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Efficacy of Rate Modulators in Children With Single-Chamber Pacemakers

Mohammad Dalili,[1] Reza Abbaszadeh,[1,*] Mohammad-Rafie Khorgami,[1] and Shirin Hosseini[1]

[1]Rajaie Cardiovascular Medical and Research Center, Iran University of Medical Sciences, Tehran, IR Iran

[*]*Corresponding author*: Reza Abbaszadeh, Rajaie Cardiovascular Medical and Research Center, Vali-Asr St., Niayesh Blvd, Tehran, IR Iran, E-mail: Rasemani95@yahoo.com

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Abstract

Background: Pacemaker implantation is a well-approved method for certain bradyarrhythmias. In children with single-chamber pacemakers, and in those with sinus node dysfunctions, there are no intrinsic mechanisms for rate modulation. Rather, rate modulators serve to provide the required rate.

Objectives: The aim of this study was to assess the efficacy of pacemaker rate modulators in children.

Patients and Methods: Twenty pacemaker-dependent children with single-chamber ventricular pacemakers were compared with the same number of children of the same age range without pacemakers. Efficacy of the rate modulators was assessed with treadmill exercise testing and compared with controls. Basal heart rates, exercise tolerance, maximal heart rates, and rate change slopes were studied.

Results: Basal heart rates, maximal heart rates, and exercise tolerance were significantly lower in the children with pacemakers. Age, sex, and body mass index had no effect on the heart rate slope during the exercise test. There was no significant difference between epicardial and endocardial pacemakers.

Conclusions: In the children in this study, pacemaker accelerometers failed to meet physiological demands.

Keywords: Arrhythmia, Children, Pacemaker, Congenital Heart Disease

1. Background

Pacemaker implantation is the only approved method for several types of cardiac conduction defects in adults and children (1). The most frequent indication for cardiac pacing in children is complete heart block. Complete heart block may present as a congenital electrical disease of the heart or as a complication of cardiac surgery for correcting congenital heart defects. Sinus node function remains intact in most children with atrioventricular block. With dual-chamber pacing, the native sinoatrial node serves as the rate modulator of the heart, thus, precluding the problem of rate modulation in various physiological situations. However, dual-chamber pacing systems are not recommended in small children owing to the concern over size and the possibility of vascular or valvular damage. Epicardial pacing systems are also implanted as a single-chamber system in most small children because of the simplicity of the procedure and comparable results. With a single-chamber pacing system, rate modulation during different physiological states depends on the ability of the device to increase or decrease the heart rate.

Several types of rate modulators have been devised and included in pacing systems. Accelerometers sense body movements and regulate the pacing rate according to these movements (2, 3). Another rate modulation system is the impedance-based system. With increasing activity, respiration becomes deeper and produces impedance changes between the pacing lead and the generator. This impedance change serves as the trigger for subsequent rate changes (4). Several attempts have been made to design artificial pacemakers that are more similar to the intrinsic cardiac pacemaker. Closed-loop systems focus on increasing cardiac muscle contractility as the trigger for rate increments. Some manufacturing companies have sought to employ a combination of the available mechanisms to improve their products (5).

As children are physically active, the role of rate modulation is important in maintaining activity tolerance and avoiding cardiac arrhythmias. Although the incidences of iatrogenic heart block and sinus node dysfunction have been lowered, most pacemaker implantations are done in children who have had previous cardiac surgeries. Rate modulation may play a considerable role in this pediatric group, since these are patients in whom cardiac contractility may be affected by surgical damage.

2. Objectives

The aim of the present study was to assess the efficacy of pacemaker rate modulators in children.

3. Materials and Methods

Twenty pacemaker-dependent children with single-chamber ventricular pacemakers were included. Our control group was selected from patients within the same age range (5 - 15 years) with no pacemakers and normal findings in outpatient examinations. The variables were compared between the pacemaker group and the control group. The exclusion criteria were having physical or mental inabilities pertaining to exercise or noncooperation and reduced ejection fraction (EF < 50%) in an echocardiography study before the exercise test. None of the cases and controls used beta blockers or other antiarrhythmic agents. The study was done in Rajaie cardiovascular, medical and research center, a tertiary cardiology center in Tehran, Iran.

For all patients, the pacemaker was set in the VVIR mode with a lower rate of 60 beats per minute (bpm) and an upper sensor rate of 170. The accelerometer was set at a lower threshold and a higher slope. All of the children underwent treadmill exercise testing with the modified Bruce protocol (CardioMed). Exercise tolerance, maximal heart rate, heart rate slope, rate recovery after exercise, and rhythm patterns were recorded. All findings were based on the Bruce treadmill protocol, which is shown in Table 1.

Table 1. The Bruce Treadmill Protocol as Used in the Current Study

Stage[a]	Belt Speed, mph	Incline (Grade %)	METs[b]
Modified Bruce	1.7	0	2.3
Modified Bruce	1.7	5	3.5
1	1.7	10	4.5
2	2.5	12	7.0
3	3.4	14	10.0
4	4.2	16	12.9
5	5.0	18	15.0
6	5.5	20	16.9
7	6.0	22	19.1

[a] 3-minute stages.
[b] METs are multiples of resting O_2 uptake. One MET equals an O_2 uptake of 3.5 mL/kg/min.

3.1. Statistical Analysis

Results are presented as mean ± standard deviation (SD) for quantitative variables. For categorical variables, data were summarized by absolute frequencies and percentages. Normality was assessed by the Kolmogorov-Smirnov test. Categorical variables were compared using the chi square test or Fisher's exact test when more than 20% of cells with expected counts of less than 5 were observed. Quantitative variables were also compared with t-tests or non-parametric Mann-Whitney U tests. Repeated measures analysis of variance (ANOVA) was used for heart rate stages. For the statistical analyses, we used the statistical package for the social sciences (SPSS) version 19.0 for Windows (SPSS Inc., Chicago, IL, USA). P values of 0.05 or less were considered statistically significant.

4. Results

This study was comprised of 40 patients (14 girls) with a mean age of 9 ± 2 years. Of these, there were 20 pacemaker-dependent children with single-chamber ventricular pacemakers. Another 20 patients comprising the control group were selected with no pacemakers and normal findings in outpatient examinations.

Basal heart rate, exercise tolerance (METs), and maximal heart rate in the control group were significantly higher than in the pacemaker group (P < 0.001). None of the underlying factors such as sex, age, and body mass index had significant effects on heart rate modulation. The demographic data of both the study group and controls are summarized in Table 2.

Table 2. Demographic Data and Main Findings in the Study Groups

Data	Pacemaker Group	Control Group	P Value
Age, y	9 ± 2.2	10 ± 2.6	0.149
Body mass index, kg/m^2	16.27 ± 3.4	17.05 ± 4.22	0.525
Sex (male/female)	12/8	14/6	0.507
Basal heart rate, bpm	69.25 ± 17.12	100.00 ± 15.85	< 0.001
Exercise tolerance, METs	11.28 ± 1.77	13.03 ± 0.70	< 0.001
Maximal heart rate, bpm	118.94 ± 26.15	181.05 ± 31.27	< 0.001

The pacemaker brands used in the children were Medtronic (n = 11) and St. Jude (n = 9). All of the pacemakers had accelerometers as the mode of rate regulation.

An assessment of heart rate variability at rest in the various stages of the exercise test in both groups showed significant heart rate changes. During the first to forth stages of the exercise test, there were gradual increments in heart rate slope, and during first and second stages of recovery, there were decrements in heart rate slope in both groups.

The average heart rate during rest in the pacemaker group was significantly lower than in the control group. The test stages are defined in Table 3.

Table 3. Heart Rate Variability Data During the Rest and Exercise Test Stages

Stage	Pacemaker Group	Control Group	P Value
Rest	69.25 ± 17.12	100.00 ± 15.85	< 0.001
Stage 1	87.10 ± 21.99	133.15 ± 20.04	< 0.001
Stage 2	104.75 ± 30.66	150.45 ± 17.85	< 0.001
Stage 3	113.95 ± 28.49	168.75 ± 17.56	< 0.001
Stage 4	118 ± 13.44	181.05 ± 31.27	< 0.001
Recovery 1	122.40 ± 27.88	165.30 ± 28.40	< 0.001
Recovery 2	76.50 ± 15.50	110.50 ± 18.63	< 0.001

Exercise tolerance and peak heart rate during maximal activity were significantly lower in the pacemaker group (P = 0.004) (Figure 1).

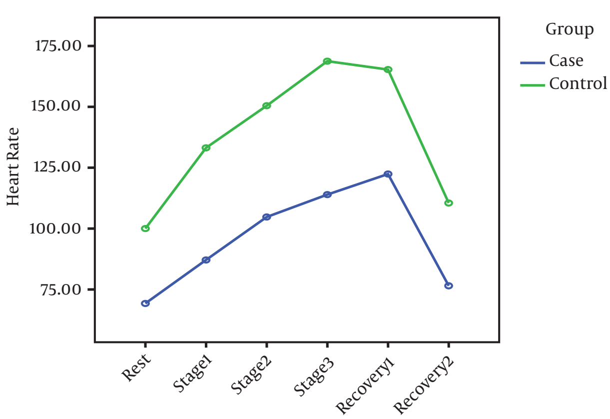

Figure 1. Comparison of the Heart Rate Slopes Between the Pacemaker and Control Groups

The data were also compared between the epicardial and endocardial pacemakers. There were 9 (45%) epicardial and 11 (55%) endocardial pacemakers. There were no significant differences between the epicardial and endocardial pacemakers with regard to maximal heart rates and exercise tolerance (Figure 2).

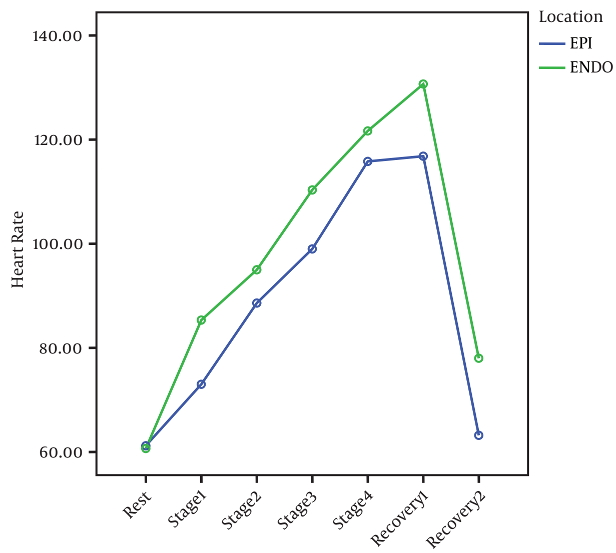

Figure 2. Comparison of the Heart Rate Slopes Between the Two Pacemaker Types

5. Discussion

Many clinical situations such as exercise, emotional stress, fever, and increased metabolic demands necessitate physiological changes in heart rate. Because of these circumstances, the use of sensors that optimally regulate the function of the sinus node has been discussed (6, 7). Since 1960, various parameters have been drawn upon as triggers for artificial pacemakers. Several artificial sensors have been designed based on the changes in pH, body temperature, oxygen saturation, respiratory rate, minute ventilation, QT interval, and heart contractility. Rate modulators are classified based on performance (primary, secondary, tertiary) or the type of technology (based on the QT interval, impedance, activity) (8, 9). The primary types of sensors directly measure factors controlling the sinus node function such as autonomic nerve activity and catecholamine levels. These sensors may seem more physiological, but there are some limitations to their use. The secondary type of rate modulator determines the parameters that can be changed by exercise. The tertiary type of rate modulator records external changes such as exercise-induced vibrations or body movements (10-14). For a long time, all pacemaker studies were done in the adult population. However, new interventional and surgical techniques for repairing congenital heart defects have led to a rise in pacemaker implantation in children. One study showed that artificial pacemakers are associated with lower mortality and morbidity rates in children with congenital heart defects (15). Although the indications for pacemaker implantation are somewhat clear in children, there are still many doubts and challenges with respect to optimal implantation tools and routes. Timing for pacemaker upgrade to the dual-chamber form is also not universal (16). In many children, single-chamber pacemakers are implanted because of the concern over size. Moreover, most investigations have demonstrated no long-term superiority for dual chamber pacing in small children. Nonetheless, single-chamber pacing in small children may seem adequate to maintain basal cardiac output, but it may fail to confer a normal active life. Limited activity could be a great problem in a child physically and mentally; thus, in a child with a single-chamber pacemaker, rate modulation is much more important than that in a less active adult.

Accelerometers are the oldest and perhaps the most efficient tools for rate modulation (17). Accelerometers can sense minimal exercise movements with high accuracy, but their sensitivity during supine or sitting isometric exercises may be reduced (18). Furthermore, not only do accelerometers fail to provide physiological responses, but their considerable shortcomings have also led to the development of other systems such as impedance meters (19). Previous research has shown that the Tei index exhibits significant improvements with the DDD mode compared with the VVIR mode. However, the DDD-CLS combination mode provides physiological heart rate variability and results in a less pronounced decrease in heart rate and fall in diastolic pressure than does the DDD mode alone (8, 20). The impact on the hemodynamic properties of the heart by mental stress underscores the need for a rate-adaptive sensor that responds to mental loads (21). Another form of modulator can measure changes in myocardial contractility a reflection of sympathetic tone and catecholamine levels during rest and nonphysical activities. Additionally, this type is capable of recording changes in myocardial contractility by measuring changes in impedance between the leads of the pacemaker and the pacemaker generator (18, 22). There is a significantly higher heart rate for close-loop stimulations than for the accelerometer sensor, and there is also good sensitivity of close-loop stimulation-based rate adaptation to mental stress (9). Close-loop stimulation was created to mimic this physiological response. Nonetheless, as much as the early results were encouraging, the technique has yet to be universally approved (12).

To date, only a few studies have been conducted on the efficacy of pacemaker rate modulators, and all of these limited investigations were on adult populations with diminished activity levels (9). In the present study, we examined active children in whom the rate modulation, and consequently exercise tolerance, are two of the most salient aspects of life. Our findings showed marked differences in exercise tolerance and maximal heart rate between the children with and without pacemakers; however, their rate acceleration slopes were similar. The major difference was in basal heart rate, with the mean heart rate at exercise initiation in the pacemaker and non pacemaker groups being 66.83 ± 14.72 and 100.00 ± 15.85 bpm, respectively. This finding suggests that heart rate in normal children significantly increases due to sympathetic tone before exercise. When we compared the basal heart rates (before starting the exercise) between the pacemaker and control groups, the difference was significant. To date, no artificial mechanism is available to substitute this intrinsic mechanism. It might have been helpful had we set the basal pacing rates higher and measured exercise tolerance again. However, we could not have set the basal pacing rates at 100 bpm, a rate that was recorded in the normal children before the test, because of excessive battery usage and the likelihood of clinical discomfort.

5.1. Study Limitations

The major limitation for our study was the small sample size. Differences in cardiac anatomy and surgical lesions may have additional roles for restricting heart rate and/or chronotropic responses; however, we did not enroll these differences within this study.

5.2. Conclusions

In the children recruited for the present study, the usual rate modulation accelerometers failed to provide physiological heart rates for maximal physical activity. The major difference between the children with and without pacemakers was their basal heart rates before exercise, which might have been due to mental factors. No substitute mechanisms for artificial pacemakers are currently available.

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