Efficacy of the DDD+ Overdrive Algorithm for the Suppression of Atrial Tachyarrhythmias

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Summary

The prevention of atrial fibrillation has become a major focus of medical research due to the increased risk of morbidity and mortality associated with this disease. Recently, new algorithms have shown their ability to ensure pacing slightly over the intrinsic rhythm in order to maintain atrial pacing more than 95% of the time. To verify the effectiveness of the DDD+ algorithm in the Philos DR pacemaker in the reduction or even elimination of atrial tachyarrhythmia episodes, this prospective, randomized, controlled, single-blind, crossover study included patients with paroxysmal or persistent atrial fibrillation with or without bradycardia. In total, 34 patients were randomized into one of two groups (DDD or DDD+). The first evaluation occurred 1 month after implantation, the second at 6 months, and the third after the crossover at 12 months. Patients were evaluated using a 24-hour Holter, an echo-Doppler cardiogram, and pacemaker telemetry. Compared with DDD pacing, overpacing clearly decreased atrial tachyarrhythmia and improved diastolic ventricular function as well as atrial size, demonstrating the value of its electrical and mechanical remodeling.

Key Words

Atrial fibrillation, overdrive pacing, atrial tachyarrythmias

Introduction

Atrial fibrillation (AF) persists as the most challenging arrhythmia in clinical practice, and it currently affects an estimated 400 million people worldwide. We view AF as the most common sustained supraventricular tachyarrhythmia, for it is associated with extensive morbidity and mortality [1]. According to some studies, AF is responsible for numerous hospitalizations, which result in significant increases in the cost of healthcare [2]. Permanent pacing has been regarded as a safe option in the prevention of atrial tachyarrhythmias (AT), especially AF, and it has been the focus of extensive investigations. Some studies have demonstrated that atrial pacing (AAI or DDD) is clearly associated with a lower incidence of paroxysmal and permanent AF [3-6] when compared with single-chamber ventricular pacing. Recently, new targeted pacing algorithms have been integrated into dual-chamber pacemakers for the prevention or even the elimination of ATs, adding an innovative perspective in the management of these arrhythmias. Among them is overdrive pacing, which is based on preventive atrial overpacing slightly above the sinus rate. It provides additional benefits by reducing the dispersion of refractoriness [7,8], the delay in interatrial conduction, and the frequency of ectopic beats [9,10].

The DDD+ mode of the Philos DR system (Biotronik, Germany) is an algorithm based on a normal, P-wave-synchronized, atrioventricular pacing (DDD) mode. Moreover, the overdrive pacing mode (DDD+) increases the basic rate after every valid atrial sensed event. The algorithm reacts to an intrinsic atrial beat classified as sinus rhythm by the device with a pro-

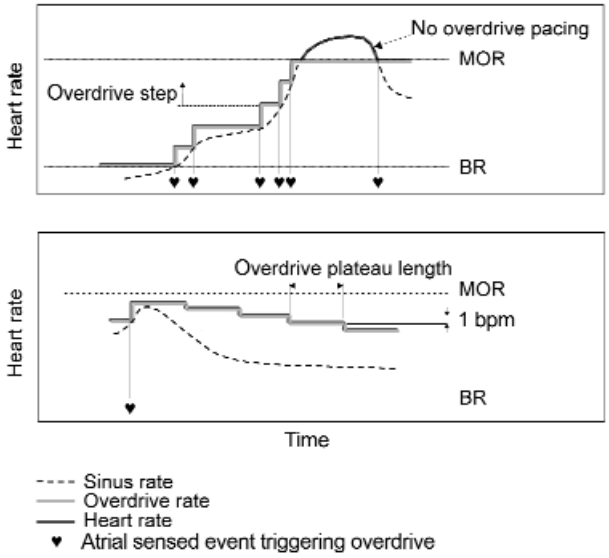

Figure 1. Panel a) Increase in the overdrive rate. Panel b) Decrease in the overdrive pacing rate. MOR = maximum overdrive rate, BR = basic rate.

grammable rate increase called "overdrive step size" (4 – 12 beats/min, nominal 8 beats/min). The pacing rate cannot exceed the maximum overdrive rate (MOR, nominal 120 beats/min) (Figure 1a). In the absence of an atrial sensed beat, the pacing rate is gradually decreased by 1 pulse/min every n-cycle (n: 1 to 32 cycles, nominal: 20 cycles), preventing permanent overstimulation at non-physiologically high rates (Figure 1b). In this way, pacing in the atrium is maintained more than 95% of the time.

The aim of this study is to evaluate the efficacy of this new dynamic overdrive algorithm in the prevention of AT.

Materials and Methods

Study Population

We enrolled 35 patients, without an upper age limit, who presented with sinus node disease (SND) with atrial electric instability (frequent atrial extrasystoles, paroxysmal AF, and non-sustained AT) and two episodes of AF within the 6 months before implantation. Patients were excluded if they had unmanaged angina pectoris, malignant ventricular arrhythmias, and symptomatic chronotropic incompetence. In addition, patients were excluded if they presented with any of the following during clinical follow-up: unresolved problems with atrial or far-field sensing, intolerance to overpacing, even after reprogramming of parameters, and development of chronic AF. All patients received a Philos DR DDD+ pacemaker.

Study Design

The study was a prospective, randomized, single-blind, crossover trial. Both the study protocol and patient consent form were approved by the local ethics review committee. The first follow-up was performed 2 months after implantation. The pacemaker was interrogated, and all statistical functions were printed out. Standard sensing, pacing threshold, and impedance tests were performed. Every parameter was adjusted according to the requirements of each patient. The arrhythmia frequency zones and the atrial precocity criteria were adjusted, and the following values were defined as a counter standard: atrial tachycardia frequency zone: 140 beats/min; atrial flutter frequency zone: 250 cycles/min; AF frequency zone: 340 fibrillatory waves/min; precocity criteria for extrasystole count (in percentage): 20%. All patients were submitted to a 24-hour ECG Holter and an echo-Doppler cardiogram.

The patients were randomized to DDD (Group I) or DDD+ pacing (Group II). The second follow-up was conducted 6 months after the randomization. The patients were submitted to a 24-hour ECG Holter, a telemetry analysis (event counter and Mode Switch (MS) number), and a second echo-Doppler cardiogram. At this time, the group crossover was performed: Group I received an adjusted DDD+ algorithm, while those in Group II were programmed to the DDD mode. The third and last follow-up occurred 12 months after

Patients	35	
Sex: male	16	46%
Age (years)	61.4 ± 13	
Sinus bradyarrhythmia	34	97%
Atrioventricular block	14	40%
Baseline disease		
Chagas disease	18	51%
Myocardiosclerosis	14	40%
Others	3	9%

Table 1. Patient's baseline characteristics.

the randomization. All the parameters were adjusted according to the needs of each patient. The patients were submitted to a new 24-hour ECG Holter, telemetry analysis (event counter and MS counter), and echo-Doppler cardiogram exam.

Statistical Analysis

All descriptive data are given as means ± standard deviations. A paired Student's t-test and a McNemar's chi-square test were used to analyze the differences between the two groups in continuous and categorical variables, respectively. Pearson´s correlation coefficient test was performed to verify the correlation between pacemaker parameters and complementary exams. A p-value < 0.001 was considered statistically highly significant. The analysis was performed using STATA statistical software, version 7.0 (STATA Corporation, USA).

Results

The study included 35 patients, 54% female, mean age 61.4 ± 13 years. The patients' baseline characteristics are summarized in Table 1. The basic rate was programmed to 65 ± 3 beats/min (DDD+ mode) and 63 ± 5 beats/min (DDD mode), the overdrive step size was programmed to 8 ± 2 beats/min, and the overdrive plateau length to 20 ± 2 cycles (range 10 – 32 cycles). The maximum overdrive rate was 124 ± 15 beats/min. These settings resulted in an atrial pacing percentage of 98% ± 3% (range 85% – 100%) in the DDD+ mode, and 65% ± 32% (range 1% – 100%) in the DDD mode. None of the patients presented any of the problems listed in the exclusion criteria during follow-up.

The statistical analysis of the intraindividual comparison DDD versus DDD+ is shown in Figures 2 – 5; in most cases more favorable results were found in the DDD+ mode. The results of the pacemaker telemetry are represented in Figures 2 and 3, where values refer to periods of 6 months each. There was a significant decrease in the number of AT and AF episodes by more than 90%. The echo-Doppler cardiogram analysis revealed a significant decrease in atrial size, which had been reduced by more than 22%. The results of the echo-Doppler cardiograms are presented in Figure 4. The 24-hour ECG Holter showed the results of the telemetry's tendency in reducing supraventricular extrasystoles and tachyarrhythmias, with statistical significance. (Figure 5)

Discussion

The most important finding of our study was the effectiveness of the DDD+ algorithm in the prevention of ATs. This dynamic overdrive algorithm decreased the amount of mode switching activation, atrial extrasystoles, and also reduced the size of the left atrium. The earliest evidence that atrial pacing could prevent AF was revealed in previous non-randomized and retrospective studies, which suggested a marked reduction in mortality, heart failure, AF, and stroke with atrial pacing as compared with ventricular pacing. The Danish Study [3], a prospective and randomized trial, verified the definite benefits of atrial pacing in reducing the incidence of AF and mortality in comparison with VVI pacing. Afterwards, the Canadian Trial on Physiologic Pacing (CTOPP) [5] analyzed the mortality and incidence of AF in patients with VVIR vs. DDDR pacing. This study showed that after 2 years of follow-up the incidence of AF did not reach statistical significance, but after 4 years of device therapy the statistical difference was demonstrated and increased with time [5]. The MOST trial [6] has shown a large (22%) decline in AF with dual-chamber pacing, an improvement in quality of life, and a tendency to limit the incidence of heart failure.

Overdrive pacing is considered effective in reducing pauses following ectopic beats, suppressing ectopy, and also reducing dispersion of refractoriness by maintaining rate control and rhythm. When it is used as a fixed high rate, this could be uncomfortable for the patient, or can induce cardiomyopathy. It might decrease ventricular function in time and lose its preventive effect for AF if the atrial rate exceeds the programmed pacing rate.Dynamic overdrive pacing, such as DDD+, can be regarded as an evolutionary step in this type of pacing. Dynamic overdrive algorithms can achieve a higher pacing rate by incrementally increasing it after each sensed beat, which respects the circadian patient's rhythm and prevents long-short cycle length sequences, without the drawbacks of a high fixed rate.

Initial experience with the DDD+ algorithm in the Inos^2 CLS (Biotronik) pacemaker has shown a tendency to diminish the incidence of AF during overdrive pacing, but without a statistically significant reduction in the prevalence of AF [11]. Otherwise, our study could have demonstrated a better performance of the Philos DR DDD+ algorithm in the prevention of AF, as well as evidenced a decrease in left atrial size in

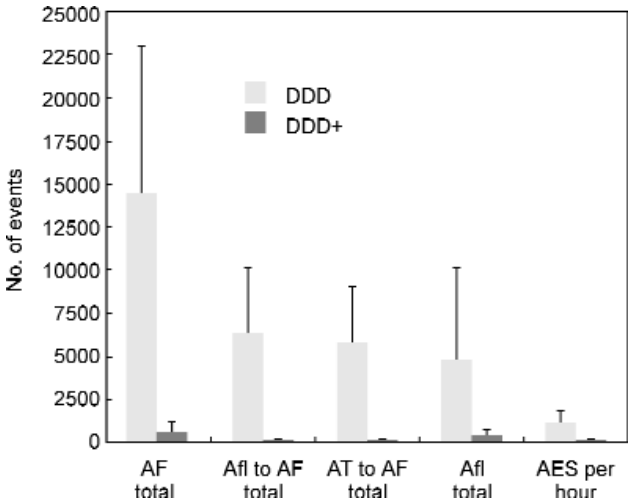

Figure 2. Results obtained from pacemaker telemetry (stored according to increased heart rate classification): AT = atrial tachyarrhythmia, Afl = atrial flutter, AF = atrial fibrillation, AES = atrial extrasystoles. p < 0.001.

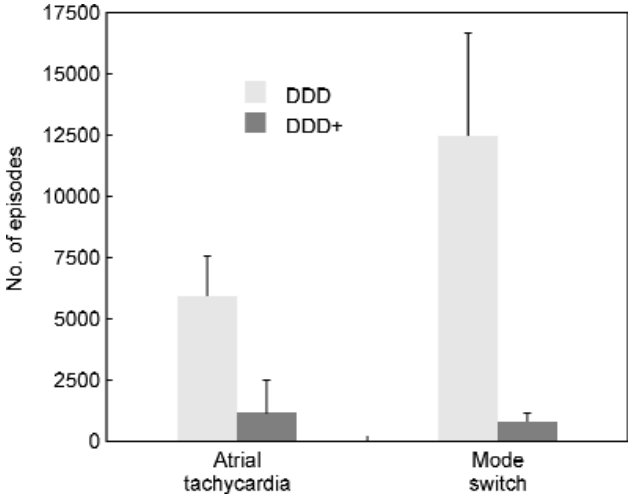

Figure 3. Results obtained from pacemaker telemetry concerning the total number of atrial tachyarrhythmias and the number of mode switching activations. p < 0.001.

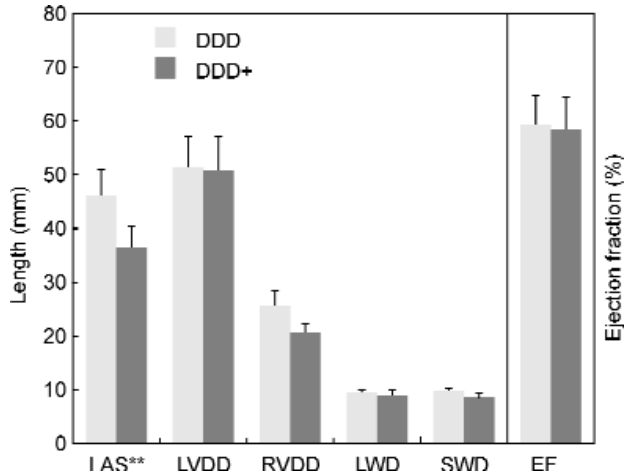

*Figure 4. Results from echo-Doppler cardiography. LAS = left atrial size; LVDD = left ventricular diastolic diameter; RVDD = right ventricular diastolic diameter; LWD = left wall diameter; SWD = septum wall diameter; EF = ejection fraction. **p < 0.001.*

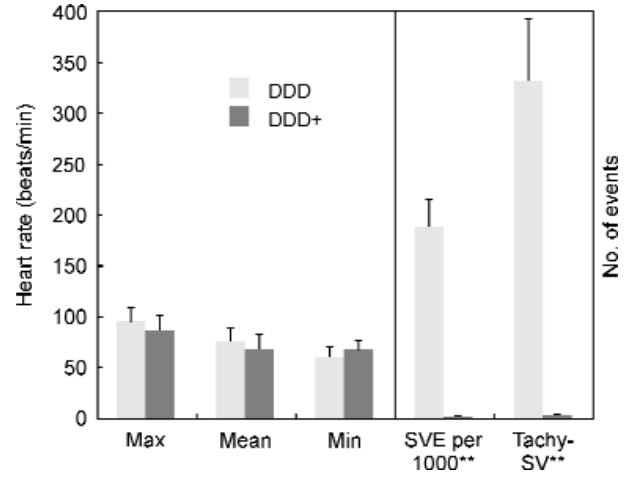

*Figure 5. Results from 24-hour ECG Holter. SVE = the number of supraventricular extrasystoles per 1000 beats; Tachy-SV = supraventricular tachyarrhythmias. **p < 0.001.*

patients with the DDD+ mode. Experimental studies [12,13] have shown that AF induces a significant electrical remodeling in the atrial myocardium, thereby increasing inducibility and stability of AF by shortening the atrial refractory period. Similar abnormalities have been reported in patients with AF [14,15]. Additional studies have verified that AF not only changed the electrophysiological properties of the atrial myocardium, but could also cause functional (contractile) and structural remodeling [16,17]. A good correlation between atrium size and the incidence or duration of AF has been shown in many studies [18,19]. Consequently, DDD+ overdrive pacing seems to modify the electrophysiologic substrate and the susceptibility to AT

associated with specific triggers; in addition, this pacing mode promotes a reversal of electrical remodeling and gradually makes AT initiation more difficult.

Conclusion

New pacing algorithms have been improving the ability of devices to treat AT; therefore, it is highly possible that they will become a standard function in future dual-chamber devices. DDD+ pacing has clearly decreased ATs, preventing the initiation of AF, improving atrial size, and preventing the electrical and mechanical remodeling status of AF. Although the long-term efficacy and safety of pacing algorithms for the treatment of AF have not yet received full recognition, this method currently represents one of the most promising approaches to treating AF.

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