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STRATEGIES TO PROMOTE LONG-TERM CARDIAC IMPLANT SITE HEALTH: CURRENT UPDATE

Cardiology

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ABSTRACT

Active implantable medical devices (AIMDs) are used for diagnostic, therapeutic, and rehabilitation purposes. Implants and devices improve the quality of life and well-being of the recipient. These include cardiac pacemakers (for controlling heart rhythm), ventricular assist devices (heart support), spinal cord stimulators (chronic pain management), deep brain stimulators (control symptoms of conditions, such as Parkinson's disease, essential tremor, epilepsy, and depression), cochlear implants (enable hearing) and, more recently, bionic eyes (restore vision). Implant life and strategies to enhance it is of paramount importance. The use of non-invasive techniques like Raman Spectroscopy to match the implant and recipient characteristics and non-invasive diagnosis of rejection would be the way forward.

KEYWORDS

INTRODUCTION & BACKGROUND

Cardiovascular implantable electronic device infections have increased along with a parallel increase in procedures performed in recent years. Prevention of this implant relation infection has been a major research area in the last decade. Patient device and procedural factors can add to this risk. Hence risk mitigation strategies revolve around pre-procedure screening, device selection, and periprocedural preparation and treatment.

REVIEW

The long-term success of novel biomaterials, biomedical devices, and tissue-engineered products necessitates a detailed understanding of biological response to implanted materials[2,3]. The changes that occur at the tissue material interface is of paramount importance in this regard. Basically, the body mounts an inflammatory response by the adherent macrophages and material surface chemistry modulates the same by altering the behavior of these like adhesion, apoptosis, fusion, and cytokine secretion. Emerging techniques of tissue engineering and regenerative medicine combine biomaterials with proteins and cells creating hybrids that find applications in the functional regeneration of damaged tissues. The host and syngeneic, allogeneic, xenogeneic or stem cells of implants would be subjected to inflammatory mediators and signalling molecules resulting in activation, differentiation, proliferation, or migration[4,5]. Reactive oxygen radicals, degradative enzymes, and pH would further decide the implant host reaction. Emergence from this compromised state to the optimal environment is essential for optimal survival of implants and reduction of morbidity. Creation of desired cell behavior or specific bio mimetic environment that ensures cell survival is some of the current techniques employed to achieve this effect. Myriads of challenges that ensue can be best understood and tackled with extensive knowledge of biomaterials and inflammatory and wound healing responses to these materials. The role of the immune system in this regard is paramount.

The goals of implant materials are that they must be durable, biomechanically sound with minimal or adverse tissue reactions. As far as joint replacement implants are considered they are well tolerated as long as the bulk form is retained and they achieve mechanical stability within the bone without colonization by microorganisms. When excessive wear of the materials sets in the generation of wear particles of ionic complexes induce periprosthetic osteolysis and loss of bony support with subsequent implant failure [6,7].

For CIED (cardiac implantable electronic devices) a biological cellulose wrap around with anti-adhesive and non-resorbable properties has been recommended. This leads to both the generator and proximal leads being free of fibrotic tissue and makes revision surgeries simple [9,10,11]. Micron-scale surface topography is an independent parameter that can be modified without affecting the bulk mechanical or chemical properties of a target substrate. Antibiotic strategies to mitigate CIED infections are well known and they include cefazolin, vancomycin, bacitracin washes, cephalexin, cefadroxil, and antibiotic-impregnated meshes. Antibiotic impregnated meshed can offer some protection but the real future lies in the development of leadless battery-less pacemakers.

Metal hypersensitivity is generally believed to be a Type IV (delayed hypersensitivity) reaction mediated by T lymphocytes. In reactions attributed to Type IV hypersensitivity as the primary mechanism, the metal ions released from implants are believed to act as haptens that bind to endogenous (internal) proteins to form hapten-protein complexes which act as antigens[12].

The corrosion of metallic implants, generation of wear debris, or problems with the structural integrity of the metallic implants can lead to the release of metal ions which may potentially increase the genotoxicity and carcinogenic risk. Induction of oxidative stress resulting in damage to cellular components including DNA, interference with DNA repair, and deregulation of cell proliferation are described as the three primary mechanisms associated with the genotoxicity/carcinogenic effects of metals[13].

Immunotoxicity testing guidance describes the five major immunological effects -hypersensitivity (Type I and Type IV), chronic inflammation, immunosuppression, immunostimulation, and autoimmunity - associated with devices and provides examples of the specific types of tests that might be used for the evaluation of these immune responses. The classical view of the CNS as a canonical site of “immunologic privilege” due to the blood-brain barrier has been refined in recent years through the study of highly specialized lymphatics associated with the CNS Specific local tissue responses depend on the device or biomaterial and peri-implant tissue type as well as patient-related characteristics. Hence the importance of preoperative screening is to identify those who might develop an adverse reaction to that particular biomaterial in the implant.

Cardiovascular implants in addition may trigger the coagulation cascade also. Endothelium injury and foreign body placement lead to the activation of platelets at the site of the implant with the recruitment of circulating leukocytes. Coagulation occurs through extrinsic and

intrinsic pathways, with the generation of thrombin and fibrinogen, and conversion to fibrin. Infections are due to device, lead, or pocket contamination. Patient-related factors like fever or leucocytosis, males, diabetics, renal failure, bacteraemia, use of steroids, and anticoagulants are associated with a higher risk for infections. Application of nano- and molecular-scale technologies for design and fabrication of the implantable circuitry can lead to remarkable advancement in integration density and dynamic power dissipation, enabling neuro-electronic interfacing and nano-bio-robotics[14]. Measures to counter CIED infections include patient and device selection criteria, provider and surgical site preparation, proper operation theatre conditions, surgical techniques that avoid hematoma, prophylactic antibiotics, and proper postoperative care with appropriate interventions like evacuation when needed[15].

RESULTS CONSISTENT WITH THE DIAGNOSIS

- Patients with CIED infection should have complete blood count (CBC) with differential, electrolytes, serum creatinine, C-reactive protein (CRP), chest x-ray, and two sets of blood cultures drawn at admission and a swab should also be sent for bacterial cultures.
- Localised infection may show as normal in blood workup.
- Positive blood cultures should undergo transesophageal echocardiography (TEE) to detect any vegetations on CIED leads or heart valves.
- PET/computed tomography (CT) can be helpful to confirm or exclude CIED infection in cases where clinical findings or TEE images are indeterminate.
- CT scan of the chest -suspected pulmonary emboli.
- When planning explants the device, swabs and tissue specimens from generator pocket should be submitted for bacterial cultures.
- Sonication of the explanted generator and leads can be a useful adjunctive measure to enhance microbial detection.
- Mycobacterial and fungal stains and cultures – for chronic or recurrent infection which are culture negative.
- Lead tip cultures should be submitted in cases of device-related endovascular infection.

Treatment Principles

Management Of CIED Infection Includes:

- Removal of infected device including leads
- Sending pocket swab and tissue for cultures; send the leads for culture.
- Antimicrobial therapy directed at causative pathogen
- Implantation of a new device once acute infection is controlled

Removal Of Infected Device

- Complete removal of the infected device, including generator and leads for curing acute infection and relapse prevention
- Patients should be assessed as to whether they need ongoing device therapy.
- Percutaneous extraction is generally considered safe, even in cases in which a large vegetation (>1 cm) is attached to the device leads.
- Cardiac surgery should be consulted in cases in which infection is complicated by valvular endocarditis, intracardiac abscess formation, perforation, or dehiscence of native or prosthetic valves and cases in which percutaneous extraction fails or poses significant risk to the patient[16].

Choice And Duration Of Anti Microbial Therapy

- In cases in which infection is limited to the device pocket, 10-14 days of anti-infective therapy is adequate.
- Patients with device-related bacteraemia (without evidence of endocarditis on TEE) should be treated with at least 2 weeks of parenteral anti-infective therapy based on identification and susceptibility of the causative pathogen. Therapy may be extended to 4 weeks in cases of S. aureus bacteraemia.
- Device-related endocarditis should be treated with 4-6 weeks of parenteral antibiotic therapy based on American Heart Association (AHA) guidelines for treatment of infective endocarditis.

Timing Of Implantation Of New Device

- A new device can be placed on the contra-lateral side once the infected device has been removed and blood cultures obtained after device removal are negative for at least 72 hours.
- In cases where admission blood cultures are negative, a new device may be implanted as soon as infected pocket has been adequately debrided.
- Implantation of a new device should be delayed for 14 days (from the first negative blood culture) in cases where device infection is complicated by valvular endocarditis.

Local milieu like the presence of uterine natural killer cells may add on to the burden of leukocyte lineage in specific body areas. Microbial dysbiosis has been recognized as an important factor in the connection of pelvic inflammatory disease with intra uterine implants. The use of Raman spectroscopy and newer advances in the diagnosis of implant health is appealing as it brings individualized care to the forefront. The newer setup enables the collection of Raman spectra of single cells at 785 nm excitation with 10 s exposure time [1].

Future

Raman spectroscopy is an analytical method by which chemical data are obtained through the inelastic scattering of light. A summary of these techniques is given in table Conventional Raman microscopy gives a non-destructive spectral analysis of chemicals at sub-micrometer resolution. Excessively long acquisition times due to the low Raman cross-section and the strong fluorescence background make this technique less suitable for the large scale mapping of tissues. Additional disadvantages: tissue must remain unstained and uncovered, resulting in the tissue drying out and risking contamination. A multidisciplinary approach that involves the proceduralist, anaesthetist, cardiologist, and IAEP is ideal for safe perioperative CIED management. The decision-making process should be tailored to individual patients and their needs, with the aim of preventing hemodynamic embarrassment consequent to CIED malfunction.

CONCLUSIONS

Immunological cross-talk that is determined genetically may finally maintain the pro-anti inflammatory balance the understanding of which would be a key factor in material selection and implant success in the future. Advancement of closed-loop systems will facilitate simultaneous stimulation and high-resolution sensing of both natural and evoked activity, with utility in intricate surgical procedures and neuromodulation. Sophisticated neuroprosthetics and artificial organs, further developments in brain-computer interfacing will enhance our ability to alter cognitive or sensory-motor functions in humans. The treatment of graft versus host disease will involve multiple modalities, like enhancement of suppressor cytokines and cellular subsets, modulation of immunologic checkpoints, graft manipulation, modulation of the microbiome, and other donor-based prophylaxis strategies. Individual-based identification strategies of implant acceptance using non-invasive methods like Raman Spectroscopy would predict implant individual compatibility preoperatively in the future.

REFERENCES:

1. Dochow, S.,: Quartz microfluidic chip for tumor cell identification by Raman spectroscopy in combination with optical traps. Anal Bioanal Chem. 405:2743-2746.
2. Charlson ME, Pompei P, Ales KL, MacKenzie CR: A new method of classifying prognostic co morbidity in longitudinal studies: development and validation. J Chronic Dis 1987; 40:373–383. [PubMed] [Google Scholar]
3. R Core Team (2014). R: A language and environment for statistical computing R Foundation for Statistical Computing, Vienna, Austria: URL http://www.R-project.org/. [Google Scholar]
4. Sohail MR, Eby EL, Ryan MP, Gunnarsson C, Wright LA, Greenspon AJ. Incidence, Treatment Intensity, and Incremental Annual Expenditures for Patients Experiencing a Cardiac Implantable Electronic Device Infection: Evidence From a Large US Payer Database 1-Year Post Implantation. Circ Arrhythm Electrophysiol. 2016; 9(8). [PubMed] [Google Scholar]
5. Kuehn C, Graf K, Heuer W, Hilfiker A, Chaberny IF, Stiesch M, et al. Economic implications of infections of implantable cardiac devices in a single institution. Eur J Cardiothorac Surg. 2010;37(4):875–9. 10.1016/j.ejcts.2009.10.018 [PubMed] [CrossRef] [Google Scholar]
6. Ludwig S, Theis C, Brown B, Witthohn A, Lux W, Goette A. Incidence and costs of cardiac device infections: retrospective analysis using German health claims data. J Comp Eff Res. 2018; 7(5):483–92. 10.2217/cer-2017-0080 [PubMed] [CrossRef] [Google Scholar]
7. Podoleanu C, Deharo JC. Management of Cardiac Implantable Electronic Device Infection. Arrhythm Electrophysiol Rev. 2014; 3(3):184–9. 10.15420/aer.2014.3.3.184 [PMC free article] [PubMed] [CrossRef] [Google Scholar]
8. Baddour, LM, Epstein, AE, Erickson, CC. "Update on cardiovascular implantable electronic device infections and their management". A scientific statement from the American Heart Association. vol. 121. Circulation 2010. pp. 458-77.
9. Sohail, MR, Uslan, DZ, Khan, AH. "Management and outcome of permanent pacemaker and implantable cardioverter-defibrillator infections". J Am Coll Cardiol. vol. 49. 2007. pp. 1851-9.
10. Klug, D, Balde, M, Pavin, D. "Risk factors related to infections of implanted pacemakers and cardioverter-defibrillators: results of a large prospective study". Circulation. vol. 116. 2007. pp. 1349-55.
11. Dy Chua, J, Abdul-Karim, A, Mawhorter, S. "The role of swab and tissue culture in the diagnosis of implantable cardiac device infection". Pacing Clin Electrophysiol. vol. 28. 2005. pp. 1276-81.
12. Uslan, DZ, Dowsley, TF, Sohail, MR. "Cardiovascular implantable electronic device infection in patients with Staphylococcus aureus bacteraemia". Pacing Clin Electrophysiol. vol. 33. 2009. pp. 407-13.

13. de Oliveira, JC, Martinelli, M, Nishioka, SA. "Efficacy of antibiotic prophylaxis before the implantation of pacemakers and cardioverter-defibrillators: results of a large, prospective, randomized, double-blinded, placebo-controlled trial". Circ Arrhythm Electrophysiol. vol. 2. 2009. pp. 29-34.
14. Sohail, MR, Eby, EL, Ryan, MP, Gunnarsson, C, Wright, LA, GREENSPON, AJ. "Incidence, Treatment Intensity, and Incremental Annual Expenditures for Patients Experiencing a Cardiac Implantable Electronic Device Infection: Evidence From a Large US Payer Database 1-Year Post Implantation". Circulation: Arrhythmia and Electrophysiology. vol. 9. 2016. pp. e003929
15. Sohail, MR, Baddour, LM. "Role of PET Imaging in Management of Implantable Electronic Device Infection*". JACC Cardiovasc Imaging. vol. 9. 2016. pp. 291-293.
16. Sohail, MR, Palraj, BR, Khalid, S. "Predicting risk of endovascular device infection in patients with Staphylococcus aureus bacteraemia (PREDICT-SAB)". Circulation: Arrhythmia and Electrophysiology. vol. 8. 2015. pp. 137-144.