Overdrive Pacing as an Effective Tool for Suppressing Paroxysmal Atrial Fibrillation: Two Case Reports

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Summary

The international multicenter study "Suppression of Atrial Fibrillation by Overdrive Pacing with Inos² CLS" aims to reduce atrial ectopic activity, and thus to prevent atrial fibrillation (AF), by homogenizing atrial depolarization and repolarization patterns. The Inos² CLS pacemaker uses the so-called DDD⁺ mode, which is a newly developed algorithm that can be downloaded via telemetry to the software-based pacemaker. As participants in the study, we present two cases of patients who already have completed the study with successful suppression of AF during DDD⁺ mode as opposed to the standard DDD mode. In the first patient, the percentage of time spent in AF was reduced from a maximum of nearly 6 % (5.96 %) in DDD mode to 2.64 % in DDD⁺ mode, and the duration of sustained AF episodes was reduced from 1.35 to 0.61 hours/day. In the second patient, the total number of AF episodes was reduced from 312 in the DDD mode to only one in the DDD⁺ mode over a period of 3 months in each. In conclusion, the DDD⁺ mode represents a new algorithm for atrial pacing that seems to be highly effective as a tool for suppressing the incidence of paroxysmal AF. The final results of the study are expected by the end of the year 2001.

Key Words

Atrial fibrillation, overdrive pacing, DDD⁺ mode

Introduction

Worldwide, atrial fibrillation (AF) is by far the most common reason for hospitalization that is due to cardiac arrhythmia. Since AF is especially a burden for the elderly, the prevalence of this arrhythmia is increasing with the increasing age of the population and the incidence of cardiac disease [1]. Treatment of AF with drugs to restore or stabilize sinus rhythm is often not effective enough, and may be accompanied by adverse effects. Bradycardia due to increased vagal tone, premature atrial activation with extrasystoles, and increased sympathetic tone with or without underlying heart conditions lead to the inhomogeneous atrial activation and repolarization patterns that are responsible for generating AF. The preventive effects of elevated atrial pacing rates above the sinus rate to suppress paroxysmal AF have been described earlier by several working groups [2-3]; pacing in this manner homogenizes atrial electrical activity and suppresses atrial premature beats.

Implementation of overdrive pacing with recently developed algorithms in cardiac pacemakers from different companies all aim at preventing AF [4]. The DDD⁺ mode by Biotronik, Germany, is a novel algorithm to treat paroxysmal AF. As participants in the international multicenter trial "Suppression of Atrial Fibrillation by Overdrive Pacing with Inos² CLS/DR", we present the cases of two study patients in the trial who were treated successfully using the DDD⁺ mode.

Materials and Methods

Criteria for including patients in the study were indications for implantation of a DDD-pacemaker and evidence of paroxysmal atrial tachyarrhythmias. The history of AF should contain at least two episodes of sustained AF in the last 3 months, or one AF episode per month and more than three consecutive premature atrial beats. Exclusion criteria were unresolved atrial sensing problems, permanent AF, malignant ventricular tachycardia, and symptomatic chronotropic incompetence. Implantation of the pacemaker device was performed in the catheter lab according to standard procedures. In accordance with the study protocol, all patients received an Inos^2 CLS/DR pacemaker (Biotronik, Germany). The physician was allowed to select the leads, but the atrial lead had to be bipolar. Stable atrial sensing should be achieved within a period of 3 months after implantation for patients with new leads, and within a period of 1 month for patients with leads that were already in place. Within this period, a stable antiarrhythmic drug therapy was to be established. Any change of antiarrhythmic medication during the investigational period was an exclusion criterion.

The patients were informed of the details of the study and had to give their written informed consent. They were randomly separated into two study groups (Group 1: DDD→ DDD$^+$/Group2: DDD$^+$→ DDD), and were not informed of which group they were being placed into. At this phase, the AF-suppression software was downloaded to the pacemaker, providing extended Holter features (cumulative AF duration on the basis of the Mode Switch function) and the modality for DDD$^+$ mode. The design and details of the ongoing study, as well as the algorithm of the DDD$^+$ mode, have been described previously [5-7].

The investigational phase started 3 months after pacemaker implantation. The pacemakers were set to DDD mode with the lower rate programmed between 45 and 60 beats/min (bpm) to provide only atrial sensing and AV-synchronous ventricular pacing. During this period, the incidence of AF and premature atrial beats was recorded with extended Holter features. AF detection was established by setting the "Mode Switch Intervention Frequency", which detects AF when the atrial rate increases beyond the intervention rate; 5 out of 8 beats above the intervention rate starts the AF period, and the AF period ends if the atrial rate falls below the intervention rate for 8 out of 8 beats. AF was counted as sustained if it lasted longer than one minute; at below one minute it was counted as a non-sustained AF episode. The date and time of the first 64 Mode Switch episodes were registered. The premature atrial beats were counted according to the prematurity criteria. The Mode Switch intervention rate was set to 170 or 180 bpm in our center depending on the setting of the upper tracking rate. In addition, patients were requested to note any symptoms or discomfort to a protocol paper.

Over a 1-year follow-up period, patients received therapy at the standard DDD mode with a lower rate of 60 bpm or DDD$^+$ mode for the first 6 months, and then the modes were crossed at the 6-month follow-up according to the randomization. In both patient groups, the extended Holter settings were active. The tested DDD$^+$ mode is supposed to reduce the incidence of atrial tachyarrhythmias by overdriving the spontaneous sinus rhythm, smoothing irregular atrial activity by suppressing atrial ectopic and premature activation, and thus homogenizing atrial depolarization and repolarization patterns.

In the DDD$^+$ mode, the occurrence of a sinus beat is followed by an increase in the pacing rate, overdriving the intrinsic rate within 1 second. The physician predefines this increase by programming the "overdrive step size" (standard 10 bpm). Thereafter, the pacing rate will decrease in steps of 1 bpm after passing of a so-called overdrive plateau length. The duration of the plateau length is programmable up to 32 beats (standard 20 beats).

Case 1 (Patient from Group 2)

Notable events in the medical history of the 49-year-old male were an accident during work in 1973 with loss of the right thumb and polyfracture of the right forearm with muscular hypotrophy, and a carcinoma of the colon with partial colon resection in 1988. In January 1999, the patient fell off his bicycle, breaking his right forearm again. On the same evening, the patient was admitted to the local hospital after experiencing syncope for the first time. During the next day, the patient suffered syncope four more times while being monitored in an intensive care unit. At that time the patient was still strongly under the influence of alcohol. The diagnosis was intermittent, complete AV-block with Adam-Stokes seizures. Hypertrophy of the left ventricle was found on echocardiography, and the

ECG revealed first degree AV-block and a positive Sokolow index for left heart hypertrophy. Over the next few days, the PR time had normalized and no further episodes of AV-block were seen; the patient was then transferred to general ward.

Over the course of the next few days, the patient had felt for the first time left thoracic stitches during exercise lasting about 10 minutes. Treadmill exercise testing was performed whenever an elevated blood pressure of 220/115 mmHg was detected. The patient was transferred to our hospital for further cardiological examinations. We saw a 48-year-old man in normal physical condition (height 189 cm, weight 80 kg). The only cardiac risk factor was arterial hypertension. Coronary angiography revealed normal coronary arteries, but an increased left-ventricular end-diastolic pressure of 13 mmHg, which would indicate hypertensive heart disease. Electrophysiologic testing was also performed; it revealed normal sinus node recovery time, normal AV-conduction, increased atrial vulnerability with repetitive induction of short episodes of atrial flutter, and AF with spontaneous conversion to sinus rhythm. Tilt table testing was not performed. Based on a strong suspicion that the patient had overshooting parasympathetic autonomous regulation and neurocardiogenic syncope, he was implanted with an Inos^2 CLS/DR pacemaker. During the pre-follow-up period, the patient noted episodes of palpitation with increased and irregular pulse and exertional dyspnea. The pacemaker Holter device revealed evidence of intermittent AF with 10 % Mode Switching during the period. At that time, the patient received 100 mg metoprolol as an antiarrhythmic medication.

After giving written informed consent, the patient was admitted to the investigational phase of the trial.

Case 2 (Patient from Group 1)

The patient said he had arterial hypertension since 1977, increasing varicosis of both legs, and diabetes mellitus since 1995, which was treated with a diabetes diet only. In January of 1998, the patient was admitted to our hospital; he presented unstable angina pectoris with a new development of T-wave inversion in the V1 to V3 leads of Wilson ECG. Coronary angiography revealed a severe coronary three-vessel disease but normal heart performance. The patient was operated on with three coronary artery bypass grafts; he developed thrombosis of the right lower limb during the postoperative period. For this reason, the patient was given warfarin therapy. In October of 1998, the patient noticed an irregular pulse, intermittent palpitations, as well as headaches and dizziness. Since that time, the patient felt dyspnea under effort and his blood pressure fluctuated greatly. The patient was thus admitted to our hospital again. The blood pressure was stabilized by further antihypertensive medication. The symptoms improved, and electrical cardioversion was suggested for AF. In April of 1999, the patient was admitted for dizziness caused by bradyarrhythmia with frequencies between 35 and 45 bpm and still-ongoing AF. A DDD-pacemaker was then implanted, and the patient was put on amiodarone medication. Electrical cardioversion was successful in July of 1999. After cardioversion, sinus rhythm of 50 bpm and first degree AV-block were documented. For the first 6 weeks after cardioversion, the pacemaker was programmed to DDD-CLS mode with a basic rate of 70 bpm. Since the sinus rhythm was stable, the patient was informed of the trial and he provided written consent. Antiarrhythmic medication with amiodarone 200 mg was established and sustained. For the pre-follow-up period, pacemaker programming was set to DDD mode with a basic rate of 60 bpm.

Results

In both patients, atrial and ventricular sensing was excellent, as were the atrial and ventricular pacing thresholds. Lead impedance for all electrodes was stable during the entire investigational period. During the pre-follow-up period of the patient from Case 1 in DDD mode (60 bpm), there was 96 % atrial sensing and 4 % atrial pacing. AF was documented in 10.4 % of this study period. In this patient, DDD$^+$ mode was programmed for the next study period with an overdrive step size of 15 bpm. In the first 3 months, the total duration of AF was reduced to 5.03 %, but the patient complained of a persistent fast heart beat. The incidence of atrial pacing was 99 %, and of atrial sensing 1 %. The overdrive step size was then reduced to 8 bpm. While still in DDD$^+$ mode over the next 3 months, a further reduction of the total AF duration was observed, down to 2.6 %. The total number of AF episodes decreased from 1658 to 723, and the number of sustained AF episodes decreased from 778 to 395 (Figure 1). Although the overdrive step size was reduced from 15 to 8 bpm, the incidence of atrial pacing increased to 100 %. The patient was almost free of

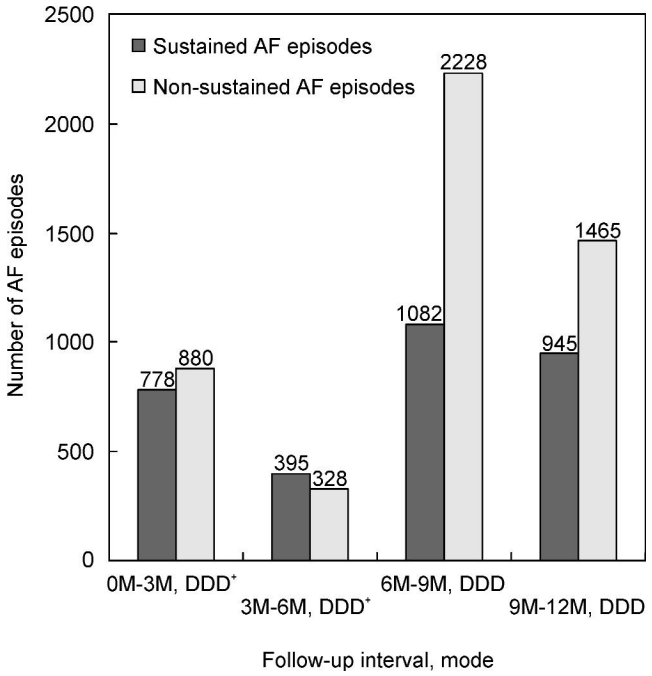

Figure 1. Number of sustained (> 60 s) and non-sustained atrial fibrillation (AF) episodes in DDD+ mode during the first 6 months and in DDD mode during the second 6 months of the 1-year follow-up for patient 1.

symptoms. After this first 6 months, a crossover to DDD mode with 60 bpm lower rate had to be performed. During this time, there was an increase of total AF duration (5.01 %) as well as in the total number of AF episodes (3310) and sustained AF episodes (1082). In the next 3 months of using the DDD mode, a further increase in total AF duration to nearly 6 % (5.96 %) was documented (Figure 1). In terms of the duration of sustained AF episodes per day, a reduction from 1.16 to 0.61 hours/day was achieved with DDD+ mode, and an increase back to 1.10 and 1.35 hours/day was seen upon switching back to DDD mode (Table 1).

The patient from Case 2 was taken from DDD-CLS mode at 70 bpm to DDD mode at 60 bpm for the pre-follow-up period after determining that the sinus rhythm was stable. During pre-follow-up, the total AF duration was only 0.04 %, and nine episodes of sustained AF and 93 non-sustained AF episodes were documented. For the subsequent 6 months, DDD mode with 60 bpm was programmed due to randomization. The number of sustained episodes did not change appreciably, but the number of non-sustained episodes decreased (Figure 2). The proportion for atrial sensing and atrial pacing was 36 % to 64 % and 39 % to 61 % for the first two 3-month periods (Table 2). At the 6-month follow-up, the mode was programmed to DDD+ mode with an overdrive step size of 6 bpm, which was not changed. This was enough to maintain almost 100 % atrial pacing. In the first three months of DDD+ mode, eight sustained AF episodes occurred but non-sustained AF episodes were reduced markedly to fourteen. In the second 3 months of DDD+ mode, only one episode of non-sustained AF was documented overall (Figure 2, Table 2).

Follow-up interval, mode	0M-3M, DDD+	3M-6M, DDD+	6M-9M, DDD	9M-12M, DDD
Follow-up duration	106d:00h:47m	92d:20h:54m	95d:03h:15m	90d:22h:24m
Time without AF	100d:16h:51m	90d:09h:58m	90d:08h:55m	85d:12h:21m
Time in AF	5d:07h:56m	2d:10h:56m	4d:18h:20m	5d:10h:03m
Time in AF (%)	5.03	2.64	5.01	5.96
Total number of AF episodes	1658	723	3310	2410
As (%)	1	0	73	64
Ap (%)	99	100	27	36
Intervention rate (bpm)	180	180	180	180
Mean atrial rate (bpm)	91	89	74	68
Basic rate (bpm)	60	60	60	60

Table 1. 1-year follow-up Holter data for patient 1. The clinically relevant parameters of atrial fibrillation (AF) are based on the Mode Switch function. As and Ap are the proportion of atrial sensed and paced events based on the atrial histogram.

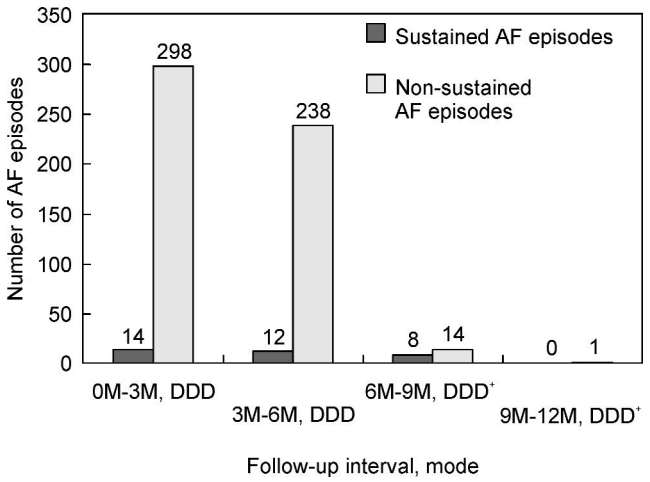

Figure 2. Number of sustained and non-sustained atrial fibrillation (AF) episodes in DDD mode during the first 6 months and in DDD⁺ mode during the second 6 months of the 1-year follow-up for patient 2.

Discussion

The two patients presented two different types of cardiac disease, as well as two different patterns of AF. In both patients, DDD⁺ mode was superior to DDD mode in suppression of paroxysmal AF. The effect of DDD⁺ mode was not as great in the first 3 months, but it increased in the second 3 months of the study period in DDD⁺ mode. As electromechanical remodeling is a common problem in stabilizing sinus rhythm, the reversibility of this electrophysiological phenomenon under stable atrial pacing may contribute to the observed improvement [8]. This might be supported by the observation that non-sustained AF was suppressed to a greater extent in both patients, and by the fact that premature atrial beats often act as a trigger for AF. The DDD⁺ mode also reduces the number of premature atrial beats, thus removing the trigger of induction of AF [9].

Conclusion

Although the data from these two patients do not allow stringent conclusions, the positive effect of the DDD⁺ mode to suppress paroxysmal AF was evident. DDD⁺ mode seems to be a promising, highly effective tool for suppressing paroxysmal AF. Nevertheless, the final results of the study will provide evidence of the power of the new tool, as well as how to tune overdrive step size and overdrive plateau length.

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Follow-up interval, Mode	0M-3M, DDD	3M-6M, DDD	6M-9M, DDD⁺	9M-12M, DDD⁺
Follow-up duration	95d:04h:58m	90d:22h:45m	89d:01h:08m	78d:00h:27m
Time without AF	95d:03h:15m	90d:21h:22m	89d:00h:43m	78d:00h:27m
Time in AF	0d:01h:43m	0d:01h:23m	0d:00h:25m	0d:00h:00m
Time in AF (%)	0.08	0.06	0.02	0.00
Total number of AF episodes	312	250	22	1
As (%)	36	39	0	0
Ap (%)	64	61	100	100
Intervention rate (bpm)	170	170	170	170
Mean atrial rate (bpm)	67	68	81	83
Basic rate (bpm)	60	60	60	60

Table 2. 1-year follow-up Holter data for patient 2. The clinically relevant parameters of atrial fibrillation are based on the Mode Switch function. As and Ap are the proportion of atrial sensed and paced events based on the atrial histogram.

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