EP & Arrythmia

How Long Should Prophylactic Antibiotics be Prescribed for Permanent Pacemaker Implantations? One Day versus Three Days

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Background: The implantation of a pacemaker is frequently a life-saving procedure. However, the process of implantation may carry an uncommon but potentially life-threatening infective complication. The prescription of prophylactic antibiotics is an effective way to reduce the risk of infection. The aim of the present study was to investigate the efficacy of 2 prophylactic antibiotic schemes and the possible risk factors associated with device-related infections.

Methods: A total of 194 consecutive patients who received permanent pacemaker (PPM) implantations were enrolled in this study. Prophylactic antibiotics were prescribed for every patient with a duration of either 1 day or 3 days. The follow-up period was 3 months, and any event of device-related infection was recorded.

Results: Out of the total 194 patients, there were 5 patients who experienced infective complications after PPM implantation (1 patient in the 1-day group and 4 patients in the 3-day group). The rate of infective complications showed no significant difference between the 2 kinds of antibiotic regimens (1.7% vs. 2.9%, $p > 0.99$). In the multivariate analysis, only the presence of pocket hematoma was an independent risk factor for infective complications (odds ratio = 3.14, $p = 0.018$).

Conclusions: Our study showed that the efficacies for prevention of PPM-related infections were similar between the 1-day and 3-day regimens of prophylactic antibiotics. Pocket hematoma was an independent risk factor of infective complications, and a longer duration of antibiotic treatment may be considered for these patients. Otherwise, a 1-day course of antibiotic prophylaxis may be effective enough to prevent device-related infections, and may further reduce the lengths of hospitalizations.

Key Words: Complication • Infection • Permanent pacemaker implantation • Prophylatic antibiotics

INTRODUCTION

More and more intracardiac devices have been developed, such as the permanent pacemaker (PPM), implantable cardioverter-defibrillators (ICDs), and cardiac resynchronization therapy (CRT), to extend patient lifespan and quality of life. In addition to maintaining sufficient heart rhythms, the indications for device implantations have broadened to include prevention of fetal arrhythmias and treatment of advanced heart failure.[1-3] However, the implantation procedures may cause uncommon but potentially life-threatening infec-

Received: August 16, 2012 Accepted: October 23, 2012

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tive complications, with an incidence rate ranging from 0.5% to 5.2%.[4-6]

The complications of device implantations occurred more frequently in repeated procedures and generator replacements than in first implants, and when procedures were performed by inexperienced medical personnel. Although there has been some debate as to whether prophylactic antibiotics should be routinely used for device implantations,[7] its usefulness in reducing infective complications has been proven by subsequent trials and has now become standard practice.[8] A recent meta-analysis also suggested that systemic antibiotic prophylaxis significantly reduced the incidence of potentially serious infective complications after PPM implantation, and supported the use of prophylactic antibiotics at the time of PPM insertion to prevent short-term pocket infection, skin erosion or septicemia.[9]

Recently, Bertaglia et al. investigated the safety and efficacy of antibiotic prophylaxis with a single-dose cefazolin for PPM implantations, and demonstrated that the complication rate was only 0.7%.[10] However, this study did not enroll a comparison group to receive prophylactic antibiotics for different durations. Therefore, the proper duration of prophylactic antibiotics remains undetermined. Thus, the aims of the present study were: (1) to evaluate the efficacy of different durations of prophylactic antibiotics (single dosage versus 3 day dosage) for PPM implantations, and (2) to disclose possible factors which may help us to determine the individualized strategy for optimum use of prophylactic antibiotics.

METHODS

Study population and study design

We prospectively enrolled consecutive patients who received implantations of PPMs with a single- or dual-chamber system at Taipei Veterans General Hospital in Taiwan from June 2008 to October 2009. These patients received prophylactic antibiotics based on one of the following protocols: a 1-day regimen of first generation Cephalosporin with 1 gram intravenous infusion before and after implantation (group 1); or a 3-day regimen of first generation Cephalosporin with 1 gram intravenous infusion before implantation and then 1 gram intravenous infusion every eight hours for a total of 3 days after implantation (group 2). No oral antibiotics were prescribed after finishing the 1-day or 3-day intravenous antibiotics. The strategy was determined by patient choice. The 1st dosage of antibiotics was administered within one hour before implantation for both groups. The data about patients' demographics, physical characteristics, baseline biochemistry, device-related factors (including types and modes of generator, timing and number of manipulations, characteristics of procedures), indication for PPMs, post-operative wound condition, and infective complications were carefully collected. Patients who had a past history of autoimmune diseases or were lost to follow-up after implantations were excluded from the study. Additionally, patients who had received any antibiotics within 30 days prior to the procedures, or received antibiotic treatment unrelated to the device implantations during the follow-up period were also excluded. The occurrence rates of device-related infective complications were compared between group 1 and group 2.

Implantation technique

Four cardiologists who each had a minimum of 3 years experience with device implantation performed all of the procedures. Before the implantation, skin was prepared by beta-iodine and alcohol solutions for sterilization of insertion-site. Prior to incision, local anesthesia was administered. New leads were inserted transvenously through the cephalic vein or through the subclavian vein. Generators were positioned subcutaneously on top of the fascia of the pectoral muscle. During pulse generator replacement or upgrading, the fibrotic capsule of the old pocket was excised before the new generator was positioned. After completing the procedures, sand bag compression was applied to avoid formation of hematoma.

Follow-up

Patients were followed-up regularly in the outpatient pacemaker clinic 2 weeks after operation, and every 1 to 3 months thereafter for any symptom or sign of device-related infection. Furthermore, patients were instructed to visit the clinic if they encountered any problem about the wounds or devices. The follow-up duration was 3 months.

The occurrences of infective complications were defined according to guidelines used in the study by Bertaglia et al.[10] The major infective complications were comprised of septicemia, endocarditis, pocket abscess, and erosions. Minor infective complications included inflammatory signs around the pocket (cellulitis, pain, erythema, and edema) and fever defined as a skin temperature of > 38.0 °C for > 2 consecutive days.

The presence of hematoma was defined as swelling of the pocket site without obvious signs of infection during the hospitalization for the implants. No additional antibiotics were prescribed for the presence of hematoma without coexisting infections.

Statistical analysis

Differences between continuous values were assessed using an unpaired 2-tailed *t* test for normally distributed continuous variables, the Mann-Whitney test for skewed variables, and the chi-square test for nominal variables. A logistic regression analysis was used to identify the factors associated with infective complications. Variables with p values < 0.2 in the univariate analysis were analyzed in the multivariable regression analysis. All statistical significances were set at $p < 0.05$, and all statistical analyses were carried out by SPSS 17.0 (SPSS Inc. Chicago, IL, USA).

RESULTS

Patient population and characteristics

A total of 212 patients were studied initially, and 18 of them were excluded (9 patients were lost to follow-up after implantations, 5 patients received antibiotics within 30 days prior to the procedures, and 4 patients received antibiotic treatment for non-device related infections during the follow-up period**)**. Ultimately, there was a total of 194 patients enrolled in the present study. The mean age of the study population was 77.0 ± 10.3 years old (range, 33-93 years), and 63% of patients were male. Among these 194 participants, 96 (49.5%) patients received generator replacement, 82 patients (42.3%) received new implantations of dual-chamber PPMs, and 8 patients (4.2%) first had temporary pacemakers (TPM) implanted due to symptomatic bradycardia, which was followed by a second surgery for new PPM implantation.

Study participants were divided into two groups, such that 58 patients would receive a one-day regimen (group I) and 136 patients would receive a 3-day regimen (group II). The baseline characteristics of study patients are summarized in Table 1. There were no significant differences of baseline characteristic between group 1 and 2 (p all > 0.05, Table 1). In the subgroup of

Table 1. Baseline characteristics in both prophylactic treatment groups

	Group 1 (n = 58)	Group 2 (n = 136)	p value
Age (years)	76 ± 10	77 ± 11	0.22
Female gender, n (%)	21 (36%)	51 (38%)	0.86
Underlying diseases			
Diabetes, n (%)	7 (12%)	29 (21%)	0.13
Hypertension, n (%)	40 (69%)	98 (72%)	0.66
CHF, n (%)	16 (28%)	20 (15%)	0.04
CAD, n (%)	21 (36%)	32 (24%)	0.07
VHD, n (%)	13 (22%)	23 (17%)	0.37
Use of warfarin, n (%)	4 (7%)	11 (8%)	> 0.99
Insertion of TPM, n (%)	2 (4%)	6 (4%)	> 0.99
WBC (CUMM)	6109 ± 1524	6361 ± 1670	0.27
Serum creatinine (mg/dl)	1.35 ± 0.87	1.29 ± 1.07	0.25
Fasting glucose (mg/dl)	100 ± 28	101 ± 27	0.60
Implantation procedures			
Generator replacement, n (%)	33 (57%)	63 (46%)	0.33
Dual-chamber system, n (%)	25 (43%)	57 (42%)	0.88
Duration of procedure (min)	47 ± 20	48 ± 23	0.97
Pocket hematoma, n (%)	1 (1.8%)	2 (1.5%)	> 0.99
Infection rate, n (%)	1 (1.7%)	4 (2.9%)	> 0.99

CAD, coronary artery disease; CHF, congestive heart failure; TPM, temporary pacemaker; VHD, valvular heart disease; WBC, white blood count.

patients with new implants (82 patients), the implant rate of the dual-chamber system exhibited no significant differences between the two groups [group I: 12 patients (48%) vs. group II: 28 (42%), p = 0.47]. The indications for implantation, including sick sinus syndrome, atrioventricular block, and atrial fibrillation with slow ventricular rate, were also similar between the 2 groups (p = 0.35) (Figure 1).

Outcome of implants and infective complications

The incidence of pocket hematoma (1 patient, 1.8% vs. 2 patients, 1.5%, in group I and II, respectively, p = 1.00) was similar between the two groups. There were no major infective complications among these patients. During routine follow-up, there were 5 patients who experienced minor infective complications after PPM implantations (1 patient in group 1 and 4 patients in group 2). The complication rates were similar between group 1 and group 2 (1.7% versus 2.9%, p = 1.00). Besides, a subgroup of patients with new implants was also analyzed. There was no significant difference in the rate of infective complications in patients who received the dual-chamber or single-chamber system [1 patient (1%) vs. 4 patients (4.1%), p = 0.40].

Risk factors for infective complications

Several possible factors which may influence the occurrence of infective complication after PPM implantation were analyzed, including the clinical conditions such as hypertension, diabetes, coronary artery disease, valvular heart disease and congestive heart failure, use of warfarin, replacement of generator or new implant, duration of procedure time and pocket hematoma. The characteristics of patients with and without infections were shown in Table 2. All these factors were similar between the patients with or without infection, except for pocket hematoma. Pocket hematoma seemed to be a possible

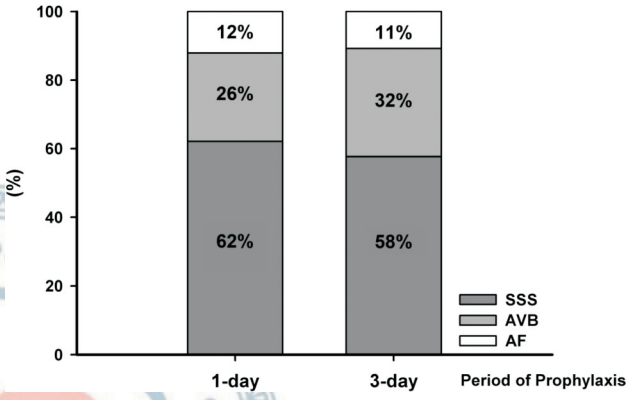

Figure 1. *The bar chart demonstrates the indications for PPM implantation in patients receiving 1-day and 3-day regimens of prophylactic antibiotics. The indications for implantations, including sick sinus syndrome (SSS), atrioventricular block (AVB), and atrial fibrillation (AF) with slow ventricular rate, were similar between 2 groups (p = 0.35). PPM, permanent pacemaker.*

Table 2. Baseline characteristics in patients with and without post-procedural infections

	Infection (n = 5)	No infection (n = 189)	p value
Age	79 ± 7	77 ± 10	0.86
Female gender, n (%)	1 (20)	71 (38)	0.65
Underlying diseases			
Diabetes, n (%)	2 (40)	34 (18)	0.23
Hypertension, n (%)	4 (80)	134 (71)	0.66
CHF, n (%)	2 (40)	34 (18)	0.23
CAD, n (%)	2 (40)	51 (27)	0.62
VHD, n (%)	0 (0)	36 (19)	0.59
Use of warfarin, n (%)	1 (20)	14 (7)	0.33
Insertion of TPM, n (%)	0	8 (4.3)	1.00
WBC (/mm^3)	6778 ± 1017	6272 ± 1641	0.36
Serum creatinine (mg/dl)	1.47 ± 0.70	1.31 ± 1.02	0.24
Fasting glucose (mg/dl)	107 ± 15	101 ± 28	0.25
Implantation procedures			
Generator replacement, n (%)	0	96 (51)	1.00
Dual-chamber system, n (%)	1 (20)	81 (43)	
Duration of procedure (min)	52 ± 26	47 ± 22	0.67
Pocket hematoma, n (%)	1 (20)	2 (1.1)	0.08

CAD, coronary artery disease; CHF, congestive heart failure; Min, minutes; TPM, temporary pacemaker; VHD, valvular heart disease; WBC, white blood cell count.

risk factor for infective complications (p = 0.08). In the multivariate logistic regression analysis, which included the presence of pocket hematoma and different regimens of antibiotics, the presence of hematoma was an independent risk factor for infective complications (odds ratio = 23.12, p = 0.02).

DISCUSSION

Main finding

The main findings of the present study were: (1) that the infective complication rates were similar between patients receiving 1-day and 3-day regimens of prophylactic antibiotics, and (2) post-procedural hematoma may be an important risk factor of infective complications.

Previous studies and clinical applications

Previous studies showed that the infective rate of PPM implantations is low, ranging from 0.5% to 5.2%.[4-6] Previous studies also confirmed the benefits of prophylaxis administration of various durations and types of antibiotics to reduce post-procedural infections,[9,11] though some centers do not routinely give prophylactic antibiotics. Our study aimed to reconfirm the efficacy of the prophylactic treatment that covers the duration of the surgical procedure. Based on the results of the present study which suggested an equal level of efficacy between the 1-day and 3-day regimens of prophylactic antibiotics, patients may receive fewer dosages of antibiotics, a shortened duration of hospital stay, and reduced healthcare costs, especially in the era of Diagnosis Related Groups of the Taiwan National Health Insurance.

The infection rate (2.6%) in our cohort was similar to that of other studies, and the present study represented one of the few reported studies focusing on the infection rate of PPM implantations in Taiwan. Our report has provided useful data which may be beneficial to clinicians when explaining the risk of infection to patients who plan to receive PPM implantations.

In our study, we did not observe any major infective complications. The reason may be attributed to the relatively short follow-up period and small sample size. Further, we excluded patients who had undergone more complicated procedures, such as ICD and CRT implantations. It may be the same reason why there were no difference related to the known risk factors between the groups (with and without infections in our cohort), such as primary implants, replacement of generator, prior TPM placement, dual-chamber system, and duration of procedure. However, in the multivariate analysis, hematoma could be a possible risk factor for infective complications. This finding may underscore the importance of adequate hemostasis during the implantation procedure, and post-operative compressions may be helpful for patients with bleeding tendencies. Furthermore, for patients with pocket hematoma, the prolonged course of antibiotics may be necessary to reduce the possibility of further infections.

Limitations of the study

There were several limitations of the present study. First, patients were not randomly assigned to receive different durations of prophylactic antibiotics. The selection of antibiotic regimen was based solely on patient choice. Second, the number of cases in our study may not be sufficient to distinguish the modest difference in complication rates between the 2 treatment groups. A further large-scale and multi-center trial is necessary to confirm the findings of the present study. Third, other intracardiac devices such as CRT and ICD were not incorporated into our trial. Therefore, the short-term prophylaxis may not be applied to more complicated procedures.

CONCLUSIONS

Our study demonstrated that the efficacies for prevention of PPM-related infections were similar between 1-day and 3-day regimens of prophylactic antibiotics. Pocket hematoma was an independent risk factor of infective complications, and a longer duration of antibiotic treatment may be considered for these patients. Otherwise, a 1-day course of antibiotic prophylaxis may be sufficiently effective to prevent device-related infections, and may further reduce the lengths of hospitalizations.

ACKNOWLEDGEMENTS

The authors would like to thank Ms. Chi for her ex-

pert technical assistance. This study was partially supported by research grants from the VGHUST Joint Research Program. (VGHUST100-G7-6-1)

COMPETING INTEREST STATEMENT

The authors state that they have no conflict of interest.

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