Initial clinical experience with a new heparin-coated chronic hemodialysis catheter

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Abstract

In this paper we wish to report our clinical experience with a new heparin-coated dialysis catheter with a symmetric tip. Over a 16-month period, 60 heparin-coated Tal Palindrome™ catheters were placed in 57 patients. Catheter patency, catheter-related complications, and reasons for catheter removal were recorded. The patient's initial cause of end-stage renal disease, underlying diseases, and site of access were recorded as well. Patients were specifically followed for development of heparin-induced thrombocytopenia. Patient ages were 34–91 (average 66). Fifty-four percent of patients had a history of diabetes. Sixty catheters were placed for a total of 5353 catheter-days. The average catheter indwell time was 107 days (range of 2–381 days). Catheter-related infection occurred in 6 patients over the study period, with a rate of 1.12/1000 catheter-days. Bacteremia occurred in 3 patients with a rate of 0.56/1000 catheter-days. Six catheters were removed or exchanged due to malfunction. There was no incidence of heparin-induced thrombocytopenia. Initial clinical experience with the heparin-coated Tal Palindrome™ hemodialysis catheter demonstrated safe, reliable use, and low infection rates.

Key words: Hemodialysis, hemodialysis catheter, catheter infection

INTRODUCTION

In the United States, the number of newly diagnosed patients with end-stage renal disease (ESRD) is steadily rising. In addition, the ages and comorbidities of these patients are on the rise. Accordingly, complications associated with dialysis access are increasing, particularly with dialysis catheters. Dialysis catheters are vital to the delivery of hemodialysis in patients awaiting kidney transplantation, maturation of arterio-venous fistula or synthetic fistula (PTFE graft) and, in a select population of patients, serve as the sole means of dialysis access. In recent years, the use of hemodialysis catheters has increased significantly from 13% of ESRD patients in 1995 to 24% of ESRD patients by 2000.[1] In the United States, as many as 1 in 5 new dialysis patients start their dialysis with tunneled cuffed catheters.[2] Owing to the high incidence of catheter-related complications including infection, central venous stenosis, and thrombosis, NKF-K/DOQI guidelines recommend that $<10\%$ of chronic renal failure patients be maintained on dialysis catheters.[3–5] The annual costs of hemodialysis catheter placement and management have reached between US$1 billion and US$1.5 billion.[6]

The systemic anticoagulation effect of heparin is an important consideration when using implantable devices with heparin coating. There is a low, although not insignificant, chance of heparin-induced thrombocytopenia (HIT), as evidenced in previous studies of heparin-coated pulmonary artery catheters and cardiac stents.[7,8] The heparin-coated catheter studied here employs a bonding technology to immobilize the drug at the inner and outer surfaces of the catheter to concentrate its effect while minimizing the risk of HIT.

In this paper, we evaluate the clinical outcome and clinical function of this new heparin-coated catheter.

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DOI:10.1111/j.1542-4758.2009.00339.x

MATERIALS AND METHODS

The study is a retrospective review of all heparin-coated Tal Palindrome™ (Covidien, Mansfield, MA) tunneled hemodialysis catheters that were placed between October 1, 2006, and February 1, 2008 (16 months). Fifty-seven patients were entered into the study. Patient selection was based on availability of the heparin-coated catheter and physician preference. Patient demographics, catheter dwell time, catheter insertion location, any interventional procedures and complications, development of HIT, and indication for removal were obtained from radiology records, referring nephrologists, and dialysis nursing staff. Institutional review board approval was obtained for this study.

Catheter placements, removals, and exchanges

All procedures were performed by an experienced interventional radiologist (M. S., M. T., H. M., J. P.) in the interventional radiology suite.

Insertion of the catheter was performed in the standard manner. Access was initially made to the internal jugular vein under real time ultrasound guidance. The catheter was then tunneled from an incision below the clavicle to the venous puncture site using the provided tunneler. The catheter was then inserted to the internal jugular vein either by utilizing the provided valved peel away sheath or over-the-wire utilizing the VenaTrac™ (Covidien, Mansfield, MA) device (Figure 1). All catheter insertion procedures were performed in the angiography suite. No antibiotics were administered. Under sterile conditions, the dermatotomy and the subcutaneous tunnel were infiltrated with buffered lidocaine hydrochloride 1%. The catheters were tunneled in an antegrade fashion and inserted using a standard technique. The tip of the catheter was placed in the mid to upper right atrium.

Flow rates were also recorded on most catheters. Flows of <300 mL/min defined a poorly functioning catheter requiring intervention.

VenaTrac over the wire insertion stylets were used for catheter exchanges. For exchanges, the catheters were bluntly dissected from the tunnel and retracted to the brachiocephalic vein. Injection of contrast was then performed with digital subtraction imaging over the chest. The presence of a fibrin sheath or thrombus was recorded. A new catheter was then inserted over a guide wire (Terumo Medical Corporation, Somerset, NJ) through the insertion stylets. The new catheter was advanced under fluoroscopic guidance.

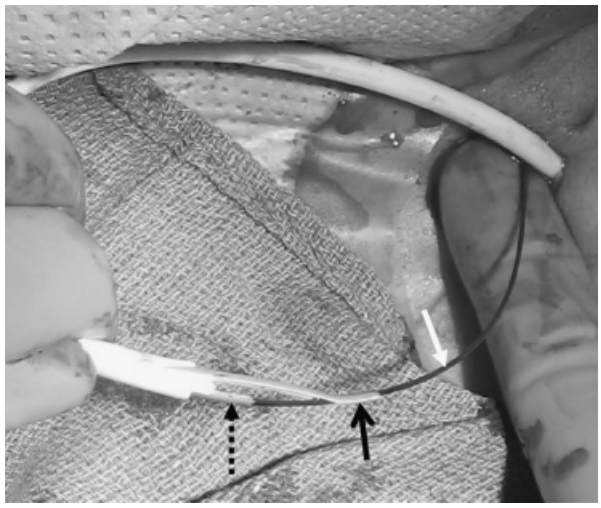

Figure 1 Image of the VenaTrac™ device. The device is comprised of 2 "D"-shaped stylets that occlude the catheter lumen. A wire (white arrow) is advanced through the tip of the longer stylet (black arrow) and into the shorter stylet (dashed arrow). The VenaTrac™ device allows over-the-wire exchange and insertion of the Tal Palindrome™ catheter without risk of air embolism.

In patients with clinical signs of infection, catheters were removed without venography and the tip was sent for culture and sensitivity.

Data recording

Data were collected prospectively in the interventional radiology suite. Every heparin-coated chronic tunneled dialysis catheter placed was entered into an excel database. Follow-up was performed during follow-up visits and using the computerized patient charts. The computerized patient charts allowed access to all notes, laboratory results, and imaging studies. Data analysis was performed at the end of the study period.

Thirty patients were followed until the removal or exchange of their hemodialysis catheters. Indications for catheter removal or exchange included poor function, infection, cuff exposure, maturation of fistula or graft, resolution of the acute renal disease, and death. The remaining 27 patients still had functioning catheters at the time of data collection.

Rates of occurrence of all complications and infection were calculated by dividing the number of catheters removed for that reason(s) by the total indwelling time of all catheters. This figure was expressed as occurrence per 1000 catheter-days.

RESULTS

A total of 60 heparin-coated Tal Palindrome™ catheters were placed in 57 patients during the study. It included 52 males and 8 females, with an age range from 34 to 91 (average 66). Fifty-four percent of patients had history of diabetes and 82% had history of hypertension.

Forty-three catheters (72%) were placed as initial placements while 17 catheters (28%) were over-the-wire exchanges. Most catheters were placed from the right internal jugular vein (53 catheters, 88%), followed by the left internal jugular vein (7 catheters, 12%). No insertional or exchange complications were seen during this study. No subclavian or femoral access was performed during the study period. Tip to cuff lengths of the catheters used in this study had the following breakdown: 12 (20%) at 19 cm, 38 (63%) at 23 cm, and 10 (17%) at 28 cm.

Follow-up information, including the reason for removal and dwell time, was available for 53 catheters. At the time of data collection, 27 catheters were still functioning without complications. Dwell time ranged from 2 to 381 days for a total of 5353 catheter-days (median 17.5 days, average 107 days). The most common indication for catheter removal or termination of catheter use was infection (6 of 33, 18%). In 6 additional patients (18%), the catheter was removed because of poor flows. The total infection rate was 1.12/1000 catheter-days. Three patients (5%) had proven catheter-related bacteremia, with a bacteremia rate of 0.56/1000 catheter-days. One exit site infection was recorded. Two additional patients had clinical signs of catheter infection without positive blood cultures.

Six catheters were exchanged due to poor flows and no fibrin sheath visualized on venography. Three catheters were exchanged due to cuff exposure, 1 catheter was exchanged due to a cracked backend connector, and 1 was exchanged due to a hole in the catheter. Two patients died of unrelated causes during the study while having functioning catheters. During the study period, follow-up blood work did not show any laboratory evidence of HIT and there was no clinical evidence of HIT.

DISCUSSION

While tunneled hemodialysis catheters are the least desirable method of hemodialysis access, there are a substantial number of patients who rely on these catheters when other means of dialysis (fistula, graft, or peritoneal dialysis) are not available.[9] Catheter-related thrombosis complications remain a major concern and a significant cause of failure to deliver adequate hemodialysis. Complications leading to catheter exchange and removal not only cause patient discomfort but also increase hospital costs. There is clearly a need for better catheter technology. Heparin coating on medical devices has been used for over 30 years and has been evaluated in vitro and in vivo on numerous medical devices including cardiopulmonary bypass circuits, stents, central venous catheters, and implanted pacemakers. Studies demonstrated that heparin-coated medical devices can improve biocompatibility,[10,11] reduce platelet deposition,[12] and reduce the occurrence of device-related thrombosis.[13–15]

The use of antithrombogenic surface technologies on the catheters might reduce the likelihood of complications such as thrombosis or infection. Heparin is the most widely used anticoagulant today and its properties and structure are well documented.[16–18] The compound interacts with the plasma protein antithrombin and repels charged platelets, leading to decreased bacterial trapping within fibrin clots and sheaths. There is evidence that low-dose heparin solution may decrease thrombus formation at the catheter tip.[19] Hydrophobic and electrostatic interactions can also decrease direct bacterial adhesion onto catheter polymer. Heparin immobilized on a plastic surface has been reported to diminish both fibronectin deposition and to decrease bacterial adherence in vitro.[20,21]

A new type of heparin-coated chronic hemodialysis catheter, the Tal Palindrome™ Emerald and Sapphire dialysis catheters (Covidien), has been developed with the aim of minimizing catheter-related thrombotic complications associated with tunneled, cuffed dialysis catheters. This heparin-coated catheter consists of a spiral-z tip design with laser-cut side slots. These features enable the catheter to be used in the forward or reverse flow position with minimal recirculation.[22] The heparin coating technology on the catheter (BioInteractions Ltd., Berkshire, UK) targets several aspects of hemocompatibility. The coating has been applied to the internal and external surfaces of the catheter (Figure 2). The polyethylene glycol groups in the coating material have been shown to minimize both protein adsorption and platelet adhesion.[23] The coating also contains sulfate and sulfonate groups that are negatively charged and have been shown to repel cells and reduce cellular attachment of erythrocytes and platelets (Figure 3).[24]

In a review of this small series of patients followed over several months, we demonstrated that the new heparin-coated catheter may be effective in mitigating some of the more serious risks associated with long-term hemodialysis catheter use. Via its primary proposed mechanisms of

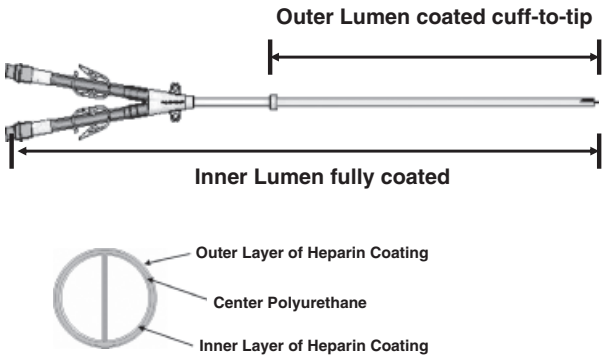

Figure 2 Schematic drawing of the catheter showing the extent of heparin coating covering the internal surface throughout and external surface of the catheter from the cuff centrally.

decreasing thrombosis and inhibiting fibrin sheath formation, the catheter may also facilitate hemodialysis efficiency and prevent catheter-related infections.

The major prospective clinical study of heparin-bonded central venous catheters is a 1996 study by Appelgren et al.[20] The clinical study, while small (32 patients), showed that heparinized catheters are associated with a significant decrease in catheter-associated bacteremia compared with uncoated catheters (26% vs. 0%, P=0.047). Our study findings also fall within this low range, with a bacteremia rate of 0.56/1000 catheter-days.

Complications related to thrombosis and infection have significant impact on catheter longevity. Up to 50%–91% of hemodialysis catheters fail within a year and mechanical catheter malfunction (malposition, thrombosis, and fibrin sheath formation) accounts for one-half to two-thirds of catheter loss.[25] Mean patency time for uncoated hemodialysis catheters has been reported to range between 73 and 92 days.[26] In this study, we find the coated catheter's mean indwell time to be 107 days. A recent paper by Spector et al.[27] describing outcome with a similar design catheter without heparin coating showed that 13.9% of the catheters were removed due to clinical signs of infection compared with 10% (6 of 60) in this paper. The total infection rate with noncoated catheters was 1.4/1000 catheter-days compared with 1.12/1000 catheter-days in this paper. In the noncoated catheters, fibrin sheath was deemed as the reason for exchange in 10 catheters (8.7%), no fibrin sheath was identified in the heparin-coated catheters.

A randomized clinical study comparing the various chronic hemodialysis catheters would be necessary to substantiate the significance of this difference.

While various methods of precoating catheters with heparin have been developed, a number of these technologies allow heparin to leach from the precoated surface over a number of days or months, potentially causing a systemic response. The bonding technology in the Tal Palindrome™ heparin-coated catheter is new and is designed to eliminate the risk of systemic effects and HIT. Although the number of patients in this series was small, our results did not demonstrate any evidence of HIT. Because the incidence of HIT is also low in previous studies

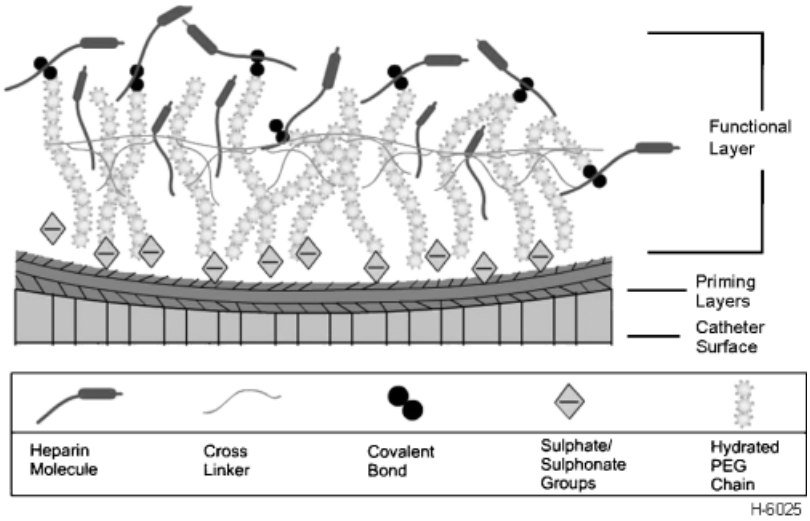

Figure 3 Schematic drawing of the molecular composition of the heparin coating of the catheter. A nonbiodegradable copolymer containing heparin, polyethylene glycol, sulfate, and sulfonate groups in conjunction with numerous polyethylene glycol groups.

of coated catheters, definitive long-term HIT benefit remains to be proven with future clinical trials.

The results of our clinical experience described in this paper suggest that the heparin-coated catheter may be effective both in mitigating thrombosis and inhibiting fibrin sheath propagation without leading to the systemic effect of heparin use. These qualities, if proven in a larger, prospective clinical trial, might have significant positive impact on catheter-dependent ESRD patients. Randomized-controlled human clinical trials are necessary to substantiate the clinical benefits, if any, of this new heparin-coated catheter. This new technology should also be evaluated on a cost-benefit ratio with conventional catheters and with other coating technologies such as silver ions and antibiotics.

ACKNOWLEDGMENT

Conflict of interest statement: Michael Tal is a consultant for Covidien Inc. None of the other authors identified any conflict of interest.

Manuscript received July 2008; revised September 2008.

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