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P Wave Dispersion in Children with Breath-holding Spells

Soluk-tutma Nöbetli Çocuklarda P Dalga Dispersiyonu

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Summary

Objective: A breath-holding spell (BHS) is a clinical feature frequently seen in infancy and early childhood and generally bringing children to pediatric cardiology outpatient clinics with the suspicion of cardiac disease. In this study, P wave dispersion (PWD), which is a marker of regional differences in atrial depolarization in electrocardiography and has been demonstrated to be beneficial in defining the risk of supraventricular tachycardia in various patient groups, was studied in children who presented with breath-holding spells.

Materials and Methods: Forty-seven patients with breath-holding spells and 36 healthy children as a control group were included in this study. We performed electrocardiography and transthoracic echocardiography on patients and controls. PWD, which is defined as the difference between maximum and minimum p wave duration, was also calculated. Statistical analysis in the study was performed using SPSS version 22.0 and $p<0.05$ was accepted as significant.

Results: Our study indicated that there were no statistically significant differences between the patients and controls in minimum, maximum p wave duration and PWD.

Conclusion: Our findings suggest that atrial conduction is probably unaffected in children with breath-holding spells.

Keywords: Breath-holding spells, electrocardiography, p wave dispersion, supraventricular tachycardia

Öz

Amaç: Soluk-tutma nöbetleri sıklıkla süt çocukluğu ve erken çocukluk çağında görülen ve kalp hastalığı şüphesiyle çocuk kardiyoloji kliniklerine çocukların götürüldüğü klinik bir tablodur. Bu çalışmada elektrokardiyografide (EKG) atriyal depolarizasyona ait bölgesel farklılıkların bir göstergesi olan ve çeşitli hasta gruplarında supraventriküler taşikardi riskini belirlemede yararlı olduğu kanıtlanmış olan p dalga dispersiyonu soluk tutma nöbeti ile başvurmuş çocuklarda çalışılmıştır.

Gereç ve Yöntem: Çalışmaya hasta grubu olarak 47 soluk-tutma nöbetli ve kontrol olarak da 36 sağlıklı çocuk alınmıştır. Her 2 gruba EKG ve ekokardiyografi yapılmıştır. P dalga dispersiyonu, maksimum ve minimum p dalga süreleri arasındaki fark olarak hesaplanmıştır. İstatistiksel analizde SPSS 22.0 programı kullanılmış olup $p<0,05$ anlamlı olarak kabul edilmiştir.

Bulgular: Hasta ve kontrol grubunda p minimum, p maksimum ve p dalga dispersiyonu süreleri arasında anlamlı farklılık bulunmamıştır.

Sonuç: Soluk-tutma nöbetli çocuklarda atrial iletinin olasılıkla etkilenmediği gösterilmiştir.

Anahtar Kelimeler: Soluk-tutma nöbeti, elektrokardiyografi, p dalga dispersiyonu, supraventriküler taşikardi

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Introduction

Breath-holding spells (BHS) are unexpected, reflexive, and non-epileptic clinical entities that are frequent in infancy and early-childhood. Patients with this symptom usually refer to pediatric cardiology and pediatric neurology clinics for exclusion of cardiac disease or epileptic seizures. Although the etiology is not known, autonomic dysfunction and increased vagal tonus, which lead to cardiac arrest and cerebral anoxia are considered to play a role. This problem can gradually resolve with autonomic system maturation (1). Paroxysmal rhythm abnormalities must be considered in the differential identification of these attacks (2). An association with iron deficiency anemia and BHS has been reported (3).

P wave dispersion (PWD) is defined as the difference between the longest and shortest duration of p waves in an electrocardiogram (ECG). PWD is a useful method for non-invasive assessment of the heterogeneity of repolarization within the atrial myocardium using surface electrocardiography, which also shows the risk of serious atrial arrhythmia. PWD can be used in the evaluation of the diffusion of sinus stimulus and duration of atrial transmission. Irregular and slow atrial stimulus transmission has been suggested to lengthen the duration of p waves and increase PWD (4). Atrial function under various pressure and volume loads, and thus the secondary changes in the atrial tissue due to these loads causes decreased intra-atrial and inter-atrial conduction and irregularity of conduction. The importance of the duration of the p wave in various clinical conditions such as paroxysmal atrial fibrillation, left atrial hypertension, and left atrial dilation has been demonstrated (4,5). Irregular and intermittent atrial conduction has been evaluated with PWD in patients with paroxysmal atrial fibrillation.

The literature review revealed no studies on PWD in BHS. In this study in children with BHS, the measurement of p wave lengths and PWD in 12-derivation ECG was performed, in addition to echocardiographic parameters. The children were also evaluated in terms of increased risk of supraventricular arrhythmia compared with normal children and its role in the etiopathogenesis of BHS was analyzed.

Materials and Methods

Forty-seven patients who presented to the outpatient clinics of Pediatric Cardiology and Pediatric Neurology of Harran University Faculty of Medicine between August 2013 and August 2014 were included in this study. Patients were included in the study after a thorough anamnesis, which revealed the presence of witnessed BHS. Families were questioned in terms of the beginning of the episodes and frequency and severity of the attacks, color changes in the patient (cyanotic and pallid), accompanying disease, and the presence of BHS and sudden death in the family. A detailed physical examination was performed in each patient. Patients were excluded in the presence of retarded neuromotor development and other pathologic findings in the physical examination, and structural cardiac disease detected in the echocardiography. Subsequently, a 12-derivation surface ECG was performed. Approval of the Ethics Board of Harran University Faculty of Medicine was obtained (Dated March 17, 2014, decision number 07, session number 04).

The control group included children who had presented to the pediatrics outpatient clinics of the Harran University Faculty of Medicine, without any systemic diseases, and were of the same age as those in the patient group. These patients were also questioned for their family history of BHS and the presence of sudden death. They were included in the study following the exclusion of any structural cardiac diseases by means of echocardiography. The parameters of ECG findings evaluated in the patient group were also evaluated in the control group.

Electrocardiographic evaluations were performed using a 12-derivation ECG device working at a speed of 25 mm/sec and 10 mm/mV standardization. All measurements were performed manually by a single individual. The following basic evaluations: rhythm, speed, QRS axis, atrial dilation, and ventricle hypertrophy and repolarization disorders in the ECG, which were all detected as normal, and the duration of p waves in all derivations of the ECG were calculated.

Statistical Analysis

The Kolmogorov-Smirnov test was used to determine the normal distribution of the continuous variables. The comparison of normally distributed and non-normally distributed variables in two independent groups was performed using Student's t-test and the Mann-Whitney U test, respectively. Categorical variables were analyzed using the chi-square test. Descriptive statistics are expressed as mean±standard deviation. Statistical analysis was performed using SPSS for Windows version 22.0 and $p<0.05$ was accepted as significant.

Results

Twenty boys and 27 girls with an age range between 6 months and 5 years (23±13 months) who were determined to have prior BHS were included in the study. Spells were described in detail by the family members and some of the patients. For the control group, 15 healthy boys and 21 healthy girls who presented to the child or pediatric cardiology outpatient clinics with innocent murmurs between the ages of 6 months and 5 years (26±11 months) were included in the study. No statistical difference was detected in age between the patient and control groups ($p=0.356$). The demographics of group 1 (patient) and group 2 (control) are shown in Table 1. No significant differences were found between the patient and control groups in the demographic characteristics.

The physical examinations and neuromotor development of all patients included in the study were normal. Basic evaluations

Table 1. Demographics of group 1 (patient) and group 2 (control)

Variables	Group 1 (n=47)	Group 2 (n=36)	p
Age* (months)	22.67 (12.94)	25.19 (11.26)	0.356
Female/male†	27/20	21/15	0.935
Height* (cm)	82.35 (11.40)	85.49 (9.44)	0.185
Weight* (kg)	11.42 (3.13)	11.89 (2.58)	0.471
BMI*	16.77 (2.45)	16.14 (1.37)	0.170
Surface area*	0.52 (0.10)	0.53 (0.09)	0.432

BMI: Body mass index, *Numerical variables are expressed as mean (standard deviation) and †categorical variables are expressed as (numbers) $p<0.05$

(rhythm, speed, QRS axis, atrial dilation, and ventricle hypertrophy and repolarization disorders) in the ECG were performed and no pathologies were detected. All patients were evaluated with a color Doppler echocardiography and no structural cardiac disease was demonstrated in either the patient or control group. In echocardiography, aortic thickness, intraventricular septum thickness, left ventricle diastolic thickness, left ventricle systolic thickness, left ventricle posterior wall thickness, left ventricle ejection fraction, and shortening fraction values were measured and the patient and control group values were compared. A comparison of the patient and control group echocardiographic parameters is shown in Table 2. No statistical difference was detected between the patient and control groups.

Heart rate, p minimum, p maximum, and PWD values were calculated using echocardiography. ECG values of the patient and control groups are shown in Table 3. No significant difference was detected between the two groups.

P maximum and p minimum in the patient group were 0.070±0.02 sec and 0.040±0.02 sec, respectively, and in the control group they were 0.070±0.02 sec and 0.045±0.02 sec, respectively. The PWD value, which is the difference between the two values stated above, was 0.025±0.17 sec and 0.219±0.01 sec in the patient and control groups, respectively; the difference between the two groups was not significant (p=0.271).

Table 2. A comparison of the patient and control group echocardiographic parameters

Variables (mean, standard deviation)	Group 1 (n=47)	Group 2 (n=36)	p
Ao dia (cm)	1.40 (0.25)	1.45 (0.23)	0.409
LA dia (cm)	1.88 (0.29)	1.96 (0.32)	0.367
IVSd (cm)	0.54 (0.08)	0.59 (0.10)	0.116
LVIDd (cm)	2.75 (0.39)	2.96 (0.43)	0.120
LVIDs (cm)	1.65 (0.28)	1.79 (0.32)	0.122
LVPWd (cm)	0.48 (0.09)	0.67 (0.24)	0.101
EF%	71.68 (7.78)	71.19 (6.91)	0.783
FS%	39.87 (6.94)	40.06 (6.71)	0.887

*p<0.05, Ao dia: Aortic diameter, LA dia: Left atrium diameter, IVSd: End-diastolic interventricular septum, LVIDd: Left ventricular end-diastolic interior diameter, LVIDs: Left ventricular end-systolic interior diameter, LVPWd: Left ventricular posterior wall end diastolic, EF: Ejection fraction, FS: Shortening fraction

Table 3. Electrocardiography values of the patient and control groups

Variables (mean, standard deviation)	Group 1 (n=47)	Group 2 (n=36)	p
P minimum (sec)	0.04 (0.02)	0.045 (0.02)	0.569
P maximum (sec)	0.07 (0.02)	0.07 (0.02)	0.339
P wave dispersion (sec)	0.025 (0.17)	0.219 (0.01)	0.271
Heart rate (beat/min)	133.59 (31.04)	132.97 (28.46)	0.993

*p<0.05

Discussion

Breath holding is an involuntary, reflexive, non-epileptic entity of childhood. The incidence is reported between 0.1% and 4.6% (2). The spells usually begin during the first 6 to 12 month of life and resolve by 4 years of age (2,6). A genetic penetrance is known, and autosomal-dominant inheritance has been suggested (7). PWD is an easy and non-invasive method for assessing the risk for serious atrial arrhythmia and sudden cardiac death. Increased PWD indicates non-homogeneous atrial repolarization within the myocardium, which causes rhythm abnormalities. Increased PWD has been demonstrated to be related to increased risk of arrhythmia and sudden death in various patient groups (8). Dilaveris and Gialafos (9) and Hallioglu et al. (10) found PWD values in adult patients with paroxysmal atrial fibrillation to increase compared with healthy individuals.

However, no study concerning the supraventricular repolarization in BHS was found in our literature survey. To our knowledge, this is the first study to evaluate PWD in patients with BHS.

The incidence of arrhythmia and sudden death had not been studied extensively in patients with BHS. On the other hand, respiratory sinus arrhythmia was found more commonly in pallid spells (11). In addition, in patients with BHSs, severe bradycardia and asystole may occur and permanent pacemaker implantation may even be required (12). Autonomic nervous system dysregulation is thought to be the primary abnormality in the pathophysiology of BHS. These children have an exaggerated oculocardiac reflex. There is increasing knowledge about ion channel disorders that cause paroxysmal symptoms in various systems due to impaired electrical activity. Our data are not sufficient to speculate about the presence of a milder type of ion channel mutation in patients with BHS. However, further studies in this field would be helpful for understanding the etiology and mechanism that causes these attacks. The frequency of complications and increased PWD indicate the need for further investigation into arrhythmia and autonomic dysfunction in this patient group.

Electrocardiographic parameters were previously studied in children with BHS; however, there are no studies in the literature on p wave length and duration of PWD in these children (1,13).

The present study was performed on children with BHS and durations of p minimum, p maximum, and PWD were evaluated and found similar in the patient and control groups. However, considering the changes in cardiac rate and atrial depolarization process, which is affected due to sympathetic discharge during the spells, the requirement of recordings during BHS must be emphasized. With this result, it can be concluded that atrial conduction is not affected in children with BHS. Nevertheless, future studies with larger scales of patients are required to reach such a conclusion.

Various techniques have been used in the measurement of p waves. Manual measurement on paper, manual measurement in a high-resolution computer medium, and automated measurement in a high-resolution digital medium may be performed (14). The main reason for the mistakes in the manual measurement on paper is the lower start of the p waves and derivations or bulges in the amplitude of p waves. In a study by Dilaveris et al. (14), the duration of p waves and PWD values in patient and control groups

were compared using three different methods and the lowest rate of error was in the manual measurement made in a high-resolution computer medium.

In settings with more developed recording and follow-up systems, patients are being followed up for longer durations and thus the imputed risk of development of disease can be evaluated more objectively. In the present study, PWD can be stated to be unchanged in the patient group; however, patients should be followed up and PWD in these patients should be re-studied in order to make more concrete and clear decisions.

Additionally, measurements of p wave length were performed manually on paper in this study. As stated above, the lowest rate of errors can be achieved in manual measurements made in a high-resolution computer medium. This condition is a limitation that affects the reliability of the results of this study.

Conclusion

The duration of PWD used in the evaluation of variability of atrial conduction time has been accepted as a predictor of supraventricular arrhythmia. In the present study, no difference was found in echocardiographic and electrocardiographic parameters between the patient and control groups.

Studies in patient groups with larger scale and longer follow-up, in addition to using technological equipment in the evaluation of patients to prevent errors are needed for a more reliable evaluation of the risk of disease development.

Ethics

Ethics Committee Approval: Approval of the Ethics Board of Harran University Faculty of Medicine was obtained (Dated March 17, 2014, decision number 07, session number 04), Informed Consent: Consent form was filled out by all participants.

Peer-review: Externally peer-reviewed.

Authorship Contributions

Surgical and Medical Practices: Tahsin Gider, Bülent Koca, Concept: Ali Yıldırım, Savaş Demirpençe, Design: Mustafa Çalık, Data Collection or Processing: Tahsin Gider, Bülent Koca, Analysis or Interpretation: Tahsin Gider, Bülent Koca, Literature Search: Tahsin Gider, Bülent Koca, Writing: Tahsin Gider, Bülent Koca.

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