Heart Rate Variability Analysis Before and After Pacemaker Implantation in Neuromediated Syncopal Patients

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Summary

Closed Loop Stimulation has been proven to be an effective pacing method for controlling the recurrence of neuromediated syncope during a patient's daily activities. In eight consecutive patients who were referred to our institution for recurrent syncopal episodes of neurally-mediated origin, an Inos^{2+} CLS pacemaker was implanted. The aim of our study was to assess in this group of patients the response to Closed Loop Stimulation in terms of heart rate variability. We focused on four parameters of heart rate variability: the mean heart rate; the number of pairs of adjacent RR intervals that differ by more than 50 ms in the entire recording, divided by the total number of RR intervals; the standard deviation of the averages of NN intervals in all 5-minute segments of the entire recording; and the standard deviation of all RR intervals. No significant differences were observed between heart rate variability indexes before and after pacemaker implantation.

Key Words

Closed Loop Stimulation (CLS), neurally-mediated syncope, heart rate variability (HRV)

Introduction

The Inos^{2+} CLS pacemaker (Biotronik, Germany), which is capable of delivering Closed Loop Stimulation (CLS), is a rate-responsive, dual-chamber device modulated by variations in myocardial contraction dynamics, and therefore, is involved in the physiological cardiovascular control mechanism. The pacemaker detects the time course of the unipolar intracardiac impedance in the neighboring ventricular lead tip, which reflects chan-ges in the volume of blood going to the myocardium during the observed ventricular contraction. Previous studies have demonstrated a good correlation between unipolar intracardiac impedance and right ventricular maximum pressure gradient dp/dt_{max} ($R^2 > 0.92$), i.e., myocardial contractility [1,2]. As the algorithm detects an increase in the impedance signal, suggesting an increasing hemodynamic need, the pacemaker reacts promptly with an adequate increase in the stimulation rate [3,4]. CLS makes the implanted pacemaker an integral part of the natural cardiovascular control loop and enables the heart rate to be managed by the information coming from the autonomic nervous system. The pacemaker becomes fully integrated into this physiological control system and can contribute in specific and adequate ways to situations of imbalance [5,6]. During neurally-mediated syncope, when chronotropy is temporarily impaired and contractility becomes the sole means to control the cardiac output, CLS establishes an artificial sinus node controlled by the sympathetic/parasympathetic drives. The "node" converts the load-dependent variations in contractility into individualized pacing rates, and restores an artificial and physiological chronotropy [7].

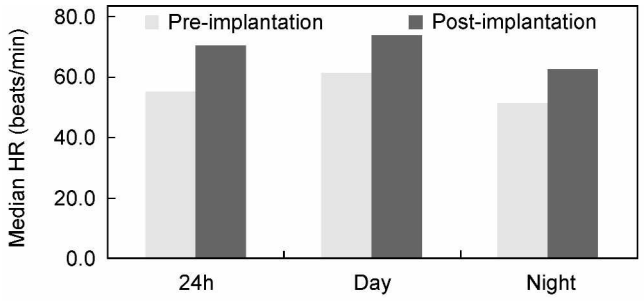
Patient Code	Gender	Age	Implant	HUTT	Carotid Sinus Massage	Cardiopathy
BG05	M	69	06/03/00	Pos	Neg	
GA08	M	76	19/04/00	Neg	Pos	Hypertensive
GP10	M	73	14/06/00	Pos	Pos	Ischemic
FP11	M	62	19/07/00	Pos	Neg	Ischemic
TG12	M	61	05/10/00	Neg	Pos	
CD13	M	75	11/10/00	Neg	Pos	Dilatative Cadiomyopathy
PG14	M	72	25/10/00	Neg	Pos	Ischemic
CR15	M	68	03/11/00	Neg	Pos	

Table 1. Characteristics of the eight patients enrolled in the study.

Patients included in our study showed neurally mediated syncopal episodes, but usually did not show pathologic patterns in heart variability during their daily activities. As many investigations have demonstrated, patients with neurally-mediated syncopes often develop an autonomic imbalance, with consequent pathologic RR-variability aspects, just before and during the syncopal episode [8-10]. The purpose of

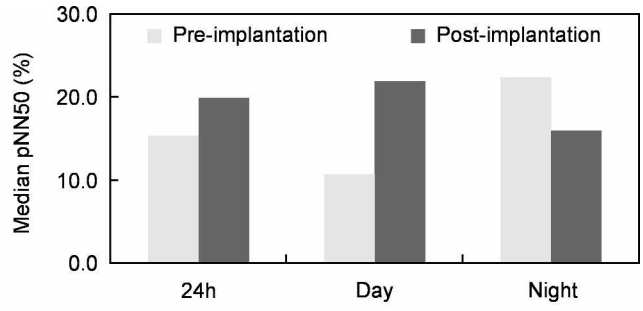
Patient Code		24-hour				Day				Night			
		HR (beats/min)	pNN50 (%)	SDANN (ms)	SDNN (ms)	HR (beats/min)	pNN50 (%)	SDANN (ms)	SDNN (ms)	HR (beats/min)	pNN50 (%)	SDANN (ms)	SDNN (ms)
BG5	Pre-impl	52.4	25.9	272.5	301.2	61.8	16.3	180.9	209.2	40.7	51.4	106.0	173.2
	Post-impl	60.8	18.4	89.3	152.9	69.3	66.7	97.4	165.1	63.0	54.6	40.1	115.5
	Delta	8.4	-7.53	-183.2	-148.4	7.5	50.4	-83.5	-44.1	22.3	3.2	-65.9	-57.7
GA8	Pre-impl	78.9	0.6	107.7	111.2	86.2	0.3	59.3	61.5	68.4	0.8	50.2	65.5
	Post-impl	86.4	21.3	68.1	87.8	90.6	24.1	58.5	79.2	81.6	10.6	38.4	63.0
	Delta	7.5	20.7	-39.5	-23.4	4.4	23.8	-0.9	17.7	13.2	9.7	-11.9	-2.5
GP10	Pre-impl	52.8	53.9	107.0	154.4	55.6	46.6	91.5	130.0	48.4	68.8	56.8	152.3
	Post-impl	73.5	22.5	131.3	177.9	71.3	26.7	92.6	123.6	79.2	14.6	191.4	242.8
	Delta	20.7	-31.4	24.2	23.5	15.7	-1.9	1.2	-6.4	30.8	-54.2	134.6	90.5
FP11	Pre-impl	51.2	3.1	146.0	181.3	54.8	3.0	128.8	160.1	47.5	3.2	110.2	162.6
	Post-impl	59.8	20.3	115.6	148.3	63.3	20.1	103.2	139.0	54.1	17.7	64.1	104.8
	Delta	8.6	17.2	-30.3	-33.0	8.5	17.1	-25.5	-21.1	6.6	14.6	-46.2	-57.8
TG12	Pre-impl	52.7	25.8	177.3	211.8	55.2	21.7	101.1	147.2	43.7	40.3	64.0	114.2
	Post-impl	70.5	12.8	114.3	134.5	76.1	17.4	114.3	134.5	62.2	4.2	48.0	65.0
	Delta	17.8	-13.0	-63.1	-77.3	20.9	-4.3	13.1	-12.7	18.5	-36.1	-16.0	-49.3
CD13	Pre-impl	81.3	51.2	96.4	116.7	88.2	51.8	41.5	65.5	70.8	55.1	78.6	130.2
	Post-impl	81.8	44.6	73.9	99.3	86.3	41.6	55.8	84.0	74.8	45.6	62.4	102.0
	Delta	0.5	-6.5	-22.5	-17.4	-1.9	-10.2	14.3	18.5	4.0	-9.5	-16.2	-28.3
PG14	Pre-impl	57.3	5.4	122.6	149.9	60.9	5.3	129.3	156.9	54.1	5.2	65.3	100.9
	Post-impl	64.5	20.1	60.5	84.1	66.7	20.5	61.1	85.1	61.9	18.7	30.9	61.7
	Delta	7.2	14.7	-62.1	-65.8	5.8	15.2	-68.2	-71.9	7.8	13.6	-34.4	-39.2
CR15	Pre-impl	70.0	1.2	126.7	184.4	75.0	1.1	120.7	123.0	63.6	1.5	49.94	66.5
	Post-impl	70.0	4.5	111.2	116.5	77.6	5.2	81.9	56.9	62.0	3.2	32.9	46.3
	Delta	0.0	3.3	-15.6	-67.9	2.6	4.1	-38.9	-66.1	-1.6	1.6	-17.0	-20.2

Table 2. Heart rate variability data collected in the eight patients before and after pacemaker implantation, grouped for the complete 24-hour observation time, diurnal and nocturnal periods. Delta = difference between post- and pre-implant value.



		24h	Day	Night
Pre-implantation	Mean ± SD (beats/min)	62.1 ± 12.7	67.1 ± 14.0	54.7 ± 11.6
Post-implantation	Mean ± SD (beats/min)	70.9 ± 9.5	75.2 ± 9.5	67.4 ± 9.8
	P	0.1588	0.2252	0.0499

Figure 1. Comparison of heart rate (HR) values before and after pacemaker implantation on a 24-hour basis, a diurnal basis, and a nocturnal basis.



		24h	Day	Night
Pre-implantation	Mean ± SD (%)	20.9 ± 22.1	18.2 ± 20.6	28.3 ± 28.5
Post-implantation	Mean ± SD (%)	20.6 ± 11.4	27.8 ± 18.7	21.2 ± 18.9
	P	0.9728	0.3647	0.5734

Figure 2. Comparison of the number of pairs of adjacent RR intervals that differ by more than 50 ms in the entire recording, divided by the total number of RR intervals (pNN50), before and after pacemaker implantation on a 24-hour basis, a diurnal basis, and a nocturnal basis.

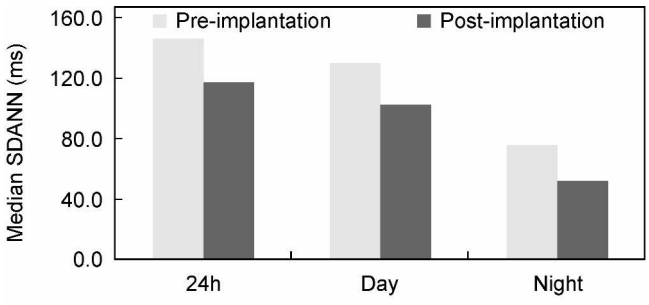
this evaluation was to analyze and compare heart rate variability (HRV) [11] before and after the implantation of an Inos^{2+} CLS pacemaker in this group of patients.

Materials and Methods

Our evaluation included eight consecutive patients, all males, ranging in age from 61 to 76 years (with a mean age of 69.5 years). They were referred to our institution for syncopal episodes between March and November, 2000. All patients had a clinical history of recurrent, neurally-mediated syncope, with at least two episodes in the last year, and no signs of sick sinus syndrome. They all met the cardiac pacemaker implantation guidelines established by the ACC/AHA task force [12], i.e., when neurally-mediated pre-syncope or syncope is associated with an asystolic period greater than 3 seconds, or with a hypersensitive cardioinhibitory response, include the carotid sinus syndrome for a Class I indication and the malignant vasovagal syncope for a Class IIb indication.

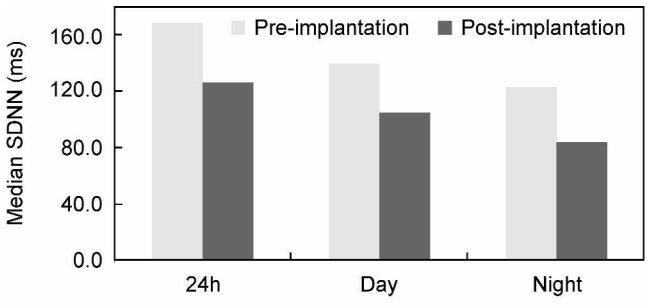
One of the patients had arterial hypertension, three had ischemic cardiopathy, and one had dilatative cardiomyopathy. No other pathologies associated with neural and cardiovascular systems were detected. All patients were evaluated with the head-up tilt test (HUTT) and carotid sinus massage. The syncope was reproducible in all cases, and two patients in particular showed a positive HUTT with a cardio-inhibitory response (Type 2A). Five patients had a positive carotid sinus massage with pauses longer than 5 s, and one patient showed both a positive HUTT with a pure vasodepressive (Type 3) response and a positive carotid sinus massage with a pause longer than 5 s.

A 24h ECG and HRV analysis were performed using a SYNETEC Holter analyzer (Rel. 1.10, ELA Medical, France), before and after implantation of the Inos^{2+} CLS pacemaker. Four HRV variables were chosen to assess the variability pattern. The mean heart rate (HR), the number of pairs of adjacent RR intervals that differ by more than 50 ms in the entire recording and are divided by the total number of RR intervals (pNN50), the standard deviation of the averages of NN intervals in all 5-minute segments of the entire recording (SDANN); and the standard deviation of all RR intervals (SDNN) were analysed as 24h global results that were divided into diurnal (from 8 AM to 9 PM) and nocturnal results (from 11 PM to 6 AM). The population observed in this study is too small to



		24h	Day	Night
Pre-implantation	Mean ± SD (ms)	144.5 ± 57.7	106.6 ± 43.8	72.6 ± 23.8
Post-implantation	Mean ± SD (ms)	95.5 ± 26.1	83.1 ± 22.4	63.5 ± 53.2
	P	0.0649	0.2182	0.6712

Figure 3. Comparison of the standard deviation of the averages of NN intervals in all 5-minute segments of the entire recording (SDANN) values before and after pacemaker implantation on a 24-hour basis, a diurnal basis, and a nocturnal basis.



		24h	Day	Night
Pre-implantation	Mean ± SD (ms)	176.4 ± 60.9	131.7 ± 49.4	120.7 ± 41.4
Post-implantation	Mean ± SD (ms)	125.2 ± 33.8	108.4 ± 37.2	100.1 ± 62.8
	P	0.0761	0.3227	0.4652

Figure 4. Comparison of the standard deviation of all RR intervals (SDNN) before and after pacemaker implantation on a 24-hour basis, a diurnal basis, and a nocturnal basis.

be considered a reliable sample for a statistical analysis. However an attempt of statistical evaluation was performed, applying on HRV variables before and after pacemaker implantation a two-sided Student's t-test for independent values and different variances.

Results

The data collected in the eight patients are individually reported in Table 2 for each observed period. Median HR values of the study group are depicted as histograms in Figure 1. Because a Basic Rate is programmed in pacemakers to guarantee the patient's safety, HR increases slightly after pacemaker implantation. The results of HRV analysis are reported in Figures 2 – 4. For pNN50, it must be taken into account that increase and decrease of pacing rate is performed using discontinual steps, e.g., an increase from 60 to 61 beats/min will correspond to a stepwise decrease of RR intervall from 1000 to 984 ms. Thus, pNN50 will be affected by pacing. Nevertheless, HRV is well maintained in both groups of measurements and the two groups of data do not evidence trends on SDNN and SDANN variability that differ with statistic significance.

Discussion and Conclusion

Notwithstanding the observed population of patients is limited and not sufficient to perform an accurate and reliable statistical equivalence analysis, the data collected before and after implantation are comparable and no statistically significant difference is verifiable. This is confirming that the CLS performed by the Inos^{2+} CLS pacemaker maintains a physiological heart rate variability. Furthermore, no additional syncopal episodes were observed in the studied patients during a (mean) 7.3 month follow-up (range 4 – 12 months). As already proven by other investigations [13,14], these data confirm that the CLS algorithm is highly specific and effective in the treatment of neurally-mediated syncopes.

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