Review Article

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Large-Bore Catheter as Vascular Access Must Be Improved

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Introduction

Billions of central venous catheters are inserted annually for intravenous and/or extracorporeal therapy worldwide. For therapeutic apheresis (TA) methods a blood access is necessary. Besides venipuncture of the peripheral or cubital veins, an arterio-venous fistula can be inserted in patients with access problems or side effects like hematomas and/or sclerotic tracks for performing TA treatments. In acute situations or for a special treatment time a large-bore- or double-lumen catheter can be inserted by percutaneous puncturing of the internal jugular, or subclavian, veins [1]. In central venous catheters, catheter-related bacteremia (CRB) is a major cause of morbidity among hemodialysis patients [2].

The source of CRB is usually a bacterial biofilm consisting of a polysaccharide matrix that forms either in the lumen or on the outer surface of the catheter [3,4]. The biofilm, most consisting of bacteria such as Staphylococcus aureus, cannot be destroyed or eliminated by a systemic antibiotic therapy, because of antimicrobial resistance. Rough catheter surfaces and protein deposits are an ideal situation for the colonization of bacteria, and they could produce and become covered with a slim layer. In this 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 bacteria toxins can penetrate the slim layer the patient blood provoking a catheter infection. A biofilm is a microbial derived sessile community characterized by cells that are irreversible attached to a substratum or interface to each other, embedded in matrix extracellular polymeric substances that have produced. Such biofilm can be the origin of fibrin sheath formations leading to catheter dysfunction. The catheter must be removed immediately, or exchange it over a guide-wire with a new catheter and additional antibiotic therapy. The majority of CRBs are associated with central venous catheters (CVCs) than with peripheral venous catheters, or arterio-venous fistula [1,5]. Important is a continued nursing staff and physicians training and the introduction of never catheter technologies, and catheter materials, which have contributed to reduce the incidence of infections to improved patients outcomes, and decreased the high costs of CRB and catheter-induced endothelial damage [3,6].

A further problem is the biocompatibility of the synthetic material of the catheters. The interaction of blood with synthetic surfaces causes coagulation and activation of the complement system, which leads to the adsorption of various proteins and the formation of a layer of protein on the synthetic Surface. Thrombocytes, bacteria, and other cells adhere to the layer of proteins and a thrombi may form which can lead to blood flow disturbances and catheter dysfunction [4]. New developments to influence CRB are available, such as new catheter materials, coating of the material surface with antibiotic-heparin, or silver and/or silicone, cuffs on the outer surface, catheter for tunneling, installation of an antibiotic-anticoagulant lock into the catheter between the treatments [2]. Surface-engineered biomaterials for catheter can reduces the rate of infection, thrombogenicity, and other catheter-related complications without adversely affecting the basic design function of catheters. Some examples are conventional coating process such as depending and spraying, vacuum-deposition techniques, and surface modification approaches such as diffusion (e.g., nitriding, carburizing), laser and plasma process, chemical plating, grafting or bonding, and bombardment with energetic particles as in plasma immersion or ion implantation. One of the available techniques based on ionized particle bombardment have particularly successful in biomaterial surface modification, primarily because they combine versatility and low-temperatures processing with superior control, reliability, and reproducibility [3].

Catheter Technology

The ion-beam based technology for the treatment of catheters, is the ion-beamed-assisted deposition (IBAD; Spi-Argent®, Spire Corporation, Bedford MA, USA) [3]. The process is typically performed at low temperature under high vacuum. The typical films with the affected layer deposited by the IBAD process is in the order of one µm or less vacuum compatible catheter materials may therefore, be treated without adversely affecting bulk mechanical properties. The IBAD is line-of-directly: however, parts with complicated geometries may be manipulated for uniform coverage of all surfaces [7].

The significant reduced infection rate with surface treated catheter in a preliminary investigation from 2001 cannot been seen in another investigation from 1992-2007 [1]. The explanations could be that all the patients in the record were included in the latter investigation and therefore data available for analysis was much larger, and in the group with the surface treated catheters only the outer surface of the catheters was treated and not the inside. The untreated catheters showed a higher positive culture for bacteria of 55 % versus 52 % to the surface treated catheter after removing, but without significance [1]. The first results with only outer surface treated catheters were encouraged, therefore the inner surface of the catheters must be treated, too, because the untreated inner surface is an ideal part for the colonization of bacteria.

The microdomain structured surfaces are considered the most biocompatible because the mimic the structure of natural biological surfaces (PUR-SMA coated catheter, Gambro, Germany) [4]. Microdomain structures are used to match the multiple requirements for improved catheter surfaces, which is reproduced thrombogenicity and improved antimicrobial properties. The PUR-SMA-modifies polyurethane coating consists of hydrophobic and hydrophilic microdomain in range below 50 nmm. Up to 50 % of the molecule are presented to the surface and create microdomain-structured surfaces, and if the domains are below a critical dimension of approximately 100 nmm, theoretical considerations indicate that interaction with proteins, blood cells, or even bacteria will be unstable and therefore not occur as frequently as on non-microdomain structured surfaces [7].

The advantage of the PUR-SMA surface treatments is the coating of the inner and outer surface of the catheters, which prevents contact of blood components with barium sulphate, possibly leading to leaching as particles or dissolved in the surrounding media [4]. Results with PUR-SMA coated catheters showed good biocompatibility with no deposits of hematic debris and low thrombogenicity and coagulation activity, and bacterial growth was very low [2]. Here, larger studies with these large-bore catheters are needed. Large-bore catheters are used for vascular access in 65 % of incident hemodialysis (HD) patients, and in 25 % of prevalent HD populations [4]. The first choice of vascular access is the vena cava superior over the internal jugular vein. However, large-bore catheters used for extracorporeal detoxification need large improvement.

One of the main complication rates of central venous catheter are infections with the source of a bacterial biofilm in the inner and outer surface of the catheters [8]. The biofilms are organized aggregate of microorganisms living an extracellular polymeric matrix that produce and irreversibly attached of fetish or living surface which will not remove unless rinse quickly [9], and consist most of Staphylococcus aureus, which cannot be destroyed or eliminated by a systemic antibiotic therapy. Especially on rough surfaces the bacteria could colonize, and produce and become covered with a slim layer, which is resistant to an antibiotic therapy. The toxins produced by the bacteria can penetrate the slime layer and provoke a catheter infection [7]. Biofilm is a microbial derived sessile community characterized by cells that irreversible attached to a substratum or interface to each other, embedded in a matrix of extracellular polymeric substances that have produced. The bacterial colonies in a biofilm generally consist of many types of micro-communities, which coordinate with one another multiple aspects, and coordinate a crucial role in exchange of substrate, distribution of important metabolic products and excretion of metabolic products [9]. The origin of a sheath formation can be such a biofilm which leads to catheter dysfunction due to blood reducing and to blood disturbances. The interaction of blood with synthetic surfaces causes coagulation and activation of the complement system and can lead to the adsorption of different proteins, thrombocytes, other cells and bacteria, and may form thrombi in the catheter, and flow disturbances and/or catheter dysfunction [4].

Surface modification processes and new catheter materials are needed to reduce the infection rate, thrombogenicity, and other catheter-related complications. The IBAD technology must use for both surfaces of the catheters and not only the outer surface, and the catheter coated with PUR-SMA on both surfaces have shown good results as shown [4]. However, larger studies are necessary.

Antibiotics on the catheter surfaces or administration to patients or disinfection substances can develop a resistance by mutation or other mechanisms. Therefore, new materials and new surgical techniques are necessary. 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 [4]. Several studies showed that tunneled dialysis catheters have a lower rate of bloodstream infection than non-tunneled catheters [10,11].

Methicillin-resistant Staphylococcus aureus (MSRA) and Vancomycin Intermediate Staphylococcus Aureus (VISA) organisms have increased [12]. One of the proposed mechanism of Vancomycin-resistance is the bacterial cell wall thickening following Vancomycin exposure [13]. Vancomycin´s activity may be decreased activity due to the thickness of bacterial cell; the result are MSRA and VISA [14].

Concepts of prevention of implant-infections must involve the impregnation of the devices the inner and outer surface with

antibiotics, antimicrobial substances, metals, and/or nanoparticle [4,15,16]. To understand the process leading to the development of CRB in order to can offer effective preventive and therapeutic possibilities [17]. To reduce the risk for biomaterial-mediated inflammatory reactions are new polymer-antibiotic systems in inhibiting bacterial biofilm formation and in reducing neutrophils activation after surface contact on different biomaterials [18-20]. Further developments are new biofilms to serve in a communication system termed quorum sensing, or molecule that inhibits quorum sensing signal generation among organism could block microbial biofilm formation [21,22]. The new engineering techniques and biomedical materials such as micro/nano surface patterning and conjugation of antimicrobial peptides, enzymes, metal cations, and hydrophilic polymers on the surface has been suggested recently [23]. All new catheter technologies are not enough to solve all problems with CRB. Therefore, large-bore catheters need larger improvements to decrease the tremendous discomfort of patients and the very high costs of CRB complications [4].

The improvement of the handling of the catheters by attending staff is most important, which is recommended in numerous available guidelines to reduce the tremendous high costs treat the CRB and discomfort and mortality and morbidity of patients [4]. The incidence of CVC-related complications is clearly associated with the nursing staff experience and respect of catheter-handling protocols [24]. A specific training program and protocolized handling procedure should be defined and adapted to their results. For the staff must be included the use of sterile materials and additive protecting barriers and resort to an auxiliary caregiver to facilitate connection to the machine while preventing contaminations [25].

Conclusion

Central venous catheters are increasingly used for intensive medical treatment and/or extracorporeal detoxification methods. They are the most common source of hospital-acquired bloodstream infections and has estimated tremendous high costs. Therefore, new catheter technologies and new surface treated methods are necessary to reduce the discomfort of patients and the tremendous high costs of treating CVC complications of millions dollars [4]. The Centers of Disease Control and Prevention have released many guidelines to help prevent and reduce CRB, and this has helped bring down the rate of infections significantly and the tremendous high costs of the CRB-related complications and to help the patients´ outcome. To create a surface of a catheter with an absolute “zero” adherence appears impossible due to thermal-dynamical reasons and due to the fact that a modified material surface is *in vivo* rapidly covered by plasma and connective proteins. However, all who are involved in this part of medicine must try all the time to come near and nearer the absolute “zero”.

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