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The Frequency of Cardiac Involvement in Children with Henoch-Schonlein Purpura

Henoch Schonlein Purpurası Tanılı Çocuk Hastalarda Kardiyak Etkilenme Sıklığı

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ÖZ

Amaç: Henoch-Schonlein purpurası (HSP) çocukluk çağının en sık görülen vaskülitidir. Bu çalışmanın amacı HSP'li çocuklarda kardiyovasküler sistemin etkilenme sıklığı ve tipinin araştırılmasıdır.
Araçlar ve Yöntem: Bu çalışmaya HSP tanısı alan 38 hasta ve kontrol grubu olarak 20 sağlıklı çocuk dâhil edildi. Hasta ve kontrol grubuna alınan olgular fizik muayene, elektrokardiyografi (EKG), ekokardiyografi (EKO) ve 24 saatlik EKG izlemi (Holter izlemi) ile değerlendirildi.
Bulgular: Hasta grubunda yaş ortalaması 9.3±3.2 yıl (aralık=4-17 yıl) idi. Hastaların 22'si kız hasta (%57.8) olup kız/erkek oranı 1.37 idi. Kontrol grubunda yaş ortalaması 9.7±3 yıl (aralık=4-14 yıl) idi. Kontrol grubunun 8'i kız (%40) olup kız/erkek oranı 0.66 idi. Henoch-Schonlein purpurası tanılı hastalarda cilt tutulumu %100, eklem tutulumu %71, gastrointestinal sistem tutulumu %71, böbrek tutulumu %31 oranında görüldü. Hasta grubunda EKG'de belirlenen kalp hızı ortalaması kontrol grubuna göre anlamlı olarak yüksekti (p=0.03). Hasta grubunun EKO incelemelerinde ortalama maksimum aort kapak akım hızı (AOVmax.) ve ortalama maksimum pulmoner kapak akım hızı (PULMmax.) değerleri kontrol grubuna göre anlamlı olarak düşüktü (p=0.02, p=0.03). Fakat iki grup arasında sistolik ve diyastolik kardiyak fonksiyonlar açısından anlamlı bir fark yoktu (p>0.05). Hasta grubunda bir hastada minimal perikardiyal efüzyon tespit edildi. Holter izleminde hasta ve kontrol grubunda kalp hızı ortalama değerleri (p=0.79) ve kalp hızı değişkenliği ortalama değerleri açısından anlamlı bir fark yoktu (p=0.60, p=0.57). Ayrıca her iki grupta klinik açıdan önemli bir aritmi veya iletim bozukluğu tespit edilmedi.
Sonuç: Henoch-Schonlein purpurası tanılı hasta grubunda kardiyak etkilenme sık değildir. Hastalar kardiyak etkilenmeye işaret edebilecek klinik bulgular var ise EKO ile değerlendirilebilir.

Anahtar Kelimeler: çocuk; henoch-schonlein purpurası; kardiyak etkilenme

ABSTRACT

Purpose: Henoch-Schonlein purpura (HSP) is the most common vasculitis in childhood. The aim of this study was to determine the prevalence and type of cardiac involvement in HSP.
Materials and Methods: Thirty-eight children with HSP (patient group) and 20 healthy children (control group) were included in the study. Physical examination, electrocardiography (ECG), echocardiography (ECHO), and 24-hour ECG monitoring (Holter monitoring) were performed.
Results: The mean age of patient and control groups were 9.3±3.2 years old (range=4-17 years old) and 9.7±3 years old (range=4-14 years old), respectively. Also, the female to male ratios were 1.37 and 0.66, respectively. The percentages of involvement of systems and organs were as follows: skin 100%, joint 71%, gastrointestinal system 71%, and kidney 31%. The mean heart rate (MHR) in ECG was significantly higher in the patient group (p=0.03) and the mean values of maximum aortic valve velocity (AOVmax.) and maximum pulmonary valve velocity (PULMVmax.) were significantly lower in the patient group than the control group (p=0.02, p=0.03) in the ECHO examination. However, systolic and diastolic cardiac functions were similar between the groups (p>0.05). In the patient group minimal pericardial effusion was detected in only one case. In 24-hour Holter monitoring MHR values (p=0.79) and heart rate variability parameters were similar between the patient and control groups (p=0.60, p=0.57). Also, no clinically important arrhythmia and other conduction disorders were detected in both groups.
Conclusion: Cardiac involvement in patients with HSP is not common. The patients may be assessed with the ECHO if signs and symptoms related to cardiac involvement were observed.

Keywords: child; henoch-schonlein purpura; cardiac involvement

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INTRODUCTION

Henoch-Schonlein purpura is the most frequent vasculitis of childhood. Disease is characterized by immunoglobulin A deposits in the small vessels of skin, joints, gastrointestinal system and kidney.[1] It rarely involves genitourinary system, central nervous system, eyes, lungs and cardiovascular system.[2,3] Cardiac involvement is rare and mostly reported as case reports.[4,5] In the present study, we aimed to evaluate the frequency and type of cardiac involvement in children with the diagnosis of HSP.

MATERIALS and METHODS

Atatürk University Faculty of Medicine Ethics Committee approved the study (Date 18.08.2011, session no 7, approval number 20). It is designed as a prospective study. Thirty-eight consecutive children with the diagnosis of HSP (study group) and 20 comparable healthy subjects (control group) were enrolled in the study. The study was performed on the children who were admitted to the outpatient clinics of general pediatrics and pediatric nephrology between June 2011 and July 2014.

The demographic characteristics, such as age, gender, weight, and height were recorded. Patients were evaluated in terms of cardiological findings between the first 1-20 days after diagnosis and before any treatment. Twenty healthy children without any cardiac and/or other systemic diseases were formed the control group.

Both groups were examined in terms of cardiovascular problems, and ECG, ECHO and Holter monitorization were performed.

All ECHO examinations were performed by the same pediatric cardiologist by using Vivid 7 Pro (General Electric, USA) ECHO device. Traditional ECHO measurements were done in conjunction with the methods offered by "American Society of Echocardiography".[6] Tei index for the right and left ventricle was measured from anterior commissure of mitral valve and anterior commissure of right ventricle.[7] All measurements were taken in 3 consecutive cardiac cycles and the mean value was used.

Using DMS 300-7 Holter monitoring recorder (DMS Inc., New York, United States of America), Holter monitorization recordings were obtained from the study and control groups. The recordings included a complete day and night cycle. All recordings were analyzed using DMS Cardioscan program (DMS Cardioscan 11 Holter analysis program, DMS Inc.), and QRS complexes were identified as artefacts and ectopic and normal beats. Further, all were re-evaluated by a pediatric cardiologist. Heart rate variability was measured by calculating time- and frequency-domain indices from 24-hour recordings. Also, all recordings were evaluated in terms of all other arrhythmias.[8] Average, minimum and maximum heart rates and the longest RR intervals were recorded.

Statistical Analysis

The data were expressed as proportions and mean±standard deviations. The normality of the data was analyzed by using Kolmogorov-Smirnov and Shapiro-Wilk's tests. Histograms were also evaluated. Data with normal distribution were compared by using the Wilcoxon test, and others by using the Mann-Whitney U test. Frequencies were compared by using the chi-square test. A p-value less than 0.05 was accepted as statistically significant for all tests.

All statistical analyses were performed using the SPSS 11.0 package program (Statistical Package for the Social Sciences, Chicago, Illinois, United States of America).

RESULTS

In the present study, a total of 44 children with the diagnosis of HSP were evaluated. Six patients were excluded due to the long interval between diagnosis and evaluation (n=1), absence of Holter monitorization (n=2), and insufficient ECHO data (n=3). The remaining 38 patients formed the study group. Twenty healthy children who were comparable with the study population formed the control group (Table 1).

The mean age of the study group was 9.3±3.2 years, and 22 (57.8%) of the participants were female (female/male ratio was 1.37). The same values for the control group were 9.7±3 years, 8 (40%) and 0.66, respectively. Both

groups were comparable in terms of their mean age, height, weight, and gender distribution (Table 1).

The ratio of affected organ systems in patient group is given in Table 2.

Table 1. Age, weight, height and genders of the patients from the study and control groups

Variables	Study group (n=38) Mean±SD	Control group (n=20) Mean±SD	p	
Age (years)	9.3±3.2	9.7±3	0.64	
Weight (kg)	30.5±14.4	36.5±14.5	0.14	
Height (cm)	131.9±19.3	137±18.5	0.34	
			X^2	p
Gender (F/M ratio)	22/16 (1.37)	8/12 (0.66)	1.68	0.19

F: female; M: male.

Table 2. Affected organ systems in patient group

Variables	n (n=38)	%
Skin	38/38	100
Joint	27/38	71
Arthritis	19/27	70
Artralgia	8/27	29
Gastrointestinal system	27/38	71
Abdominal pain	27/27	100
Melena	7/27	25
Invagination	1/27	3
Kidney*	12/38	31
Group 1	2/12	16
Group 2	1/12	8
Group 3	5/12	41
Group 4	1/12	8
Group 5	3/12	25
Group 6	0/12	0
Other organs	0/38	0

*Kidney involvement has been classified in terms of MEADOW classification.[22]

In clinical evaluation of cardiovascular system, innocent murmur was detected in 8 patients and hypertension in one patient with renal involvement.

Comparison of the MHR and PR intervals in 12 lead surface ECG in both groups are given in Table 3. The mean heart rate in patient group was significantly higher than in the control group (p=0.03). None of the cases had prolonged PR interval in terms of the age and heart rate. In a 6-year-old female patient, T wave was negative in DIII and aVF, and flat in DII.

Echocardiography revealed minimal pericardial effusion in one patient, and it was disappeared in a short time. An additional case was diagnosed as having a small atrial septal defect. Comparisons of ECHO measurements are given in Table 4.

Table 3. Comparison of the MHR and PR intervals in surface electrocardiography

Variables	Study group (n=38) Mean±SD	Control group (n=20) Mean±SD	p
Heart rate (bpm)	99.03±21.5	87±15.6	0.03
PR interval (seconds)	0.12±0.01	0.13±0.01	0.19
Prolonged PR (n)	0	0	-

Table 4. Comparisons of ECHO measurements

Variables	Study group (n=38) Mean±SD	Control group (n=20) Mean±SD	p
AOVmax (m/s)	1.08±0.13	1.18±0.14	0.02
PULMVmax (m/s)	1±0.12	1.08±0.15	0.03
AO (mm)	22.6±3.4	21.6±3.4	0.3
LA (mm)	26±3.2	27.3±4.5	0.2
LA/AO	1.17±0.12	1.28±0.12	0.03
LVEDD (mm)	37.3±5.6	38.9±5.9	0.32
LVESD (mm)	22.5±3.8	23.4±3.6	0.43
EF (%)	70.1±5.9	70.7±5.2	0.74
KF (%)	39±5	39.5±4.9	0.75
IVSd (mm)	7±1.1	6.9±1.1	0.59
LVPWTd (mm)	6.6±1.3	6.4±1.2	0.71
ME (m/s)	0.22±0.28	0.11±0.01	0.1
MA (m/s)	0.15±0.22	0.06±0.01	0.06
ME/MA	1.8±0.61	1.8±0.45	0.84
TE (m/s)	0.2±0.17	0.2±0.22	0.99
TA (m/s)	0.16±0.12	0.11±0.02	0.09
TE/TA	1.3±0.49	1.4±0.45	0.19
MTei	0.45±0.14	0.44±0.08	0.9
TTei	0.43±0.16	0.41±0.12	0.73

AOVmax: maximum velocity at aortic valve; PULMVmak: maximum velocity at pulmonary valve; AO: aortic diameter; LA: left atrial diameter; LVDd: left ventricular end diastolic diameter; LVDs: left ventricular end systolic diameter; LVPWTd: left ventricular posterior wall diastolic thickness; IVSd: end diastolic thickness of the interventricular septum; EF: ejection fraction of the left ventricle; SF: shortening fraction; ME: peak early filling velocity of mitral valve; MA: peak late filling velocity of mitral valve; TE: peak early filling velocity of tricuspid valve; TA: peak late filling velocity of tricus-pid valve; MTei: left ventricular Tei index; TTei: right ventricular Tei index.

The mean AOVmax (p=0.02), PULMVmax (p=0.03) and LA/Ao ratio (p=0.03) were significantly lower in the patient group.

Comparison of the MHR parameters and the MHR variability parameters obtained from Holter monitorization are given in Table 5 and Table 6, respectively. Infrequent ventricular premature beats in one patient and infrequent supraventricular premature beats in two patients from study group, infrequent ventricular premature beats in three patients and infrequent supraventricular premature beats in two patients from control group were detected.

No significant difference was detected between the MHR parameters (Table 5) and the MHR variability parameters (Table 6) obtained from Holter monitorization.

Tablo 5. Comparison of the heart rate parameters obtained from Holter monitoring.

Variables	Study group (n=38) Mean±SD	Control group (n=20) Mean±SD	p
Average heart rate (bpm)	93±17.7	83.3±11.1	0.79
Minimum heart rate (bpm)	54.9±10.2	50.1±5.6	0.60
Maximum heart rate (bpm)	156±18.6	155.2±17	0.57
Longest RR interval (ms)	1173.4±256.3	1329.4±150.9	0.43

Table 6. Mean heart rate variability parameters obtained from Holter monitoring recordings

Variables	Study group (n=38) Mean±SD	Control Group (n=20) Mean±SD	p
SDNN Index (ms)	114.1±48.9	138.8±43.6	0.74
SDANN (ms)	96.4±41.9	117.9±40.3	0.44
SDNN (ms)	57.1±24.3	76.8±24.7	0.62
rMSSD (ms)	44.1±24.2	55.6±21.1	0.60
pNN50	18.7±15.7	25.6±13.4	0.64
Total power (ms^2)	3493.9±2662	5687.7±3211.2	0.60
VLF (ms^2)	2161.8±1876.4	3738.2±2364.1	0.66
LF (ms^2)	733.7±461.3	1183.7±590.2	0.44
HF (ms^2)	536.8±452	695.3±394.5	0.54
LF/HF	1.9±1.1	1.8±0.55	0.99
nLF (ms^2)	0.59±0.12	0.61±0.06	0.69
nHF (ms^2)	0.36±0.12	0.34±0.06	0.86

SDNN index: mean of the standard deviations of all normal sinus R–R intervals for all 5-minute segments of the entire recording; SDANN: the standard deviation of the means of all R–R intervals for all 5-minute segments of the analysis; SDNN: the standard deviation of all R–R intervals over 24 hours; rMSSD: the square root of the mean of the sum of squares of differences between adjacent R–R intervals over the length of the analysis; pNN50: the amount of adjacent R–R intervals that are greater than 50 milliseconds for the whole analysis. Total power: Variability in all NN ranges, VLF: Very low frequency, LF: low frequency, HF: high frequency, nLF: normalized low frequency, nHF: Normalized high frequency.

DISCUSSION

Henoch-Scholein purpura is the most frequent vasculitis in childhood. It mostly affects skin, gastrointestinal system, joints and kidney. The disease rarely affects genitourinary system, central nervous system, eyes, lungs, and cardiovascular system.[2,3] In severe cases of HSP, cardiac involvement had been reported as rare case reports.[4,5] We are not aware of any prospective study performed in children investigating the cardiac involvement in children with HSP.

In adults with HSP, complete atrioventricular (AV) block,[9] elevated creatinine kinase level with left bundle branch block,[10] escape rhythm and myocardial infarction,[4] nodal rhythm with elevated troponin T level,[5] congestive heart failure,[11] myocardial infarction with microangiopathy,[12] cardiac dysfunction and dilation,[13] Mobitz type II block,[14] and myocardial infarction due to coroner thrombus[15] had been reported.

Lutz et al.[14] reported negative T waves in DII, DIII, aVF and V4-V6 in a 19-year-old patient. The patient had developed asymptomatic ectopic atrial ritm and Mobitz type II AV block in following period. Gulati et al.[16] reported association of HSP and rheumatic carditis in a 8-year old patient. Güven et al.[17] reported Mobitz type II AV block in a 9-year-old patient with HSP and rheumatic fever.

In our study, in the patient group, the MHR in surface ECG was found to be significantly higher than that of the control group (p=0.03). That was thought to be the result of the systemic inflammatory status and the accompanying abdominal pain and the arthralgia. In another patient, nonspecific T wave changes were observed. Mean PR interval was also similar between two groups. Also, Holter monitoring did not reveal any other asymptomatic rhythm and conduction abnormality.

In Holter monitoring mean of average, minimum and maximum heart rates and longest RR intervals were similar between study and control groups (Table 5). No significant arrhythmia was detected except for the infrequent premature beats. Additionally, the mean values of heart rate variability parameters were similar between the patient and control groups (Table 6). These results suggest that the HSP does not have a significant effect on the autonomic nervous system.

In children with HSP mild pericardial effusion and mild mitral regurgitation,[16] periluminal coronary artery thickening,[18] severe mitral regurgitation, left ventricular dilatation and hypertrophy and mitral valv prolapse,[19] pericardial tamponed[20] and left ventricular dilatation with depressed left ventricular systolic functions[21] had been reported. Lutz et al.[14] reported some magnetic resonance findings indicating myocardial involvement in a 19-year-old patient.

In our study, spontaneously disappearing mild pericardial effusion was detected in only one patient. Systolic and diastolic function parameters for both ventricles were found to be similar between study and control groups (Table 4). Aortic and pulmonary valve flow velocities showed some

differences, but it did not indicate a clinical significance (Table 4).

In conclusion, our results suggest that HSP rarely affects the cardiovascular system. Our study is important as it is the first prospective study performed on a relatively large child group. New studies performed on larger patient groups may show new results.

Conflict of Interest

We have no conflict of interest.

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Ethics Committee Permission

Atatürk University Faculty of Medicine Ethics Committee approved the study (Date 18.08.2011, sesion no 7, approvel number 20).

Authors' Contributions

Concept/Design: FB, NC, FL, HO. Data Collection and/or Processing: FB, NC, FL, HO. Data analysis and interpretation: FB, NC, FL, HO. Literature Search: FB, FL. Drafting manuscript: FB, NC. Critical revision of manuscript: FB, NC. Supervision: NC.

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