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Antibiotic Prophylaxis and Treatment in Early Cardiac Implantable Electronic Devices Infection

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ABSTRACT

Background: Cardiac implantable electronic devices – PM, ICD, and CRTs- are well-proven life-sustaining and the ultimate destination for many heart conditions. Based on scientific evidence, there is a worldwide incremental increase in CIED implantations numbers. **Objective**: Early infection of cardiac implantable electronic devices (CIED)– pacemaker (PM), implantable cardioverter-defibrillator (ICD), and cardiac resynchronization therapy (CRT)– is a growing health challenge. We examined the effectiveness of antibiotic prophylaxis and treatment of early infection of CIED in a single center. **Methods:** This is a retrospective, single-center observational study. Data were collected from patients' records from July 2017-July, 2019. All Patients received intravenous ceftriaxone 2gm before incision, Gentamicin 120mg pocket irrigation, and oral Amoxicillin/Clavulanate for 5 days post-implantation. **Results:** A 639 consecutive CIED implantations – PM (n=474, mean age, 64yr, female=49%), ICD (n=106, mean age 56yr, female=17%) and CRT (n=59, mean age, 54yr, female=20%)- were performed over 3years. The incidence of early infection was 1.9% (12 cases), female=41%. PM=5/474, ICD=5/106, and CRT=2/59. Three out of the 12 patients had total device explant due to pocket abscess; one PM had a generator changed; one ICD who had a pneumothorax, and the third one had reimplantation after ICD lead perforation. Nine cases were managed conservatively using saline dressing and oral Amoxicillin/Clavulanate, 3/9 patients developed a hematoma, 4/9 patients developed purulent suture line infection. None of them had infection recurrence on three months follow up. **Conclusion:** Early infection of CIED is a rare complication with multiple predisposing factors. Our protocol is reassurance and prompt initiation of management protocol to prevent and treat this issue's sequences.

Keywords: Cardiovascular Infections, Surgical Wound Infection, Cardiac implantable electronic devices, Cardiac resynchronization therapy, Implantable cardioverter defibrillator, Pacemaker.

1. BACKGROUND

Cardiac implantable electronic devices (CIED) - PM, ICD, and CRTs- are well-proven life-sustaining and the ultimate destination for many heart conditions. Based on scientific evidence, there is a worldwide incremental increase in CIED implantations numbers (1-5). Unfortunately, related complications are amplified. Infection is one of these complications, which negatively impacts patient health, budget, and expectations (4-6).

Infection occurred early (0-28 days), late (29–364 days), and delayed (at least one year after device implantation) (1, 2), and it has been emphasized that the risk of CIED infection was 25%, 33%, and 42% respectively (1, 2). Recently, data confirmed that 45% of patients presented after one year following their last CIED-related procedure (3). Early and late infections might be due to contamination during implantation, while the delayed infection is mostly due to a bloodstream infection.

Clinical practice and management strategies for preventing and treating the CIED infection demonstrated a great worldwide disparity (4) with the lack of consensus regarding the effective antibiotic regimen in preventing and treating CIED infection.

2. OBJECTIVE

We aimed in this study to examine the effectiveness of antibiotic prophylaxis and treatment protocols of EI of CIED in our Department of Cardiology at Queen Alia Heart Institute.

3. METHODS

A retrospective, single-center observational study. Data collected from consecutive CIED patients' records implanted between July 2017-July 2019 at Queen Alia Heart Institute. A total of 639 patients were included in this study. Patients' medical records were reviewed for their age, gender, comorbidities, diagnosis, clinical history and physical examination findings, type and time of device implantation, procedure-related complications, medical treatment received, type of intervention if present, and the outcome of the final management plan. Diagnosis is made based on clinical, laboratory data, ultrasonic, and blood culture findings.

The implantation procedure was carried out with preoperative skin preparation by povidone-iodine, intraprocedural sterile techniques, and pocket hematoma prevention by tight packing dressing. All patients received 2 grams of intravenous ceftriaxone just before skin incision, pocket irrigation with 120 mg of Gentamicin before wound closure, and dismissal medications including oral amoxicillin 500 mg /clavulanate potassium 125 mg twice daily for 5 days, except for penicillin-allergic patients who received alternatively 1 gram of intravenous vancomycin just before skin incision, Gentamicin pocket irrigation and dismissed on oral Lincomycin Capsule 500 mg twice daily for 5 days. Serial blood cultures were taken from all patients who presented with fever, local pocket symptoms, and signs. Pocket ultrasound was performed for all patients with purulent discharge or new pocket deformities. Infected CIED Patients who presented more than four weeks after implantation were excluded from this study.

4. RESULTS

A 639 consecutive CIED implantations – PM (n=474, mean age =64yr, female=49%), ICD (n=106, mean age =56yr, female=17%) and CRT (n=59, mean age =54yr, female=20%)- were performed over 3yrs (Table 1). EI incidence was 1.9% (12 cases), out of these: PM=5/474, ICD=5/106, and CRT=2/59 (Figure 1). About 60% of our infection group were males, and 60% were below 40. The median period of the presentation was 5 days post device emplacement. Out of 50% of infections were following the first implantation, while 25% were following reimplantation, and the remainder 25% were after the generator changed. All had negative blood cultures. No penicillin allergy was reported.

Out of these, 3/12 patients had total device explants due to pocket abscess (Table 2); one PM had a generator changed; the second was ICD, who had a pneumothorax. And the third had reimplantation after ICD lead perforation.

Other cases (n=9) were managed conservatively, in whom saline dressing and oral amoxicillin 500 mg / clavulanate potassium 125 mg twice daily for 10 days (Table 3). 2/9 had superficial skin Infection. 3/9 developed hematoma, 2/3 were anticoagulated. 4/9 developed purulent suture line infection. First, with ICD, became afebrile 48hr before the implant. Second, female with ICD who underwent second redo implantation because of recurrent Twiddler's syndrome. Third, PM reimplantation in renal impaired patients, and fourth had prolonged CRT implantation. None of them had infection recurrence on three months follow up.

A 639 consecutive CIED[a] implementations over three years			
	PM[b]	ICD[c]	CRT[d]
Number	474	106	59
Mean age in years	64	56	54
Female ratio	49%	17%	20%

a. CIED= cardiac implantable electronic devices
b. PM= Pacemaker
c. ICD= Implantable cardioverter-defibrillator
d. CRT= Cardiac resynchronization therapy

Table 1: A 639 consecutive CIED implementations.

3/12 patients had total device explants due to pocket abscess	
1. PM[a]	had a generator changed
2. ICD[b]	had a pneumothorax
3. ICD[b]	had reimplantation after ICD[b] lead perforation

a. PM= Pacemaker
b. ICD= Implantable cardioverter-defibrillator

Table 2: 3/12 patients had total device explants.

9/12 Patients had saline dressing and oral amoxicillin 500 mg / clavulanate potassium 125 mg twice daily for 10 days.			
Superficial skin Infection		2 out of 9	
Hematoma	Anticoagulation	3 out 9	2 out of 3
Purulent suture line infection		4 out of 9	
Total cases		9	

Table 3: saline dressing and oral amoxicillin 500 mg / clavulanate potassium 125 mg twice daily for 10 days.. CRT= Cardiac resynchronization therapy, ICD= Implantable cardioverter-defibrillator, PM= Pacemaker

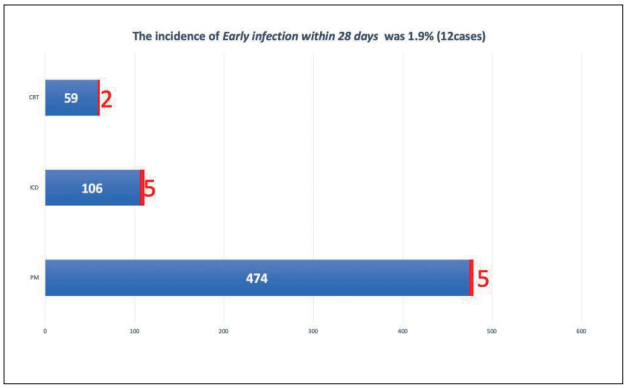

Figure 1. The incidence of early infection within 28 days

5. DISCUSSION

The recent large Danish cohort data demonstrated that the combined incidence of infection during the de-

vice lifetime was 1.19% for PM, 1.91% for ICD, 2.18% for CRT-P, and 3.35% for CRT-D, and the incidence of early infection ranged from 0.16% to 0.30% at 30 days (5). As compared with this European data (5), our analysis showed a higher total combined incidence of early infection = 1.9%, with an incidence of 4.7%, 3.4%, and 1% for ICDs, CRTs, and pacemakers, respectively. But it is still lower than the incidence of the early infection in the middle east country like Lebanon, in which 9.1% suffered from infection 0 to 28 days after implantation (6).

Young age and male sex were independent patient-related risk factors associated with higher device-related infection risk (5). About 60% of our infection group were male gender, and 60% below 40 years.

Any microorganism can cause CIED infection. However, the most common pathogens are coagulase-negative staphylococci (68%) and Staphylococcus aureus (23%) (2). The majority of cellulitis cases are non-yielding culture results, and therefore the micro-organisms are unknown (7). Our data did not demonstrate any positive blood or pocket cultures, and it may be due to prior antibiotics prescriptions.

Optimal preprocedural decolonization of the site of implantation is the mainstay in the prevention of CIED infections. The application of chlorhexidine–alcohol reduced the risk of surgical-site infection by 41% compared with using aqueous povidone-iodine (8). In one study, the type of antiseptic solution used for skin preparation also had a clear effect on the device infection rate; 5.8% of patients receiving topical antisepsis with povidone-iodine had device infection, compared to 1.5% of those receiving antisepsis with chlorhexidine-alcohol (P=0.0001) (9). These findings necessitate the need for reevaluation and changing our preoperative skin preparation by the povidone-iodine solution.

De novo implantations had a lower risk of infection in all device types. At the same time, any reoperation was associated with a significantly increased risk of Device related infection, independent of the type of device and the type of reoperation (5, 10). However, our findings showed that 50% of CIED infection occurs in de novo implantation, 50% after pocket reopening procedures (25% after reimplantation, and 25% post generator replacement). Concomitant procedure-related complications, complexity, and duration of the procedure (5, 11) increased CIED early infection risks. One case of pneumothorax was subacute ICD right ventricular lead perforation, and hemothorax, a case CRT who had prolonged LV lead implantation procedure that was more than 4 hours due to anatomical barrier, and three cases of hematomas (12).

In a previously published meta-analysis, certain comorbidities like chronic heart failure, chronic renal disease (13), chronic obstructive pulmonary disease, corticosteroid use, anticoagulation, pre-procedural fever (14) and diabetes mellitus, skin disorders, history of the previous device infection, preoperative temporary pacemaker (14), are high-risk predictors for CIED infection (11).

In our study, all five pacemaker patients had temporary pacemakers before the implant; two out of three hematoma patients were on oral anticoagulation and aspirin. Four patients had chronic kidney disease, and six patients had diabetes and heart failure. Only one patient just afebrile 48 hours before implantation. Of note, 6 patients had a BMI of more than 30, but also, we had two patients underweight with a BMI of less than 20 (15).

The strategies of antibiotic prophylaxis differ between clinicians. Some use pre-operative intravenous antibiotics, pocket irrigation with antibiotics, Antibacterial envelop, and post-operative intravenous, oral, or topical antibiotics.

An early meta-analysis demonstrated that systemic antibiotic prophylaxis significantly reduces the incidence of serious infective complications after permanent pacemaker implantation (16). Clinical practice guidelines for antimicrobial prophylaxis in surgical cardiac device insertion procedures recommends a single dose of cefazolin or cefuroxime before device implantation or generator replacement in a PM, ICD, or CRTs. However, prophylaxis with vancomycin is warranted for patients known to be colonized with MRSA and/or patients at high risk for MRSA infection (17).

In the Heart Rhythm Society Survey conducted by Basil and colleagues (18), pre-incision prophylaxis for new and replacement pacemakers and ICD was nearly universal. Pocket irrigation with the antibiotic solution (most commonly gentamicin, vancomycin, or both) was common (53% to 62%). In contrast, an antibiotic-impregnated pouch was more frequent for replacement procedures (16% vs. 6% for new implants). The use of additional post-procedure intravenous (25% to 50%) or oral (22% to 36%) antibiotics after the wound's closure. Concomitant procedure-related complications, complexity, and duration of the procedure (5, 11) increased CIED early infection risks. One case of pneumothorax was subacute ICD right ventricular lead perforation, and hemothorax, a case CRT who had prolonged LV lead implantation procedure that was more than 4 hours anatomical barrier, and three cases of hematomas (12).

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As a tradition in our center, all our study patients received pre-incisional 2 grams of ceftriaxone, a third-generation cephalosporin. It is a broad-spectrum bactericidal antibiotic that creates a defect in cell walls that lead to cellular death. Has a long half-life (6.4 hours) and high penetrability, administered once or twice daily. It can be used for infective endocarditis prophylaxis and pre-incisional prophylaxis (19).

Even though the current guidelines did not recommend pocket irrigation with antibiotics to reduce pocket infection, one of the international surveys suggested that pocket irrigation with antibiotics during implantation is widely used in current practice (54% believe in the effectiveness of antibiotic pocket irrigation to reduce CIED infection; 33% are uncertain, and few consider this strategy ineffective 13% or offered no opinion) (20). A recent meta-analysis demonstrated a significantly protective effect on preventing PM infection with antimicrobial pocket irrigation, regardless of antimicrobial class (21). Our protocol includes pocket irrigation with 120 mg of gentamycin before wound closure.

A new development in the prevention of CIED infection is the TYRX absorbable multifilament wrapper covered with rifampin and minocycline (22). WRAP-IT trial addressed that The TYRX envelope significantly lowered major CIED infections by 40% and major pocket infections by 61% (23). Anyhow, despite promising results of WRAP-IT, none of our patients received a TYRX envelope. Post implantation, we used to maintain oral amoxicillin 500 mg /clavulanate potassium 125 mg twice daily for 5 days. This is not uncommon practice based on the Heart Rhythm Society Survey as they found that 22% to 36% of physicians keep additional post-procedure oral antibiotics after pocket closure (18). On the other hand, PADIT Trial demonstrates that the variation in infection rates was not statistically significant in incremental antibiotics use groups to reduce device infection (24).

Infections of CIED may ensnare either the surgical pocket, the leads, and the endocardium. The pocket involvement either early or late by a superficial skin infection, cellulitis (purulent or non-purulent), or socket abscess. Patients with early infection were more likely to present with localized inflammation, whereas those with late infection were more likely to have pocket erosion or valvular endocarditis (25). All of our patients presented clinically with fever and pocket related symptoms (dolor, calor, rubor, and tumor) and signs (erythema, warmth, tenderness, and induration). Five out of twelve patients presented with non-purulent cellulitis. The other seven patients presented with purulent cellulitis; six patients described local purulent discharge: four cases in form of suture line infection with small superficial abscesses and stitch sinus, and only three patients had a pocket abscess which confirmed by pocket ultrasound, while transesophageal echocardiography did not show lead or valvular vegetations. A superficial wound infection without connection to the pocket should be differentiated from a pocket infection because it does not require CIED system removal (26). A total of nine out of twelve patients have purulent and non-purulent superficial incisional cellulitis, with negative blood culture and TTE findings, these patients were treated conservatively with saline dressing and oral amoxicillin 500 mg /clavulanate potassium 125 mg twice daily for 10 days. None of them showed recurrence of infection after three months of follow up. All patients who developed pocket abscess underwent complete device removal.

6. CONCLUSION

EI of CIED is a rare complication with multiple predisposing factors. The total incidence of EI was 1.9% in this study. Even though our protocol seems reassuring in preventing and treating this issue's sequences, we still need to implement more effective strategies to miniature the CIED infection risks.

- **Patient Consent Form**: All participants were informed about the study's subject, and the ethical and research committee of royal medical services approved conducting and publishing the data.
- **Author's Contribution**: all authors gave substantial contributions to the conception and design of the work in acquisition, data analysis, preparing for drafting and revising it, and they gave final approval of the version to be published and agreed to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.
- **Conflicts of interest**: There are no conflicts of interest.
- **Financial support and sponsorship**: Nil.

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