INOS² DR and Neurocardiogenic Syncope: First Experiences in Four Cases

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Summary

Vasovagal syndrome is a much discussed indication for pacemaker implantation. In searching for answers to this question, this study reports the initial results of 4 carotid sinus syndrome patients with organic bradycardia who were implanted with a pacemaker that can evaluate the sympathetic tone via intracardiac impedance (INOS² DR, BIOTRONIK). Decrease in blood pressure and heart rate responses were observed during a head-up tilt test before and after pacemaker implantation. With positive results before implantation, 3 out of 4 patients tested negatively in the second head-up tilt test and were completely asymptomatic.

Key Words

Intracardiac impedance, carotid sinus syndrome, neurocardiogenic syncope, head-up tilt test

Introduction

Malignant vasovagal syndrome is a much discussed indication for pacemaker implantation. Nevertheless, the incidence of cardiac inhibition with pauses exceeding 5 s during the head-up tilt test is low (about 4.5%). With most patients responsive to drug therapy [1-4], pacemaker implantation does not have to be the first solution.

Pacemaker implantation for vasovagal syncope, also known as vasodepressor syncope and neurocardiogenic syncope, is beginning to be studied. The physiopathologic mechanism underlying these cases of syncope is not well known, but it is related to the medullar centers. A recent study shows that a high pacing rate controlled by a special algorithm that can analyze the cardiac rate decrease could be of benefit to a large portion of highly symptomatic patients with positive head-up tilt test results (and also with bradycardia) [5-8].

We tested the eventual benefit of a new physiologic sensor for treating neurocardiogenic syncope. This pacemaker seems to be able to evaluate the sympathetic tone by analyzing the heart contractility caused by the catecholamine release. The pacemaker evaluates the differences in intracardiac impedance values during the contraction and ejection phases of the myocardium [9-13].

Materials and Methods

Four male patients (mean age: 77.2 ± 6.6 years) were implanted with the INOS² DR (BIOTRONIK) pacemaker for treating recurrent presyncope and syncope events. As documented in an electrophysiologic study, each patient has an organic cause behind the fainting for which cardiac pacing is indicated. In addition, all patients have hypertensive cardiopathy, thus requiring anti-hypertensive therapy. The clinical histories of these patients prevent a distinction between vasovagal fainting and fainting due to extrinsic or intrinsic conduction dysfunctions. Prior to implantation, the head-up tilt test was positive for each patient. After pacemaker implantation and manual initialization of the rate-adaptive algorithm, a second head-up tilt test was initiated.

The head-up tilt test is performed in a quiet, dark room after a 10-min resting period in the decubitus position. The table is raised to a 60° upright position for 30 min, the cardiovascular system is continuously monitored. Blood pressure is taken every minute at the arm with a blood pressure cuff (dynamap). In the event of a negative result for the first part of the test, 0.3 mg of Trinitrine is administer-ed sublingually in decubitus, and after 5 min the table is raised again for 15 min. The head-up tilt test is positive when a presyncope or syn-

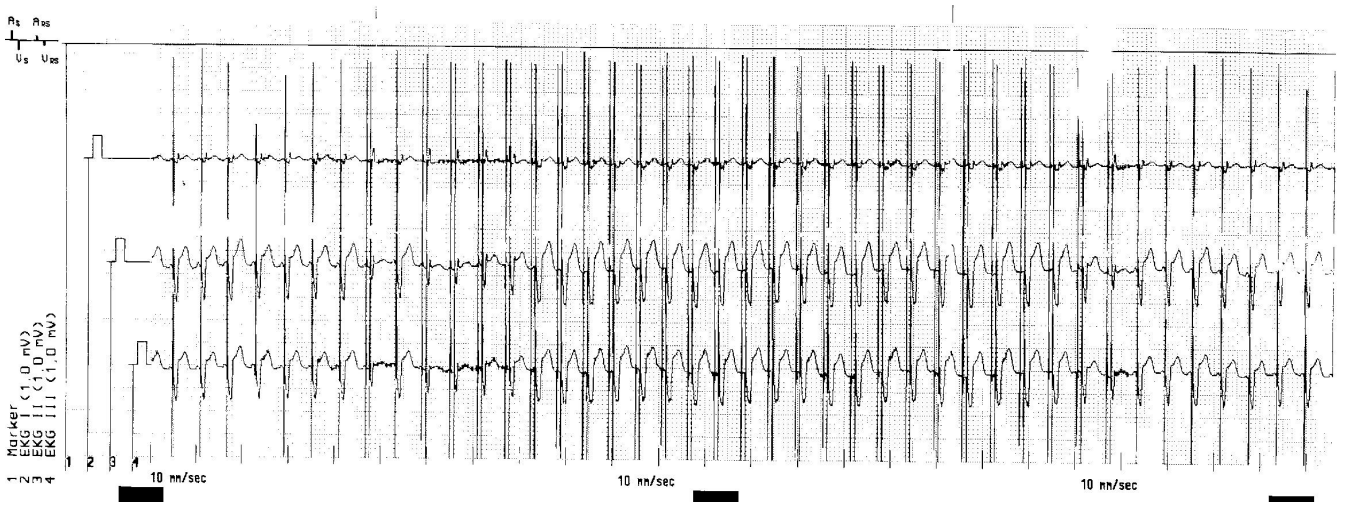

Figure 1. ECG recording of a typical syncope. Twice, an accelerated rhythm is followed by a bradycardic period.

cope event occurs which is associated with a blood pressure decrease and/or bradycardia.
Therapy is not modified between the different tests.

Results

Before implantation, the mean number of presyncope and syncope events per patient is 6.7 and 1.5, respectively. Syncope has been present for an average of 30 months (range: 1 to 60 months).
The electrophysiologic study revealed one case of isolated cardioinhibitory carotid sinus syndrome and two paroxysmal atrioventricular blocks associated with vasodepressive carotid sinus syndrome in one case and mixed carotid sinus syndrome in the other. The last patient was observed to have sinus node dysfunction, but with chronotropic competence, and mixed carotid sinus syndrome.
During the first head-up tilt test, accelerated cardiac rhythm was documented (mean increase: 28.5 ± 9.4 bpm). The mean maximal decrease in blood pressure measured during syncope is 97.7 ± 18.8 mmHg, preceded by a moderate bradycardia for 3 patients (range: 10 to 44 bpm) (e.g. in figure 1). This first head-up tilt test used sensitization for 3 in 4 patients.
After pacemaker implantation, the second head-up tilt test was performed. Each test was sensitized. The time elapsing between the two tests was 13.5 ± 13 days (range: 3 to 31 days). The mean decrease in blood pressure was only 66.6 ± 18.8 mmHg. In 3 completely asymptomatic patients, the head-up tilt test was negative. In these three cases, the mean fall in blood pressure was only 57.6 mmHg versus 101 mmHg prior to pacemaker implantation.
For the last patient, the second head-up tilt test was positive. The results showed the same delay as after the first sensitized test, and the patient was symptomatic. The decrease in blood pressure was approximately identical. The pacemaker response is always the same, alternating VDD mode and dual-chamber pacing with sinus overdriving ranging from 5 to 10 bpm.
See table 1 for a summary of patient data and results.

Discussion

This preliminary study shows that head-up tilt tests are negative for 75% of the patients implanted with an INOS² DR pacemaker.
From their etiology, it could not be predicted which patients would respond to the therapy. The exact physiopathologic mechanism must be defined, it might be the periodic acceleration of the heart rate which modifies the baroreceptor reflex. This hypothesis would explain the results obtained by other authors who established a decrease or a disappearance of symptoms in 80% of the vasovagal patients who were implanted with a pacemaker possessing a specific "rate-drop-sensing" algorithm which estimates the relative decrease in heart rate [5-8]. Nevertheless, these studies are unreliable because the placebo effect of the pacemaker was not researched. Likewise, possible modifications of the vasodilative therapy are not specified.

	Patient 1	Patient 2	Patient 3	Patient 4
Age/sexe	83/M	71/M	83/M	72/M
Card. Des.	HT	HT	HT	HT
Treatment	Vasodil.	Vasodil.	Vasodil.	Vasodil.
Pre-syncope	2	5	10	10
Syncope	3	0	3	0
Period of occurrence	60 months	2 months	60 months	1 months
Day/pacing	27/10/97	06/01/98	27/02/98	06/03/98
Pac. Indic.	Ssc ci	Avb / vd ssc	Snd / mi. ssc	Avb / mi. ssc
Delay/ 2 Tests	31 days	16 days	3 days	4 days
Increase after injection of adrenaline	27 bpm	41 bpm	18 bpm	28 bpm
Vasodep.1st tilt	88 mm Hg	89 mm Hg	126 mm Hg	88 mm Hg
Vasodep.2nd tilt	53 mm Hg	53 mm Hg	67 mm Hg	93 mm Hg
Bradyc.1st tilt	30 bpm	0 bpm	44 bpm	10 bpm
Sens.1st tilt	No	Yes	Yes	Yes
Sens.2nd tilt	Yes	Yes	Yes	Yes
Negat. 2nd tilt	Yes	Yes	Yes	No

Table 1. Summary of patient data and results. CSS, carotid sinus syndrome; ci, cardioinhibitory; AVB, atrioventricular block; vd, vassodepressive; SND, sinus node dysfunction.

Thus, these results must be interpreted carefully. A number of limitations can be pointed out in our study as well:

- Small patient number: The reason for this choice was to include only patients with organic bradycardia. Negative head-up tilt tests were possibly just lucky coincidence. Nevertheless, a number of researchers have shown the reproducibility of these tests [14-19], especially important for short intervals between tests as was the case in our study.
- Anti-hypertensive therapy: Pharmacological therapy had to be maintained because of patient cardiopathy. But since the pharmacological environment is the same during both head-up tilt tests, interpretation errors are limited.
- Placebo effect: The negative head-up tilt test was attributed to the specific algorithm of this pacemaker. We cannot exclude a possible placebo effect related to the pacemaker and the intervention.
- Sensing hypercontractility: If hypercontractility caused by catecholamine release during stress can be sensed with other physiologic sensors [20], it is also highly probable with the INOS² DR. However, the response of the pacemaker during the head-up tilt test cannot confirm this. Impedance is measured at regular intervals during dual-chamber stimulation. Intermittent DDD-mode overdrive pacing does not necessarily equal hypercontractility detection. A real-time impedance monitoring appears to be necessary for affirming varying contractility and attaining real-time parameters which control the pacemaker response.

Conclusion

Our study set out to answer questions about implanting pacemakers to treat malignant vasovagal syndrome. Using a state-of-the-art pacemaker that is based on a principle of measuring contractility via intracardiac impedance, three-quarters of the patients appeared to be assisted by the device. Repeated testing over a longer follow-up period will reveal more data, enabling more informed conclusions to be drawn. With this initial groundwork laid, the task is now to perform wider clinical studies and compare data, where possible.

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