Chapter 16. Prevention of Intravascular Catheter-Associated Infections

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Background

Central venous catheters inserted for short-term use have become common and important devices in caring for hospitalized patients, especially the critically ill.[1] While they have important advantages (eg, ability to administer large volumes of fluid), short-term vascular catheters are also associated with serious complications, the most common of which is infection. Intravascular catheters are one of the most common causes of nosocomial bacteremia;[2] and catheter-related bloodstream infection (CR-BSI) affects over 200,000 patients per year in the United States.[3] This chapter focuses primarily on short-term central venous catheters. Two relatively recent reviews address prevention of infection due to other types of vascular catheters.[4,5] We review use of maximum barrier precautions (Subchapter 16.1), central venous catheters coated with antibacterial or antiseptic agents (Subchapter 16.2), and use of chlorhexidine gluconate at the insertion site (Subchapter 16.3). We review several promising practices, as well as some common ineffective practices (Subchapter 16.4).

Definitions and Microbiology

Catheter-related infections can be subdivided into those that are local and those that are bacteremic. Local infection involves only the insertion site and manifests as pericatheter skin inflammation. *Local infection* is usually diagnosed when there is evidence of an insertion-site infection (eg, purulence at the exit site). *Catheter colonization* is defined by growth of an organism from the tip or the subcutaneous segment of the removed catheter. Growth of greater than 15 colony-forming units (CFU) using the semiquantitative roll-plate culture technique is often used to define catheter colonization.[6] Alternatively, the presence of more than 1000 CFUs per catheter tip segment by quantitative culture using a method such as sonication indicates evidence of catheter colonization.[7] Signs of local infection may or may not be present when there is significant catheter colonization; evidence of local infection is observed in at least 5% of patients with catheter colonization.

Bacteremic catheter-related infection (often also referred to as CR-BSI) is defined as a positive blood culture with clinical or microbiologic evidence that strongly implicates the catheter as the source of infection.[1] This includes: 1) evidence of local infection with isolation of the same organism from both pus around the site and bloodstream; or 2) positive cultures of both the catheter tip (using either semi-quantitative or quantitative methods) and bloodstream with the same organism; or 3) clinical evidence of sepsis (eg, fever, altered mental status, hypotension, leukocytosis) that does not respond to antibiotic therapy, but resolves once the catheter is removed.[1,5] Some have proposed additional methods of diagnosing CR-BSI, including paired blood cultures (drawn from both the central venous catheter and from a noncatheterized vein)[8] and a technique in which time to culture positivity for blood drawn from the central venous catheter is compared with that for the blood drawn from percutaneous venipuncture.[9]

The most common organisms causing catheter-related infections are staphylococci, gram negative rods, and *Candida* species.[10,11] The pathophysiology of these infections include several mechanisms, the most important of which involve the skin insertion site and the catheter hub.[1] Bacteria migrate from the insertion site on the skin along the external surface of the catheter and

then colonize the distal tip.[12,13] The hub can also lead to infection when bacteria are introduced via the hands of medical personnel. These organisms then migrate along the internal surface of the lumen and may result in bacteremia.[14]

Less commonly, catheter-related infection can result from hematogenous seeding of the catheter from another focus[15] or from contaminated infusates.[16]

Prevalence and Severity of the Target Safety Problem

A recent quantitative review found that of patients in whom standard, non-coated central venous catheters are in place on average for 8 days, 25% can be expected to develop catheter colonization and 5% will develop CR-BSI.[17] The risk of CR-BSI from this estimate is similar to the rate reported by the Federal Centers for Disease Control and Prevention (CDC). The CDC has reported an average CR-BSI rate of 2.8 to 12.8 infections per 1000 catheter-days for all types of intensive care units and average rates of 4.5 to 6.1 infections per 1000 catheter-days for medical/surgical intensive care units.[18]

CR-BSI is associated with an increased risk of dying, but whether this association is causal remains controversial.[17] Some argue that hospitalized patients who develop CR-BSI may differ in their clinical and physiologic characteristics, and thus may have a higher risk of dying due to intrinsic factors. Proponents of this view believe that the development of CR-BSI is primarily a marker of severe underlying disease or deficient immunity rather than an independent risk factor for dying. Unfortunately, the few studies evaluating attributable mortality due to CR-BSI have conflicting results.

Pittet and colleagues estimated that the attributable mortality of CR-BSI was 25% in a matched case-control study.[19,20] Another matched study estimated that the attributable mortality was 28%.[21] Other investigators have found a much smaller attributable mortality associated with CR-BSI. DiGiovine et al, in a matched case-control study of 136 medical intensive care unit patients, found a non-significant attributable mortality of CR-BSI (4.4%; p=0.51).[22] A recent, carefully matched cohort study of 113 patients by Soufir and colleagues also failed to detect a statistically significant increase in mortality associated with CR-BSI.[23] Nevertheless, given the small sample size, these authors concluded that their findings are consistent with a 10% to 20% increased mortality due to CR-BSI.[23] Further research to clarify the mortality associated with CR-BSI is needed, but the available data are consistent with an attributable mortality of CR-BSI ranging between 4% and 20%.

Central venous catheter related infection also leads to increased health care costs. Though there is substantial variability in the economic estimates, a recent review estimates that an episode of local catheter-related infection leads to an additional cost of approximately $400, while the additional cost of CR-BSI ranges from about $6005 to $9738.[17] Some have estimated that each episode leads to even higher costs, approximately $25,000 per episode.[19,20]

Prevention

Unnecessarily prolonged catheterization should be avoided. Because of the increased risk of infection with prolonged catheterization, many clinicians attempt to reduce this risk with routine changes of the catheter, either over a guidewire or with a new insertion site. However, the available data do not support this practice.[24] Eyer et al[25] randomized 112 surgical patients receiving a central venous, pulmonary arterial, or systemic arterial catheter for more than 7 days into three groups: a) weekly catheter change at a new site; or b) weekly guidewire exchange at the same site; or c) no routine weekly changes. No significant difference was noted in the incidence of local or bacteremic infection.[25] Cobb and colleagues[26] randomized 160 patients with central venous or pulmonary arterial catheters to either replacement every 3 days at a new site or over a guidewire, or replacement only when clinically indicated. In those with replacement catheters at new sites, the risk of infectious complications was not decreased and the number of mechanical complications was increased. Those undergoing routine replacement via a guidewire exchange showed a trend towards a higher rate of bloodstream infections compared with those who had catheter replacement only when clinically indicated.[26] A recent meta-analysis has confirmed that routine changes of central venous and systemic arterial catheters appear unnecessary;[24] attempts should be made, however, to limit the duration of catheterization. Strict adherence to proper handwashing and use of proven infection control principles is crucial (see Chapters 13 and 14).[27,28]

Subchapter 16.1. Use of Maximum Barrier Precautions During Central Venous Catheter Insertion

Practice Description

Catheter-related infections often result from contamination of the central venous catheter during insertion. Maximum sterile barrier (MSB) precautions may reduce the incidence of catheter contamination during insertion and thus reduce the rate of CR-BSI. MSB precautions consist of the use of sterile gloves, long-sleeved gowns, and a full-size drape as well as a non-sterile mask (and often a non-sterile cap) during central venous catheter insertion.

Opportunities for Impact

The proportion of patients receiving central venous catheters in whom maximum barrier precautions are employed is not currently known. If maximum barrier precautions are not used, then the standard insertion technique involves the use of only sterile gloves and a sterile small drape. Given the additional time required to employ MSB, it is likely that many patients are not receiving maximum barrier precautions during catheter insertion.

Study Designs

One randomized and one non-randomized study have evaluated the use of maximum barrier precautions (Table 16.1.1). The clinical trial randomized 176 patients to catheter insertion using MSB and 167 patients to control (use of sterile gloves and sterile small drape).[29] A non-randomized before-after observational evaluation assessed the effect of a 1-day course on infection control practices and procedures on physician compliance with MSB use and incidence of catheter-infection.[30]

Study Outcomes

Both studies evaluated rates of catheter-related infection (Level 1), including local and bloodstream infection.

Evidence for Effectiveness of the Practice

There is moderately strong evidence that use of maximum barrier precautions decrease the risk of catheter-related infection (Table 16.1.1). Furthermore, the evidence that health care providers—specifically physicians-in-training—can be taught proper use of barrier precautions and thereby decrease the incidence of infection is reasonably strong.

Potential for Harm

There is virtually no harm associated with this intervention.

Costs and Implementation

The use of maximum barrier precautions will cost more than not using this technique in both materials and time. Additionally, teaching health care providers how to properly use maximum barrier precautions is also time-consuming and expensive. Sherertz and colleagues estimated the overall cost of their educational program and supplies to be $74,081.[30] However, when the costs of preventing catheter-related infection are also included, use of MSB has been estimated to be cost-saving in simplified "back-of-the-envelope" cost studies.[29,30] Formal economic evaluation is required to fully assess the economic consequences of full adoption of maximum barrier precautions.

Comments

Use of MSB appears to be a reasonable method of preventing catheter-related infection. Though achieving full compliance with this method of catheter insertion is likely to be challenging, a relatively simple educational intervention has demonstrated effectiveness in improving adherence and reducing infection rates. Given the excellent benefit-to-harm ratio of this patient safety practice, it seems reasonable to strongly consider employing MSB for all patients requiring central venous catheters. The economic consequences of full implementation of this practice are still not entirely clear.

Table 16.1.1. Studies of vascular catheter-related infection*

Study Description; Intervention	Study Design, Outcomes	Results (p-value or 95% CI)†
343 patients in a 500-bed cancer referral center; catheters inserted under maximal sterile barrier precautions (mask, cap, sterile gloves, gown, and large drape) vs. control precautions (sterile gloves and small drape only)[29]	Level 1, Level 1	CR-BSI per 1000 catheter days: 0.08 vs. 0.5, (p=0.02) Catheter colonization: 2.3% vs. 7.2% (p=0.04)
6 ICUs and a step-down unit in an academic medical center in NC; 1-day course for physicians-in-training on the control of vascular catheter infection, emphasizing use of full-size sterile drapes[30]	Level 2‡, Level 1	Primary bloodstream infection and catheter-related infection decreased 28% (p<0.01) Use of full-size sterile drapes increased from 44% to 65% (p<0.001)
Meta-analysis of 12 RCTs (2611 catheters) comparing central venous catheters coated with chlorhexidine/silver sulfadiazine with standard, non-coated catheters[44]	Level 1A, Level 1	Odds of CR-BSI with chlorhexidine/silver sulfadiazine catheter vs. standard catheter: OR 0.56 (0.37-0.84)
High-risk adult patients at 12 university-affiliated hospitals in whom central venous catheters were expected to remain in place for • 3 days; minocycline/rifampin vs. chlorhexidine/silver sulfadiazine catheters[46]	Level 1, Level 1	Incidence of CR-BSI: minocycline/rifampin 0.3% vs. chlorhexidine/silver sulfadiazine 3.4% (p<0.002) Both types of catheters had similar efficacy for approximately the first 10 days
Meta-analysis of 7 RCTs (772 catheters) comparing tunneling with standard placement of short-term central venous catheters[61]	Level 1A, Level 1	Catheter-related septicemia: RR 0.56 (0.31-1); excluding 1 study of placement in internal jugular: RR 0.71 (0.36-1.43) Catheter colonization: RR 0.61 (0.39-0.95); excluding 1 study of placement in internal jugular: RR 0.59 (0.32-1.10)
Meta-analysis of 12 RCTs comparing prophylactic heparin use (in different forms) with no heparin use on the following outcomes: central venous catheter colonization (3 trials), CR-BSI (4 trials), and catheter-related deep venous thrombosis (7 trials)[59]	Level 1A, Level 1	CR-BSI: RR 0.26 (0.07-1.03) Catheter colonization: RR 0.18 (0.06-0.60) Catheter-related deep venous thrombosis: RR 0.43 (0.23-078)

Meta-analysis of 12 RCTs (918 patients, • 1913 catheters) assessing the effect of guidewire exchange and a prophylactic replacement strategy (change every 3 days) on central venous catheter-related colonization (8 trials), exit site infection (4 trials), bacteremia (8 trials), and mechanical complications (9 trials) in critically ill patients[24]	Level 1A, Level 1	Catheter colonization: RR 1.26 (0.87-1.84) Exit site infection: RR 1.52 (0.34-6.73) Bacteremia: RR 1.72 (0.89-3.33) Mechanical complications: RR 0.48 (0.12-1.91) Prophylactic catheter replacement every 3 days was not found to be better than as-needed replacement

* CI indicates confidence interval; CR-BSI, catheter-related bloodstream infection; OR, odds ratio; RCT, randomized controlled trial; and RR, relative risk.

† Results are reported as intervention group vs. control (standard or usual care) group.

‡ Prospective before-after study design.

Subchapter 16.2. Use of Central Venous Catheters Coated with Antibacterial or Antiseptic Agents

Practice Description

Recent studies have indicated that central venous catheters coated with antimicrobial agents reduce the incidence of catheter-related bloodstream infection (CR-BSI). Implementing use of these catheters would be simple, primarily involving the replacement of standard, non-coated vascular catheters. However, these catheters, such as chlorhexidine/silver sulfadiazine-impregnated catheters and minocycline/rifampin-coated catheters, are more expensive than standard catheters. Thus, the cost-effectiveness of these catheters needs to be considered by decision makers.

Opportunities for Impact

Currently, it is not known precisely what proportion of patient who require central venous catheterization receive an antimicrobial catheter, however, it is probably the minority of patients.

Study Designs

Multiple randomized trials have compared chlorhexidine/silver sulfadiazine central venous catheters with standard, non-coated central venous catheters.[31-43] In addition, a recent meta-analysis used a fixed effects model to combine the results of these chlorhexidine/silver sulfadiazine trials.[44] A large, multicenter study has compared minocycline/rifampin coated catheters with non-coated, standard catheters.[45] Additionally, a recent multicenter randomized trial of minocycline/rifampin versus chlorhexidine/silver sulfadiazine catheters has also been reported.[46] The majority of the patients enrolled in the individual studies cited above had a central venous catheter in place for 8 days on average (range of average duration, 5 to 11 days). Details of the characteristics and results of the trials comparing central venous catheters coated with chlorhexidine/silver sulfadiazine to control catheters are in Tables 16.2.1 and 16.2.2.

Study Outcomes

Most studies reported the incidence of catheter colonization and CR-BSI. Though the precise outcome definitions in some of the studies varied, in general the definition of catheter colonization and CR-BSI used in most of these studies was explicit and appropriate.

Evidence for Effectiveness of the Practice

The evidence for the efficacy of chlorhexidine/silver sulfadiazine catheters is fairly substantial. The recent meta-analysis found a statistically significant decrease in the incidence of CR-BSI (odds ratio 0.56, 95% CI: 0.37-0.84).[44] There is also reasonable evidence that minocycline-rifampin catheters reduce the risk of CR-BSI compared with standard, non-coated catheters. The recent randomized trial of minocycline/rifampin versus chlorhexidine/silver sulfadiazine catheters found a significant and clinically important decrease in the incidence of CR-BSI in the group of patients using minocycline/rifampin compared with chlorhexidine/silver sulfadiazine catheters (0.3% vs. 3.4%, $p<0.002$).[46] Of note, both types of coated catheters had similar efficacy for approximately the first 10 days of catheterization.

Potential for Harm The potential for occurrence of immediate hypersensitivity reaction in association with the use of chlorhexidine/silver sulfadiazine impregnated catheters is of

concern. Although there have been no reports of hypersensitivity reactions to chlorhexidine/silver sulfadiazine impregnated central venous catheters in the United States (out of more than 2.5 million sold), 13 cases of immediate hypersensitivity reactions have been reported in Japan, including one potentially associated death.[47] There were 117,000 antiseptic-impregnated catheters sold in Japan before their use was halted because of these cases.[47] It is not clear why there have been no reports of hypersensitivity reactions in the U.S; this heterogeneity may be caused by a higher previous exposure of patients in Japan to chlorhexidine or by a genetic predisposition.

Minocycline and rifampin are both occasionally used as systemic antimicrobial agents; thus, their use on catheters raises the important theoretical issue of increased antimicrobial resistance. At this time, there has been no conclusive evidence that antimicrobial resistance has or will increase due to the use of these catheters.

Costs and Implementation

Formal and informal economic analyses indicate that central venous catheters coated with antibacterial agents (such as chlorhexidine/silver sulfadiazine or minocycline/rifampin) are likely to lead to both clinical and economic advantages in selected patients. In terms of formal economic comparisons, a recent analysis compared chlorhexidine/silver sulfadiazine catheters to standard catheters and found that chlorhexidine/silver sulfadiazine catheters lead to both clinical and economic advantages in patients receiving central venous catheterization for 2 to 10 days and who were considered high risk for infection (ie, critically ill or immunocompromised patients). Specifically, the chlorhexidine/silver sulfadiazine catheters led to a significant decrease in the incidence of CR-BSI and death, and a cost savings of approximately $200 per catheter used.[47] Importantly, the risk of hypersensitivity reaction to the chlorhexidine/silver sulfadiazine catheters was considered in the analysis, but had little effect on the overall clinical and economic outcomes.[47]

However, given the recently demonstrated efficacy of the minocycline/rifampin catheter compared with the chlorhexidine/silver sulfadiazine catheter,[46] a formal cost-effectiveness analysis comparing these two types of coated catheters is necessary. This is especially important since the minocycline/rifampin catheter costs about $9 more per catheter than the chlorhexidine/silver sulfadiazine catheter.

Implementation of either of these catheters would be straightforward. Stocking the appropriate antimicrobial catheter in areas of the hospital that are likely to require such catheters (eg, intensive care unit, operative room, hematology-oncology floor) would be a relatively simple way of translating the research findings into actual practice.

Comment

In light of the substantial clinical and economic burden of catheter-related infection, hospital personnel should adopt proven cost-effective methods to reduce this common and important nosocomial complication. The bulk of the evidence supports the use of either chlorhexidine/silver sulfadiazine or minocycline/rifampin central venous catheters rather than standard (non-coated) catheters in high-risk patients requiring short-term central venous catheterization (eg, for 2 to 10 days). Choosing between the 2 antimicrobial catheters requires a formal cost-effectiveness analysis since the minocycline/rifampin catheter costs significantly more than the chlorhexidine/silver sulfadiazine catheter. There are 2 primary issues that should be addressed when comparing these catheters: the expected duration of catheterization and the risk of antibiotic resistance to the patient, the hospital, and society. Though each minocycline/rifampin catheter costs more than the chlorhexidine/silver sulfadiazine catheter, using minocycline/rifampin catheters may actually result in cost-savings for at least some patient populations given their improved overall efficacy. Of note, the improved efficacy of the minocycline/rifampin catheters may be a result of coating both the internal and external surfaces with these substances; the chlorhexidine/silver sulfadiazine catheters evaluated to date have only had the external surface coated with the antiseptic combination.

Table 16.2.1. Characteristics of trials comparing central venous catheters coated with chlorhexidine/silver sulfadiazine to control catheters*

Study Description	Number of Catheters (Treatment, Control)	Mean Catheter Duration in Days (Treatment, Control)	Catheter Colonization†	Catheter-Related Bloodstream Infection†
Tennenberg[31]: 282 hospital patients (137 treatment, 145 control) in variety of settings; double- and triple-lumen catheters without exchanges over guidewires	137, 145	5.1, 53	SQ (IV, SC, >15 CFU)	SO (IV, SC, site), CS, NS
Maki[32]: 158 ICU patients (72 treatment, 86 control); triple-lumen catheters with catheter exchanges over guidewires	208, 195	6.0, 6.0	SQ (IV, >15 CFU)	SO (>15 CFU, IV, hub, inf)‡
van Heerden[33]§: 54 ICU patients (28 treatment, 26 control); triple-lumen catheters without catheter exchanges over guidewires	28, 26	6.6, 6.8	SQ (IV, >15 CFU)	NR
Hannan[34]: ICU patients; triple-lumen catheters	68, 60	7, 8	SQ (IV, $>10^3$ CFU) ¶	SO (IV, $>10^3$ CFU), NS
Bach[35]§: 26 ICU patients (14 treatment, 12 control); triple-lumen catheters without catheter exchanges over guidewires	14, 12	7.0, 7.0	QN (IV, $>10^3$ CFU)	NR
Bach[36]§: 133 surgical patients (116 treatment, 117 control); double- and triple-lumen cathetes without exchanges over guidewires	116, 117	7.7, 7.7	QN (IV, $>10^3$ CFU)	SO (IV)
Heard[37]§: 111 SICU patients (107 treatment, 104 control); triple-lumen catheters with exchanges over guidewires	151, 157	8.5, 9	SQ (IV, SC, >14 CFU)	SO (IV, SC, >4 CFU)
Collin[38]: 119 ER/ICU patients (58 treatment, 61 control); single-, double-, and triple-lumen catheters with exchanges over guidewires	98, 139	9.0, 7.3	SQ (IV, SC, >15 CFU)	SO (IV, SC)
Ciresi[39]§: 191 patients receiving TPN (92 treatment, 99 control); triple-lumen catheters with exchanges over guidewires	124, 127	9.6, 9.1	SQ (IV, SC, >15 CFU)	SO (IV, SC)
Pemberton[40]: 72 patients receiving TPN (32 treatment, 40 control); triple-lumen catheters without exchanges over guidewires	32, 40	10, 11	NR	SO (IV), Res, NS

Ramsay[41]§: 397 hospital patients (199 treatment, 189 control) in a variety of settings; triple-lumen catheters without exchanges over guidewires	199, 189	10.9, 10.9	SQ (IV, SC, >15 CFU)	SO (IV, SC)
Trazzera[42]§: 181 ICU/BMT patients (99 treatment, 82 control); triple-lumen catheters with exchanges over guidewires	123, 99	11.2, 6.7	SQ (IV, >15 CFU)	SO (IV, >15 CFU)
George[43]: Transplant patients; triple-lumen catheters without exchanges over guidewires	44, 35	NR	SQ (IV, >5 CFU)	SO (IV)

* BMT indicates bone marrow transplant; CFU, colony forming units; CS, clinical signs of systemic infection; ER, emergency room; ICU, intensive care unit; IV, intravascular catheter segment; inf, catheter infusate; NR, not reported; NS, no other sources of infection; QN, quantitative culture; Res, resolution of symptoms upon catheter removal; SC, subcutaneous catheter segment; SICU, surgical intensive care unit; site, catheter insertion site; SO, same organism isolated from blood and catheter; SQ, semi-quantitative culture; and TPN, total parenteral nutrition.

† Catheter segments (or site) cultured and criteria for a positive culture are given in parenthesis

‡ Organism identity confirmed by restriction-fragment subtyping

§ Additional information provided by author (personal communications, 1/98-3/98)

¶ Culture method reported as semiquantitative; criteria for culture growth suggests quantitative method

Table 16.2.2. Results of trials comparing central venous catheters coated with chlorhexidine/silver sulfadiazine to control catheters*

Study	Catheter Colonization			Catheter-related Bloodstream Infection		
	No. (%) Positive		Odds Ratio (95% CI)	No. (%) Positive		Odds Ratio (95% CI)
	Treatment	Control		Treatment	Control	
Tennenberg[31]	8 (5.8%)	32 (22.1%)	0.22 (0.10-0.49)	5 (3.6%)	9 (6.2%)	0.57 (0.19-1.75)
Maki[32]	28 (13.5%)	47 (24.1%)	0.49 (0.29-0.82)	2 (1.0%)	9 (4.6%)	0.20 (0.04-0.94)
van Heerden[33]†	4 (14.3%)	10 (38.5%)	0.27 (0.07-1.00)	–	–	–
Hannan[34]	22 (32.4%)	22 (36.7%)	0.83 (0.40-1.72)	5 (7.4%)	7 (11.7%)	0.60 (0.18-2.00)
Bach[35]†	0 (0%)	4 (33.3%)	0 (0-0.65)	–	–	–
Bach[36]†	2 (1.7%)	16 (13.7%)	0.11 (0.02-0.49)	0 (0%)	3 (2.6%)	0 (0-1.28)
Heard[37] †	60 (39.7%)	82 (52.2%)	0.60 (0.38-0.95)	5 (3.3%)	6 (3.8%)	0.86 (0.26-2.89)
Collin[38]	2 (2.0%)	25 (18.0%)	0.10 (0.02-0.41)	1 (1.0%)	4 (2.9%)	0.35 (0.04-3.16)
Ciresi[39]†	15 (12.1%)	21(16.5%)	0.69 (0.34-1.42)	13 (10.5%)	14 (11.0%)	0.95 (0.43-2.10)
Pemberton[40]	–	–	–	2 (6.3%)	3 (7.5%)	0.82 (0.13-5.24)
Ramsay[41]†	45 (22.6%)	63 (33.3%)	0.58 (0.37-0.92)	1 (0.5%)	4 (2.1%)	0.23 (0.03-2.11)
Trazzera[42] †	16 (13.0%)	24 (24.2%)	0.47 (0.23-0.94)	4 (3.3%)	5 (5.1%)	0.63 (0.17-2.42)
George[43]	10 (22.7%)	25 (71.4%)	0.12 (0.04-0.33)	1 (2.3%)	3 (8.6%)	0.25 (0.02-2.50)

* CI indicates confidence interval.
† Additional information provided by author (personal communications, 1/98-3/98)

Subchapter 16.3. Use of Chlorhexidine Gluconate at the Central Venous Catheter Insertion Site

Practice Description

Microbial populations on the skin are routinely suppressed with antiseptic agents prior to catheter insertion. Using an antiseptic solution for skin disinfection at the catheter insertion site helps to prevent catheter-related infections. The physician uses an agent that has antimicrobial properties to thoroughly cleanse the skin just prior to insertion of a central venous catheter. In the United States, povidone-iodine (PI) is overwhelmingly the most commonly used agent for this purpose. Recently, several studies have compared the efficacy of PI and chlorhexidine gluconate (CHG) solutions in reducing vascular catheter-related infections.

Opportunities for Impact

If PI is the most commonly used agent for site disinfection in the United States even though CHG may be superior, substantial opportunity exists for impact by switching to CHG.

Study Designs

The study characteristics of 6 randomized trials[48-53] comparing any type of CHG solution with PI solution for vascular catheter site care are shown in Table 16.3.1. The mean duration of catheterization for the CHG and PI groups was comparable in most of the studies. There was no significant difference in the sites at which catheters were inserted between the CHG and PI groups. Several formulations of CHG were used, including[9,12-14] an alcoholic solution and an aqueous solution. All studies used 10% PI solution for the control arm.

Study Outcomes

All studies[48-53] evaluated catheter colonization (Level 2 outcome) and all but one[52] evaluated CR-BSI (Level 1 outcome). All studies evaluating CR-BSI as an outcome required the recovery of the same microbial species from both the catheter segment and a blood culture.

Evidence for Effectiveness of the Practice

Most clinical trials have revealed that the use of CHG solution results in a significant decrease in catheter colonization, but the evidence is not clear for CR-BSI (Table 16.3.2). Most of the individual trials showed a trend in reducing CR-BSI incidence in patients using CHG solution. The lack of significant results may be a result of insufficient statistical power in the individual studies. A formal meta-analysis of the published trials would be valuable in assessing the comparative efficacy of PI versus CHG for central venous catheter site disinfection. Using explicit inclusion criteria and accepted quantitative methods, a meta-analysis[54-56] can often help clarify the features of individual studies that have divergent results[57] and increase statistical power since several small studies can be pooled.[58]

Potential for Harm

Only one study reported adverse effects from the use of either antiseptic solution. Maki et al[48] found erythema at the insertion site in 28.3% of catheters in the PI group and in 45.3% of catheters in the CHG group (p=0.0002). However, there was no statistically significant difference in erythema among these 2 groups and those patients whose site was disinfected with alcohol. Hypersensitivity reactions to chlorhexidine-silver sulfadiazine impregnated central

venous catheters and to use of CHG for bathing have been reported. Hypersenstivity reactions were not reported in any of the studies, but clinicians should be aware of such potential side effects. Another concern is the development of bacterial resistance. However, there have been few reports of bacterial resistance to CHG despite its widespread use for several decades.

Costs and Implementation

The cost of CHG is approximately twice that of PI with an absolute difference of $0.51 (approximately $0.92 versus $0.41 for a quantity sufficient to prepare a central venous catheter insertion site). If meta-analysis suggests that CHG use is effective in reducing the risk of CR-BSI, a formal economic evaluation of this issue is required.

Comment

The use of chlorhexidine gluconate rather than povidone-iodine solution for catheter site care may be an effective and simple measure for improving patient safety by reducing vascular catheter-related infections. Formal meta-analysis and economic evaluations are required before strongly recommending that CHG replace PI for central venous catheter site disinfection in appropriate patient populations.

Table 16.3.1. Characteristics of studies comparing chlorhexidine gluconate (CHG) and povidone-iodine (PI) solutions for vascular catheter site care*

Study Description†	Number of Catheters (Treatment, Control)	Mean Catheter Duration in Days (Treatment, Control)	Catheter Colonization‡	Catheter-Related Bloodstream Infection‡
Maki[48]: 441 ICU patients (2% aqueous CHG solution in 214, PI in 227)	214, 227	5.3, 5.3	SQ (>15 CFU)	CX, NoSource, Sx
Sheehan[49]: 189 ICU patients (2% aqueous CHG solution in 94, PI in 95)	169,177	NA	SQ (>15 CFU)	CX, NoSource, Sx
Meffre[50]: 1117 hospital patients (CHG solution of 0.5% alcohol 70% in 568, PI in 549)	568, 549	1.6, 1.6	SQ (>15 CFU) or QN (>10^3 CFU/mL)	[Local or Sx] or [CX, NoSource]
Mimoz[51]: ICU patients (Biseptine®§ vs. PI)	170, 145	4.5, 3.9	QN (>10^3 XFU/mL)	CX, Sx
Cobett and LeBlanc[52]: 244 hospital patients (0.5% alcohol 70% in 8, PI in 161)	83, 161	1.6, 1.7	SQ (>15 CFU)¶	NA
Humar et al[53]: 3374 ICU patients (0.5% alcohol in 193 and 181/193	193, 181	5.3, 6.	SQ (>15 CFU)	CX, Molec, NoSource

* CFU indicates colony forming units; CX, same organism or species matched between blood and catheter segment culture; ICU: intensive care units; Local: local signs of infection; Molec: same organism confirmed by molecular subtyping; NA:not available; NoSource: no other source of infection; QN: quantitative; Sx: clinical symptoms of bloodstream infection; SQ: semiquantitative.

† All studies used 10% povidone-iodine solution.

‡ Catheter segments (or site) cultured and criteria for a positive culture are given in parenthesis.

§ Biseptine® consists of 0.25% chlorhexidine gluconate, 0.025% benzalkonium chloride, 4% benzyl alcohol.

¶ Required one of the following symptoms: fever, erythema, heat at the site, and pain.

Table 16.3.2. Results of Studies Comparing Chlorhexidine Gluconate (CHG) and Povidone-iodine (PI) Solutions for Vascular Catheter Site Care *

	Catheter Colonization (Positive Cultures)		RR (95% CI) CHG vs. PI	Catheter Related Bloodstream Infection		RR (95% CI) CHG vs. PI
	CHG Solution	PI Solution		CHG Solution	PI Solution	
Maki[48]	5/214	21/227	0.25 (0.10,0.66)	1/214	6/227	0.18 (0.02,1.46)
Sheehan[9]	3/169	12/177	0.22 (0.06,0.75)	1/169	1/177	1.05 (0.07,16.61)
Meffre[50]	9/568	22/549	0.40 (0.18,0.85)	3/568	3/549	0.97 (0.20,4.77)
Mimoz[51]	12/170	24/145	0.43 (0.22,0.82)	3/170	4/145	0.64 (0.15,2.81)
Cobett and LeBlanc[52]†	6/83	23/161	0.49 (0.31,0.77)	-	-	-
Humar[53]	36/116	27/116	1.33 (0.87,2.04)	4/193	5/181	0.75 (0.20,2.75)

* CI indicates confidence interval; RR, relative risk.
† Additional information was provided by authors

Subchapter 16.4. Other Practices

Practices That Appear Promising

Use of heparin with central venous catheters. Because an association has been shown between thrombus formation and catheter-related infection, clinicians usually use heparin, in a variety of forms: 1) as flushes to fill the catheter lumens between use; 2) injected subcutaneously; or 3) bonded on the catheter. A meta-analysis of 12 randomized trials evaluating prophylactic use of heparin in patients using central venous catheters has shown that prophylactic heparin decreases catheter-related venous thrombosis (Level 2 outcome; RR 0.43, 95% CI: 0.23-078) and bacterial colonization (Level 2 outcome; RR 0.18, 95% CI: 0.06-0.60) and may decrease CR-BSI (Level 1 outcome; RR 0.26, 95% CI: 0.07-1.03).[59] Since subcutaneous heparin also offers benefit in reducing venous thromboembolism in certain patient populations (see Chapter 31), this is likely to be a reasonable strategy even though CR-BSIs have not definitely been shown to be reduced. However use of heparin is associated with several side effects, such as heparin-induced thrombocytopenia and bleeding.

Tunneling short-term central venous catheters. Since the primary site of entry for microorganisms on the central venous catheter is the site of cutaneous insertion,[60] tunneling the catheter through the subcutaneous tissue may decease the incidence of infection. Several trials have evaluated the effect of tunneling on catheter-related infection. A recent meta-analysis has summarized the potential benefit.[61] The meta-analysis included 7 trials and found that compared with patients receiving standard catheter placement, tunneling decreased bacterial colonization (Level 2 outcome; RR 0.61, 95% CI: 0.39-0.95) and decreased CR-BSI (Level 1 outcome; RR 0.56, 95% CI: 0.31-1).[61] However, the benefit of tunneling came primarily from one trial using the internal jugular as the site of catheter placement; the reduction in CR-BSI no longer reached statistical significance when data from the several subclavian catheter trials were pooled (RR 0.71; 95% CI 0.36-1.43).[61] The authors concluded appropriately that current evidence does not

support the routine use of tunneling central venous catheters. This could change if the efficacy of tunneling is clearly demonstrated at different placement sites and relative to other interventions (eg, antiseptic coated catheters).[61]

Ineffective Practices

Intravenous antimicrobial prophylaxis. There is no evidence to support the systemic use of either vancomycin[62] or teicoplanin[63] during insertion of central venous catheters. The randomized studies evaluating the use on intravenous vanomycin or teicoplanin have failed to demonstrate that this intervention reduces CR-BSI (Level 1 outcome).[62, 63] Given the theoretical risk of developing resistance to the antimicrobial agents used for prophylaxis, this practice is not recommended.

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Final Comment to Chapter 16

Infections due to central venous catheters are common and lead to substantial morbidity and health care costs. Several practices will likely reduce the incidence of this common patient safety problem, including the use of maximum sterile barrier precautions during catheter insertion, use of catheters coated with antibacterial or antiseptic agents, and use of chlorhexidine gluconate at the insertion site. Additionally, use of heparin and tunneling of the central venous catheter may prove to be effective in reducing CR-BSI. However, the relative efficacy of these interventions is unclear. Also, a clear and formal delineation of the economic consequences of combining several of these patient safety practices is necessary.