Prevention & Treatment of Central Venous Catheter Infections

Kimberly Walsh

St. Catherine University
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written by

Kimberly Ann Walsh

and have found that it is complete and satisfactory in all respects,
and that any and all revisions required have been made.

Graduate Program Faculty

Name of Project Advisor

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Date

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Central venous catheters (CVCs) have been widely utilized since the 1970’s. They have become essential in the medical field for a variety of uses throughout an array of different patient populations. The most common function of a CVC is safe administration of intravenous medications such as chemotherapy and antibiotics. They are also used for blood product transfusions, nourishment such as total parenteral nutrition (TPN), and dialysis for patients with impaired renal function. These catheters have allowed patients to live a more normal life outside of the hospital. However, in the United States, central venous catheters are the leading source of nosocomial bloodstream infections, causing 2,400 to 20,000 deaths. Not only are catheter related blood stream infections (CRBSIs) costly, they also are associated with a negative impact on patients’ quality of life, therefore prevention of CRBSIs is key. Prevention of CRBSIs begins with using maximum precautions to create a sterile field during the insertion of a CVC and continues with appropriate maintenance of the site. Practitioners need to be knowledgeable about what organisms commonly cause CRBSIs, and the most effective way to treat them. Such treatments include removal of the catheter, antibiotic therapy, antibiotic lock therapy, and ethanol lock therapy.
# Prevention & Treatment of Central Venous Catheter Infections

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Introduction

Central venous catheters (CVCs) have been widely utilized since the 1970’s. They have become essential in the medical field for a variety of uses throughout an array of different patient populations. The most common function of a CVC is safe administration of intravenous medications such as chemotherapy and antibiotics. They are also used for blood product transfusions, nourishment such as total parenteral nutrition (TPN), and dialysis for patients with impaired renal function. Additionally, central venous catheters are used to collect blood samples from patients in order to lessen the pain caused by numerous needle sticks. These catheters have allowed patients to live a more normal life outside of the hospital.

In the United States alone, approximately five million central venous catheters are inserted annually (Maiefski, Rupp, & Hermsen, 2009). Despite technological advances, an estimated 250,000 catheter related blood stream infections occur annually (Hanna et al., 2004). In the United States, central venous catheters are the leading source of nosocomial bloodstream infections, causing 2,400 to 20,000 deaths. These infections are extremely costly. It is estimated that in the United States alone, central venous catheter related blood stream infections account for approximately 2 billion health care dollars annually (Lane & Matthyay, 2002). This number breaks down to a range of approximately $4000 to $56,000 for each episode (Opilla, Kirby, & Edmond, 2007). CVC related bloodstream infections also prolong hospitalization by an average of 6.5 days (Maiefski et al. 2009). Increased mortality rates may also be attributed to the effects of CVC infections. Probably the most significant problem created by a central venous catheter infection is the negative impact one can have on a patient’s quality of life. Repeated hospitalizations, potential job loss, time spent away from family, and increased medical bills are all factors that contribute to a patient’s mental well being (Opilla et al. 2007).
In order to better care for patients with central venous catheters it is important to know the different types of central venous catheters, how they are inserted, and the best practices in which to care for these lines to effectively prevent infection.

**Prevention of Central Venous Catheter Infections during Insertion**

Central venous catheter infections most commonly occur from one of three ways: colonization of the catheter tip during insertion, contamination at the catheter hub with routine use, and infection from another source within the body that spreads through the blood stream and attaches to the lumen. Rarely CVCs can become infected from contaminated infusions (Band 2010).

Prior to placement of a CVC several things need to be taken into consideration. For example the location of insertion, and type of catheter to be used, including number of lumens and what type of material the catheter is made of all impact how likely it is that the catheter will become infected. The first step in the prevention of catheter related infections takes place during insertion of the catheter. Proper placement of the CVC in an area where skin flora is less dense is the optimal choice if possible. Lines placed in the jugular or femoral areas have a higher incidence of infections. Once the optimal location has been chosen, proper skin cleansing is the next step in ensuring a successful insertion. Currently two options are available. Povidone Iodine has been the most widely used antiseptic in the United States, however new studies have shown that using a chlorhexidine gluconate solution has proven to lower the rate of infection (CDC, 2002).

Aseptic technique during the actual insertion process is also of extreme importance. Standard precautions including good hand washing along with sterile gloves and small drapes are
no longer sufficient. A study performed by Raad et al., (1994) showed a significant decrease in catheter related infections when maximum precautions were used during catheter insertion. This includes mask, cap, sterile gown and gloves, and a large sterile drape. They also concluded that this practice was cost-effective. Furthermore, the level of experience by the provider placing the catheter has an impact on the occurrence of infections once the CVC has been placed. Central venous catheters inserted by a practitioner who has placed greater than fifty catheters are less likely to become infected than those placed by less experienced practitioners (McGee & Gould, 2003).

The material a catheter is made of plays an important role in how well it is able to resist adherence of organisms. Catheters are made out of such materials as Teflon, silicone elastomer, and polyurethane. Currently studies are being performed to evaluate the effectiveness of anti-microbial impregnated catheters. The two most commonly used antimicrobial catheters are impregnated with silver sulfadiazine and chlorhexidine or minocycline and rifampin. Studies have shown using anti-microbial impregnated catheters have reduced the rate of blood stream infections to 1.6 infections per 1000 catheter days down from 7.6 infections per 1000 catheter days (McGee & Gould, 2003). Maki, Stolz, Wheeler & Mermel, (1997) found in a controlled, randomized clinical trial, that catheters coated with a chlorhexidine/silver sulfadiazine combination had a five-fold decrease in CRBSIs compared to a standard polyurethane catheter. The antimicrobial activity of these catheters decreases over time limiting their effectiveness in patients who will maintain the catheter for an extended period of time (CDC, 2002). Due to their broad-spectrum inhibitory activities, the use of catheters coated with minocycline and rifampin have proven to be significantly superior to those coated with chlorhexidine and silver sulfadiazine (Raad et al., 1997). The half-life of antimicrobial activity associated with catheters
coated with minocycline and rifampin against S. epidermidis is 25 days compared to 3 days for catheters coated with chlorhexidine and silver sulfadiazine (CDC, 2002). A potential drawback to using antimicrobial impregnated catheters is the risk for anti-biotic resistance. Although it is possible for resistance to occur with these anti-septic agents, it is far less frequent than with antibiotics (Maki et al. 1997). In the study conducted by Raad et al. (1997) no evidence of resistance to minocycline or rifampin was found. Furthermore, they determined that using coated catheters to prevent CRBSIs could decrease the use of systemic antibiotics therefore reducing the likelihood of resistance to common agents used to empirically treat bloodstream infections. In a study performed by Hanna et al., (2003), following the introduction of catheters coated with minocycline and rifampin the rate of vancomycin resistant enterococcus (VRE) decreased significantly. Currently, the CDC recommends the use of antimicrobial impregnated catheters in patients with an increased risk for CRBSIs (Raad et al. 1997).

**Guidelines for Care and Maintenance of the Central Venous Catheter**

Central venous catheter care and maintenance has evolved significantly over the past 40 years. Various cleansing options and dressings are available to clean, cover and protect the exit site from infection. Considering that approximately 60% of CRBSIs stem from the flora found on the patient’s skin, it is of utmost importance that catheters be properly cleansed (Olson & Heilman, 2008). Overwhelming evidence has shown using a 2% chlorhexidine antiseptic cleansing solution reduces the rate of catheter-related bloodstream infections by up to 50% (Chambers et al., 2005). Chlorhexidine solutions are superior to alcohol or povidone-iodine solutions for many reasons. One reason being the antimicrobial effects of chlorhexidine are almost immediate and continue to last for up to six hours, compared to the antimicrobial effects of povidone-iodine which occur as it dries and leaves no residual antimicrobial activity (Zitella,
2003). Chlorhexidine has also been recommended for use in cleansing of CVC hubs prior to manipulation of the line (Casey & Elliott, 2010).

Several dressings are available to cover and protect the catheter following the cleansing process. They range from semipermeable, transparent polyurethane dressings to standard gauze and tape. Numerous research studies have been conducted regarding which dressing provides the most optimal protection against CRBSIs. These studies have resulted in inconclusive evidence. Additionally, studies performed on the frequency of dressing changes have shown variable results. Because of this standardized catheter care guidelines are unavailable causing inconsistencies in practice (Zitella, 2003). Benefits of using a semipermeable transparent dressing include ability to visualize the exit site and less frequent dressing changes. Semipermeable transparent dressings are generally changed once every 7 days unless the dressing is soiled, moist, or is lifting up. A standard gauze dressing is commonly recommended for newly placed catheters to absorb any blood or oozing. Standard gauze dressings require more frequent changes, approximately every 2 days, because of the inability to visualize the exit site to monitor for infectious process (Casey & Elliott, 2010).

In addition to dressings, other items such as the Biopatch and Statlock have been integrated into central line catheter care. The Biopatch, a chlorhexidine-impregnated sponge, is placed around the catheter at the exit site prior to being covered by a transparent dressing and provides antimicrobial activity directly to the skin. Use of the Biopatch has shown to aid in reducing catheter infections (Zitella, 2003). A drawback to using the Biopatch includes additional and continued training of staff for proper placement of the disk. Also the disk is opaque inhibiting the view of the exit site for monitoring purposes. Most recently another product has been introduced which includes a transparent dressing with a chlorhexidine
gluconate gel pad built in. This reduces the number of steps needed to perform a dressing change and also eliminates clinician error in applying the Biopatch. The gel pad is transparent so visualization of the exit site is not hindered (Olson & Heilman, 2008). Use of a sutureless securement device such as the Statlock has proven to reduce the number of catheter related infections in comparison to routine securement by sutures. In addition, sutureless devices eliminate the risk of needle stick injuries to healthcare professionals while suturing the catheter (CDC, 2002).

**Most Common Organisms that Cause CRBSIs**

According to Lane & Matthay (2002), CRBSIs are defined as the presence of fungemia or bacteremia in a patient with a central venous catheter along with one of the following conditions: signs and symptoms of infection such as chills; fever; hypotension; or tachycardia; no other apparent source of infection besides the CVC; and positive blood cultures growing the same organism in both the central venous catheter as well as in the peripheral blood. Gram positive organisms are responsible for most catheter related blood stream infections. The most common causative organism is coagulase-negative Staphylococci also known as Staphylococcus epidermis. However, gram-negative organisms account for up to 28% of infections (Bagnall-Reeb, 2004). Occasionally more than one organism may be responsible for a CRBSI (Band, 2010). Other common organisms include Staphylococcus aureus, Candida albicans, and aerobic gram-negative bacilli such as Escherichia coli (Galloway, 2010).

CRBSIs are increasingly difficult to treat when a biofilm is formed. Biofilms generally develop within 3 days of catheter insertion (Cirioni et al., 2006). The process begins when bacteria adhere to artificial surfaces and communities of surface-adherent organisms become
embedded in extracellular matrices. This results in a bubble of protection for bacteria to harbor thus preventing penetration from phagocytes and systemic antibiotics (Lane & Matthay, 2002). Since biofilms are resistant to the immune response and antibiotic therapy even at very high concentrations, these catheters generally need to be removed (Ciroioni et al., 2006). For this reason alternatives to antimicrobial therapy such as antibiotic lock therapy (ALT), and ethanol lock therapy (ELT) have been researched in order to find new ways to eradicate these biofilms and prevent catheter removal as well as relapse of the infection.

**Antibiotic Therapy**

When a CRBSI is suspected, determining whether or not to remove the catheter is the first issue a clinician is confronted with (Lane & Matthay, 2002). If maintaining the catheter is necessary, prompt evaluation of the patient and their catheter are important to determine which steps will be taken to treat the infection. The standard of care for treatment of intravenous catheter related blood stream infections in the neutropenic patient includes prompt evaluation, culturing, and broad spectrum antibiotic therapy. Two to three days after initiation of antibiotic therapy, blood cultures should be obtained to determine response to treatment. Empiric therapy generally includes antibiotics which cover both gram-negative and gram-positive organisms (Jones, 1998).

Determining which antibiotic is appropriate for treatment of a CRBSI can be quite difficult. Antibiotic resistance is becoming increasingly more common creating a barrier to successful eradication of the organism causing the infection. According to Lane & Matthay (2002), p. 441, “more than 50% of S. aureus and more than 80% of Staphylococcus isolates are resistant to oxacillin, 25% of enterococci are resistant to vancomycin, and 23% of Pseudomonas
aeruginosa are resistant to quinolones.” Because of the presence of methicillin-resistant staphylococci (MRSA), vancomycin has become the antibiotic of choice. In addition, the use of a third or fourth generation cephalosporin should be considered in severely immunocompromised patients for gram-negative coverage. If a fungal infection is suspected, intravenous amphotericin B or fluconazole should be administered. Once the patient’s condition has stabilized and antimicrobial sensitivities are determined, oral antibiotics such as ciprofloxacin, Bactrim, or linezolid can be used. These oral agents are the drug of choice due to their high tissue penetration and superior bioavailability (Lane & Matthay, 2002).

Determining the duration of antibiotic therapy in the treatment of a CRBSI involves continued observation of the patient’s symptoms, blood culture surveillance, and monitoring the catheter for further complications. Although conclusive data regarding the appropriate duration of therapy does not exist, the Infectious Disease Society of America offers guidelines for length of therapy. In the case of an uncomplicated gram-negative bacillus, a 10 to 14 day course of antibiotics is appropriate. For an uncomplicated S. aureus infection, 14 days of therapy should be sufficient to clear the organism. If a Candida species is identified, treatment needs to be continued for 14 days past the last positive blood culture. For complicated or persistent bacterial infections, therapy should continue for 4 to 6 weeks (Lane & Matthay, 2002). Intravenous antibiotic therapy has proven to be 66% effective in clearing central line infections, however within 12 weeks of therapy 20% of patients have episodes of recurrent bacteremia (Krzywda & Edmiston, 2002).

**Antibiotic Lock Therapy**
In the late 1980’s, antibiotic lock therapy was developed to treat or prevent CRBSIs. Combinations of different antibiotics instilled in a variety of ways have been studied in order to find the best way to utilize this therapy and treat CRBSIs. ALT involves instilling 2-5 ml’s of concentrated antibiotic solutions into a catheter and allowing it to dwell for a defined period of time. This period of time can range anywhere from six to twelve hours. The main goal of this therapy is to sterilize the catheter in an attempt to reduce the level of biofilm. Common drugs that have been used for ALT include gentamicin, vancomycin, amphotericin B, and ciprofloxacin (Opilla et al., 2007).

In a study conducted by Messing, Peitra-Cohen, Debure, Beliah, & Bernier (1988), ALT was used in home parenteral nutrition (HPN) patients with catheter related sepsis. In total, 11 patients who were hospitalized for catheter related infections were treated using one of three antibiotic solutions. The solutions included; minocycline, vancomycin, or amikacin. During the hospitalization, 2mls of the antibiotic solution was instilled each morning into the catheter and allowed to dwell for a period of 12 hours. Upon discharge, prepared antibiotic solutions were drawn up in syringes and sent home with the patients who were trained to continue the therapy for a total of 2 weeks. The goal of ALT in this study was catheter salvage in order to continue HPN without interruption while maintaining control of catheter sepsis. This was achieved with 90% of the patients involved in the study.

Several different techniques have been studied in an effort to enhance ALT such as combining these antimicrobials with anticoagulation agents such as edentate calcium disodium (EDTA), and heparin. Several weaknesses have been noted with this therapy including expense, lack of stability, and availability. An additional drawback posed by ALT is the risk for developing antibiotic resistance. For this reason the Centers for Disease Control and Prevention
state that using vancomycin as a lock therapy is not recommended due to the possible risk of developing vancomycin resistant enterococcus (VRE) (Opilla et al, 2007).

**Ethanol Lock Therapy**

Ethanol is an antiseptic agent which exhibits bactericidal and fungicidal activity against a wide range of organisms including Gram-negative and Gram-positive bacteria. It is readily available, inexpensive, and currently no resistance to microorganisms has been discovered. In contrast to antibiotic lock therapy, ethanol works by denaturization therefore the effect does not depend on microorganism resistance or sensitivity. For these reasons this therapy has sparked interest within the medical field to safely develop a standard process for its use in the prevention and treatment of CRBSI (Dannenberg, Bierbach, Rothe Beer, & Korholz, 2003).

Between January 2000 and December 2001, Dannenberg, Bierbach, Rothe, Beer, and Korholz (2003), enrolled 79 pediatric oncology patients in their study involving ethanol lock therapy. In this study half of the patients with a central catheter infection were treated empirically with antibiotic therapy while the other half were treated with ethanol lock therapy in addition to the same antibiotic therapy. The ethanol lock technique consisted of filling the catheter lumen with a 74% ethanol solution and allowing it to dwell for 20 to 24 hours. Following the dwell period the solution was flushed through the line to prevent clotting. Each port of the catheter was locked on alternating days so that the other port could be used for antibiotic therapy. No severe adverse reactions were reported with the ethanol flushes, they were well tolerated with only mild side effects which included tiredness, nausea, headaches, light-headedness, and dizziness. The ethanol lock technique was used 24 times. Results showed 67%
of the patients remained infection free in the treatment group compared to 47% in the control group.

Onland, Shin, Fustar, Rushing, and Wong (2006), conducted a retrospective review of patients treated with ELT. Medical records from June of 2004 through June 2005 were included. The patient population consisted of 75 children who were being cared for at the Childrens Hospital Los Angeles in Los Angeles, California. Criteria for inclusion was six months of age and older, no known allergy to ethanol, a functioning silicone catheter prior to the initiation of ethanol lock therapy, and positive blood cultures that persisted following 48 hours of intravenous antibiotic therapy. The technique consisted of instilling an ethanol lock for a dwell time of 12 to 24 hours. Following this period of time, the ethanol lock was extracted and discarded and the line was cleared with a sodium chloride flush. The process was repeated for a total of five days consecutively. Successful treatment was defined as a patient being afebrile within 24 hours of initiating therapy, no further positive blood cultures growing the same organism, and catheter salvage. Treatment failure occurred with catheter removal due to persistent infection, or recurrence of the same organism within 30 days. Of the initial 75 patient records which were reviewed, 35 were excluded for various reasons including mechanical problems with the line, discontinuation of the line because it was no longer needed, and the presence of viral infection. The remaining 40 patients successfully retained their central catheters following ethanol lock treatment and experienced no adverse effects.

Broom et al., (2008) performed a prospective trial involving 19 patients with tunneled central venous catheters. All of the 17 patients included in the study had infections which were attributed to their central venous catheter. Study inclusion criteria were to have a tunneled central venous catheter, no allergy to ethanol, and have a bacterial infection with the central line
as the source. Patients were excluded if they had an allergy to ethanol, evidence of an exit site infection or metastatic infection, or if they were pregnant or breastfeeding. In addition to appropriate antibiotic therapy, the patients were treated with 70% ethanol locks. The locks were instilled in both lumens of the patients’ catheters and allowed to dwell for 4 hours over a period of 5 days. Successful treatment occurred if blood cultures obtained from all lumens on day 6 showed no evidence of the original infecting organism and preservation of the catheter for 14 days. Seventeen patients completed the 5 day ethanol lock therapy. Of these 17 patients, none of the day 6 surveillance blood cultures were positive for the original infecting organism. Additionally, 12 of the 17 patients maintained their lines for more than 14 days following treatment and no considerable side-effects from the therapy were reported.

Use of ethanol lock therapy was also examined by Mouw, Chessman, Lesher, & Tagge (2008). Medical records of 10 pediatric patients who received ethanol lock therapy were reviewed. All of these patients had a diagnosis of short bowel syndrome and required a central venous catheter for the administration of parenteral nutrition (PN). The exact methods involved with the ethanol lock therapy varied from patient to patient. Half of the children began ELT after having the catheter for a number of days, while the other half began ELT the day the CVC was placed. Dwell times also varied in this group depending on each patient’s specific PN cycle. The shortest dwell time was 4 hours and the longest 14. A 70% ethanol lock solution was used for all of the patients. Findings were as follows; prior to ELT the rate at which a catheter related infection (CRI) occurred was 11.15 CRIs per 1000 catheter-days, following initiation of ELT, the rate of CRIs was 2.07 per 1000 catheter-days. It was determined that parental nonadherence was the cause for persistent catheter infections in one of the children. No adverse reactions to therapy were noted.
The use of ELT was again evaluated in the prevention of catheter related blood stream infection in home care patients receiving parenteral nutrition. Opilla, Kirby, and Edmond (2007) began selecting patients who were followed by the Virginia Commonwealth University Medical Center Nutrition Support Team. Nine patients were selected. All experienced recurrent line infections. The use of ELT was presented to them not as a research study, but as a possible strategy to prevent future infections. Methods used included instilling 3mls of a 25% to 70% ethanol solution into each lumen of the catheter. A minimum dwell time of 2 hours was recommended, and instillation of the ethanol solution occurred 2 to 7 days per week. Following the dwell period, the ELT was cleared through the line using standard flushing protocol. Prior to starting ELT the nine patients experienced a total of 81 line infections and sixty-nine catheter changes. Following ELT the number of line infections was reduced to 9 with only one catheter change. Negative effects experienced by the patients included a sensation of lightheadedness, dizziness and nausea after the ethanol was flushed through the line. In an attempt to lessen these side effects, patients decreased the frequency of ELT, changed the ethanol concentration from 70% to 25%, and decreased the flush volume from 3mL to 1mL. The patients reported no improvement in symptoms following these changes, however they did convey a decreased awareness of these sensations over time.

**Conclusion**

In summary, central venous catheters are an invaluable tool in the medical field for use in treating a variety of illnesses. Catheter related blood stream infections are a serious complication associated with the use of CVCs and continued research is needed to further medical professionals’ knowledge base in preventing and treating CRBSIs. Not only are CRBSIs costly, they also are associated with a negative impact on patients’ quality of life, therefore prevention
of CRBSIs is key. Prevention of CRBSIs begins with using maximum precautions to create a sterile field during the insertion of a CVC and continues with appropriate maintenance of the site. Having experience with which organisms commonly cause CRBSIs as well as which antibiotics are used to treat them is also important. Although no specific guidelines are currently in place, the use of ALT or ELT may be appropriate in certain patient situations. ELT appears to be safe, well tolerated, and effective in preventing and treating CRBSIs.
References


