The Effect of Chlorhexidine Catheter Coating Compared to an Uncoated and Biomimetic Catheter on the Reduction of Fibrin Sheath Formation in an in vivo Clinically Simulated Ovine Model

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INTRODUCTION

The Peripherally Inserted Central Venous Catheter (PVC) is widely used for vascular access in all age groups. Initially, the PVC was associated with a decreased risk for venous complications associated with subclavian and jugular central venous catheter insertion and catheter-related bloodstream infection (CRBSI). PVCs are associated with thrombotic events such as thrombophlebitis, superficial and deep vein thrombosis, septic thromboplasty, post-thrombotic syndrome and pulmonary embolism. However, PVC infection rates are on the increase along with thrombotic events [1]. PVCs are more commonly used in settings where patients are at increased risk of acquiring CRBSI such as extremes of age, immunosuppression, renal failure, recent surgery, longer hospital stay, prolonged mechanical ventilation, and patients on an antibiotic arm and older age[2].

The presence of a catheter in the smaller vessels of the upper extremity may cause vessel wall injury, and the shearing forces generated by the catheter as it is advanced down the vessel lumen, cause thromboembolism and venous occlusion, all of which in turn increase the risk of CRBSI. The ideal antimicrobial coatings have been developed to reduce the risk of CRBSI but lacking anti-thrombogenic technology. The use of a catheter with a surface that is both anti-infective and anti-thrombogenic would be significant clinical benefit.

PURPOSE

The purpose of this study in an in-vivo clinically simulated ovine model is to compare anti-thrombotic properties of a chlorhexidine coated catheter (CH) to an uncoated catheter (C1) and an anti-thrombotic/bioactive surface treated catheter (C2).

METHODS

Catheterization

This study was approved by an institutional IACUC for animal subjects. Eighteen adult male or female sheep weighing between 40-65 kg were randomly assigned to receive either a test catheter: 5 Fr. chlorhexidine (CH) coated, 5 Fr. double lumen (DL) PICC, 5 Fr. biocompatible coated DL PICC, 5 Fr. Polyurethane, 5 Fr. Male, n=9 sheep were assigned to the 12 day catheterization group and nine assigned to a 31 day catheterization group.

The sheep were anesthetized and the right or left jugular vein was chosen by random selection. The neck was clipped and prepared with betadine. A 21 gauge刺 puncture needle was used to pierce the skin and subcutaneous tissue. The catheter was then inserted with a guidewire and a needleless connector closed the catheter for the duration of the study. Catheters were secured in place with promethesutol, a chlorhexidine foam (Biopatch) and neck wrapped with vet wrap. Daily observations of body temperature, food intake, activity, posture and behavior were performed. Insertion site care was done twice per week with Chloraprep solution, Biopatch and vet wrap. Blood sampling included CBC, chem panel, pro-thrombin time. All animals were euthanized at the group study endpoints; 12 or 31 days.

Fibrin sheath, catheter and vessel sample analysis

After euthanasia the jugular vein was dissected and removed en bloc. The vein was longitudinally excised and fibrin sheath length and weight were measured. The fibrin sheath was stripped from the catheter and weighed. A histological sample was taken from the middle sheath of each sample and stained with H&E for histological evaluation. Histologic evaluation was done in the 31 day group only by a veterinary pathologist.

RESULTS

The mean fibrin sheath length and weight of the fibrin sheath were modelled using an ANOVA, with catheter type (Test CH catheter, Control 1 (C1): 5 Fr. DL PICC, Control 2 (C2): 5 Fr. biocompatible coated DL PICC, 5 Fr. Polyurethane, 5 Fr. Male) as the main effect of interest. The main effects were the catheter type and the interaction between the catheter type and the number of days. The ANOVA was used to compare the Control 1 and Control 2 to the Test CH catheter. All analyses were performed using the statistical software package Minihl v. 16.

Figure 1: Test catheter with central axis. Bifurcated tissue formation, insertion site size 4 mm length, size 2 at 0 cm axial insertion site size. Length is 4 mm from insertion site. Bifurcated tissue is formed at 4 mm length. Test catheter is composed of arterial fibroblasts and entrapped fibrin.

Figure 2: Subcutaneous tract length and weight of the fibrin sheath. Mean, median, confidence and confidence intervals are notal values. All analyses were performed using the statistical software package Minihl v.16

Figure 3: Subcutaneous tract length and weight of the fibrin sheath. Mean, median, confidence and confidence intervals are notal values. All analyses were performed using the statistical software package Minihl v.16

Figure 4: Catheter tract and lumen surface (left) lined with intact endothelium and connective tissue cells, no inflammatory infiltrate. Right: Distal fibrin sheath composed of dense layers of organized fibrin, the vein wall and connective tissue cells (up to 100 µm thick) involving approx. 25% of the vein wall, connective and adipose tissue. No changes of media or adventitia.

Figure 5: Catheter tract and lumen surface (left) composed of fibroblastic tissue with amorphous fibrin, RBCs, WBCs and fibroblastic tissue. No changes of media or adventitia.

Figure 6: Catheter tract and lumen surface (left) lined with intact endothelium. The vein (right) has focal area of necrosis, the wall of the tract is continuous with the vein and consists of fibroblasts and granulation tissue. Th e vein wall, connective and adipose tissue (up to 100 µm thick). No changes of media or adventitia.

Figure 7: Catheter tract and lumen surface (left) lined with intact endothelium. The vein (right) is covered with dense amorphous fibrin, RBCs, WBCs and fibroblastic tissue. No changes of media or adventitia.

Figure 8: Catheter tract and lumen surface (left) lined with intact endothelium. The vein (right) is covered with amorphous fibrin, RBCs, WBCs and fibroblastic tissue. No changes of media or adventitia.

CONCLUSIONS

• There was a trend in the data toward reduction of fibrin sheath formation in the the CH group compared to the control groups.

• The mean weight of fibrin sheath was lowest in the CH catheter group. Although there is no statistically significant difference in fibrin sheath weight between the groups, there was a trend for less weight in the CH group compared to both control groups.

• The mean fibrin sheath length was lowest in the CH catheter group. Although there is no statistically significant difference in fibrin sheath weight between the groups, there was a trend for less weight in the CH group compared to both control groups.

• There was no evidence of bacteria colonies on Gram stained sections in any of the 12 Day or 31 Day cases.

• Based on the histology changes, the only differences between study groups were in sections of vein at approximately midway between catheter insertion and phlebectomy. Based on approximate percentage of luminal circumference, the severity of intimal hyperplasia was less in the CH group than the C2 group. The CH and C1 had decreased or similar circumference of intimal hyperplasia. The CH and C1 had decreased or similar circumference of intimal hyperplasia.

• There was no statistically significant difference in fibrin sheath lengths among the control catheters on Day 12 (C1 versus C2 p-value = 0.9971). There were no statistically significant differences in mean fibrin sheath lengths among the control catheters on Day 31 (C1 versus C2 p-value = 0.8964, C1 versus C2 p-value = 0.9413, C1 versus C2 p-value = 0.8944, C1 versus C2 p-value = 0.8944).

REFERENCES