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Review

The significance of *Candida* infections of medical implants

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Infection of medical implants is acquired at the time of instrumentation or surgery. It is an early complication of this intrusive procedure. Biofilm formation on implanted implants such as dentures, catheters or a prosthetic heart valve may lead to *Candida* infections. Factors affecting the biofilm formation and the risk factors associated with the implantation of the various medical devices are highlighted in this paper. The modification of biomaterial surface with anti–infective agents to enhance biocompatibility of the indwelling medical devices is discussed.

Keywords: *Candida albicans*, medical implants, biofilm, biomaterial manufacture.

INTRODUCTION

Biofilms are structured microbial communities that are attached to surfaces and encased in a matrix of anionic exopolymeric material. They are indispensable to the development of clinical infections (Davey et al., 2000).

The surface of an indwelling medical implant should be similar to that of the blood vessel in a healthy human body A single microbial species or a mixture of bacterial or fungal species may cause biofilm infections. The implant-related infections are caused by microorganisms growing on the surface of medical devices such as catheters, joint replacements, dentures and prosthetic heart values (Donlan, 2001).

More than half of the nosocomial infections are linked with the use of medical implants (Richards et al., 2000). The medical implications of device-related infections can be enormous such as increased resistance to antifungal therapy and failure of the medical implant. This review describes biofilm formation by *Candida* species and infections associated with medical devices commonly used by patients.

Biofilm formation in *Candida* Infections and resistance to antimicrobial agents

In other to colonise any surface, microorganisms must adhere to biomaterial surface by producing extracellular polymers, leading to the formation of a microbial biofilm (Donlan, 2001). An implanted device such as a urinary catheter is associated with nosocomial infections and biofilms can be detected on such device. The other medical devices totally implanted in the body that are liable to *Candida* infection are cardiac pacemakers, joint replacements and prosthetic heart valves. Organisms may be introduced from the hands of nursing staff or the patient's skin microflora (Douglas, 2003).

The commonest superficial *Candida* infection is denture stomatitis. This is caused by *Candida* infection of the oral mucosa. The surface of a close fitting acrylic denture has a mixed species biofilm which contains bacteria (streptococci) and yeasts (Darouichie, 2001).

Patients with silicone rubber voice prostheses are liable to infection with *Candida* spp in polymicrobial biofilms. The biofilm may cause malfunction of the valve mechanism thereby leading to the failure of the prostheses within months of placement (Van de Mei et al., 2000). A mixture of morphological forms is characteristic of fully matured *Candida* biofilms. It consists of a dense network of yeasts, hyphae and pseudohyphae in a matrix of polysaccharides, carbohydrates, protein and unknown components (Chandra et al., 2001).

In order to inhibit microorganisms, antimicrobial agents must diffuse through the biofilm matrix. Biofilm resistance is related to the slow uptake of these agents. The formation and structure of *Candida* biofilms is influence by environmental factors, *Candida* morphogenesis and the nature of the contact surface. High glucose medium significantly favours growth of *Candida* spp. This is important for *Candida parapsilosis* as it has the potential to produce large amounts of biofilm when grown in 8% glucose.

Biofilm formation by *C. albicans* is slightly increased on

latex or silicone elastomer when compared with polyvinyl chloride (PVC).Similarly, conditioning films of serum or saliva promoted biofilm formation on denture acrylic (Chandra et al, 2001).

Orthopaedic devices/ joint replacements

The commonly infected implanted joint prostheses are mainly those of the hip and the knee. The organisms are introduced during surgery and there may be a haematogenous spread from another focus of infection within the body. Due to factors such as the long duration of operations, there is a higher risk for *Candida* infection of knee and hip prostheses than other joint prostheses (Stocks and Janssen, 2002). Early or late manifestation of infections determines the clinical presentation. Early infections include those that appear less than or equal to three months after surgery. These symptoms include pain, oedema,late wound healing, erythema and fever. The late manifestations or presentations include persistent pain, early loosing of protheses with or without pyrexia. (Zimmerti and Ochsner, 2002) Although early surgical debridement could save the device from being removed if the infection is not well established (Romamohan *et al*., 2001).

Urinary Catheters in immunocompromised patients

Urinary catheters are hollow, latex or silicone implants that are passed through the urethra into the bladder to collect urine during surgery or control urinary incontinence (Kaye and Hessen, 1994). Catheter systems may be open or closed. Patients with the closed systems are much less susceptible to urinary tract infections. Most urinary tract infections are related to catheter implant. Candiduria with multiple underlying illnesses in patients with funguria may be responsible for the high mortality observed. The isolation of *Candida* species from urine specimens of patients may represent several clinical states such as catheter infection, cystitis and unidentified septicaemia (Kauffman et al., 2000). A growing problem amongst immunocopromised patients with indwelling catheters is haematogenous candidemia. *Candida albicans* has been implicated in 37% of candidemia in some hospitals in Brazil (Colombo, 2000).

Indwelling intravenous Catheters

The surgically implanted device most commonly infected is the central venous catheter which is used for administration of fluids, nutrients and cytotoxic drugs.

Patients with central venous catheters are prone to primary bloodstream infections. Surgical implantation of prosthetic heart valve leads to the platelet and fibrin accumulation at the suture site and on the device as well as tissue damage. C*. albicans* accounts for up to 63% of all cases of candidemia (Richards et al., 2000). Maximal treatment of central venous catheter-related infections depends on the kind of catheter used, the type of causative agent and the severity of illness. Treatment of complicated and uncomplicated *Candida* infections of tunneled and nontunnelled central venous catheter is by catheter removal and systemic antifungal therapy (Nucci and Anaissie, 2002).

Dialysis vascular grafts

Patients with end-stage renal disease requiring hemodialysis or peritoneal dialysis can be infected. The predisposing factors to infection are metabolic acidosis, underlying diseases. In addition to the high glucose concentration and low pH, the immune system cannot handle microorganisms in such compromised patients (Kojic and Darouiche, 2004).

Intrauterine devices

The use of Intrauterine devices (IUDs) has been linked to pelvic inflammatory disease. IUDs removed from women have been shown to be severely contaminated with *Candida albicans.* The sheathed tail of the IUD may be a source of contamination by acting as a wick to allow bacteria to travel by capillary action and enter the endometrial cavity. Evidence for biofilms on IUDs has been proven by scanning electro microscopy and transmission electron microscopy (Jaques et al., 1986).

Central Nervous System Implants

The most commonly used devices of the central nervous system (CNS) are the ventriculoperitoneal shunts which are made of silicone polymers. Obstruction of fluid flow and infections are the most common complications with *Candida* infections.

Predisposing factors for *Candida* shunt infections and meningitis include use of antibiotics prior to or parallel bacterial meningitis, leakage of the cerebrospinal fluid, bowel perforation and or abdominal operation, use of steroid and implanted catheters (Montero et al., 2001).

The clinical presentation of *Candida* shunt infections differs mainly due to the location of the infection. If the infection is at the distal end, (vascular site or peritoneum), there may be fever and malaise. Proximal *Candida* shunt infections are evidenced by symptoms such as headache, nausea, vomiting.

MODIFICATION OF BIOMATERIAL SURFACE USED FOR DEVICE MANUFACTURE

The biocompatibility of a medical implant may be increased by surface treatment. This will modify the device properties and decrease the susceptibility to bacterial adhe-

sion. Such device properties include hydrophilicity and surface free energy.

Medical devices can be made from plastic or metals and are hydrophobic having high coefficients of friction that heighten the scale of infection. The hydrophilicity of the devices can be increased to reduce bacterial adhesion. This involves the use of hydrogel technology, which is a process that applies biocompatible water absorbable polymer hydrogels to medical device surfaces. Most microorganisms find it difficult to adhere to hydrogel-coated surface (Ista et al., 1996)

Examples of hydrogel polymers are polyvinyl pyrolidone and polyethylene glycol. The urinary catheters having a hydrogel coating performed better than silicone-coated ones.

The use of anti-infective agents to modify medical implants

The incorporation of non-toxic, anti-infective agents on device surface provides an alternative method to ensure a bacterial free surface. The advantages are that the bulk properties of the implant are not altered and they appear to increase biocompatibility and resist microbial adhesion than on medical implants (Shintani et al., 2004).

Other advantages are that the anti-infective agents provide a chemical barrier against intruding organisms, for example, Silver metal has been used on orthopedic external fixation pins by ion beam assisted deposition to prevent infections. Entrapment of anti-infective agents in a polymer matrix has been studied. Silver sulfadiazine and chorhexidine in a polyurethane matrix when applied to central venous catheters reduced the qualitative level and frequency of microbial colonisation . (Shintani et al., 2004).

Conclusion

An indwelling medical device must be biocompatible and free of microbial adherence. The 'ideal' medical implant surface should have the same surface properties as that of a healthy living body.

The understanding of microbial biofilm structure and the use of modern technology to bring about modification of the medical devices will lead to decreased microbial infection of medical devices.

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