Circadian pattern of atrial pacing threshold in the young

Massimo S. Silvetti1*, Antonella De Santis1, Simona Marcora1, Tiziana De Santo2, Nicoletta Grovale2, and Fabrizio Drago1

1Dipartimento Medico-Chirurgico di Cardiologia, Ospedale Pediatrico Bambino Gesù, Piazza S. Onofrio 4, 00165 Roma, Italy; and 2Medtronic Italy, Italy

Received 19 October 2007; accepted after revision 20 December 2007

Aims The aim of this study was to evaluate the circadian variation of atrial pacing threshold in young patients.

Methods and results Atrial Capture ManagementTM (ACM) algorithm is a Medtronic EnPulse pacemaker (PM) feature that uses two algorithms: atrioventricular conduction (AVC) (atrial pacing and spontaneous SVC) and atrial chamber reset (ACR) [intrinsic atrial activity with atrioventricular block (AVB)]. For this prospective, non-randomized study, ACM automatically measured and recorded thresholds every 4 h. Data are reported as median (range) or mean ± SD. In 2004–05, 14 consecutive patients (11 males, 79%), aged 12 years (1 day–24 years) received an EnPulse DDD/R PM for AVB (eight patients, 57%) or sinus node dysfunction. A new pacing system was implanted in eight patients (57%) and a replaced PM in six patients. Epicardial leads were implanted in 10 patients (71%). The follow-up duration is 11 (1–18) months: 9742 threshold measurements were attempted (6328 AVC, 3414 ACR), of which 3797 (39%) were successful (1807 AVC, 29%, 1990 ACR, 58%) in 11 (79%) patients. Three infants had no successful measurements. Measurement success was 42 ± 34% (AVC 27 ± 39%, ACR 41 ± 29%). Higher thresholds were found between 00.00 and 12.00 and lower between 12.00 and 20.00.

Conclusion Young patients show a circadian variability of atrial threshold with higher thresholds between 00.00 and 12.00.

KEYWORDS Cardiac pacing; Paediatric age; Circadian variability; Pacing thresholds

Introduction Pacemaker (PM) algorithms in use for the automatic ventricular pacing threshold detection, the AutocaptureTM (St Jude Medical CRMD, Sylmar, CA, USA) and the Ventricular Capture ManagementTM (VCM) (Medtronic, Inc., Minneapolis, MN, USA), have been shown to be effective and safe in measuring ventricular thresholds in children and therefore may improve battery longevity.1–9 Pacing threshold is not fixed but varies during the day and during various activities.9,10 Recently, a new algorithm capable of automatically measuring the atrial threshold has been developed, the Atrial Capture ManagementTM (ACM) (Medtronic, Inc.)11 and it is utilized in the Medtronic EnPulse pacemaker series, but there are no data about the atrial threshold variations in paediatric patients. The aim of this study was to evaluate the circadian variation of atrial pacing threshold in paediatric patients who underwent implantation of an EnPulse E2DR01 PM.

Methods Patient population This was a prospective, non-randomized study involving patients who underwent implantation of an EnPulse E2DR01 DDD/R PM between 2004 and 2005 at our institution, either as a first PM and lead implantation (‘acute leads’), or as a generator replacement only (‘chronic leads’).8 All patients were enrolled in the EnPulse Italian registry. Informed consent was signed at the enrolment by patients or by their parents.

Pacemaker implantation The procedures used in our Institution for the implantation of pacing systems in paediatric patients with transvenous or epicardial leads have been already described.15 Briefly, the endocardial leads were inserted with transcutaneous puncture of the subclavian vein and positioned in the right ventricular apex and in the right atrial appendage with tined or screw-in leads or, in patients after cardiac surgery, in appendage remnants or in the lateral atrial wall with screw-in leads. The PM generator was placed in a pre-pectoral pocket. For epicardial pacing, the PM generator was placed in the abdominal wall in a subcutaneous or submuscular (generally in neonates and infants) pocket. The leads were inserted by standard surgical techniques either through a sternotomy or through a

* Corresponding author. Tel: +39 06 68591; fax: +39 06 6859 2257. E-mail address: silvetti@opbg.net

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Thoracotomy, based on anatomical or operative characteristics, and fixed on the right atrium and on the non-systemic ventricle.

Atrial capture management algorithm

Atrial capture management algorithm uses two methods according to the patient’s spontaneous rhythm:11 atrial chamber reset (ACR), used in the presence of AV block (AVB) with intrinsic atrial/sinus rhythm, and AV conduction (AVC) in patients with paced atrial rhythm and spontaneous AVC. The device evaluates the intrinsic patient rhythm and automatically selects one of these two algorithms. By default, ACR is the first to be performed in the presence of spontaneous atrial rhythm.

Atrial capture management was turned on (adaptive mode) in all patients from enrolment. The threshold search was performed every 4 h, with a safety margin of two times the threshold or minimum adapted amplitude 1.5 V. This lower limit for output was chosen to ensure atrial capture.

Follow-up

Clinical and diagnostic data were collected at implantation, enrolment, and at 1, 3 and 6 months and then every 6 months, and saved to disk for later analysis. At each follow-up, the PM was interrogated for daily ACM thresholds and aborted measurements. Furthermore, manual atrial thresholds, automatic and manual sensing values, and lead impedance were measured at every follow-up visit.

Statistical analysis

Continuous data were expressed as mean ± standard deviation (SD) or median with range and categorical variables as percentage. Differences between categorical variables were evaluated with the χ² test or Fisher’s exact test when appropriate. Differences between continuous variables were evaluated with the t-test or Mann-Whitney test. The general linear model (GLM) for repeated ventricular septal defect status post repair (tal heart defects (CHD) were present in nine (64%) patients: sinus node dysfunction in six patients (43%). Other congenital patient rhythm and automatically selects one of these two algorithms. By default, ACR is the first to be performed in the presence of spontaneous atrial rhythm.

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Statistical analysis

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Results

Patients’ characteristics

Fourteen consecutive patients (11 boys, 79%) who underwent implantation of a Medtronic EnPulse EZDR01 DDD/R PM were enrolled. Median age was 12 years, range 1–24 years. Indications for PM implantation were AVB in eight (57%) patients (post-operative in three patients) and sinus node dysfunction in six patients (43%). Other congenital heart defects (CHD) were present in nine (64%) patients: ventricular septal defect status post repair (n = 2 patients), tricuspid atresia status post-Fontan operation (n = 2 patients), transposition of the great arteries (S, D, D) status post-Senning operation (n = 1), aortic and pulmonary stenosis (n = 1), AV septal defect status post-repair (n = 1), hypothyroid obstructive cardiomyopathy (n = 1).

Epicardial atrial leads were implanted in 10 patients (71%): Medtronic 4965 (n = 7), bipolar, steroid-eluting, Medtronic 4968 (n = 1), bipolar, steroid-eluting, and Cordis Encor (n = 2), bipolar, non-steroid-eluting. Endocardial atrial leads were implanted in four patients (29%): Medtronic 4574 (n = 1) and Medtronic 4524 (n = 1), both bipolar, steroid-eluting, tined and Medtronic 5076 (n = 2), bipolar, steroid-eluting, screw-in.

Eight patients (57%) underwent a first PM and lead implantation, whereas six received only a generator replacement. The pacing mode was DDD in 11 patients (79%) and DDD/R in the other three. Baseline characteristics of patients with epicardial and endocardial leads were compared, showing no significant difference between patients with epicardial (median 6 years, range 1 day–24 years) and endocardial (median 19, range 12–22 years) leads. No patient was taking an anti-arrhythmic drug that might affect pacing thresholds.10 Median follow-up was 11 months (range 1–18).

Threshold measurements

A total of 9742 (6328 AVC, 3414 ACR) automatic threshold measurements were performed in 11 (79%) patients, and 3797 (39%) threshold measurements were successful: AVC 1807 (29%), ACR 1990 (58%). Average measurement success was 42 ± 34% (AVC 27 ± 39%, ACR 41 ± 29%) and maximum success was 98%. The three patients with totally unsuccessful measurements were neonates with complete congenital AVB and epicardial pacing systems implanted in the first year of age. The two ACM algorithms, divided for endocardial and epicardial pacing, showed no significant difference in success rate: total success was 69 ± 14% (endocardial) and 31 ± 34% (epicardial). AVC success was 41 ± 47% (endocardial) and 21 ± 37% (epicardial); ACR success was 52 ± 29% (endocardial) and 34 ± 30% (epicardial). Unsuccessful measurements were more common in younger patients and epicardial pacing systems associated with higher sinus rates (100 bpm is the upper limit for function of the algorithm). The younger patients in whom threshold measurement by ACM was ineffective were managed with manual threshold measurement and output adjustment, leaving the ACM algorithm turned on for monitoring.

There were no statistically significant differences between electrical parameters of all patients measured at implantation and at all follow-up visits (respectively, P-wave 3.4 ± 1.8 vs. 4.5 ± 1.5 mV; far-field R-wave 1.8 ± 1.2 vs. 1.2 ± 1.0 mV; unipolar impedance 389 ± 155 vs. 328 ± 97 ohm, bipolar impedance 516 ± 121 vs. 510 ± 70 ohm). All thresholds were calculated at 0.40 ms of pulse duration. We also compared at follow-up automatic (0.8 ± 0.6 V) and manual thresholds (0.7 ± 0.4 V), and the differences were not statistically significant. There was, in contrast, a significant difference between manual thresholds at implantation (1.1 ± 0.5 V) and at follow-up (0.7 ± 0.4 V) (P = 0.017) and between manual thresholds measured in ‘chronic’ and in ‘acute’ leads during follow-up (respectively, 0.9 ± 0.5 vs. 0.5 ± 0.2 V, P = 0.031). Differences in automatic threshold measurements between ‘chronic’ and ‘acute’ leads were not statistically significant (respectively, 1.1 ± 0.7 vs. 0.6 ± 0.3 V). Differences between patients with endocardial and epicardial pacing system are reported in Table 1. One patient with a chronic epicardial atrial lead showed stable thresholds higher than 2 V throughout the follow-up. None of the patients developed thresholds >5.0 V/1.0 ms where there would be failure to capture with ACM.

Atrial arrhythmias and evidence of loss of atrial capture did not occur during follow-up.
Circadian threshold variations

Threshold measurements obtained throughout the day were grouped into six 4 h intervals, and all the measurements for each patient obtained during each time interval were averaged. Figure 1 shows the circadian threshold variability of all patients. Although this circadian variability was not statistically significant during the day, there was a trend toward higher threshold values between 00.00 and 12.00 a.m., with the maximum threshold value at 08.00–12.00 (mean 1.2 ± 0.7 V, median 1.0 V). Thresholds decrease in the afternoon and rise again in the evening. The lowest value was 0.8 ± 0.6 V (median 0.625 V) at 12.00–16.00. Maximum daily range of automatic threshold was 0.26 ± 0.20 V (median 0.25, range 0.125–0.75 V): for endocardial leads, it was 0.16 ± 0.06 V (median 0.125, range 0.125–0.250 V) and for epicardial leads 0.32 ± 0.23 V (median 0.25, range 0.125–0.750 V).

There were no significant differences of circadian threshold variability measured in patients with epicardial or endocardial leads, although the latter tended to be higher (GLM for repeated measures P = 0.23) (Figure 2).

Highest thresholds occurred at slightly different times in patients with endocardial and epicardial leads: the peak threshold for epicardial leads occurred between 08.00–12.00, at the same time as in all patients combined (Table 1), whereas the peak threshold in endocardial leads occurred between 00.00 and 04.00. However, caution must be applied in the interpretation of these data because of the small number of patients (seven with epicardial systems, four with endocardial systems).

Discussion

Only recently, the algorithm for ACM has became useful in clinical practice.11 The ACM algorithm, differing from the VCM algorithm,7–9 does not use the evoked response detection because of its small amplitude, but rather the resetting of the spontaneous atrial cycle (ACR method) or the spontaneous AVC of a paced atrial beat (AVC method). To our knowledge, there are no data about the circadian variability of the atrial pacing threshold in young patients. The knowledge of the daily atrial threshold variability is useful for the correct programming of the ACM algorithm and for physiopathological analysis. Our data show a pattern of atrial threshold variability (Figures 1 and 2), with highest values after midnight and in the morning until 12.00, and a decrease in the afternoon. In the evening, thresholds started to rise again. The average variability is actually rather low (0.26 ± 0.20 V), and tended to be lower for endocardial than for epicardial leads, although the difference was not statistically significant. The circadian atrial threshold pattern resembles that of ventricular threshold in young patients9 and in adults,10 in whom the highest thresholds were recorded between 00.00 and 06.00 a.m. The highest thresholds registered during the night are likely due to alteration in cardiac size, differences in tissue-lead contact, changes in catecholamine concentration, and changes in cardiac electrolyte levels during sleep.10

The small difference between the curves of the circadian atrial
threshold in all patients and in epicardial lead patients (Figures 1 and 2) and that of ventricular threshold might be due to the difference in the data sampling times (every 2 h for the ventricular threshold study, every 4 h in this study), and to the smaller number of cases in this study. The small number of cases in this study, particularly with this high number of epicardial leads, might have influenced the poor results of the algorithm (mean ACM success 39%).

The high number of unsuccessful measurements was due to the high heart rate of our young patients and to the theoretical limitations of this algorithm, which has better success rate in patients with spontaneous AVC and low percentage of atrial pacing. In automatic ventricular threshold measurement, success increases with age. Thus, ACM should not be activated in neonates with DDD PMs, in whom the sinus rate is generally higher than 100 bpm (limit above which ACM and VCM do not work).

However, the ACM is not harmful even in patients in whom a threshold search is often unsuccessful. When the ACM algorithm cannot perform a successful threshold measurement, it keeps previously programmed values.

For patients who otherwise meet criteria for ACM (good baseline lead thresholds, appropriate resting heart rate below 100 bpm, presence of intrinsic sinus rhythm, or spontaneous AVC), it is feasible with either endocardial or epicardial leads, and once a day automatic threshold measurement during the night is sufficient in clinical practice to ensure good atrial capture. This might be particularly important in patients with operated CHD in whom AV synchronicity is more necessary and the risk of developing atrial tachyarrhythmias is higher than in patients with isolated congenital AVB. Moreover, the good function of the ACM might prolong battery life.

Conclusions

Children and adolescents show a circadian atrial threshold variability similar to that described for ventricular threshold, with thresholds higher at night and in the morning. Thresholds decrease in the afternoon and rise again in the evening. Once a day, automatic threshold search during the night, with a threshold margin of 1.5X to 2X, seems reasonable, safe, and effective in clinical practice.

Acknowledgements

We thank Prof. Stephen P. Sanders, M. D., for his help in reviewing the manuscript.

Conflict of interest: T.D.S and N.G. are employees of Medtronic Italy.

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