Indian Journal of Microbiology Research 2023;10(3):129–133

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Indian Journal of Microbiology Research

Journal homepage: https://www.ijmronline.org/

Review Article

Cardiac implantable electronic device infection: Microbiology and antibiotic prophylaxis

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ARTICLE INFO

Article history:
Received 07-07-2023
Accepted 23-08-2023
Available online 10-10-2023

Keywords:
Staphylococcus species
Blood culture
Pocket infection

ABSTRACT

Cardiovascular implantable electronic devices (CIED) improve quality of life of patients with cardiac arrhythmias and also improves chances of survival. CIEDs, however it may cause complications. To avoid these complications surgical prophylaxis in CIED insertion is required to avoid infection. Due to the rise in antimicrobial resistance the use of antimicrobial agents should be rational and under control. To prevent resistance of antibiotics their use and duration of therapy should be monitored. The high-end and restricted antibiotics should be used only if organisms grow in cultures or if suggested by infectious disease specialists. This review focuses on empirical antibiotics used as prophylaxis. The purpose of this document is to outline the antimicrobial options which can be used as an empirical prophylactic agent in CIED infections.

1. Introduction

Permanent pacemakers (PPMs), implantable cardioverter defibrillators (ICDs), and cardiac resynchronizing therapy (CRT) devices are examples of cardiovascular implantable electronic devices (CIEDs). Compared to low-income nations, high-income nations have a higher rate of CIED implantation. The implantable cardioverter-defibrillator (ICD) implantation rate in India is approximately 0.3 per 100,000 people, while the permanent pacemaker (PPM) implantation rate in India is approximately 3.3 per 100,000 people.[1] Septicaemia, pocket abscess, and skin erosion of the pulse generator or electrode can all result from CIED or PPM insertion. Nearly 40,000 CIED are implanted annually in India.[2] A survey by Indian Society of Electro cardiology and the Indian Heart Rhythm Society found Pacemaker for bradyarrhythmia was the most common (80%) of the devices implanted.[3]

After implanting a permanent pacemaker, infection-related complications that necessitate a second operation are less likely to occur if antibiotic prophylaxis is taken. *S aureus*, *E coli*, *E faecalis*, and *S epidermidis* are among the organisms that are ineffective.[4] Prevalence of these organisms can differ by countries. Diabetes, chronic renal failure, chronic obstructive pulmonary disease, renal procedures, and immunosuppressive therapy are all potential risk factors for CIED infections.[5]

2. Risk Factors of CIED Infection

1. **Patient factors:** Comorbidities (renal failure, heart failure, diabetes), fever within 24 hours before the implantation, anticoagulation, and steroid use.
2. **Device-related risk factors**: Use of more than two pacing leads and the need for early pocket re-exploration can cause central venous thrombosis.
3. **Procedure-related factors:** Procedure time, temporary pacemaker use prior to implantation, early re-intervention and postoperative haematoma at

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https://doi.org/10.18231/j.ijmr.2023.023
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the device pocket site.[6]

Table 1: Microbiology in CIED infections

S.No	Study type	Most	Least
1.	Prospective[7] Didier Klug (1997)	*S. aureus, S. epidermidis, Pseudomonas aeruginosa*	
2.	Cohort[8] Daniel Z. Uslan et al (2007)	*S aureus, Ecoli, Klebsiella, Enterococcus, CoNS, Strep pneumoniae*	*Pseudomonas*
3.	Prospective[9] Antoine Da Costa (1998)	*Staphylococcus, epidermidis, hominis, haemolyticus, Enterobacter aerogenes, Serratia marcescens*	*Enterobacter aerogenes, Serratia marcescens*
4.	Prospective[10] Eugene Y Fu. (1999)	*S. aureus, S. epidermidis*	
5.	Prospective[11] Jimmy Dy Chua 2000	CoNS, *S. aureus*	
6.	Cohort study[12] (2016) Ayman A. Hussein	MRSA (33.8%), CoNS (37.6%)	*Enterococci, staphylococci, anaerobes, fungi, mycobacteria*
7.	2013[13]	*Staph. Aureus* (66%), gram positive cocci (14%)	*E coli* (3%)
8.	Abdulla Fakhro, 2016[14]	CoNS(42%), MSSA (25%)	MRSA (4%), Fungal (2%)

* CIED - Cardiovascular implantable electronic device infections

2.1. Diagnostic workup for suspected CIED infection

2.1.1. Pre-operative

1. It is necessary to obtain a complete blood count, procalcitonin levels, C reactive protein, and erythrocyte sedimentation rate (ESR).
2. Sets of blood samples before initiating empirical antibiotic therapy.
   (a) Blood cultures for aerobic, anaerobic and candida species should be sent.
   (b) One Bactec plus one aerobic/F bottle and one Bactec lytic/10 anaerobic/F bottle of blood should be taken and incubated for five days on an automated Bactec FX instrument.
   (c) Blood cultures of fungal and mycobacterial organisms in culture-negative CIED infections; with immunocompromised hosts and central venous catheters.
3. Transoesophageal echocardiogram (TEE) should be performed in patients with positive blood cultures or who have systemic symptoms but negative blood cultures as a result of previous antibiotic therapy.

2.2. Intra-operative

1. Swab samples from the device for gram stain, and bacterial culture sensitivity.
   (a) If suspected, consider fungal and mycobacterial cultures and acid-fast bacillus (AFB) smears.
2. Generator pocket tissue samples for culture and susceptibility testing.
3. Device sonication.
   (a) Place the extracted device into a sterile jar/container with 50 to 100 ml of sterile saline and seal before submitting to the microbiology laboratory.[15]

3. Pathogenesis of Infection

During implantation or subsequent manipulation, lead and/or pulse generator contamination can result in cardiac implantable electronic device infections.[9] The host, microorganism, or device can all play a role in the infection of the cardiac implantable electronic device (CIED). The air in the operating room, the patient's own skin flora, the materials used to make the surfaces of CIED polymers—silicone and polyvinylchloride adhere better than polytetrafluoroethylene, whereas polyurethane does not adhere as well as polyethylene does. In metals steel shows more bacterial adherence than titanium.[19] The organisms isolated mostly were Gram-positive bacteria (70–90%), especially Coagulase Negative Staphylococci (37.6% of the isolates) and *Staphylococcus aureus* (30.8%), gram negative rods, *Enterobacteriaceae* and *fungi* were rare. This may differ from hospital to hospital or country to country. Studies of CIED infections have shown 33.8% Methicillin Resistant *S aureus*, 37.6% coagulase negative staphylococci. In Italy, 92.5 percent of isolates were gram positives, while coagulase-negative staphylococci (CoNS) were found in 69% of cases and *S. aureus* in 13.8%. Lead or lead material cultures, blood cultures, pocket tissue cultures, and pocket swab cultures can all be used to identify the source of infection.[12] Systemic infection related to endocarditis on pacemaker leads studied where the duration

Table 2: Antimicrobial prophylaxis used in different studies (2010-2023)

S.No.	Study	Antimicrobial prophylaxis	Time/Duration
1.	Cohort (2019) [16]	Cephalosporin - cefazolin, cefuroxime Alternatives: vancomycin (also for MRSA), clindamycin	1 hr prior 2 hrs prior
2.	Review [17] (2022) Post - OP Early management	Cephalexin TMP/SMX, Clindamycin	7-10 days
3.	Review [18]	Vancomycin / Daptomycin	Duration varies according to infection
4.	Update from AHA (2020) [19]	Cefazolin (1-2 gm), vancomycin (15mg/kg), Flucloxacillin (1-2gm) 1st line Vancomycin 2nd line Daptomycin or Linezolid	Cefazolin (1 hr prior), vancomycin (2 hrs prior) Should be tailored according to sensitivity reports.
5.	Sohail MR et al, (2022) [20]	Cefazolin 1gm, vancomycin	Cephazolin 1hr prior
6.	Cohort study, Kabulski GM et al (2019) [21]	Cephalexin (44.3%), doxycycline (10.9%), Clindamycin (8.1%), trimethoprim/ sulfamethoxazole (4.5%)	Post OP- Vancomycin for 14 days (prior MRSA) infection) Cephalexin for 14 days (with existing ICD)
7.	Michael Koutentakis et al. (2014) [22]	Vancomycin, teicoplanin, ciprofloxacin	40-57 days post operative
8.	2011 [23]	Cephazolin (1st generation cephalosporin)/ Vancomycin (if oxacillin resistant staphylococci) Linezolid/daptomycin (if allergic to all above)	Cephazolin (1hr prior) Vancomycin (90-120min prior) **Duration after CIED removal:** 1. 10-14 days pocket site infection 2. 14 days blood stream infection 3. 4-6 weeks complicated infections
9.	2011 review [24]	Cloxacillin / cephalexin 1. Suspected endocarditis with >2 cm vegetation	7-14 days according to blood culture reports. 1. 24-72 hrs post extraction of device, 7-14 days for re-implantation depending upon bacteraemia.
10.	Post operative management (2017) [25]	1. Cefazolin 2. Vancomycin (If not tolerating above antibiotics) 3. Levofloxacin	1. 2gm IV over 5 mins of incision repeated intraoperatively after 3 hrs. 2.1gm IV over 60 min, repeated at every 6 hrs if procedure is ongoing. 3.500 mg every 24 hrs for 2 doses.
12.	Retrospective cohort study [26]	Vancomycin (83.1%), daptomycin (12.0%), linezolid (2.4%), cephalosporins (1.7%), rifampin (35.6%), gentamicin (14.0%)	

of antibiotic therapy before lead ablation was 9.7±6.1 days in patients with a positive lead culture versus 15.3±6.2 days in patients with a negative lead culture. [7]

4. Clinical Diagnosis

There are four types of CIED infection: Patients with

1. Local inflammatory changes at the generator pocket site, such as erythema, swelling, pain, discomfort, drainage, or erosion of the generator and/or leads through the skin.
2. Fever and no local changes at the generator pocket site.
3. Bacteraemia and no local changes at the generator pocket site.
4. Lead thrombus or vegetation on echocardiography. [15]

5. Discussion

Antibiotic prophylaxis can reduce the risk of complications which require repeat operation. [4] Before insertion of CIED it should be ensured that patients do not have signs of infection. CIED infections are differentiated as Pocket Hematoma, Post-implantation inflammation, Superficial infection of surgical wound and uncomplicated pocket infection. [27] The use of antibiotics for surgical prophylaxis has varied from cefazolin to higher end or restricted antibiotics. Vancomycin is an alternative for patients who are allergic to cephalosporins of the first generation. Additionally, daptomycin or linezolid are alternatives if

patient is allergic to both vancomycin and first-generation cephalosporin.[28] Antibiotics taken post-operatively do not significantly differ from pre-operative antibiotics. One case with a history of MRSA received vancomycin for 14 days and another one with existing ICD received 14 days of cephalexin prophylaxis. Another patient with prior methicillin-resistant *S. aureus* bacteraemia as a result of infected haemodialysis fistula, received 14 days of vancomycin for initial placement of a single-chamber pacemaker prophylaxis.[21] If superficial infection is suspected, oral empirical antibiotics can be started for 14 days after collection of blood samples. The pocket infection should be differentiated clinically from soft tissue infection, hematoma and allergic reactions to dressings, tapes or disinfectants. Monotherapy with cephalexin, clindamycin, trimethoprim-sulfamethoxazole, doxycycline, linezolid or cephalexin in combination with doxycycline or trimethoprim-sulfamethoxazole are suggested options. The use of Linezolid is restricted to infectious disease specialists.[18] The treatment should cover *Staphylococcus aureus* as it is most common in CIED infections. Due to the lack of current data on MRSA prevalence and use, treatment decisions should be based on the institution's or patients' risk.[19] The duration of antimicrobial therapy varies from 6 weeks in valve vegetation or septic phlebitis and osteomyelitis to 2 weeks in CIED erosion through skin without obvious purulence.[18] Yeast infections are rare. But candida species are most frequent including *C. parapsilosis* and *C. albicans*. In these cases, empirical amphotericin B, either with or without 5-flucytosine, or an echinocandin, can be used as the first line of treatment. It can be then deescalated to fluconazole 400–800 mg daily according to sensitivity of microorganisms or negative cultures.[29] Complete device removal is the only effective measure for the eradication of CIED infections. Michael Koutentakis et al. the study has treated 6 CIED infections caused by staph species; the postoperative course of antibiotics was 40-57 days.[22]

6. Conclusion

Antibiotic prophylaxis has reduced the infections associated with CIED. In the complicated infections extraction of CIED system remains the option. Though staphylococcus species are leading cause in infections, empiric antimicrobial coverage should be decided based on clinical findings, epidemiologic factors and results of blood cultures and sensitivity. After collection of blood cultures, antibiotics should be tailored according to sensitivity reports. 1st generation cephalosporins are usually recommended as empiric surgical prophylactic. As the antimicrobial resistance is at rise; the use of Vancomycin and Linezolid should be restricted to infectious disease specialists.

7. Source of Funding

None.

8. Conflict of Interest

None.

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Cite this article: Paralkar SS, Godbole D, Mundhe S. Cardiac implantable electronic device infection: Microbiology and antibiotic prophylaxis. *Indian J Microbiol Res* 2023;10(3):129-133.