The Effect of Chlorhexidine Catheter Coating Compared to a Biomimetic Catheter on the Reduction of Fibrin Sheath Formation in the presence of Staphylococcus aureus colonization in an in vivo Clinically Simulated Ovine Model

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INTRODUCTION

Intravascular catheters are the most frequently used medical devices in healthcare. They are also associated with serious and life-threatening complications. A catheter in the bloodstream crosses from non-sterile to sterile tissue spaces and interfaces with the circulatory flow. Both the cutaneous insertion site and the internal lumen of the catheter serve as entry points for microbial contamination. Over 150 years ago, Virchow observed that reduced blood flow, vessel wall injury, and alterations in coagulation promoted the formation of thrombus and propagation of thrombotic events. In addition to vessel trauma and venous stasis, the catheter itself becomes a thromogenic surface when exposed to blood. Platelets are instantly adherent to the catheter on blood contact. This proteineous "conditioning layer" in turn promotes platelet and leukocyte activation, reducing the risk of "parachute" microembolization into the bloodstream. The release of the inflammatory mediators then in turn induces thrombogenesis. The adherent plasma proteins present attachment sites for adhesion of microorganisms to the catheter surface. Bacterial infection is accompanied by leukocyte infiltration and procoagulant pathways.

The correlation of catheter-related infection and thrombosis has been observed clinically[1]. The "conditioning layer" of platelets and proteins is an outgrowth of interventions to reduce the risk of catheter-related bloodstream infection (CRBSI) by being instrumental in reducing the risk of catheter-related infections. These interventions are directed primarily towards the prevention of microbial contamination during the insertion procedure and have no relationship with post-insertion infection and thrombosis prevention. Pathogenesis-based strategies including catheter surface modification technology could lead to improved resistance against CRBSI and thrombotic events.

The efficacy of a chlitoxilene (CH) coated catheter was previously studied in an in vivo ovine model. The CH-coated catheter reduced fibrin sheath formation on the extra- and intraluminal surfaces[2]. The surface of fibrinolytic material on the catheter surface may influence the potential for catheter colonization. The use of a catheter that is both antithrombotic and antimicrobial would be of significant clinical benefit.

METHODS

The study was approved by an institutional IACUC for animal subjects. Ten adult male or female sheep weighing between 40-65 kg were randomly assigned to receive either a Test catheter (5.5 Fr Teleflex (CH) chlitoxilene coated double lumen (DL) PICC, Teleflex Medical, Research Park Triangle, NC) or one of 2 control catheters; Control 1 (C1) or Control 2 (C2). C1: 5 Fr. biotopic coated DL PICC, H. Vascular, Maple Grove, MN in the right or left jugular vein. Sheep were anesthetized and the neck was clipped and shaved with soap and water followed by application of 70% IPA. A 2 cm area of skin over the insertion site was marked with a sterile surgical marking pen and incised with a 15g incision using a sterile scalpel. The catheter was inserted under sterile conditions following standard technique per manufacturers’ instruction through the incised skin. The catheter tip was positioned in the left internal jugular vein and confirmed by fluoroscopy. Catheters were flushed with heparin and a neutrudeal neutralizing catheter connector used to prevent infection. Catheter usage varied in length with protein tangle and covered with sterile gause and sterile wet wraps. Daily observations of body temperature, food intake, attitude, posture and behavior were performed. Insertion site culture was done twice per week with sterile saline cleaning and sterile gauze. If the sheep displayed clinical signs of infection such as decreased food intake, depression, elevated body temp (≥ 40°C), increased WBC count, they were euthanized. If the sheep displayed clinical signs of infection such as decreased food intake, depression, elevated body temp (≥ 40°C), increased WBC count, they were euthanized. Insertion site skin cultures were taken weekly and prior to euthanasia.

Fibrin sheath, catheter and vessel sample analysis

After euthanasia the jugular vein was dissected and removed on ice. The vein was acoustically longitudinally excised and fibrin sheath length and weight were measured. The fibrin sheath was stripped from the catheter and weighed. The jugular vein was frozen at −80°C and used for pathologic evaluation by a pathology pathologist. The catheter and fibrin sheaths were shipped in sterile vials and each vial contained separate aliquots of the vein and catheter samples. The vein and venous samples were treated with DE broth for chlitoxilene neutralization before analysis. Representative 5 cm sections of the vein (insertion, middle, and tip) were excised, sonicated, serial diluted, plated and incubated overnight. Colony counts are expressed in CFU/cm². The fibrin sheath was homogenized, sonicated, serial diluted, plated and incubated overnight. Colony counts are expressed as CFU/gm.

Statistical analysis

Statistical analysis was performed separately on each of the length and weight of the fibrin sheath, and on the bacterial log densities using a one-way ANOVA, with catheter type (C1, C2 and CH) as the factor. ANOVA was used to compare the CH catheters to the C1 and C2 catheters. Tukey tests and confidence intervals for all parameters were calculated with the SAS/STAT software package (version 9.2). All analyses were performed using the statistical software package Minitab 16.

RESULTS

The results are shown in Figure 1. Figure 2 shows the estimated median values of the fibrin sheath length for each of the groups. Note that the CH catheter was statistically significantly different from C1 (p-value = 0.0019) and the CH catheter was statistically significantly different from C2 (p-value = 0.0002). The two control catheters were not statistically significantly different from each other (p-value = 0.3960).

Figure 3 shows the % reduction in relation to either the length or weight of the fibrin sheath achieved by CH when compared to either C1 or C2 catheters.

Figure 4 shows the mean log density and SD of bacteria on the catheter's surface. The CH catheter was statistically significantly different from both the C1 (p-value = 0.0019) and the C2 catheters (p-value = 0.0066). The two control catheters were not statistically significantly different from each other (p-value = 0.325).

Figure 5 shows the mean log density and SD of the bacteria in the fibrin sheath. Note that the CH catheter was statistically significantly different from both the C1 (p-value = 0.0019) and the C2 catheters (p-value = 0.0066). The two control catheters were not statistically significantly different from each other (p-value = 0.325).

CONCLUSIONS

The CH-coated catheter showed a statistically significantly smaller fibrin sheath than either of the control catheters. The CH-coated catheter showed a clinically significant reduction in fibrin sheath formation. The CH-coated catheter showed a statistically significantly reduced bacterial burden both on the catheter surface and in the fibrin sheath. There was an impressive macroscopic and microscopic reduction in cells, thromboplastic and necrosis of the tissues surrounding the catheter tract of the CH-coated catheter compared to the control catheters. Based on histologic findings, there was less intraluminal hyperplasia in the veins of the catheters with no evidence of infection (all chlitoxilene catheters and one control catheter). The CH-coated catheter was protective for 31 days against thrombotic events in ovine models. The CH catheter was statistically significantly different from all other catheter types and the two control catheters were not statistically significantly different from each other (p-value = 0.0066).

REFERENCES