

## Short Review

### Large-Bore Catheters for Extracorporeal Detoxification Methods Need Large Improvements

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#### Abstract

Catheter-Related Bacteremia (CRB), thrombosis and stenosis are among the most frequent complications associated with catheters, which are inserted in vessels as vascular access. These problems are usually related to the handling of the staff, the catheter materials and the surface properties of the catheter. To reduce the tremendous high costs of the CRB and improve the patient outcome and discomfort, other technologies, which include the outer and the inner surface are necessary. New materials and new technologies must be developed, which should have a better biocompatibility.

**Keywords:** Large-bore catheter; Vena jugularis interna; Catheter-related bacteria; Biocompatibility; Surface treatment; High costs of infections

#### Introduction

Despite all technical innovations in hemodialysis, the problem of finding a temporary or permanent vascular entry point appears to have found no satisfactory solution. Temporary vascular access, in particular, still presented considerable problems over years. In 1979, the author became aware of the problems associated with vascular points for acute hemodialysis and the author introduced the canalization of the superior vena cava over the internal jugular vein with a modified large-bore catheter [1]. With the introduction of catheterization, the previously necessary application of a Scribner shunt has become

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superfluous. Catheterization of the internal jugular and subclavian vein as temporary access points is suitable for almost all treatments situations [2]. In the following years, the author was involved in the development of new large-bore catheter types [3]. Several years later, he found a company in the USA, which treated the outer surfaces of different materials. The company treated large-bore catheters with silver or Silicone (Spire Corporation, Bedford, MA, USA) [4].

Contraindications for the internal jugular vein catheterization are such as inflammations at the point of puncture and unidentified anatomical conditions, e.g., extended stream or tumors in the neck area and one of the most frequent are jugular vein thrombosis. After insertion of the catheter in the internal jugular or subclavian vein, the position of the catheter tip should be checked by fixing the catheter with a suitable cutaneous suture. In order to avoid x-ray control, the author has been locating the catheter tip with an intra-arterial electrocardiogram passed over the catheter [5].

Synthetic catheters are increasingly used for intensive medical treatment and extracorporeal detoxification procedure since several decades. Correspondingly, typical complications such as infections and thrombosis are also on the increase. Infections present a particular problem as they can appear any time, even years after an implantation, and may affect all materials. Complication rates due to infections for venous catheters are given at between 34 % and 40 % [6]. Catheter-related complications represent a significant burden on the management of the Renal Replacement Therapy (RRT) program and mortality risk for the dialysis patient. The incidence of catheter-related complications is significantly higher than with arterio-venous fistula [7].

In the first retrospective study (1979-1990) with 2,626 large-bore catheters in 1,627 patients, the frequency of infections, thrombosis, bleeding, and other side effects was investigated. All complications together are presented dependent upon vascular route and were seen in total in 502 treatments (44.3 %) [8]. In the second retrospective study (1992-2007), outer surface treated catheter with silver (n = 54) versus untreated catheters (n = 105), who needed a large-bore catheter, were investigated [9]. The results of the preliminary investigation from 2001, which showed 75 % decline in the infection rate with the surface treated catheter, cannot be confirmed with the present investigation. One reason may be that in the surface treated catheters only the outer surface was coated with silver and the possibility of contamination by handling during the extracorporeal treatments [10].

Dialysis catheters are used for vascular access in 65% of incident Hemodialysis (HD) patients, and in 25 % of the prevalent HD populations [11]. Today the first choice of vascular access is the vena cava superior over the internal jugular vein [12].

However, large-bore catheters used for extracorporeal detoxification need large improvements, due to the complication rates. Catheter improvements must develop together from scientists, physicians and industries, which are involved in the catheter production.

## Discussion

Catheter-Related Bacteremia (CRB) is a major cause of morbidity among hemodialysis patients. Treatment with systemic antibiotics alone without removal of the catheter fails definitely eradicates the infection in most patients [13]. CRB must managed by either catheter removal with delayed placement of a new catheter or manage of the infected catheter with a new catheter over a guide-wire and additional systemic antibiotic therapy. These CRBs are contributing factors to increasing cost of medical care. They are responsible for patient readmissions and longer hospital stays as well as patient discomfort, morbidity, and occasions mortality.

The source of CRB is in most patient's abacterial biofilm, which forms in the catheter lumen or on the outer surface. This biofilm, most consisting of *Staphylococcus aureus*, cannot be destroyed or eliminated by a systemic antibiotic therapy because of antimicrobial resistance [14]. Bacteriae could most the time colonize, of rough surfaces [15]. The combination of rough surfaces and protein deposits should be an ideal situation for colonization of bacteria. The bacteria could produce and become covered with a slime layer, in which case antibiotic drugs have no influence on the bacteria. The bacteria under the slime layer use the organic substances of the catheter material for their metabolism. The toxins of the bacteria can penetrate the slime layer and enter the patient blood provoking a catheter infection [16]. Biofilm is a microbial derived sessile community characterized by cells that irreversibly attached to a substratum or interface to each other, embedded in a matrix of extracellular polymeric substances that have produced [17]. Such a biofilm can be the origin of fibrin sheath formations leading to catheter dysfunction due to blood reducing and to blood disturbances. The therapy must be remove the catheter immediately, or exchange it over a guide-wire with a new catheter and additional systemic antibiotic therapy.

Biocompatibility of synthetic materials is another major problem. The interaction of blood with a synthetic surface causes coagulation and activation of the complement system. This can lead to the adsorption of various proteins and the formation of a layer of protein on the synthetic surfaces. Thrombocytes, other cells and bacteria adhere of this layer of protein so that thrombi may form which can lead to blood flow disturbances and catheter dysfunction [9].

Surface modification processes can reduces the rate of infection, thrombogenicity, and other catheter-related complications without adversely affecting the basic design function of catheters. Examples include conventional coating process such as depending and spraying: vacuum-deposition techniques (e.g., sputtering), and surface modification approaches such as diffusion (e.g., nitriding, carburizing), laser and plasma processes, chemical plating, grafting or bonding, and bombardment with energetic particles (as in plasma immersion or ion implantation). Of the available bombardment have particularly successful in biomaterial surface modification, primarily because they combine versatility and low-temperature processing with superior control, reliability, and reproducibility [18].

Another possibility shows the developed catheter material, the microdomain structured surface (PUR-SMA coated catheter, Gambro Germany) [19]. Microdomain surfaces are considered the most biocompatible because the mimic the structure of natural biological surfaces. Microdomain structures are used to match the multiple requirements for improved catheter surfaces that are reduced

thrombogenicity and improved antimicrobial properties. An SMA-modified polyurethane coating consists of hydrophobic and hydrophilic microdomain in range below 50 nm. Up to 50 percent of the molecules are presented to the surface and creates microdomain-structured surfaces. If the domains are below a critical dimension of approximately 100 nm, theoretical considerations indicate that interaction with proteins, blood cells, or even bacteria will unstable and therefore not occur as frequently as on non-microdomain structured surfaces.

Other new materials must developed, which should have better biocompatibility to reduce side effects so that they can be left in situ for a longer time, because the part of dialysis patients with vascular access problems is increasing in the last decades. However, about 30 % of all hemodialysis patients, because the age of HD patients are permanent growing up [20]. As the requirement for more and more artificial organs and/or organ replacement increases, especially in elderly patients, there will be a definite need for new materials with better biocompatibility and for suitable technologies to solve these infection, thrombosis and medical problems to reduce the costs and get better improvement of the patients. A disadvantage of drugs such as antibiotics in the catheter surfaces or administration to patient or disinfection substances is that they can develop resistance by mutation or other mechanisms. Therefore, the need of new surgical techniques and materials are necessary [21]. However, it appears impossible to create a surface with an absolute "zero" adherence due to thermal-dynamical reasons and due to the fact that a modified material surface is *in vivo* rapidly covered by plasma and connective tissue proteins.

Recent data have suggested that Methicillin-Resistant *S. aureus* (MSRA) and Vancomycin Intermediate *S. Aureus* (VISA) organisms have increased [22]. One of the proposed mechanisms of vancomycin-resistance is the bacterial cell wall thickening following vancomycin exposure [23]. Vancomycin's activity may be decreased activity may be decreased due to the thickness of the bacterial cell; the results are MSRA and VISA [24].

Therefore other concepts of the prevention of implant-associated infections must involve the impregnation of the devices the inner and outer surface with antibiotics, antimicrobial substances and/or metal [25,26]. Another point is to understand the process leading to the development of CRB in order to can offer effective preventive and therapeutic possibilities [27]. Such as new polymer-antibiotic systems in inhibiting bacterial biofilm formation and in reducing neutrophils activation after surface contact on different biomaterials, thus reducing the risk for biomaterial-mediated inflammatory reactions [28-30], or the development of new biofilm to serve in a communication system termed quorum sensing [31], or molecules that inhibit quorum sensing signal generation among organism could block microbial biofilm formation [32].

These CRB are contributing factors to the increasing cost of medical care. They are responsible for patient readmissions and longer hospital stays as well as patients discomfort, morbidity, and occasional mortality. Feldmann et al. calculated in 1996 the costs of the morbidity due to catheter infections will soon exceed \$ 1 billion per year [33]. Therefore he demanded to reduce vascular access-related morbidity, that strategies must be developed not only to prevent and detect appropriately early synthetic vascular access dysfunction, but to better identify the patients in a whom radial arterio-venous fistula

is a viable clinical option. The representative health care cost savings for hemodialysis catheters, given specific infection rates and potential reductions.

The cost analysis was calculated using the literature and the available costs of different companies which distribute these catheters [34]. Potential health care cost reductions that could be achieved through the use of surface treated of surface treated catheters by an annual usage of 125,971 hemodialysis catheter devices and an infection rate of 5-20 % savings per year of \$ 17.7 million, reduction about 40 %. Besides a high member of patients who die to end stage renal disease, the costs of these infections are increasingly steady. After Schwebel et al. the costs are \$2.118/intensive care unit day, and after Pronovost et al \$ 45.000 per each infection [35,36]. Toccanelli et al. estimated in 2009 the costs associated with ESRD in four European countries (France, Germany, Italy, and UK) between € 35.9 and € 163.9 million per year [37].

Central Venous Catheters (CVC) is the most common source of hospital-acquired bloodstream infections in the USA. Each infection has an estimated additional cost of \$ 25.000 per episode [38]. There are up to 250.000 episodes reported in the USA per year, each episode increasing the cost and duration of the hospital stay. The Centers of Disease Control and Prevention (CDC) have released many guidelines to help prevent and reduce CRB, and this has helped bring down the rate of infections significantly. However, the number of CVC remains close to 15 million catheter-days per year. The CDC reports a 50 % decrease in Central Line-Associated Bloodstream Infection (CLABSI) rate from 2008 to 2014 and a 9 % decrease between 2013 and 2014. The CDC introduced general guidelines to decrease and prevent CLABSI in 2009. Nevertheless, about 30,100 CLABSIs still occur in the intensive care units and wards of US acute care Facilities each year [38].

Due to tremendous high costs, it must possible of scientists, physicians, bioengineers and others to develop new techniques and new materials to reduce these high costs and increase the improvement of patients. However, besides the high costs due to catheter-related infections, the patients' longer hospital stays, and patients discomfort, mortality, and occasionally mortality are the most important problems, which must be resolved. To reduce these complications it is necessary that the handling of the catheters must be done first after the numerous recommendation and guideline available in the literature [39,40].

After various authors is important, if the use of a large-bore catheter is inevitable, insertion in the right internal jugular vein is preferred, as the incidence of complications is less likely [1,8,41-43]. Treatment of elderly patients who commence HD with a large-bore catheter should be planned considering aspects of individual clinical risk assessment [44].

Most important is the improvement of the handling of the catheters by attending staff, which is recommended in numerous available guidelines to reduce the tremendous high costs to treat the CRB and the discomfort and morbidity of the patients. The nursing staff insuring dialysis connection and disconnection usually provides CVC care. The incidence of CVC-related complications is clearly associated with nursing staff experience and respect of catheter-handling protocols [7]. For each dialysis facility, a specific training program and a protocolized handling procedure should be defined and adapted

to their results. Aseptic rules for manipulating CVC at the time of dialysis connection and disconnection should be applied at all times. They include for the nurse, the use of sterile materials and additive protecting barriers and resort to an auxiliary caregiver to facilitate connection to the dialysis machine while preventing contamination.

Therefore, new materials, new surface treatments, and new technologies are needed to serve the tremendous high costs for hemodialysis and apheresis catheters by treating the complications, to reduce infections rates, and thrombus formations to improve the patient outcomes and reduce the tremendous costs. Large-bore catheters for extracorporeal detoxification methods need large improvements to decrease the tremendous high costs of complications and the discomfort of patients.

## Conclusion

In point of view of the results and the literature data, new technologies, new materials and surface treatment of both surfaces, the inner and outer surface, are needed to save the tremendous high health costs of the catheters for extracorporeal detoxification methods, to reduce infection rates, and thrombus formations and help to improve the patients outcome.

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