Closed Loop Stimulation and Neurocardiogenic Syncope

P. GRAUX, Y. GUYOMAR, S. HEULS, R. CARLIOZ, Z. HOUCHAYMI, M. MOUKAHAL, A. DUTOIT
Cardiology Department, Hospital Group of the Catholic Institute of Lille, France

Summary

Indications for pacemaker implantation have been discussed in assessing the vasovagal syndrome. Head-up tilt testing (HUTT) is considered the standard in reproducing the symptoms and mechanisms of the vasovagal syndrome. In this study, 13 patients experienced asystole during positive tilt testing. After implantation of the INOS² CLS pacemaker with activated Closed Loop Stimulation (CLS), 8 out of 13 patients (61.5%) tested negatively in the second HUTT.

Key Words

Head-up tilt test, malignant vasovagal syndrome

Introduction

Pacemaker implantation is a much discussed indication for malignant vasovagal syndrome. Nevertheless, the incidence of cardiac inhibition with pauses exceeding 5 sec. during the HUTT is low (about 4.5%). Since most patients are responsive to drug therapy [1-4], pacemaker implantation is not the first solution. The pathophysiological mechanisms underlying these cases of syncope are not well understood, but it appears to be related to the medullar centers. Recent studies have shown that a high pacing rate controlled by a special algorithm that can analyze the decrease in cardiac rate, could be of benefit to a large portion of highly symptomatic patients with positive HUTT results (and also those with bradycardia) [5-8]. We tested the potential benefit of a new physiologic system for treating neurocardiogenic syncope. This pacemaker evaluates the sympathetic tone by analyzing the heart contractility caused by the release of catecholamines. The pacemaker evaluates the differences in intracardiac impedance values during the contraction and ejection phases of the myocardium [9-13].

Materials and Methods

Thirteen patients (10 male, 3 female; mean age: 77.3 ± 5.7 years) were implanted with the INOS² CLS pacemaker (Biotronik) for recurrent presyncope and syncope. The mean number of presyncopal episodes was 6.46 per patient and the number of syncopal episodes was 1.92 per patient in a mean period of 26.5 months (1-60 months). Eight patients experienced mild hypertension and two experienced ischemic cardiopathy
Since echocardiography and Holter ECG did not provide any information, patients underwent electrophysiological procedures which revealed the following:

- 1 cardio-inhibiting carotid sinus syndrome,
- 1 mixed carotid sinus syndrome,
- 1 sinus dysfunction,
- 1 AV block,
- 1 sinus dysfunction with an AV block,
- 4 AV block and mixed vasodepressive carotid sinus syndrome,
- 1 sinus dysfunction with mixed carotid sinus syndrome,
- 2 sinus dysfunction with AV block and mixed carotid sinus syndrome.

In each patient, the HUTT was also positive. The clinical histories prevented a distinction between vasovagal fainting and fainting due to extrinsic or intrinsic conduction dysfunction. After pacemaker implantation, the Closed Loop Stimulation was manually initialized in the first 4 patients, and automatically initialized in the last 9 patients (4 used the 1st software, 5 used the 2nd software). A 3-day waiting period was required before performing the second HUTT.
A third tilt test was performed in 2 patients; in 1 case

without the CLS mode activated and in the other, with this function switched "on".
The HUTT was performed in a quiet, dark room after a 10 min resting period with the patient in the supine position. The table was raised to a 60° upright position for 30 min, with the heart rate being continuously monitored. Blood pressure was taken every minute using an arm blood pressure cuff (Dynamap). In the event of a negative result during the first part of the test, 0.3 mg of nitroglycerine was administered sublingually with the patient in the supine position, and after 5 min the table was raised again for another 15 min. The HUTT was considered positive when a presyncopal or syncopal event occured associated with a drop in blood pressure and/or bradycardia.
Therapy was not modified between the different tests.

Results

During the first HUTT, the mean maximum decrease in blood pressure measured during syncope was 91.81 ± 19.90 mmHg. This first tilt test resulted in sensitization in 10 out of 13 patients. During syncope there was also a moderate cardiac rhythm decrease of 10 bpm (0-44 bpm). The maximum cardiac acceleration during the first part of the test was 30 ± 14 bpm.
After pacemaker implantation, a second HUTT was performed approximately 16.3 days after the first one (3 to 31 days post). Five patients remained symptomatic during the second test and their SBP fall was the same as during the first tilt test. Eight (61.5%) patients became negative; however there was always a significant SBP fall during the first tilt test (61.5 mmHg vs. 92.1 mmHg).
During the second tilt test, there was a continuous alternation in the atria between spontaneous and paced rhythm (10-20 s periods) for the patients who had manual initialization or had the first automatic software. For the patients who had initialization with the second automatic software there were only some dual-chamber accelerations during longer periods.
A third tilt test was performed in a patient 2 months after the second negative tilt test and without the Closed Loop Stimulation activation. No syncopal or near syncopal episodes occurred in DDD mode and the maximum blood pressure drop was 41 mmHg.
In 1 patient with a positive second HUTT, the delay of the symptoms were the same as during the first sensitized test, and the decrease in blood pressure was approximately identical. A third tilt test was done 3 months after the second with the automatically initialized CLS mode. The patient was asymptomatic and the maximum blood pressure drop was only 40 mmHg.

Discussion

This study shows that 61.5% of patients implanted with the INOS^2 CLS pacemaker did not experience a syncopal episode during tilt testing when CLS was aktiv. Among those patients with spontaneous and induced neurocardiogenic syncope, it was impossible to predict which would respond to the therapy. The exact interaction between pacemaker and baroreflex must be defined; it might be due to the periodic acceleration of the heart rate which modifies the baroreceptor reflex in the older software version. The new software does not need periodic dual chamber accelerations. However, 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 implanted with a pacemaker possessing a specific "rate-dropping-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.
Thus, these results must be interpreted carefully. A number of limitations can be pointed out in our study as well:

- Small patient population. We chose to include only patients with reasonable causes of paroxysmal bradycardia: carotid sinus syndrome, sinus node dysfunction, or paroxysmal AV block. Negative HUTTs were possibly just a lucky coincidence. Nevertheless, a number of researchers have reproduced these tests [14-19]. (Which is especially important for short test intervals as was the case in our study between the first two ones.)
- The mechanisms of a spontaneous and a induced neurocardiogenic syncope are analogous to one another, but are probably not exactly the same: Will a pacemaker with a contractility sensor give the same results in the two situations?
- Anti-hypertensive therapy: Pharmacological therapy had to be maintained because of patient cardiopathy.

Since the pharmacological environment is the same during both HUTTs, errors are limited.

- Placebo effect: The negative HUTT was attributed to the specific algorithm of this pacemaker. We cannot exclude a possible placebo effect related to the intervention of the pacemaker.
- Repetition of the tilt test: This might have the same effect as the continuous tilt test, resulting in a syncopal relapse [20].
- Sensing hypercontractility: Hypercontractility (caused by catecholamine release during stress) can be sensed with other physiologic sensors [21]; it is also highly probable to occur with the INOS^2 CLS. However, the response of the pacemaker during the HUTT cannot confirm this. Impedance is measured at regular intervals during dual-chamber stimulation. Intermittent DDD-mode overdrive pacing does not necessarily equal hypercontractility detection. Our knowledge will increase with the use of the new CLS software. However the response of the pacemaker during the HUTT cannot confirm this using the first version of the software. Impedance is measured at regular intervals during dual-chamber stimulation and intermittent DDD-mode overdrive pacing is not necessarily the same as hypercontractility detection.
- Real-time impedance monitoring: This appears to be necessary for confirming varying contractility, and attaining real-time parameters which control the pacemaker response.

Conclusion

It is evident that implanting the INOS^2 CLS is resulted in reducing syncope in 61.5% of patients, according to the serial HUTT results. It is hoped that further improvements in the software and implantation of state of the art pacemakers (that can measure the contractility of intracardiac impedance variations) will provide more information about the mechanisms of neurocardiogenic syncope.

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