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Abstract

Effectiveness of Antimicrobial Coated Catheters for Prevention of Blood Stream Infection in a Trauma Patient Population

Jeffrey Purvis, Doctor of Philosophy, 2013

Dissertation Directed by: Erika Friedmann, PhD, Professor, UMB

Background: Clinical leaders are faced with making the decision to utilize products with varied designs without enough evidence to make an informed decision. An example of this problem is the decision regarding whether to change from uncoated to antimicrobial or antibiotic catheters to prevent Central Line Associated Blood Stream Infection (CLABSI).

Purpose: This study compares the effectiveness of three types of central venous catheters (CVC): (1) non-coated, (2) antimicrobial (silver), and (3) antibiotic coated. The four CLABSI outcome measures were: (1) CLABSI rate per 1,000 catheter days, (2) gram positive organism cultures per total admissions, (3) gram negative organism cultures per total admissions, and (4) yeast organism cultures per total admissions.

Methods: This retrospective study assessed the comparative effectiveness of CVCs in a trauma hospital population (n = 10,680) admitted between July 1, 2006 and June 30, 2011. Monthly data were obtained for the time periods when each catheter type was purchased. Linear mixed models (LMMs), with data nested within units, were used to examine differences among the three periods in BSI rates and frequency of organism type.

Results: Antibiotic coated catheters reduced BSI rates (beta = 4.054, $p < 0.001$) and gram negative organisms (beta = 6.608, $p < 0.001$). Silver impregnated catheters reduced gram negative organisms (beta = 3.194, $p = 0.009$) compared with uncoated catheters.

Conclusion: Further improvement in CVC technology is required to be effective for broad spectrum of organisms. Large prospective randomized clinical trials are needed to determine the effectiveness of devices to inform purchasing decisions.

Effectiveness of Antimicrobial Coated Catheters for Prevention of Blood Stream Infection in a Trauma Patient Population

by

Jeffrey Purvis

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Statement of the Problem

Central line associated blood stream infections (CLABSIs) that are determined to be "health care-associated" infections are considered to be a preventable threat to patient morbidity and mortality and a considerable strain and cost to the healthcare system (CDC, 2012). BSI leads to increased length of stay, additional complications, increased cost, and sometimes death. "Attributable mortality is estimated between 2% and 35%, and length of stay in the ICU is thought to increase by 9.5 to 11.9 days causing substantial economic cost and excess morbidity" (Ramritu, p.104. 2008). According to the Centers for Disease Control, the average additional cost to treat a patient with a blood stream infection ranges from between $34,500- $56,000 (CDC, 2012).

BSI is so common that an expected incidence is recognized as difficult to avoid and is tolerated until the incidence of BSI rises beyond the historical average benchmarks. Based on surveillance metrics, efforts to prevent infection are expected to gradually improve over time and current levels derived from the standard comparative population statistics are "expected." "The Standard Infection Ratio (SIR) is calculated by dividing the number of observed infections by the number of expected infections" (CDC, 2012). "The number of expected infections, in the context of statistical prediction, is calculated using CLABSI rates from a standard population during a baseline time period," as reported in the National Healthcare Safety Network (NHSN) Report (CDC, Jan 2012). Results are of elevated concern when the comparison ratio results in >1.0 which indicates "slowing of Progress" by the healthcare provider. Any level is unacceptable and should cause concern that less than optimal conditions exist (CDC, Jan 2012). Every effort should be made to investigate and understand the specific source(s) of BSI so that improvements could be made to target a level of zero.

Clinical leaders are faced with making the decision to implement products with varied designs, such as antimicrobial or antibiotic coatings on catheters and specialized dressings in order to prevent infection, but not enough evidence exists in the literature to make an informed decision. What is the best way to monitor the outcomes of their decision? How do they evaluate the outcomes of their decision to justify the continued use and associated costs?

This study is a retrospective comparison of the outcomes of three types of catheters used consecutively over the course of over four years. The information was collected from two sources of data. The first is the source of all demographic, diagnostic and admission/discharge information which is derived from the electronic medical record. The second source is a file maintained by a member of the infection control team with the intent to track information related to each patient determined to have a BSI. By using this information, this study answers the questions of how to measure and monitor the outcomes as well as justify the decision and its associated costs based on statistical outcomes.

Introduction

Critically ill patients frequently require the need for central venous catheters to maintain direct vascular access. The catheters are inserted in large veins, typically in the groin, neck, or chest and are a means to provide nutrition, medications, fluids, as well as to collect blood samples. Unfortunately, the advantage of direct access potentially exposes the patient to infection by providing a direct pathway for organisms to enter the very core of the human body. If colonization is not controlled or prevented, this bridge into the blood stream may allow organisms to enter the body and may cause systemic BSI). "The skin around the insertion site is the most common source of colonization and infection of vascular catheters in place for less than 10 days. Skin flora migrates along the external surface into the subcutaneous catheter tract" (Corral. p.217, 2003).

Purpose

Multiple types of catheters are introduced in an attempt to address concerns that central venous catheters (CVCs) put patients at risk for BSI. Manufacturer sales representatives explain to clinicians and administrators that the catheter design has a coating or contains inherent metals that inhibit and/or kill bacterial growth. However, there are limited scientific data to support this. Clinicians implement multiple methods to prevent BSI, including consistent training of personnel, observing proper technique, and choosing lower risk sites. Unfortunately, none of these alternatives alone is highly effective in sustaining a reduction or elimination of BSI. Some institutions have attempted a bundled approach to prevent infection, however, if these fail, a product design intended to reduce infection by preventing or reducing colonization at the site of insertion could be effective in preventing infection.

The aim of this dissertation was to compare two types of central line catheter technology to a (third) standard non-coated catheter (Arrow International). The first catheter design is an antimicrobial impregnated catheter (Edwards) extruded from polyurethane combined with silver, carbon, and platinum. The second catheter design contains a coating of minocycline and rifampicin on the inner and outer surfaces (Cook Inc.). CLABSI and related organism rates of these patient groups were compared in a trauma population in a large Primary Adult Resource Center (PARC) designated metropolitan hospital.

Biophysical Model

A biophysical model was used as the basis for understanding the CLABSI source. Bong states that "CLABSI occurs when microorganisms gain access to the bloodstream via one of four routes: catheter hub contamination, colonization of organisms at the catheter insertion site, contaminated infusate, and/or haematogenous seeding and that the first two portals of entry are the most frequent routes via which BSI occurs" (Bong, 2003).

Catheter hub contamination occurs with frequent connection and disconnection at the hub site with lines, syringes, and other devices. Contaminated catheter hubs, from which organisms migrate along the internal surface of the catheter, are the most common source of organisms (Niel-Weise, 2007). This introduction through the inner cannula may carry organisms in fluids or on the inner surface of devices leading directly into the blood stream possibly leading to BSI.

Site colonization is related to the actual location of line placement (Marschall, 2008). Commonly used central line insertion sites locations include the internal-jugular vein, femoral vein, and the subclavian vein. The insertion site used is influenced by patient diagnosis, injury, patient size, and influential events at the time of insertion such as planned versus emergency insertion. Studies and historical clinical experiences suggest that the femoral site is more likely to contribute to infection (Marschall, 2008). This site is associated with increased risk of infection due to the proximity of the femoral vein to the groin, which makes it difficult to maintain a clean skin surface. Skin colonization is more likely to spread to the catheter and be introduced around the outside perimeter and skin tract as well as through the hub and inner lumen during procedures (Corral, 2003).

Migration of microbes at the insertion site occurs over time after organisms gain access to the entry point at the skin surface. BSI is not necessarily impending when the tissue around the catheter becomes colonized. However, if it isn't prevented or interrupted, "colonization can migrate along the subcutaneous insertion tract" without mechanical assistance or necessarily high skin flora levels (Ramritu, 2008).

Haematogenous seeding occurs when virulent organisms originate from the patient at other sites of infection which gain access to the bloodstream confirmed by microarray technology matching the genetic make-up of organisms (Fowler, 2005).

Contaminated infusate results from an unsuspected break in sterile techniques during preparation or administration of intravenous fluids or medications which may contribute to CLABSI.

Regardless of the method that organisms contribute to BSI listed above, a catheter designed to have a bacteriostatic or bactericidal effect when in close proximity to microbes would be expected to kill, prevent growth, and advancement of colonizing organisms on the inner and outer surface of the catheter so the designs have become a proposed strategy to reduce risk in high incidence settings (Ramritu, 2008).

Significance

The public health significance of CLABIS is twofold. One is from the clinical perspective regarding the patient's outcomes and the efforts by the clinical team to prevent infection. The second is the overall economic cost impact to healthcare that could be prevented if addressed adequately. The Division of Healthcare Quality Promotion

(DHQP) is part of the National Center for Infectious Diseases, in the CDC's Coordinating Center for Infectious Diseases. "The mission of DHQP is to protect patients, protect healthcare personnel, and promote safety, quality, and value in the healthcare delivery system by providing national leadership in key areas" (CDC, 2013). The Prevention and Evaluation Branch (PEB) of the DHQP develops and promotes the implementation of evidence-based guidelines, recommendations, and other interventions to prevent healthcare-associated infections and antimicrobial resistance, related adverse events, and medical errors. In 2008 the Centers for Medicare and Medicaid services declared central line catheter related BSI as a "Health care associated infection" that would not be reimbursed (CMS, 2008).

Patients are diagnosed with CLABSIs approximately 250,000 times annually, of which, 30,000 to 62,000 result in deaths (Clancy, 2009). In the United States alone, the CDC (2009) reported approximately 80,000 catheter related BSIs. About 25% of BSIs recorded in ICUs are secondary to proven catheter related infection and up to 80% of the so-called primary bacteremia may be caused by catheter infection (Brun-Buisson, 2004). A CLABSI is estimated to increase length of stay by 9.5 to 11.9 days (Ramritu, 2008). The average cost for the additional expense associated with a patient BSI is estimated to range between $3,240 (Rupp, 2005) to $90,000 (Moretti, 2005). Multiplying half of the cost estimated by Moretti (2005), with the CDC's reported 80,000 CLABSIs (2009), hospitals in the U.S. could lose $3.6 billion in expense that would not be reimbursed. Based on the number of hospitals registered in the U.S., according to a 2010 survey reported by the American Hospital Association (2012), the average loss per hospital is $625,652.

In 2006, The Institute for Healthcare Improvement attracted widespread participation in their “100,000 lives” campaign to encourage hospitals throughout the United States to implement best practices bundles aimed at preventing complications of hospitalization (Yokoe, 2008). With this in mind, nursing administrators are finding themselves in the position to make decisions regarding products that are allowed into a hospital’s product formulary. Budgets do not grow as quickly as the costs associated with healthcare technology, so nurse managers, responsible for maintaining budgets within limits, are forced to make decisions which provide the best care for patients, while maintaining a fiscally responsible budget. These critical decisions are becoming more frequently involved with technology designed for the prevention of infection.

Assumptions

The assumptions in this study begin with the insertion technique. It is assumed that the clinicians involved use the standard aseptic technique to avoid introducing microorganisms into the patient. Each of the catheter designs requires aseptic technique for insertion of the catheter. The site is dressed according to hospital policy and access for sampling or administration of fluids, medications or nutrition is assumed to be per hospital protocol. It is assumed that the heterogeneity among the three groups is normally distributed so that each represents a typical population at this hospital. Likewise, it is assumed that the three groups are homogenous so that over the course of time, unexpected patient differences do not contribute to differences in the outcomes. It is assumed that accepted care practices have not changed significantly during the course of the study. It is assumed that the clinical data were accurately collected by clinicians, interpreted consistently, and entered correctly into the database by the infection control center staff.

Summary

Scientific research should be used in the clinical arena to measure the effects of treatments and products to determine their effectiveness. Through careful control of practices and manipulation of approved products, multidisciplinary teams can determine which are the most effective products and apply their use to maintaining or improving patient care outcomes and justifying the associated expense. It is intended that this study provides insight into possible methods to collect clinical data to more accurately review the clinical outcomes related to new product implementations.

Chapter 2: Review of Literature and Conceptual Framework

Introduction

This chapter will review the types of catheter technologies in this study that are commercially available to prevent CLABSI. Brief descriptions of the technology will be provided as well as results of the published research relative to those designs.

"Central venous catheters (CVCs), including a variety of vascular access devices are widely used for drug delivery, intravenous feeding, monitoring and blood sampling in a variety of hospital settings" (Wang, p.1, 2010). CVCs can be placed via the subclavian route, internal jugular, and femoral sites (Dunser, p.1779, 2005). A plethora of suggested interventions are promoted as a means to prevent CLABSI, but very few alone are shown to prevent infection. Multiple sources contribute to central venous catheter related BSI, including lack of compliance with hand hygiene, improper catheter insertion technique, and inconsistent and improper application of dressing materials at the catheter insertion site. However, preventive measures can reduce the incidence of infection. Pronovost et al. (2006) demonstrated in a large scale study (n = 103 intensive care units) that an intervention bundle focused on consistent hand hygiene, use of full barrier precautions, cleansing skin with chlorhexadine, avoiding insertion of CVCs into the femoral vein, and prompt removal of unnecessary CVCs resulted in a large and sustained reduction in central line associated BSI. When multiple concurrent interventions are introduced, "the effectiveness of and potential synergy between specific combinations of interventions are unknown" (Yokoe, 2008). Collective efforts are successful but it is difficult to identify which intervention(s) worked. Possibly there are multiple concurrent sources of infection which require multiple preventative measures.

Risk Factors

Multiple risk factors are present throughout the indwelling time of a CVC which makes infection prevention difficult.

> "Risk factors for CVC-related infections include triple lumen CVC, which are often preferred by clinicians; and the site of insertion. In common with most studies, internal jugular vein insertion was shown to have the highest risk and subclavian vein insertion the lowest risk of infection. Other risk factors included more than one catheterization in the ICU; an infectious focus elsewhere in the body; exposure of the catheter to bacteraemia; the lack of systemic antimicrobial therapy; duration of catheterization; the types of dressing; and the experience of the staff inserting the device" (Corral, p.217, 2003).

These risk factors allow contamination of the skin and device at the insertion site which may lead to infection.

Development of Colonization

Contamination through previously mentioned risk factors may lead to colonization. "… catheter colonization with skin microorganisms along the external surface seems to be the most important pathogenic mechanism" (Dunser, p.1778, 2005). "The skin around the insertion site is the most common source of colonization and infection of vascular catheters in place for less than 10 days. Skin flora migrates along the external surface into the subcutaneous catheter tract" (Corral, p.217, 2003). For long-term use CVCs, contaminated catheter hubs from which organisms migrate along the internal surface of the catheter are the most common source of organisms (Niel-Weise, p. 2059, 2007). After 7-10 days, endoluminal colonization caused by contaminated catheter hubs or IV fluids becomes more prominent" (Dunser, p.1778, 2005). Depending on the length of time the catheter is indwelling, the mechanism of organism infection shifts from skin and outer surfaces of the catheter to the hub and inner surface of the catheter.

Correlation Between Colonization and Bacteraemia

"There has been debate regarding the association between colonization and bacteraemia. Polderman and Girbes suggested that approximately 20% of colonized catheters proceed to catheter related bacteraemia. Veenstra et al. found the overall bacteraemia-colonization ratio was 25%, but the range was 0-86%" (Moretti, p.144, 2005). Ramritu supported the relationship and supported its use as a measure in BSI research. "The microbiologic evidence on the role of CVC colonization in the development of catheter related blood stream infection (CLABSI) is credible, and we support others who argue that catheter colonization is a good surrogate for CLABSI and can be used as a relevant outcome in assessing effectiveness. Further exploration of this relationship should focus on the application of statistical tests of surrogacy" (Ramritu, p. 112, 2008). In a review of several studies, Moretti (p. 144, 2005) found the correlations between colonization and bacteraemia were only 0.25 and 0.22 for chlorhexadine-silver sulphadiazine (CSS)-coated and uncoated catheters, respectively however, the correlation between bacteraemia rates for the two types of catheters was 0.86. Moretti concluded that "these correlations imply that the association between colonization and bactereamia is weak and suggested that the causal linkage between colonization and bacteraemia may need re-examination" (Moretti, p.144, 2005). Outcomes are difficult to measure. "Clinical trials of antimicrobial catheters have typically failed to estimate accurately their effectiveness because of small numbers of CLABSI and tend to draw conclusions from the surrogate outcome of catheter colonization" (Ramritu, p.104, 2008). Indeed, Maki et al. stated that “CLABSI rates, rather than colonization rates, are the preferred measure when comparing CVCs” (Moretti, p.144, 2005).

Types of Coated Catheters

In order to prevent the growth and colonization of infectious organisms from failed attempts to prevent contamination, manufacturers have developed catheters with coatings and combinations of materials designed to help prevent colonization and subsequent infections. These types of catheters contain an antibiotic coating, such as minocycline, rifampin, or cefazolin, as well as silver with or without chlorhexadine which are all intended to be bacteriostatic and therefore prevent entry of microorganisms into the bloodstream via the inner or outer surfaces of the catheter. While most catheters have the coating applied to the external surface of the catheter, there are some catheters that also have the coating applied to the inner lumen. Unfortunately, the potential disadvantage to these coatings is the associated risk of developing antibiotic resistance or reactions (Chatzinikolaou, 2003).

Silver Coatings

More recently, another type of catheter was introduced which “uses an integrated antimicrobial material extruded from polyurethane, combined with the natural elements of silver, carbon and platinum” (Edwards Lifesciences website, 2010). The manufacturer’s website (2010) states that this combination “releases silver ions from the device material which kills colonizing bacteria in both the inner and outer catheter surfaces.”

Another type of CVC that has been produced is a catheter that combines chlorhexadine-silver and sulfadiazine applied to the catheter’s external surface. This application prevents the adherence and proliferation of microorganisms on the catheter (Rupp, 2005). This catheter is also associated with limitations including possible cytotoxicity, sensitivity, allergy, and a significant decrease of the amount of coating after a few days.

Ramritu (2008) conducted a systematic review to examine the evidence on the effects of antimicrobial-coated central venous catheters in lowering rates of CLABSI between 1985 and 2006 in critically ill adults. Of the 34 studies selected based on predetermined criteria, the review consisted of 5 randomized-control-trials (RCTS) that involved silver technology as part of a central line catheter. Overall, silver coated catheters and silver, platinum, and carbon coated catheters, failed to demonstrate significant relative risk reduction of BSI.

Corral, et al. (2003) examined "microbial colonization and the incidence of CLABSI associated with Oligon Vantex silver central venous catheters in critically ill patients in a prospective, randomized, controlled 17-month trial in an intensive care unit (N=206)" (Corral, p.212, 2003). In this trial comparing non-coated catheters to the coated catheters, cultures of the patients' catheter blood, skin, catheter hub, and catheter-tips were taken. Of 206 catheters, there were 103 in each group (Corral 2003). Colonization was greater in the control catheters than in the silver catheters (44% vs. 29%, respectively; $p = 0.04$) (Corral 2003). There were a total of five cases of CLABSI among the patients including one among the silver catheter group and four cases from the non-coated catheter group (Corral 2003). Rates of CLABSI were significantly lower in patients with silver catheters than in patients with non-coated catheters (0.8 per 1000 catheter-days vs. 2.8 per 1000 catheter days, respectively; $P < 0.001$) (Corral 2003).

These data demonstrate that the Oligon Vantex silver catheter reduced the incidence of catheter-colonization and the risk of CLABSI. However, as Moretti summarized, “the association between colonization and bactereamia is weak and that the causal linkage between colonization and bacteraemia may need re-examination”(Moretti, p.144, 2005).

Moretti et al. (2005) performed a prospective, randomized, controlled study to compare an uncoated catheter to a silver coated central line catheter design. The study included 514 patients (252 in the treatment group and 262 in the control group) in 10 hospitals. Cultures of the patients’ blood, distal catheter tip, and an endocutaneous segment were examined. Although the colonization rates were high (24.5%), Moretti et al. (2005) could only demonstrate that infection rates likely “depend more on non-catheter related factors such as adherence to infection control standards, selection of insertion site, duration of CVC placement and dressing change frequency” (p.140). This trial showed that there were no significant differences in the outcomes of colonization and infection between the silver impregnated catheter and the non-silver catheter.

Corral (2003) involved only ICU patients who had an average stay of 13 days where the patients in Moretti’s study (2005) averaged 6 days and used a less strict definition of CLABSI. When Ramritu (2008) combined to pool results in a meta-analysis, a potential reduction in risk of CLABSI is noted (RR, 0.54; 95%, CI: 0.16-1.85), but further trials are required to achieve a more precise estimation.

Ramritu (2008) reported that there were three qualifying studies referencing the silver ion/alloy. The studies, by Bach (1999), Stoiser (2002), and Dunser (2005), collectively contained 240 silver ion coated with 244 uncoated. Dunser only examined colonization and showed that there was no difference in colonization between the standard and silver catheters. Ramritu (2008) pooled the CLABSI rates reported by Bach and Stoiser and determined that they “gave no indication that this coating was effective in preventing CLABSI” (p.110). Ramritu also pointed out that “Stoiser et al. used a scoring system to define CLABSI and that the scoring system had a greater sensitivity than the Center for Disease Control definition” (Ramritu, p. 110, 2008). This could have possibly diluted the effect of the catheter by producing more false positives. Likewise, it could have captured true CLABSIs that would not have been identified using other less sensitive methods and therefore should not have been compared. In another study by Wang, there was a recommendation that the use of silver iontophoretic CVCs may reduce the incidence of CLABSI although tests did not reach significance (Wang, p. 9, 2010). Finally, silver might not be effective against a broad spectrum of organisms. A study by Guggenbichler et al. showed that that some strains of Enterobacteriaceae are silver-resistant (Corral, p.217-218, 2003). This review of the literature indicates that although silver reduces colonization of organisms, there is limited conclusive evidence on the effect of silver coated CVCs in preventing CLABSI. Since silver is known to have limited effectiveness, host reactivity, and possible resistant strains, manufacturers must search for alternative solutions.

Antibiotic Coatings

In recent years, there has been a concerted effort to apply antimicrobial technology to prevent infections, including the use of prophylactic antibiotics and catheters with special coatings and surface modifications (Moretti, p.140, 2005). In an attempt to find other coatings to prevent BSIs, antibiotics are used on catheter surfaces. Widespread adoption is contentious because antibiotic catheters may accelerate development of resistance among microorganisms (Ramritu, p. 112, 2008). Continued studies are required to clarify further the possibility of resistance development, especially in the setting of long term catheterization (Wang, p. 9, 2010). In animal models, resistance has been demonstrated, but evidence outside the laboratory has been scarce. Evidence of development of antimicrobial resistance associated with the use of these antibiotic-impregnated catheters was not recorded" (Ramritu, p. 111, 2008). Although there are concerns related to potential antibiotic resistance with regard to rifampicin, adverse reactions to chlorhexadine are reported (Moretti, p.140, 2005). Central venous catheters with antimicrobial agents have raised concerns regarding the possible development of antimicrobial resistance (Dunser, p.1779, 2005), and these concerns and other technical issues have limited the widespread use of antibiotic-coated catheters (Moretti, p.140, 2005).

Limited Antibiotic Solutions

Manufacturers are faced with limited choices in the antibiotics that can be used as coatings, which makes creating this technology difficult. Two considerations in using antibiotic coatings are identified by Raad (1996). The first is that the antibiotics selected for prophylactic use cannot include antibiotics considered first-line drugs for treating an established infection (Raad, p. 418, 1996). The second is that antibiotics selected should have a broad spectrum of effectiveness against the most common causes of catheter related infections. The most common organism leading to infection is S. epidermidis, followed by S. aureus, C. albicans, and some nosocomial strains of resistant gram-negative bacilli such as A. baumanii, and S. maltophilia (Raad, p.422, 1996).

Summary

Researchers involved in development of robust technology are continually searching for new designs to incorporate into central line technology with the goal to prevent infection from its multiple sources. Silver, antimicrobial, and antibiotic coatings in varying combinations seem to have an effect in reducing colonization, and in some cases BSI. However, more robust research designs are needed that can address the question of whether or not technology with organism resistant designs not only reduces colonization but prevents the incidence of BSI. Designs that prevent BSI could already be available on the market, but large, randomly controlled studies that are not sponsored by manufacturers have yet to be published.

Chapter 3: Research Design and Methods

Introduction

This study assessed the comparative effectiveness of central venous catheters in a trauma population admitted between July 1, 2006 and June 30, 2011. Three types of catheters were used in this period. The first type is the design without coating, the second type is a silver impregnated catheter, and the third type is an antibiotic coated catheter.

The cohort consisted of all patients meeting inclusion/exclusion criteria entering the trauma facility and admitted to an Intensive Care Unit (ICU), called A, B, or C. From this cohort, a subgroup of patients was identified according to development of a positive CLABSI. Information for the entire cohort was obtained from the Central Data Repository (CDR), an index extracted from the electronic medical record provided by the Department of Epidemiology at the hospital. Patient information was provided in averages per month for each unit and included demographics, admission/discharge, and multiple diagnoses. The affected subgroup was compared to the larger cohort to test for differences according to available covariates and none were found. The infected subgroup was divided into three subgroups divided according to the time period when the catheter types were purchased. This information was based on reports from the hospital's materials management information system. The system shows catalogued purchases by volume and the volume of distribution to each unit in the hospital. Patients admitted to the three units during each period were assumed to have received the type of catheter purchased at the same time. Between each period, a one month buffer period of data was omitted from the analysis in order to accommodate utilization of any remaining inventory so that any effects of the gradual conversion in catheter design would not dampen the outcomes. In addition, a buffer period may allow clinical staff to become familiar in the use of new product and prevent inclusion of outcomes resulting from an underdeveloped technique.

The silver and antibiotic designs were compared to the uncoated design based on BSIs per 1,000 catheter days and monthly totals of types of infections based on organism type. Patients were nested by unit.

Operational Definitions

The following are operational definitions necessary to describe identification of certain clinical determinations. There may be variations described in research depending on the current understanding and guidelines recommended by the CDC and experts in the field at the time it is published.

- Central catheter, central line, central venous catheter (CVC) is defined as a percutaneous vascular access devices used for drug delivery, intravenous feeding, monitoring and blood sampling in a variety of hospital settings" (Wang, p.1, 2010). CVCs can be placed via the subclavian route, internal jugular, and femoral sites (Dunser, p.1779, 2005).
- Colonization is defined as the growth of 15 or more Colony Forming Units (CFU/ml) in culture of the distal segment of the catheter by the roll plate method or more than 100 CFU in cultures (Bong, 2003).
- CLABSI or CLABSI "is defined as the isolation of the same organism (i.e. identical species) from the colonized catheter and peripheral blood in a patient with accompanying signs and symptoms of blood stream infection (BSI) and no other source of BSI" (Moretti, p. 141, 2005).

- Bacteraemia is defined as cases where the same organism was isolated from the catheter and peripheral blood cultures, regardless of documented signs or symptoms or other potential sources of infection (Moretti, p. 141, 2005).
- Biopatch is a silver-impregnated dressing/disk frequently used in conjunction with central venous catheters to prevent infection.
- Central Data Repository (CDR) is the database from which demographic, diagnostic, admission and discharge information was extracted.
- Materials Management Database is the hospital Supply Chain Management database from which materials utilization and location of distribution was extracted.
- Gram Stain is the method developed in 1884 by a Danish physician Christian Gram which involves 4 steps: 1) the heat fixed smear is covered with a solution of crystal violet; 2) the dye is washed off and then the smear is flooded with an iodine solution; 3) the iodine is washed off with water and then rinsed with 95% alcohol; 4) the smear is counterstained with safranin or Bismarck brown (Volk, p. 229, 1986).
- Gram-positive (G+) organisms are bacteria that will retain the crystal violet dye when washed in a decolorizing solution known as Gram staining. These include - *Actinomyces, Bacillus anthracis, Bacillus cereus, Clostridium, Clostridium difficile, Corynebacterium diphteriae, Enterococcus,Lactobacillus, Lactococcus, Listeria monocytogene, Microbacterium, Micrococcus, Peptostreptococcus, Pneumococcus, Staphylococcus, Staphylococcus aureus, Staphylococcus saprophyticus, Streptococcus,*

Streptococcus agalactiae (groupe B), Streptococcus β hémolytique, *Streptococcus bovis, Streptococcus mitis, Streptococcus pneumoniae (Pneumococcus), Streptococcus pyogenes, Streptococcus salivarius,* (Volk, p.229, 1986).

- Gram-negative (G-) organisms are bacteria that do not retain crystal violet dye in the Gram staining protocol. In a Gram stain test, a counterstain (commonly safranin) is added after the crystal violet, coloring all gram negative bacteria with a red or pink color. These include *Aeromonas, Bacteroïdes fragilis, Bartonella henselae, Bordetella pertussis, Bordetella parapertussis, Brucella, Burkholderia cepacia, Campylobacter, Enterobacter aerogenes, Enterobacter sakazakii, Enterobacteriaceae, Escherichia coli, Francisella tularensis, Fusobacterium, Fusobacterium Necrophorum, (gonorrhoeae meningitidis* n'existe pas), *Haemophilus, Haemophilus ducreyi, Haemophilus influenzae, Helicobacter pylori, Legionella, Legionella pneumophila, Moraxella catarrhalis,* (anciennement *Branhamella catarrhalis), Neisseria, Neisseria meningitidis, Photobacterium, Proteus, Pseudomonas, Pseudomonas aeruginosa, Salmonella, Salmonella typhi, Shigella, Stenotrophomonas maltophilia),* (anciennement *Xanthomonas maltophilia), Veillonella, Vibrio cholerae, Yersinia enterocolitica,* (Volk, p. 229, 1986).
- Yeast are fungal organisms that will not stain gram positive or negative. They include: *Candida albicans, Candida tropicalis, Candida parapsiliosis, and Candida krusei* (Volk, p. 536, 1986).

Design Inclusion/Exclusion Criteria

This retrospective comparison study was limited to patients over 21 admitted to this large metropolitan trauma hospital, as it focused only on the adult population where data were entered into the database. It was also limited to trauma patients receiving a central line catheter for at least 3 days. Exclusion criteria, used previously by Raad (1997), excluded those patients who had a central venous catheter for less than 3 days and patients who had a central venous catheter inserted for greater than 11 days. According to Raad (1997), patients with catheters indwelling for less than 3 days are not as likely to develop or show signs of hospital acquired catheter related infection within that small window. Patients with catheters inserted for more than 11 days have a greater chance in developing infection systemically, possibly due to other contributing interventions. Additional exclusion criteria excluded patients less than 21 years of age, pregnant women, patients who have a history of suspected allergies to the silver coated catheter, patients with a suspected allergy to the antibiotics minocycline or rifampin, patients with a tracheostomy, and patients with current infection at the time of admission.

Indwelling time could not be consistently collected, so inclusion criteria included all admitted adult trauma patients on the ICUs confirmed to have a central line related blood stream infection where all necessary outcome information was available.

Instruments/Data Collection

This study involved the use of existing databases maintained at the organization. All data examined came from three sources. The first was the Central Data Repository (CDR) which is the database from which demographic, diagnostic, admission and discharge information was extracted. All patient information was provided as averages per month by unit.

One factor examined from the CDR was the Abbreviated Injury (severity) Scale assessed on admission.

> "The Abbreviated Injury Scale (AIS) incorporates current medical technology providing an internationally accepted tool for ranking injury severity. The AIS© is an anatomically based, consensus derived, global severity scoring system that classifies an individual injury by body region according to its relative severity on a 6 point scale. The severity component of AIS has also been applied in health services research both as an outcome measure as well as a covariate for case mix adjustment purposes" (online http://www.aaam1.org/ais/, accessed 10/24/11)

Average Abbreviated Injury Scale was called Injury Severity Score (ISS) in the database and was provided as a monthly average per unit used as a co-variable to control for differences between unit populations as well as within the same unit populations throughout the three periods.

The second was the Materials Management Database which is the database from which materials utilization reports were run. Volumes and location of distributed central venous catheters were extracted by manufacturer and catalogue number to demonstrate conversion to alternate designs and determine adequate use in the facility.

The third was a database maintained by the infection control department to track details and attributes of patients determined to have a CLABSI. Examples of this information include the admission date, unit, and type of organism isolated by specific name or general category.

Data Utilization

Many points of data were expected to be available consistently throughout the three periods but upon review, some of the expectations were not met. Data was obtained from the CDR database and sorted according to unit and month of admission. This information was complete without missing variables and contained the elements representing age, gender, admission date, discharge, ISS, and unit.

Catheter utilization for each patient unit was obtained from the hospital's materials management database. This information was complete with monthly volumes of specific catalogued catheters used throughout the facility. This was examined to assure that the previous design was depleted and the subsequent designs were used as expected.

The infection control data base, which collected information on patients determined to have BSI, provided the admission date, unit, and isolated organism(s) from blood samples. During the span of the three periods, the method changed regarding collection of organism information. Many similar abbreviations were used for the same organism and in some cases, only the broad category of organism type was used such as "gram negative species" versus the specific organism name such as "Staphylococcus Aureus." In order to maintain consistency throughout the three periods, the three organism types, gram positive (G+), gram negative (G-), and yeast, were used only. Likewise each could only be counted for a patient once as previous multiple colony types could have been recognized as a single category. In the third period, a new coding system was used by the infection control department as a method to standardize abbreviations. All three periods were converted to a reduction of any occurrence of G+, G-, or yeast.

Four outcome measures for catheter related infections were assessed for analysis: catheter tip colonization, CLABSIs with type of organism, CLABSI days, and time to development of CLABSI.

When each catheter is removed, standard procedures include culturing of the catheter tip to assess for the presence of microbial organisms. If any organism is present at more than 15 CFU/ml, "catheter colonization" is considered positive and the presence of catheter colonization was entered into the data base. This information was not available throughout the three periods consistently and so was not able to be used as an outcome for this analysis.

Based on consistent definitions, a CLABSI was confirmed and documented by a team made up of infection control nurses and staff in the Department of Epidemiology. The presence of CLABSI was entered into the database along with any associated information related to the organisms isolated from the blood sample and was used as outcomes for this analysis.

Days of CLABSI could be determined based on symptoms, date of confirmation of infection, and surveillance of blood samples to later rule out infection.   The date when the blood is no longer positive for the BSI is recorded in the database. The number of days elapsed between diagnosis and end of CLABSI could be calculated to determine trends for the group. However, this information was not available consistently and therefore was not be used as an outcome for this analysis.

Time to development of CLABSI could be calculated based on days elapsed between date of catheter insertion and date of diagnosis of CLABSI. This information was not available consistently during the three design periods, and therefore was not be used for this analysis.

Other variables obtained from the data base included:

- Date of admission
- Trauma Severity Score on admission (Acuity scale)
- Antibiotic therapy
- Patient demographics (age, gender, race)
- Primary diagnosis
- Co-morbidities such as immunosuppression, steroids etc.
- Date of CLABSI diagnosis
- Primary medical service –(team)
- Mechanical ventilation assistance

Data Analysis Procedures

The aim of this dissertation was to compare the effects of a non-coated central line catheter, a silver impregnated catheter, and an antibiotic coated catheter on catheter related infections among trauma patients in a large PARC-designated metropolitan trauma hospital. Two outcome measures for catheter related infections will be assessed: catheter colonization type frequency and occurrence of CLABSIs.

Catheter colonization frequency by organism type and CLABSI occurrences are continuous variables. The covariates ISS and age are continuous and gender is dichotomous.

Prior to each analysis the data were checked for inconsistencies, potential coding errors (out of range data) and missing data. Normality of continuous variables was assessed and transformation was not needed. The randomness of missing data also was evaluated.

To test each hypotheses, each set of analyses began with an unconditional means model (which includes only ID as a predictor) and will followed with a model that includes all predictors.

Hypothesis Testing

Hypothesis 1 - Catheter colonization rate differs between uncoated, silver coated, and antibiotic coated catheters.

This required utilization of monthly data for each unit from the hospital's central data repository as well as data tracked for patients identified with blood stream infection through the Infection Control Department. This included all patients on the three trauma intensive care units. The measurable outcome needed was the rate of positive catheter colonization from the Infection Control database. Colonization is determined by sending the tip of the removed central line catheter to the hospital laboratory to be cultured. These data were not consistently available in each period and therefore could not be examined.

Hypothesis 2 – CLABSI rates differ among uncoated, silver coated, and antibiotic coated catheters.

This hypothesis was tested using monthly data for each of the three units from the Central Data Repository and from the Materials Management Database. BSI was measured as rate of infections confirmed per 1,000 catheter days in each month. These monthly summary data were nested within the three units. The predictors were the type of catheter used which was defined by what catheter was in use during the hospitalization based on the dates of introduction of each type of catheter as determined by the materials management database. The analysis controlled for average patient age, gender, and patient severity score each month as well as for Biopatch use. Biopatch use was defined based on its date of introduction confirmed by report from the materials management information system.

LMM analyses were used to examine differences among the three periods in number of BSIs per 1,000 catheter days. Prior to analyses, the assumptions of the LMMs were examined, including normality of the continuous variables. Two sets of analyses were performed: fixed models and random intercept models. The predictors were the dummy variables for the periods (period 2, period 3), with period 1 (uncoated catheter) as the reference point, monthly average severity score, monthly average age of patients, and monthly percent female. The interaction between average age of patients and percent female also was examined to evaluate whether the relationship of age to the outcome differed according to gender. Several models were examined including different combinations of predictors.

The superior model was chosen based on AIC and BIC criteria that "smaller is better."

Hypothesis 3 - Time to development of CLABSI differs between uncoated, silver coated, and antibiotic coated catheters.

This hypothesis was not able to be tested as the insertion times were not collected for a large enough number of infected patients in each period. This required the data set for of patients diagnosed with BSI only. The outcome was intended to be the number of days after insertion determined by the date of infection minus date of insertion of the CVC. Predictors were intended to be two dummy variables coded for the type of catheter used based on a comparison of admission date to the catheters distributed to those units at the same time. The distribution information was provided from reports from the materials management information system. The analysis would have controlled for average patient age, average severity score gender, and for Biopatch use, based on its date of introduction, confirmed by report from the materials management information system. The statistical method used would have been the Survival analysis-via generalized LMMs which considers outcome time to event, unit nesting, intra class correlation, individual level data, with the assumption that seasonality will eliminate itself.

Hypothesis 4 – Monthly rates of catheter BSI infection organisms differ between uncoated, silver coated, and antibiotic coated catheters.

This hypothesis was tested using monthly data for each of the three units from the Central Data Repository, materials management database, and information manually collected by the Infection Control Department. Type of organisms isolated from blood samples collected from patients with BSI were totaled by month. The monthly summaries of data were nested within the three units. The predictors were the type of catheter used determined by the date of introduction of each type of catheter as reported by the Materials Management Database. The analysis controlled for average patient age, gender, and patient severity score as well as for Biopatch use, based on its date of introduction reported from the materials management information system.

LMM analyses were used to examine differences among the three periods for each type of infection. Two sets of analyses were performed, fixed models and random intercept models. The predictors were the dummy variables for the periods (period 2, period 3), with period 1 (uncoated catheter) as the reference group, monthly average severity score, monthly average age of patients, and monthly percent female. The interaction between average age of patients and percent female also was examined to evaluate whether the relationship of age to the outcome differed according to gender.

Types of catheter infections were classified into three organism types: gram positive, gram negative, and yeast. Separate analyses were conducted for gram positive, gram negative, and yeast infections nested within units. It was limited to the first catheter that led to the BSI.

BSI and Organism Rate Analysis

In examining the rate comparisons, the basic analytic approach used LMM analyses to examine differences among the three periods in number of occurrences. Two sets of analyses were performed: fixed models and random intercept models. The predictors were the dummy variables for the periods (period 2, period 3), with period 1 (uncoated catheter) as the reference point, monthly average severity score, monthly average age of patients, and monthly percent female. The interaction between average age of patients and percent female also was examined to evaluate whether the relationship of age to the outcome differed according to gender.

Based on AIC criteria (smaller is better), the random intercept model or the fixed effects only model was chosen. Several covariance structure models were performed including auto regressive, compound symmetry, Toeplitz, and unstructured to choose the best covariance matrix model. Additional covariates such as demographics (age, gender, and race) and ISS acuity were added to control for possible confounding factors related to infection.

Measures for Protection of Human Subjects

IRB approval was acquired before the study began (see Appendix A). This study is classified as Human Subjects Research because it involves collection of certain de-identified data according to UMB HRPP SOP 1.3.D. & E., but there was no intervention or interaction with individuals. The database was contained on a fingerprint/password protected computer and protected according to hospital Health and Human Services and Health Insurance Portability and Accountability Act (HIPAA) guidelines.

Summary

This chapter discussed the population and the inclusion and exclusion criteria for consideration in this study. The operational definitions were provided to describe the critical terms used regarding the elements of the study. The data bases and the elements within those data bases were described as well as the methods used to prepare the data for analysis. The procedures needed to analyze the data were described. The hypotheses were included in this chapter to elaborate on the specific elements targeted as outcomes and the analysis associated with those data. Finally, the measures taken to protect human subjects and the related information were reviewed to assure that there was no critical information at risk for exposure.

Chapter 4: Results

Introduction

This study assesses the comparative effectiveness at reducing blood stream infections (BSI) of different types of central venous catheters in a trauma population admitted to an urban level X trauma center between July 1, 2006 and June 30, 2011. Three types of catheters were used during the five-year period. The first type of design was a central line catheter without coating, the second type was a silver impregnated catheter, and the third an antibiotic coated catheter.

Description of Samples

Two different types of samples were obtained: a unit level sample and a patient level sample. The unit level sample contained aggregate data from units that were used to track rates of CLABSI. The patient level sample contained data from individual patients that were used for organism specific data.

Monthly data on BSIs and total central line days were provided for each of the three units each month for the three catheter use periods. Thus, rates were calculated for the 24 months of uncoated catheter use, 13 months of silver impregnated catheter use, and 22 months of antibiotic coated catheter use.

The patient level cohort for organism identification consists of all patients (n = 10,680) meeting inclusion/exclusion criteria, entering the trauma facility, and being admitted to one of three ICUs, renamed A, B, or C. From this cohort, 240 patients were identified as having developed a BSI.

Organisms Identified in Each Period

Patients with a positive BSI were documented with the type of organism isolated from the blood sample. Organisms were classified into three categories: gram positive, gram negative, or yeast. Throughout all three periods, many patient entries contained nonspecific organism types which could have reflected multiple organisms of the same category. If a patient had multiple specific strains of organisms in the same category, they were consolidated to one occurrence for that category for that patient.

Period Subgroups

To compare catheter design related outcomes, type of catheter used was defined according to associated time of purchase based on the hospital materials management information system reporting and distribution of three types of catheters. The second (silver impregnated) and third (antibiotic coated) types of catheter were compared to the first type of catheter (uncoated) based on BSI rate and type of organism as measurable outcome data. Likewise, similar comparisons were conducted to test for differences in BSI rates according to age, gender, and the interaction effects of age and gender.

According to the CDC Device Associated Infection Module (January 2012), CLABSI rate is calculated by dividing the number of CLABSI by the number of central line days and multiplying by 1,000. The standard CDC result for comparison is the number of infections per 1,000 central line days.

In the first period (Table 1) when uncoated catheters were used, there were 4,557 admissions among the three units. Among those admissions, patients experienced 14,439 central line catheter days. Total organisms isolated from this overall patient group include 9 yeast, 73 gram negative, and 51 gram positive. One hundred and twenty two patients

Table 1 - Period Summary of Patients Experiencing Blood Stream Infection by Unit

Period	Unit	Any G+	Any G-	Any Yeast	BSI Count	Admission	Central Line Days	BSI rate
1	A	17	25	1	42	1,548	5,418	7.75
1	B	20	32	4	50	1,307	6,030	8.29
1	C	14	16	4	30	1,702	2,991	10.03
Period Total		**51**	**73**	**9**	**122**	**4,557**	**14,439**	**8.45**
2	A	11	15	2	24	792	2,351	10.21
2	B	12	21	0	29	556	2,588	11.21
2	C	7	13	2	20	808	2,606	7.67
Period Total		**30**	**49**	**4**	**73**	**2,156**	**7,545**	**9.68**
3	A	3	6	0	8	1,283	3,230	2.48
3	B	6	16	1	21	1,245	4,410	4.76
3	C	3	14	2	16	1,439	3,880	4.12
Period Total		**12**	**36**	**3**	**45**	**3,967**	**11,520**	**3.91**
Grand Total		**93**	**158**	**16**	**240**	**10,680**	**33,504**	**7.16**

Period 1 = uncoated design, 24 months, period 2 = silver design, 13 months, period 3 = antibiotic coated, 22 months

Unit A = neuro trauma, unit B = multitrauma, unit C = internal trauma

G+: Number of patients with Gram Positive organisms present; G-: Number of patients with Gram Negative organisms present; Yeast: Number of patients with yeast organisms present

BSI: Number of patients with Blood Stream Infection

Admissions are the number of patients admitted to the unit during the period

Central line days: total number of central line days recorded during the period

BSI rate: number of patients with confirmed BSI divided by the number of central line days multiplied by 1000 developed BSIs. In the first period, the BSI rate was 8.45 BSI/1,000 catheter days or simply 8.45. In the second period (Table 1) when silver impregnated catheters were used, there were 2,156 admissions among the three units. Among those admissions, patients experienced 7,545 central line catheter days. Total organisms isolated from this overall patient group include 4 yeast, 49 gram negative, and 30 gram positive. Seventy three patients developed BSIs among the three units which resulted in a BSI rate of 9.68.

In the third period (Table 1) when antibiotic coated catheters were used, there were 3,967 admissions among the three units. Among those admissions, patients experienced 11,520 central line catheter days. Total organisms isolated from this overall patient group include 3 yeast, 36 gram negative, and 12 gram positive. Forty five patients developed BSIs among the three units. The BSI rate calculated during the third period is 3.91.

Description of Units

The three units included in this sample are intensive care units in a trauma facility in a major metropolitan area. Each unit is typically designated for specific patient populations. The A unit is primarily for patients with head trauma. The B unit is designated for patients with multiple traumatic injuries that typically involve extremities. The C unit is designated for patients with abdominal wounds and multiple internal diagnoses.

Unit A, the head trauma unit, had 3,623 admissions during the three periods (see Table 2). Among those admissions, patients experienced 10,999 central line catheter days. Total organisms isolated from patients on this unit were 3 yeast, 46 gram negative,

Table 2 - Unit Summary of Patients Experiencing Blood Stream Infection by Period

Unit	Period	Any G+	Any G-	Any Yeast	BSI Count	Admission	Central Line Days	BSI /1000 days
A	1	17	25	1	42	1,548	5,418	7.75
A	2	11	15	2	24	792	2,351	10.21
A	3	3	6	0	8	1,283	3,230	2.48
Unit Total		**31**	**46**	**3**	**74**	**3,623**	**10,999**	**6.73**
B	1	20	32	4	50	1,307	6,030	8.29
B	2	12	21	0	29	556	2,588	11.21
B	3	6	16	1	21	1,245	4,410	4.76
Unit Total		**38**	**69**	**5**	**100**	**3,108**	**13,028**	**7.68**
C	1	14	16	4	30	1,702	2,991	10.03
C	2	7	13	2	20	808	2,606	7.67
C	3	3	14	2	16	1,439	3,880	4.12
Unit Total		**24**	**43**	**8**	**66**	**3,949**	**9,477**	**6.96**
Grand Total		**93**	**158**	**16**	**240**	**10,680**	**33,504**	**7.16**

Period 1 = uncoated design, 24 months, period 2 = silver design, 13 months, period 3 = antibiotic coated, 22 months

Unit A = neuro trauma, unit B = multitrauma, unit C = internal trauma

G+: Number of patients with Gram Positive organisms present, G-: Number of patients with Gram Negative organisms present

Yeast: Number of patients with yeast organisms present

BSI: Number of patients with Blood Stream Infection

Admissions: the number of patients admitted to the unit during the period, Central line days: total number of central line days recorded during the period

BSI rate: number of patients with confirmed BSI divided by the number of central line days multiplied by 1000 and 31 gram positive. Seventy four patients developed BSIs during the three periods with a calculated BSI rate of 6.73 per 1,000 central line days.

Unit B, the multi trauma unit, had 3,108 admissions during the three periods (see Table 2). Among those admissions, patients experienced 13,028 central line catheter days. Total organisms isolated from patients on this unit were 5 yeast, 69 gram negative, and 38 gram positive. One hundred patients developed BSIs during the three periods. The resulting BSI rate is 7.68 per 1,000 central line days.

Unit C, the trauma unit for patients with abdominal wounds and multiple internal diagnoses, had 3,949 admissions during the three periods (see Table 2). Among those admissions, patients experienced 9,477 central line catheter days. Total organisms isolated from patients on this unit were 8 yeast, 43 gram negative, and 24 gram positive. 66 patients developed BSIs during the three periods. The overall BSI rate for Unit C is 6.96 infections per 1,000 central line days.

Hypotheses Tests

Hypothesis 2

Hypothesis 2 states that CLABSI rates differ among uncoated, silver coated, and antibiotic coated catheters. This hypothesis required statistical comparison of composite data were the dummy variables for the periods (period 2, period 3), with period 1 (uncoated catheter) as the reference, monthly average severity score, monthly average age of patients, and monthly percent female. The interaction between average age of patients and percent female also was examined to evaluate whether the relationship of age to the outcome differed according to gender. These predictors were added to the better of the fixed or random intercept models in different combinations until the best model was identified.

Based on AIC and BIC criteria (smaller is better), the random intercept model was superior to the fixed effects only model. Several covariance models were examined including independence, exchangeable, autoregressive, and unstructured specification to choose the best model. The unstructured covariance matrix was used. The model with the random intercept and the interaction of age and gender (AIC = 1040.612, BIC = 1068.566) was superior to the model without the interaction (AIC = 1034.352, BIC = 1049.881), therefore the model without the interaction was retained. The results of the random intercept model with the type of catheter (period 2) as the predictor (see Table 3) show that the BSI per 1,000 catheter days in period 2 (silver impregnated catheter) was not significantly different (p=0.388) than the BSI per 1,000 catheter days in period 1 (uncoated catheter). In period 3 (antibiotic coated catheter), BSI per 1,000 catheter days was significantly lower (p<0.001) than in period 1 (uncoated catheter). On average, there were 4.05 BSIs per/1,000 catheter days, fewer with the antibiotic coated catheter than with the uncoated catheter. Average severity score, average age, and percent female were not significant predictors of BSI. There was no difference in BSI rates between periods when silver impregnated and uncoated catheters were used.

Table 3 - Random Intercept model – BSI

Estimates of Fixed Effects[a]

Parameter	Estimate	Std. Error	Df	t	Sig.	95% Confidence Interval	
						Lower Bound	Upper Bound
Intercept	5.237	1.318	105.425	3.973	.000	2.623	7.850
[per2=0]	-.975	1.125	163.514	-.866	.388	-3.197	1.247
[per2=1]	0[b]	0	.	.	.	.	.
[per3=0]	4.054	.949	163.925	4.272	.000	2.180	5.928
[per3=1]	0[b]	0	.	.	.	.	.

a. Dependent Variable: BSI_RATE.

b. This parameter is set to zero because it is redundant.

Based on these results, central venous catheters with antibiotic coating significantly reduced the rate of BSIs compared to an uncoated or silver coated catheter in this population**.**

Hypothesis 4

Hypothesis 4 states that monthly rates of catheter BSI infection organisms differ between uncoated, silver coated, and antibiotic coated catheters. Organisms cultured from the blood of patients with suspected BSIs were categorized according to the presence of gram positive, gram negative, and/or yeast colonies in the cultures. Separate sets of analyses were performed to compare the rate of each type of BSI as a percentage of admissions per month per unit of during each period. The number of patients admitted to each unit, each month, who developed gram negative, gram positive, or yeast BSIs were the dependent variables. The predictors were the dummy variables for the periods 2 and 3 (silver coated and antibiotic coated), with period 1 (uncoated catheter) as the reference. Monthly average severity score, monthly average age of patients, and monthly percent female were used as covariates. The interaction between average age of patients and percent female also was examined to evaluate whether the relationship of age to the outcome differed according to gender.

Gram Positive Organism Analysis

Based on AIC and BIC criteria (smaller is better), the random intercept model was superior to the fixed effects only model. Several covariance models were examined including independence, exchangeable, autoregressive, and unstructured specification to choose the best model. The unstructured covariance matrix was superior and used. The model with the random intercept and the interaction of age and gender (AIC = 1087.376, BIC = 1115.808) was inferior to the model without the interaction (AIC = 1083.476, BIC = 1105.589), therefore the model without the interaction was retained. The predictors were the dummy variables for the periods (period 2, period 3), with period 1 (uncoated catheter) as the reference, monthly average severity score, monthly average age of patients, and monthly percent female. The results of the random intercept model (see Table 4) show that gram positive organism infections in period 2 (silver impregnated catheter) were not significantly different ($p=0.216$) than the gram positive organism infections in period 1 (uncoated catheter). In period 3 (antibiotic coated catheter), gram positive organism infections were not significantly different ($p=0.429$) than in period 1 (uncoated catheter). Average age and percent female were not significant predictors of gram positive organism infections but average severity score was a significant predictor ($p=0.046$). Each increase of 1 point out of 36 total points in severity score is associated with an increase of .116 in gram positive organism infections.

Table 4 – Random Intercept Model – Gram Positive Organisms

Estimates of Fixed Effects[b]

Parameter	Estimate	Std. Error	Df	t	Sig.	95% Confidence Interval	
						Lower Bound	Upper Bound
Intercept	10.698	2.791	105.313	3.832	.000	5.162	16.233
[per2=0]	-1.353	1.089	172.456	-1.243	.216	-3.503	.796
[per2=1]	0[a]	0	.	.	.	.	.
[per3=0]	-.737	.929	171.527	-.793	.429	-2.573	1.097
[per3=1]	0[a]	0	.	.	.	.	.
AVGISS	.115	.057	135.713	2.014	.046	.002	.228
FEMPCT	-.088	.046	171.815	-1.903	.059	-.180	.003

a. This parameter is set to zero because it is redundant.

b. Dependent Variable: pctgramposofadmi.

Hypothesis 4 was not supported regarding gram positive organisms. The number of CLABSIs with gram positive organisms was no different with the antibiotic coated catheters than with uncoated catheters. There was no difference in gram positive organism rates between periods when silver impregnated and uncoated catheters were used.

Gram Negative Organism Analysis

Based on AIC and BIC criteria (smaller is better), the random intercept model was superior to the fixed effects only model. Several covariance models were examined including independence, exchangeable, autoregressive, and unstructured specification to choose the best model. The unstructured covariance matrix was used. The model with the random intercept and the interaction of age and gender (AIC = 1128.299, BIC = 1156.730) was inferior to the model without the interaction (AIC = 1124.821, BIC = 1146.935), therefore the model without the interaction was retained. The results of the random intercept model (see Table 5) with the dummy variables for the periods (period 2, period 3), with period 1 (uncoated catheter) as the reference, monthly average severity

Table 5 – Random Intercept Model – Gram Negative Organisms

Estimates of Fixed Effects[b]

Parameter	Estimate	Std. Error	df	t	Sig.	95% Confidence Interval Lower Bound	95% Confidence Interval Upper Bound
Intercept	16.857	3.415	44.594	4.936	.000	9.976	23.738
[per2=0]	-3.194	1.217	171.618	-2.624	.009	-5.597	-.791
[per2=1]	0[a]	0	.	.	.	.	.
[per3=0]	-6.608	1.038	171.226	-6.366	.000	-8.658	-4.559
[per3=1]	0[a]	0	.	.	.	.	.
AVGISS	.108	.065	172.253	1.643	.102	-.021	.238
FEMPCT	-.153	.052	171.312	-2.956	.004	-.256	-.051

a. This parameter is set to zero because it is redundant.

b. Dependent Variable: pctgramnegofadmi.

score, monthly average age of patients, and monthly percent female as predictors show that gram negative organism infections in period 2 (silver impregnated catheter) were significantly (p=0.009) different than the gram negative organism infections in period 1 (uncoated catheter). On average, there were 3.19% fewer gram negative organism infections with the silver impregnated catheter than with the uncoated catheter. In period 3 (antibiotic coated catheter), gram negative organism infections were significantly lower (p=0.000) than in period 1 (uncoated catheter). On average, there were 6.61% fewer gram negative organism infections with the antibiotic coated catheter than with the uncoated catheter. Average severity score and average age were not significant predictors of gram negative organism infections. However, percent female was significant (p=0.004) with .15% less gram negative infections for every 1% increase in female admissions.

Hypothesis 4 was supported regarding gram negative organism infections. CLABSIs with gram negative organisms were significantly lower with the silver impregnated catheters and significantly lower, to a greater degree, with the antibiotic coated catheters than with uncoated catheters. On average, there were 3.19% fewer gram negative organisms with the silver impregnated catheter and 6.61% fewer gram negative organisms with the antibiotic coated catheter than with the uncoated catheter. There was a difference in gram negative organism rates between periods when silver impregnated and antibiotic coated catheters were used versus the period of uncoated catheter use.

Yeast Organism Analysis

Based on AIC and BIC criteria (smaller is better), the random intercept model was superior to the fixed effects only model. Several covariance models were examined including independence, exchangeable, autoregressive, and unstructured specification to choose the best model. The unstructured covariance matrix was superior to the other tested covariance matrices. The model with the random intercept and the interaction of age and gender (AIC =530.288, BIC =558.719) was superior to the model without the interaction (AIC = 533.983, BIC = 559.255), therefore the model with the interaction was retained. The results of the random intercept model (see Table 7) show that yeast organism infections in period 2 (silver impregnated catheter) were not significantly different (p=0.839) than the yeast organism infections in period 1 (uncoated catheter). In period 3 (antibiotic coated catheter), yeast organism infections were not significantly different (p=0.169) than in period 1 (uncoated catheter). Average severity score and percent female were not significant predictors of yeast organism infections. Average age and the average age/percent female interaction were significant predictors of yeast infections (p=0.016) and (p=0.017) respectively. In periods 2 and 3, there was an association between the covariate percentage of women and the amount of yeast organisms identified. In addition, there was an interaction effect with percent of female and age in that for each increase in one year of average age by women there was a decrease in yeast by .004%. Table 6 shows the distribution of women in each period as a percent of the overall admissions.

Table 6 – Female Distribution

PERIOD	Unit	ADMI	FEMADI	Percent Women
1	4	1,548	417	27%
1	5	1,307	353	27%
1	6	1,702	506	30%
1 Total		4,557	1,277	28%
2	4	792	222	28%
2	5	556	162	29%
2	6	808	236	29%
2 Total		2,156	620	29%
3	4	1,283	398	31%
3	5	1,245	451	36%
3	6	1,439	475	33%
3 Total		3,967	1,324	33%
Grand Total		10,680	3,220	30%

Hypothesis 4 was not supported regarding yeast organisms. CLABSIs with yeast organisms were not significantly different with the silver impregnated catheters or antibiotic coated catheters than with uncoated catheters. However, there is an interaction where younger women with BSIs are more likely to have yeast colonization in the blood sample than older women.

Summary

Based on the results (Table 7), tests of fixed effects suggest that the silver impregnated catheter design, period 2, was not associated with lower BSIs, yeast infections, or gram

Table 7 – Random Intercept Model – Yeast Organisms

Estimates of Fixed Effects[b]

Parameter	Estimate	Std. Error	Df	t	Sig.
Intercept	-5.465	3.236	172.103	-1.688	.093
[per2=0]	-.047	.234	171.321	-.204	.839
[per2=1]	0[a]	0	.	.	.
[per3=0]	-.294	.212	171.021	-1.381	.169
[per3=1]	0[a]	0	.	.	.
AVGISS	.012	.011	156.158	1.046	.297
VAGE	.118	.064	171.307	1.843	.067
FEMPCT	.242	.099	170.968	2.439	.016
VAGE * FEMPCT	-.004	.002	171.006	-2.407	.017

a. This parameter is set to zero because it is redundant.

b. Dependent Variable: pctyeastofadmi

positive infections compared with an uncoated catheter but was associated with a decrease in gram negative infections of 3.19% (p=0.009). The antibiotic catheter design, period 3, was not associated with lower yeast or gram positive infections compared with an uncoated catheter, but was associated with reductions in BSI, 4.054514%, (p=0.000), and gram negative, 6.608919% (p=.000) infections compared to the uncoated design. These results suggest that the silver design is no different than the uncoated design except in the reduction of gram negative organisms. The results suggest that the antibiotic design is associated with lower rates of total BSI per 1,000 central line days and of incidence of gram negative organisms per admission but is not different than the uncoated design in regards to gram positive and yeast organisms.

Based on the summary of results (Table 8), it can be concluded that the antibiotic coated catheter is a better solution in preventing gram negative organism infection and overall BSI per 1,000 central line days compared to the uncoated design. Although the silver design resulted in fewer gram negative infections, compared to the uncoated design, it did not significantly change the BSI outcome.

This chapter described the samples and the review of organisms before analysis. The period and unit subgroups were described including detailed summary tables. The tests of Hypothesis 2 were described with the results regarding BSI. The tests of Hypothesis 4 were described with the results regarding gram positive, gram negative, and yeast organisms isolated in blood samples from the infected patients. All results from both hypotheses were summarized in a table.

Table 8 – Catheter Design Related Results

Period	**Design**	**Gram Positive**	**Gram Negative**	**Yeast**	**BSI**
1	**Uncoated**	reference	reference	reference	Reference
2	**Silver**	no difference	↓	no difference	no difference
3	**Antibiotic**	no difference	↓	no difference	↓

↓ Indicates a significant decrease in rate

Chapter 5: Results and Discussion

Introduction

This is a retrospective study utilizing secondary data to tests two hypotheses regarding CLABSI and organism colonization. Hypothesis 1 and 3 were not tested due to missing data. Hypothesis 2 states that CLABSI rates differ between uncoated, silver coated, and antibiotic coated central venous catheters (CVCs). Hypothesis 4 states that types of BSIs will differ between uncoated, silver coated, and antibiotic coated CVCs. This chapter will discuss the results of those tests as well as the limitations, implications, and recommendations for future research.

BSI Outcomes with Uncoated versus Silver Coated

There was no difference in BSI rates between periods when silver impregnated and uncoated catheters were used. This result is similar to the results of Ramritu's 2008 meta-analysis which summarized that this technology was not effective in several studies including Bach (1999), Stoiser (2002), and Dunser (2005). Moretti had similar results and stated, "Unexpectedly, we found no significant differences in colonization or bacteraemia rates between the test and control catheters" (Moretti, p.143, 2005).

In the hospital setting where costs are increasing and reimbursement is declining, a decision to use products that have a financial premium attached for advanced technology should be monitored for the improved outcomes described by the manufacturer. If the product is not effective at the facility within a period that provided adequate data for statistical review, then, in this author's opinion, it should be discontinued and other options pursued.

The costs for premium technology of these designs can be significant. In this case, the second period in this study was 13 months long utilizing over 1,500 catheters at a cost differential between the uncoated and silver of greater than $30 per catheter. If the use of the silver catheters had been discontinued after 6 months, it would have eliminated the use by 750 silver coated catheters. The difference in cost between uncoated and silver coated catheters would have saved is roughly $22,500.

In addition to preventing unjustified expense, discontinued use of ineffective technology allows clinicians to search for other strategies to prevent infection and possibly find a solution for patients who would not have received the benefit. Without a post-implementation review of outcomes, clinicians incorrectly assume that the choices they have made for patients are contributing to providing the best care for those patients.

BSI Outcomes with Uncoated versus Antibiotic-Coated

In period 3 where the minocycline/rifampicin (MR) coated catheter was implemented, BSI was significantly lower ($p=0.000$) than in period 1 where the uncoated catheter was used. This outcome has also been seen in other studies such as Raad (1997), Marik (1999), Chatzinikolaou (2003), Leon (2004), and Yucel (2004). Their results were reviewed in Ramritu's 2008 meta-analysis in which the "pooled estimate of effectiveness for MR-coated catheters indicates a reduction in risk of CLABSI" as well as "homogeneity in the definition of CLABSI increasing the validity and giving strong support for the effectiveness of MR CVCs in preventing CLABSI in the ICU" (Ramritu, p.110, 2008).

The MR CVCs were approximately twice the cost of the non-coated catheters. In the results section, the statistics report was that, on average, there were 4.05 fewer BSIs per 1,000 catheter days with the antibiotic coated catheter than with the uncoated catheter. In the third period, there were 11,520 CVC days. This translates to approximately 46 fewer BSIs in this period that were prevented by utilizing this design compared with use of a non-coated CVC. The added cost of using antibiotic impregnated catheters during this period was approximately $200,000. "Beyond the 10% to 25% case-fatality rate associated with catheter related bacteremia, nosocomial bloodstream infection prolongs hospitalization by 7 to 14 days and add approximately $29,000 to the cost of hospitalization" (Maki, p.262, 1997). Literature shows that BSIs "are associated with higher cost increases from $6,000 to $90,000 per patient infection" (Moretti, p.140, 2005). This range of cost applied to the possible reduction in BSIs translates to a range of cost avoidance of $276,000 to $4,140,000 during the 22 month period. Even though a direct "cause and effect" argument could not be established, hospital administrators would likely agree that the added $200,000 expense was at least recovered.

Choosing a Design Based on BSI

"Whereas some authors could demonstrate a highly significant reduction of CVC colonization rates by the use of (silver) coated catheters, our results are in line with studies from Ceresi et al. and Pemberton et al., none of whom found antiseptic catheters beneficial in reducing the incidence of CVC colonization and related bloodstream infections" (Dunser, p. 1782, 2005). Regarding a choice between the silver CVC and the MR CVC, the silver should not be selected for use regardless of the results related to colonization reductions for two reasons. The first is that "the causal linkage between colonization and bacteraemia is weaker that than previously thought" (Moretti, p.144, 2005). Studies that show reductions in colonization lead toward the possibility that BSI could be reduced by reducing the risk, but studies showing a reduction in BSI are more pertinent because of the second reason. BSI should be the true measure of effectiveness. Kaflon stated that "the ultimate purpose of an impregnated CVC must be lowering the incidence of CLABSI rather than only reducing the catheter colonization rate" (Kaflon, p.1037, 2007). Unless more robust studies are published stating results that silver CVCs reduce BSI, clinicians should not consider their use.

Differences in the Types of Organism with the Three Catheter Types

Each patient BSI had two considerations when organizing the data. First, a patient could have experienced an infection that was related to multiple organisms based on cultures from the blood sample. In the analysis, if the multiple organisms were from the separate types (gram positive, gram negative, and yeast), then the infection would count in each category for the monthly summary. The second consideration is that if a patient experienced more than one organism of the same type, it counted as one occurrence for that category. This was done to maintain consistency in the method of documentation in the data table by the infection control department.

Gram Positive Organisms

Hypothesis 4, that monthly rates of catheter BSI infection organisms differ between uncoated, silver coated, and antibiotic coated catheters, was not supported regarding gram positive organisms. The number of CLABSIs with gram positive organisms was no different with the antibiotic coated catheters than with uncoated catheters. Likewise, there was no difference in gram positive organism rates between periods when silver impregnated and uncoated catheters were used.

Although the hypothesis was not supported, the result can help in decision making regarding the prevalence of gram positive organism related BSIs among the patient population. If the large majority of infections occurring at a hospital are related to gram positive organisms, this study would indicate that the uncoated CVC is just as effective as other more costly designs and therefore BSI prevention strategies should focus on other sources of prevention.

Based on the results, the average severity score is a significant predictor ($p=0.046$) of gram positive organism infections. Each increase of 1 point in severity score is associated with an increase of .116 in gram positive organism infections. Active monitoring of severity score by clinicians could help to identify patients at an increased risk for gram positive infections and possibly contribute to improved patient care strategies to prevent infection.

Gram Negative Organisms

Hypothesis 4, that monthly rates of catheter BSI infection organisms differ between uncoated, silver coated, and antibiotic coated catheters, was supported regarding gram negative organism infections. CLABSIs with gram negative organisms were significantly lower with the silver impregnated catheters and significantly lower, to a greater degree, with the antibiotic coated catheters than with uncoated catheters. On average, there were 3.19% fewer gram negative organisms with the silver impregnated catheter and 6.61% fewer gram negative organisms with the antibiotic coated catheter than with the uncoated catheter. There was a difference in gram negative organism rates between periods when silver impregnated and antibiotic coated catheters were used versus the period of uncoated catheter use.

Regarding gram negative related BSIs, MR CVCs should be the first choice in prevention based on the higher degree of reduction of BSIs compared to the uncoated catheters and silver design catheters. This decision is further supported with the BSI related outcome described previously.

After considering the covariates average severity score, average age, and percent female, the significant predictor of gram negative organism infections is percent female (p=0.004) with .15% less gram negative infections for every 1% increase in female admissions. This points toward the male population as more likely to have gram negative related BSIs. Patient gender, in combination with other clinical indications, could be a consideration as this indicates that males are more likely to experience a gram negative infection. This could be small contributor to the decision favor of choosing MR CVCs over an uncoated CVC to prevent CLABSI in male patients.

Yeast Organisms

Hypothesis 4, that monthly rates of catheter BSI infection organisms differ between uncoated, silver coated, and antibiotic coated catheters, was not supported regarding yeast organisms. CLABSIs with yeast organisms were not significantly different with the silver impregnated catheters or antibiotic coated catheters than with uncoated catheters. This might have been due to the low number of yeast organism outcomes. A longer study with more patients is required to answer hypothesis 4.

In the yeast model however, average age and the average age and percent female interaction were significant predictors of yeast infections (p=0.016 and p=0.017, respectively). In periods 2 and 3, there was an association between the covariate percentage of women and the amount of yeast organisms identified. In addition there was an interaction effect with percent of female and age in that for each increase in one year of average age by women there was a decrease in yeast by .004%.

It could be helpful to know that approximately one in 400 female patients is likely to experience a yeast BSI and that the distribution of infected patients decreases with age. This could be helpful in planning care of women in this trauma population as well as understanding their associated rate of infection to contribute to collected information in diagnosis of a cluster of symptoms.

Limitations

There are many limitations to consider regarding this study. The data sources are based on information entered manually into hospital databases and into patient records. This could introduce error related to manual entry and subjective interpretation of information to be transcribed from various sources.

Diagnoses, which are used to calculate severity scores, are subjectively concluded by teams of clinicians based on several patient symptoms. The membership of the teams may change over time, possibly changing the collective interpretation of diagnostic information. There is no measure of inter-rater reliability to assure consistency, although interviews with members of this team confirm that at least two members were consistent throughout the study period. Also, during the course of the data collection, it could be possible that the interpretation of criteria in diagnosis of CLABSI could have changed gradually.

Some data tables are from the hospital electronic medical record (EMR) which contains all information related to patient demographics, diagnoses, admission/discharge data, and which were provided through the hospital's Department of Epidemiology. In addition to this information, other information was assembled as patients were diagnosed following a discussion among the team assigned to the patient for care. This information included the CVC site, date of removal, lab results, and organism. During the three periods of this study, the method or elements collected changed. One such change occurred throughout the study period. In the beginning, multiple points of information were transcribed together in a single field of an Excel database. Later, they were separated into separate fields. Some of those isolated fields were later discontinued. The method of transcription was not standardized and abbreviations known to the owner of the file were frequently used for convenience as this information was not necessary to be placed into a format that could be used for statistical analysis but for reference. An example of variability of data collection is the multiple ways gram negative cocci infections were documented. It was listed as GN, GNC, gram neg, or the actual gram negative organism. It also appeared that in period 2 and 3 the amount of information collected regarding organisms increased. Instead of GNC listed in the prior period, multiple gram negative organisms in a later period could have been listed for one patient. This was discussed with the clinicians collecting the information, and the solution to correct for this inconsistency was that one occurrence within the three categories was accounted for in the case of multiple like organisms. In period 3, although a dictionary of abbreviations was used as a means to code the organisms, there was some redundancy in the code list. The process of coding for the same organism could have utilized multiple abbreviations. This evolution of coding is in response to increasing needs in surveillance and will likely continue to improve as information systems are better designed to provide the data already entered into the EMR.

There are two limitations regarding the availability of alternative designs in all three periods. The first is regarding the possibility of contamination of the samples due to remaining central line catheter inventory in certain areas that existed during a time when it was expected to be exhausted. The second is that an adjoining hospital consistently maintained alternative designs for other patient populations. Although considered unlikely, it is possible that either these CVCs were brought onto the trauma facility or the trauma patients could have been taken to the adjoining hospital during their course of care and received an alternative CVC.

Insertion of CVCs by multiple clinicians with varying expertise in varying anatomical locations can introduce risk of infection to specific populations where their team is assigned.

Introduction of other dressing technology could have had some effect on outcomes. This dressing is the silver coated disc Biopatch, intended to prevent colonization on the skin surface thereby reducing the chance of migration of organisms around the skin site toward the entry point of the catheter into the bloodstream. No statistical significance was found comparing the subperiods before and after introduction within the silver design period. BSI was not different during this period compared to the non-coated CVC.

During the study in 2009 there was a campaign to reinforce education and create surveillance activities to prevent infection. These activities included introduction of a bundled approach of preventive measures and a re-education of clinicians in the insertion techniques. Surveillance of insertion techniques and proper hand washing techniques were implemented to check for individual compliance by clinicians. Education targeted proper use and application of dressings surrounding the catheter site and the prompt removal of devices when not necessary or when suspected of infection. Incorporation of a standard approach to sampling from the hubs as well as proper care and assessment of the site according to nursing protocol was implemented.

This campaign occurred during the third period and could have impacted the outcomes. "Increases in the effectiveness while concurrent interventions occurred support the postulate that the use of concurrent infection control strategies might have a synergistic effecting reducing infection risk but it should be interpreted carefully as it may reflect variation in study reporting" (Ramritu, P.112, 2008). Focused research is difficult in this area because the impetus for the need for premium technology is intolerable levels of infection. The situation warrants a multifaceted approach to elimination of infection with a secondary intent to collect the data for research purposes.

Recommendations for Future Research

This study is a retrospective analysis examining the outcomes related to sequential introduction of three designs of central venous catheters. "The randomized controlled trial is generally considered to have the highest level of credibility with regard to assessing causality; however in a hospital or public health setting, the intervention often cannot be randomized, for one or more reasons (1) ethical considerations, (2) an inability to randomize patients, (3) an inability to randomize locations, and (4) a need to intervene quickly" (Harris, 2004, p.1587).

Large RCT studies should be designed to create more robust study results. Emphasis should be placed in comprehensive, consistent data collection to allow more comparisons within groups as well as to test for other influential variables. One study by Marciante (2005) suggests that CVC technology types should be chosen for patients based on the estimated duration that the patient is expected to experience a CVC. Marciante (2005) hypothesized that silver coatings were more effective for the shorter duration and that the MR CVCs were more effective in the long term. This would require the collection and analysis of data related to insertion date and time, removal date and time, and blood sample draw date and time, so that the timeline to diagnosis could be used a continuous measure to analyze catheter related infection. These times could be manually extracted from charts but the cost to review the number of patients necessary for a strong investigation could be prohibitive.

Implementation of newer EMRs at hospitals that apply time stamps to patient care, integrate lab information, maintain admission/discharge/demographic information, and track materials charges could be built to better support data extraction for research. As hospitals across the nation build and upgrade their EMRs, clinical groups should attempt to collaborate to create standard measures that can be combined to create large databases so that tests for small effect sizes are still robust. RCTs that randomly provide alternative designs to patients over a period of several years could enable research that could provide clinicians with the necessary information that reduces the risk of infection for patients as well as allow them to make fiscally sound decisions.

Summary

This study compared the outcomes of silver coated CVCs and MR coated CVCs to a non-coated CVC. The remarkable outcome is that during the period in which MR coated CVCs were used, BSI was significantly reduced. It is unknown as to whether the source of that difference is related to the design or other influential factors. There were some differences in colonization outcomes, but published literature questions the relationship between colonization and BSI. Inferences due to differences in outcomes in colonization should not be made regarding a relationship with BSI.

Neither catheter design was different that the uncoated design regarding gram positive organism infections. According to Raad (1996), "S. Epidermidis is the most common cause of vascular catheter related infections." If this is the most common in this study of a trauma population, S. Epidermidis, a gram positive organism, was not affected by either catheter design. These results demonstrate that further improvement in technology is required to cover a wider spectrum of organisms. Large prospective RCTs are needed to reliably determine the effectiveness of these CVC designs so that hospital administration can make educated decisions that benefit their patients as well as the facility's budget.

Appendix A: IRB Approval Notification

University of Maryland, Baltimore
Institutional Review Board (IRB)
Phone: (410) 706-5037
Fax: (410) 706-4189
Email: hrpo@som.umaryland.edu

New Study Approval Notification

Date: November 10, 2010

To: Erika Friedmann
From: IRB Chair/Vice Chair: Ann Zimrin
RE: HP-00045690
Risk designation: Minimal Risk
Submission Date: 9/7/2010
Original Version #: N/A

Approval for this project is valid from 11/10/2010 to 11/9/2011

This is to certify that the University of Maryland, Baltimore (UMB) Institutional Review Board (IRB) has fully approved the above referenced protocol entitled, "*Effectiveness of Antimicrobial Coated Catheters for Prevention of Blood Stream Infection in a Trauma Patient Population*".

The IRB has determined that this protocol qualifies for expedited review pursuant to Federal regulations 45 CFR 46.110, 21 CFR 56.110, & 38 CRF 16.110 category(ies).

(5) Research involving materials (data, documents, records, or specimens) that have been collected, or will be collected solely for nonresearch purposes (such as medical treatment or diagnosis). (NOTE: Some research in this category may be exempt from the HHS regulations for the protection of human subjects. 45 CFR 46.101(b)(4). This listing refers only to research that is not exempt.)

Please be aware that only valid IRB-approved informed consent forms may be used when written informed consent is required.

Investigators are reminded that the IRB must be notified of any changes in the study. In addition, the PI is responsible for ensuring prompt reporting to the IRB of proposed changes in a research activity, and for ensuring that such changes in approved research, during the period for which IRB approval has already been given, may not be initiated without IRB review and approval except when necessary to eliminate apparent immediate hazards to the subject (45 CFR 46.103(4)(iii)).

DHHS regulations at 45 CFR 46.109 (e) require that **continuing review** of research be conducted by the IRB at intervals appropriate to the degree of risk and **not less than once per year**. The regulations make **no provision for any grace period extending the conduct of the research beyond the expiration date of IRB approval**. You will receive continuing review email reminder notices prior to study expiration; however, it is your responsibility to submit your continuing review report in a timely manner to allow adequate time for substantive and meaningful IRB review and assure that this study is not conducted beyond the expiration date. Investigators should submit continuing review reports in the electronic system at least six weeks prior to the IRB expiration date.

In addition, you must inform the IRB of any new and significant information that may impact a research participants' safety or willingness to continue in your study and any unanticipated problems involving risks to participants or others.

Research activity involving veterans or the Baltimore VA Maryland Healthcare System (BVAMHCS) as a site, must also be approved by the BVAMHCS Research and Development Committee prior to initiation. Contact the VA Research Office at 410-605-7131 for assistance.

The UMB IRB is organized and operated according to guidelines of the International Council on Harmonization, the United States Office for Human Research Protections and the United States Code of Federal Regulations and operates under Federal Wide Assurance No. FWA00007145.

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