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ORIGINAL ARTICLE

P-Wave Dispersion in Children With Acute Rheumatic Fever

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Abstract As a new and simple electrocardiographic marker, P-wave dispersion is reported to be associated with inhomogeneous and discontinuous propagation of sinus impulses. The current study aimed to investigate P-wave dispersion in children with acute rheumatic fever. The study population consisted of 47 children with acute rheumatic fever (29 patients with carditis and 18 patients without carditis) and 31 healthy control subjects. Maximum and minimum P-wave durations were measured from the 12-lead surface electrocardiogram. The P-wave dispersion was calculated as the difference between maximum and minimum P-wave durations. The maximum P-wave duration and the P-wave dispersion of the patients with and without carditis were significantly greater than those of the control subjects. The P-wave dispersion of the patients with carditis was significantly greater than that of the patients without carditis. In conclusion, the P-wave dispersion was higher in the children with acute rheumatic fever than in the healthy control subjects.

Keywords Cardiac involvement · Carditis · Electrocardiography

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Acute rheumatic fever still is an endemic disease, especially among school-age children in developing countries. Cardiac involvement, nearly 50% of which occurs at the first attack, is the most serious complication. Cardiac involvement extends from the endocardium to the pericardium [19, 26].

As a new and simple electrocardiographic marker, P-wave dispersion is reported to be associated with inhomogeneous and discontinuous propagation of sinus impulses [11, 12]. It has been defined as the difference between the shortest and longest P-wave durations [11].

Previously, P-wave dispersion has been studied in patients with hypertension, paroxysmal atrial fibrillation, mitral stenosis, and aortic stenosis, as well as during spontaneous angina pectoris and coronary angioplasty [2, 13, 15, 20, 22, 27, 28, 29]. Prolonged P-wave duration and increased P-wave dispersion are reported to carry an increased risk for atrial fibrillation [2, 11].

To the best of our knowledge, the extent of P-wave dispersion in patients with acute rheumatic fever has not been studied. In this study, we prospectively analyzed the variations of the P-wave dispersion in the surface electrocardiograms of children with acute rheumatic fever and compared the results with those of healthy control subjects.

Materials and Methods

Study Population

This study enrolled all the children who had been hospitalized with a diagnosis of acute rheumatic fever during the first attack in the Pediatric Cardiology Department of the Konya Training and Research Hospital and the Selcuk University Hospital over a period of 12-months, from

February 2010 to February 2011. The patients were eligible for participation if they met the criteria specifying a diagnosis of acute rheumatic fever based on the revised Jones criteria [8, 24] during the first attack of carditis.

Complete blood count, erythrocyte sedimentation rate, C-reactive protein level, antistreptolysin-O titer, chest radiographs, and electrocardiograms were obtained from all the patients. The diagnosis of carditis was made with echocardiographic examinations. No patient had accompanying disease or was taking drugs known to influence heart rhythm or the electrocardiogram. None of the patients were taking medications or had been previously hospitalized. None of the patients had electrolyte abnormalities.

The patients with acute rheumatic fever were categorized into two groups based on the presence of carditis. Because the population included subjects with and without carditis, we also enrolled a group of control subjects. The control group consisted of 31 age- and sex-matched healthy children. The study was approved by the local ethics committee of our institution, and written informed consent was obtained from all the patients.

Electrocardiogram Analysis

Patients' history, clinical examination findings, physical examination findings, and laboratory data (complete blood count, erythrocyte sedimentation rate, C-reactive protein level, anti-streptolysin O, 12-lead electrocardiogram, telecardiographic findings, and echocardiographic findings) were recorded. A 12-lead electrocardiogram with a paper speed of 50 mm/s and 1-mV/cm standardization (Nihon Kohden electrocardiogram, Cardiofax GEM, Model 9022K, Tokyo, Japan) was obtained at admission.

Electrocardiogram tracings of all the children were blindly analyzed by two investigators. The measurements of the two investigators showed no discrepancies. The arithmetic mean of these two measurements was taken.

To improve accuracy, measurements were performed with calipers and magnifying lens. The onset of the P-wave was defined as the junction between the isoelectric line and the beginning of the P-wave deflection, and the offset of the P-wave was defined as the junction between the end of the P-wave deflection and the isoelectric line. Heart rate, maximum P-wave duration, and minimum P-wave duration were measured from the 12-lead surface electrocardiogram. Dispersion of the P-wave was calculated as the difference between the maximum and minimum P-wave durations (P-wave dispersion = maximum P-wave duration – minimum P-wave duration) [11, 13, 14]. An acceptable electrocardiogram was determined by its ability to measure P-wave duration in at least 8 of the 12 electrocardiographic leads recorded simultaneously.

Echocardiographic Examination

All the patients underwent echocardiographic examination within 24 to 48 h after their acute rheumatic fever diagnosis and before they started antiinflammatory treatment. All ultrasound examinations were performed with a commercially available echocardiographic machine (ProSound Alpha 7; Aloka, Hitachi-Aloka Medical, Tokyo, Japan) equipped with 3- and 5-MHz transducers. A standardized cross-sectional and Doppler echocardiographic examination was performed using multiple orthogonal parasternal, apical, and subcostal views with the patient in the left lateral decubitus position.

The four criteria of mitral and aortic regurgitant jets specified by the World Health Organization Expert Committee to differentiate normal from pathologic regurgitation on an echocardiogram were used: (1) the regurgitant jet should be 1 cm long, (2) should be seen in at least two planes, (3) should have a peak velocity 2.5 m/s, and (4) should persist throughout systole (mitral valve) or diastole (aortic valve) [29]. The systolic function of the left ventricle was evaluated using M-mode echocardiography in the parasternal long-axis view. Fractional shortening was calculated as defined previously [16]. The left atrial dimension was measured from the parasternal long-axis window in M-mode echocardiography.

Statistical Analysis

Data were analyzed using nonparametric methods and reported as the mean ± standard deviation or as median and range. The Kruskal–Wallis analysis of variance test was used to compare groups, and the Bonferroni-corrected Mann–Whitney U test was used as a more conservative measure of significance for multiple comparisons. Associations between parameters were assessed using Spearman's rank correlation test. Results were considered significant when p was less than 0.05 or, in case of k comparisons, when p was less than $0.05/k$. Statistical analysis was performed using the SPSS software package for windows, version 15.0 (SPSS, Chicago, IL, USA).

Results

All the groups were similar in terms of age ($p > 0.05$). Table 1 shows the baseline demographic, electrocardiographic, echocardiographic characteristics of the three groups. The P-wave dispersion values were significantly greater in both the patients without carditis ($p = 0.004$) and those with carditis ($p < 0.0001$) than in the control subjects. Significantly higher P-wave dispersion levels were found in the patients with carditis than in those

Table 1 Comparison of groups in terms of demographic, electrocardiographic, echocardiographic characteristics

Characteristics	Control group	Patients without carditis	Patients with carditis	Controls vs. patients without carditis *P value*	Controls vs. patients with carditis	Patients without carditis vs. patients with carditis
No. of patients	31	18	29			
Age (years)						
Mean	11.4 ± 2.4	10.3 ± 2.2	12.2 ± 2.2			
Median (range)	11 (6–16)	11 (7–15)	12 (7–16)			
Male:female ratio	16:15	8:10	18:11			
P-wave minimum (ms)						
Mean	48.7 ± 8	49.8 ± 10.5	40.6 ± 9.8	0.697	0.001	0.002
Median (range)	48 (36–60)	48 (30–72)	40 (24–72)			
P-wave maximum (ms)						
Mean	86 ± 8.1	99.7 ± 13.2	103.1 ± 16.3	<0.0001	<0.0001	0.502
Median (range)	84 (72–100)	100 (76–120)	100 (80–140)			
P-wave dispersion (ms)						
Mean	37.2 ± 12	49.8 ± 14	62.4 ± 15.4	0.004	<0.0001	0.007
Median (range)	36 (20–64)	50 (28–76)	60 (40–100			
Heart rate (beats/min)						
Mean	83 ± 18	100 ± 21	96 ± 27	0.009	0.019	0.533
Median (range)	80 (48–135)	100 (66–140)	96 (64–140)			
Left atrial diameter (mm)						
Mean	24.9 ± 2.4	25.2 ± 3.4	30.2 ± 5.5	0.810	<0.0001	0.001
Median (range)	25 (19–29)	25 (20–34)	30 (21–45)			
Left ventricular ejection fraction (%)						
Mean	69.2 ± 4.5	69.2 ± 4.7	68.4 ± 6.4	0.983	0.705	0.759
Median (range)	69 (60–78)	69.5 (60–82)	68 (51–79)			
Fractional shortening (%)						
Mean	38.8 ± 4.1	38.4 ± 4.0	37.4 ± 4.8	0.843	0.255	0.474
Median (range)	38 (31–49)	38 (31–50)	37 (26–48)			

Results were compared using the Kruskal–Wallis test followed by the Bonferroni-corrected Mann–Whitney *U* test. Significance was determined by $p < 0.05$ for the Kruskal–Wallis test and $p < 0.016$ ($p = 0.05/3$) for the Bonferroni correction

without carditis ($p = 0.007$). The minimum P-wave duration was significantly shorter in the patients with carditis than in those without carditis ($p = 0.002$) or in the control subjects ($p = 0.001$). The maximum P-wave duration was longer in the patients with carditis ($p < 0.0001$) and in those without carditis ($p = 0.0001$) than in the control subjects.

The left atrial diameters were significantly greater in the patients with carditis than in the control subjects ($p < 0.0001$). They also were greater the patients with carditis than in the the patients without carditis ($p = 0.001$). However, the patients without carditis did not differ significantly from the control subjects in terms of the left atrial diameter ($p > 0.05$).

A highly significant positive correlation was detected between maximum P-wave duration and P-wave dispersion ($r = 0.793$; $p < 0.0001$), whereas a highly significant negative correlation was detected between minimum P-wave duration and P-wave dispersion ($r = –0.535$; $p < 0.0001$). However, no correlation was detected between heart rate and P-wave dispersion ($r = 0.054$; $p = 0.639$) or between P-wave dispersion and left ventricular ejection fraction ($r = 0.197$; $p = 0.084$). Besides, maximum P-wave duration and P-wave dispersion were found to be correlated positively with left atrial diameter ($r = 0.329$; $p = 0.003$ and $r = 0.378$, $p = 0.001$, respectively).

Discussion

To our knowledge, no studies have previously compared P-wave dispersion in children experiencing acute rheumatic fever with that in healthy control subjects. Our study is the first to investigate P-wave dispersion in children with acute rheumatic fever.

In the current study, maximum P-wave duration and P-wave dispersion were detected to be significantly greater in the patients with acute rheumatic fever than in the control subjects. In addition, left atrial diameter was found to be significantly greater in the patients with carditis.

Furthermore, we found a maximum P-wave duration and P-wave dispersion to be correlated positively with left atrial diameter. It has been reported previously that changes in left atrial dimension and left atrial pressure may influence P-wave duration [6]. It is reported that P-wave abnormalities are related to left atrial enlargement [7, 25], left atrial hypertension [3], altered conduction [25], or a combination of multiple factors [17, 23]. We also have found a positive correlation between left atrial diameter and P-wave dispersion in patients with acute rheumatic fever.

The combination of mitral valve disease and atrial inflammation secondary to rheumatic carditis causes left atrial dilation, fibrosis within the wall of the atrium, and disorganization of the atrial muscle bundles [1]. Consequently, these changes lead to electrical inhomogeneity, disparate conduction velocities, and inhomogeneous refractory periods within the atrial myocardium [1, 4]. This is reflected on the electrocardiogram as increased P-wave duration and P-wave dispersion [11, 12]. It has been suspected that P-wave prolongation might be caused in part by abnormalities in atrial electrical properties such as intra-atrial or interatrial conduction disturbance or block [5, 9].

Mitral valvar regurgitation in acute rheumatic fever patients may be found early in the acute episode of carditis, and pathologic, hemodynamic, and functional changes are important determinants in the worsening of valvar incompetence. The valvar leaflets become thickened and retracted, with shortening and fusion of the tendinous cords also contributing to restricted valvar closure, which may be aggravated by dilation of the annulus and left atrium. The increased volume overload and output of the left atrium resulting from the regurgitation leads to an increased diastolic volume of the left ventricle, with dilation and hypertrophy of both chambers proportional to the severity of the valvar dysfunction.

In the setting of chronic disease, as the left atrium has time to dilate, the rise in pressure is relatively low. In contrast, in acute valvar incompetence, with a normal size left atrium, the left atrial pressure rises suddenly to a marked degree [18]. Anatomic and hemodynamic changes in left atrium, left atrial dilation, and increased left atrial pressure may be the underlying causes of prolonged maximum P-wave duration and increased P-wave dispersion in patients with acute rheumatic fever compared with control subjects.

Subclinical valvitis diagnosed by Doppler echocardiography is proposed to be a major criterion in the diagnosis of acute rheumatic fever [21]. Similarly, we observed that P-wave dispersion was significantly greater in acute rheumatic fever patients with carditis and those without carditis than in control subjects. Although rheumatic carditis usually refers to the valve damage, myocardial impairment exists.

One of the most characteristic disturbances of conduction in acute rheumatic fever is first-degree heart block. However, prolongation of the PR interval relative to the heart rate is a nonspecific finding, present in more than one-third of all patients. The PR interval usually returns to normal after the disease becomes inactive. Prolongation PR can occur both with and without carditis [10].

We can explain that P-wave dispersion is increased in active rheumatic carditis patients because the intra-atrial and interatrial conduction system may be affected by inflammation during the acute phase of disease. We hypothesized that P-wave dispersion was significantly greater in patients without carditis than in control subjects because of a conduction system involvement without valvulitis.

Conclusion

In this study, maximum P-wave duration and P-wave dispersion were found to be greater in children with acute rheumatic fever than in healthy control subjects. Because a P-wave dispersion increase may reflect cardiac involvement in acute rheumatic fever, it could be a new important parameter in the diagnosis of rheumatic carditis. Furthermore, our study showed that involvement of cardiac conduction tissue may be seen in acute rheumatic fever, even in the absence of clinical or echocardiographic manifestations. Further prospective studies that include larger series with long-term follow-up evaluation are necessary to clarify the clinical utility of P-wave dispersion in children with acute rheumatic fever.

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