protective effect of chlorhexidine-impregnated dressing on the risk of catheter colonization (OR 0.40) than bloodstream or CNS infections (OR 0.58) as demonstrated in this meta-analysis is concordant with this hypothesis.

The proportion of patients with vascular catheter-related bloodstream infections in the placebo and treatment arm of the pooled intravascular catheter studies was about 3.7% (46/1247) and 2.3% (26/1149), respectively. The incidence of the catheter-related bloodstream infections in the placebo arm of this meta-analysis is consistent with the data from other studies.²² As the efficacy of the chlorhexidine-impregnated dressing varies outside a pH range of 5.5–7.0, a change of the dressing may be necessary after every 5 days if the device is soaked with wound exudate or excessive moisture. The estimated number of chlorhexidine-impregnated dressings needed to prevent one episode of intravascular catheter-related bloodstream infection was therefore estimated to be 142 [$100 \times 2/(3.7-2.3\%)$] if an average period of the vascular catheter *in situ* is 10 days and with a change of dressing every 5 days. The cost of each chlorhexidine-impregnated dressing is £2.1 (US \$3.75) and the cost of preventing one vascular catheter-related bloodstream infection would be £298 (US \$532.5). This is significantly cheaper than the cost of treating one episode of catheter-related bloodstream infection (£16 800 or US \$30 000)²³ and hence the use of chlorhexidine-impregnated dressing is very cost-effective. In fact, if we assume that the attributable mortality of an episode of catheter-related bloodstream infection is 20%,¹ the cost of using chlorhexidine-impregnated dressing to save one life will only be £1491 (US \$2663). Sensitivity analyses with different baseline rates and cost of treating one episode of catheter-related bloodstream infection reported by another study confirmed that chlorhexidine-impregnated dressing can reduce overall healthcare cost and hospital mortality if the device is used routinely in all patients with a vascular catheter.²¹ These results suggest that adding chlorhexidine-impregnated dressing to the usual transparent film or sterile gauze dressing for CVCs is likely to be beneficial and cost-effective.²⁴

The incidence of side effects of chlorhexidine-impregnated dressing was low (5.6%) and the local cutaneous reaction occurred mainly in the neonatal patients.^{15,16} Systemic adverse reactions to chlorhexidine were not reported in any of the pooled studies although anaphylactic reactions to chlorhexidine-impregnated CVCs have been reported from the Netherlands, Australia and Japan (~1 case per 9000 catheters placed in Japan).^{25,26} Induction of resistance to chlorhexidine in an isolate of *Pseudomonas stutzeri in vitro* has been reported²⁷ but there was no evidence of inducing chlorhexidine resistance in the susceptibility testing of the bacterial isolates from two of the pooled studies.^{17,19,25} Whether severe systemic reactions to chlorhexidine or bacterial resistance to chlorhexidine will become more apparent when chlorhexidine-impregnated dressings are widely used remains uncertain.

There are a few limitations with this meta-analysis. First, meta-analysis is prone to bias. In order to avoid selection bias, we have used three databases in the literature search without any language restriction. The symmetrical distribution of the study results around the overall estimate suggested that publication bias was unlikely to be a major problem (Figure 4). However, there were only two small studies assessing the effect

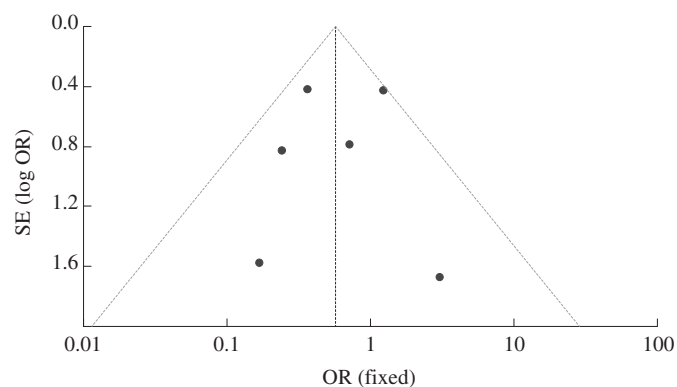


Figure 4. Funnel plot showing the absence of significant publication bias using systemic infections related to either the epidural or vascular catheter as an end point.

of chlorhexidine-impregnated dressing on the risk of epidural catheter colonization and infection. While the results of these two studies were consistent with results of other studies that assessed vascular catheters, the cost-effectiveness could be very different because the incidence of epidural-related CNS infections is much lower than vascular catheter-related bloodstream infections.⁴ Furthermore, the sample size of this meta-analysis ($n = 2396$ for vascular catheters) is still too small to confirm a statistically significant reduction in catheter-related bloodstream infections in patients treated with the chlorhexidine-impregnated dressing. A sample size of 4380 will be needed to confirm a 40% relative risk reduction in catheter-related bloodstream infection if the baseline risk of catheter-related bloodstream infection is 3.7%. Therefore, a large prospective randomized controlled study is needed to confirm the cost-effectiveness of chlorhexidine-impregnated dressing in reducing infections related to epidural and vascular catheters. Second, four studies were funded by the company that manufactured the chlorhexidine-impregnated device and also none of the included studies was double blinded. These could have introduced potential bias in the results of the studies. Third, the site of the intravascular catheter insertion was not specified in most studies and this could be a potential significant confounder if there were significant differences in the sites of catheter insertion between the treatment and placebo group.²⁸ Fourth, the largest study pooled in this meta-analysis was published in an abstract form only. Some additional data were available from reviews published by the same group of investigators but detailed assessment of the study was limited. Nevertheless, the magnitude and direction of the results on colonization of the catheters remained unchanged after excluding this study. Finally, a new slow silver-releasing catheter dressing device (Silverlon[®]) is now available.²⁹ A direct comparison of this new silver-releasing device with chlorhexidine-impregnated dressing in a large randomized controlled study is needed to confirm which device is more cost-effective.

In conclusion, chlorhexidine-impregnated dressing is effective in reducing vascular and epidural catheter bacterial colonization and is associated with a trend towards reduction in catheter-related bloodstream or CNS infections. Use of chlorhexidine-impregnated dressing is safe and may be cost-effective in adult patients with a vascular catheter. A large randomized

controlled trial is needed to confirm whether chlorhexidine-impregnated dressing is cost-effective in preventing bacterial infection related to vascular and epidural catheters.

Acknowledgements

We thank Dr Hanazaki for providing additional information from his original study. Support of this study was provided solely from the Department of Intensive Care, Royal Perth Hospital.

Transparency declarations

None of the authors has any conflict of interest with pharmaceutical or other commercial companies that have produced drugs or equipment mentioned in this meta-analysis.

References

1. Safdar N, Maki DG. Inflammation at the insertion site is not predictive of catheter-related bloodstream infection with short-term, noncuffed central venous catheters. *Crit Care Med* 2002; **30**: 2632–5.
2. Safdar N, Kluger DM, Maki DG. A review of risk factors for catheter-related bloodstream infection caused by percutaneously inserted, noncuffed central venous catheters: implications for preventive strategies. *Medicine (Baltimore)* 2002; **81**: 466–79.
3. Wang LP, Hauerberg J, Schmidt JF. Incidence of spinal epidural abscess after epidural analgesia: a national 1-year survey. *Anesthesiology* 1999; **91**: 1928–36.
4. Wang LP, Hauerberg J, Schmidt JF. Long-term outcome after neurosurgically treated spinal epidural abscess following epidural analgesia. *Acta Anaesthesiol Scand* 2001; **45**: 233–9.
5. Shapiro JM, Bond EL, Garman JK. Use of a chlorhexidine dressing to reduce microbial colonization of epidural catheters. *Anesthesiology* 1990; **73**: 625–31.
6. Safdar N, Maki DG. The pathogenesis of catheter-related bloodstream infection with noncuffed short-term central venous catheters. *Intensive Care Med* 2004; **30**: 62–7.
7. Chaiyakunapruk N, Veenstra DL, Lipsky BA *et al*. Chlorhexidine compared with povidone-iodine solution for vascular catheter-site care: a meta-analysis. *Ann Intern Med* 2002; **136**: 792–801.
8. Bhende S, Spangler D. *In vitro* assessment of chlorhexidine gluconate-impregnated polyurethane foam antimicrobial dressing using zone of inhibition assays. *Infect Control Hosp Epidemiol* 2004; **25**: 664–7.
9. O'Grady NP, Alexander M, Dellinger EP *et al*. Guidelines for the prevention of intravascular catheter-related infections. *Infect Control Hosp Epidemiol* 2002; **23**: 759–69.
10. Hanazaki K, Shingu K, Adachi W *et al*. Chlorhexidine dressing for reduction in microbial colonization of the skin with central venous catheters: a prospective randomized controlled trial. *J Hosp Infect* 1999; **42**: 165–8.
11. Rijnders BJ, Van Wijngaerden E, Peetermans WE. Catheter-tip colonization as a surrogate end point in clinical studies on catheter-related bloodstream infection: how strong is the evidence? *Clin Infect Dis* 2002; **35**: 1053–8.
12. Altman DG, Bland JM. Interaction revisited: the difference between two estimates. *BMJ* 2003; **326**: 219.

13. Higgins JP, Thompson SG, Deeks JJ *et al*. Measuring inconsistency in meta-analyses. *BMJ* 2003; **327**: 557–60.
14. Mann TJ, Orlikowski CE, Gurrin LC *et al*. The effect of the biopatch, a chlorhexidine impregnated dressing, on bacterial colonization of epidural catheter exit sites. *Anaesth Intensive Care* 2001; **29**: 600–3.
15. Garland JS, Alex CP, Mueller CD *et al*. A randomized trial comparing povidone-iodine to a chlorhexidine gluconate-impregnated dressing for prevention of central venous catheter infections in neonates. *Pediatrics* 2001; **107**: 1431–6.
16. Levy I, Katz J, Solter E *et al*. Chlorhexidine-impregnated dressing for prevention of colonization of central venous catheters in infants and children: a randomized controlled study. *Pediatr Infect Dis J* 2005; **24**: 676–9.
17. Chambers ST, Sanders J, Patton WN *et al*. Reduction of exit-site infections of tunnelled intravascular catheters among neutropenic patients by sustained-release chlorhexidine dressings: results from a prospective randomized controlled trial. *J Hosp Infect* 2005; **61**: 53–61.
18. Roberts B, Cheung D. Biopatch—a new concept in antimicrobial dressings for invasive devices. *Aust Crit Care* 1998; **11**: 16–9.
19. Maki DG, Mermel LA, Kluger D *et al*. The efficacy of a chlorhexidine-impregnated sponge (Biopatch) for the prevention of intravascular catheter-related infection- a prospective, randomized, controlled, multi-center study. In: *Programs and Abstracts of the Fortieth Interscience Conference on Antimicrobial Agents and Chemotherapy, Toronto, 2000*. Abstract 1430, p. 422. American Society for Microbiology, Washington, DC, USA.
20. Safdar N, Maki DG. Risk of catheter-related bloodstream infection with peripherally inserted central venous catheters used in hospitalized patients. *Chest* 2005; **128**: 489–95.
21. Crawford AG, Fuhr JP Jr, Rao B. Cost-benefit analysis of chlorhexidine gluconate dressing in the prevention of catheter-related bloodstream infections. *Infect Control Hosp Epidemiol* 2004; **25**: 668–74.
22. Laupland KB, Zygun DA, Davies HD *et al*. Population-based assessment of intensive care unit-acquired bloodstream infections in adults: incidence, risk factors, and associated mortality rate. *Crit Care Med* 2002; **30**: 2462–7.
23. Pittet D, Hulliger S, Auckenthaler R. Intravascular device-related infections in critically ill patients. *J Chemother* 1995; **7** Suppl 3: 55–66.
24. Gillies D, O'Riordan E, Carr D *et al*. Central venous catheter dressings: a systematic review. *J Adv Nurs* 2003; **44**: 623–32.
25. Crnich CJ, Maki DG. The promise of novel technology for the prevention of intravascular device-related bloodstream infection. I. Pathogenesis and short-term devices. *Clin Infect Dis* 2002; **34**: 1232–42.
26. US Food and Drug Administration, Centers for Devices and Radiological Health. *Potential Hypersensitivity Reactions to Chlorhexidine-impregnated Devices: FDA Public Health Notice*. Washington, DC, US Food and Drug Administration. <http://www.fda.gov/cdrh/chlorhex.html> (1 May 2006, date last accessed).
27. Tattawasart U, Hann AC, Maillard JY *et al*. Cytological changes in chlorhexidine-resistant isolates of *Pseudomonas stutzeri*. *J Antimicrob Chemother* 2000; **45**: 145–52.
28. Merrer J, De Jonghe B, Golliot F *et al*. Complications of femoral and subclavian venous catheterization in critically ill patients: a randomized controlled trial. *JAMA* 2001; **286**: 700–7.
29. Silverlon® iv catheter wound dressings. Available at: <http://www.silverlon.com> (1 May 2006, date last accessed).