Cardiology in the Young

cambridge.org/cty

Increased QT and P-wave dispersion during attack-free period in pediatric patients with migraine attacks*

Oyku Tosun[1] and Elif Karatoprak[2]

[1]Department of Pediatric Cardiology, Medeniyet University Faculty of Medicine, Istanbul, Turkey and [2]Department of Pediatric Neurology, Medeniyet University Faculty of Medicine, Istanbul, Turkey

Original Article

Cite this article: Tosun O, Karatoprak E (2019) Increased QT and P-wave dispersion during attack-free period in pediatric patients with migraine attacks. *Cardiology in the Young* **29**: 488–491. doi: 10.1017/S1047951119000088

Received: 23 November 2018
Revised: 20 December 2018
Accepted: 7 January 2019

Key words:
Autonomic nervous system; electrocardiography; migraine; pediatrics

Author for correspondence:
Oyku Tosun, Department of Pediatric Cardiology, Medeniyet University Faculty of Medicine, Istanbul, Turkey.
Tel: +905053901685; Fax: +902165666614;
E-mail: isaltosun@hotmail.com

*The study is a single-centre original retrospective article.

Abstract

Introduction: Migraine is a common neurovascular disease characterised with recurrent attacks by pain-free periods. It has been suggested that both sympathetic and parasympathetic dysfunctions play a role in its pathophysiology. *Aim:* The aim of our study was to investigate the ECG changes during attack-free period in children with migraine, in terms of QTc interval, QTc, and P-wave dispersion to evaluate the autonomic nervous system disturbance. *Methods:* Sixty children who were diagnosed with migraine were included as patient group and 50 healthy, age- and body mass index-matched children who were examined for innocent murmur were included as control group. The patients' routine ECG records were screened from the outpatient clinic files. The durations of P-wave, QT, and QTc intervals and dispersion values and heart rates (beats/minute) were compared between the patient and control groups. *Results:* P maximum and P dispersion were significantly higher, and P minimum was significantly lower in the migraine group compared with the control group. QT–QTc maximum and QT–QTc dispersion were significantly higher and QT–QTc minimum was significantly lower in the migraine group compared with the control group. *Conclusion:* According to our findings, although migraine patients were asymptomatic and no arrhythmia was detected in the surface ECG, sympathovagal balance in the sympathetic system, which may be disrupted in favour of the sympathetic system, should continue even in the attack-free period, and we should be careful in terms of serious arrhythmias that may develop in these patients.

Migraine is a common neurovascular disease characterised with recurrent attacks by pain-free periods.[1] It has been suggested that both sympathetic and parasympathetic dysfunctions play a role in its pathophysiology.[2] Disturbance of the autonomic nervous system (ANS) may affect atrial and ventricular repolarisation. Disturbed autonomic innervation of the heart may cause possible ECG changes in patients with migraine.[3] Changes in these parameters appear to correlate with the severity of the autonomic dysfunction.[4–6]

QT dispersion has been suggested to be an ECG parameter that reflects the physiological variability of ventricular repolarisation. Increased QTc interval (corrected QT) and QTc dispersion have been reported to be indicators of risk for ventricular arrhythmias and sudden cardiac death in several studies.[7,8] P-wave dispersion has been shown to be related with inhomogeneous and discontinuous propagation of sinus node impulses and atrial fibrillation.[9,10]

Cardiac arrhythmias, QTc, and P-wave dispersion during migraine attack have been reported in studies on adults.[11,12] To the best of our knowledge, there is no information about QTc interval, QTc, and P-wave dispersion during attack-free period in children with migraine.

The aim of our study was to investigate the ECG changes during attack-free period in children with migraine, in terms of QTc interval, QTc, and P-wave dispersion to evaluate the ANS disturbance.

Methods

The data of 110 children who were referred to our pediatric cardiology and pediatric neurology outpatient clinic between March 2014 and June 2018 were retrospectively analysed from the outpatient clinic records.

Study population

Sixty children who were admitted to the pediatric neurology outpatient clinic with a diagnosis of migraine, according to the International Classification of Headache Disorders, 3rd edition (beta version) criteria in 2013,[13] were included in the study as the patient group. The outpatient clinic files recorded by the pediatric neurology physician were screened, and patients with detailed cardiovascular examination reports were included in the study.

CAMBRIDGE UNIVERSITY PRESS

Table 1. Demographic features of the patient and control groups

	Control group		Patient group		p
Sex	Female	30	Female	23	0.76
	Male	20	Male	37	
Age (months)	148.86 ± 33.27		147.93 ± 38.14		0.28
BMI (kg/m^2)	18.76 ± 4.11		18.26 ± 4.21		0.54
Systolic blood pressure (mmHg)	112.4 ± 2.03		110.2 ± 1.8		0.55
Diastolic blood pressure (mmHg)	59.2 ± 5.1		58.4 ± 4.4		0.59

BMI, body mass index.
Values are presented as mean ± standard deviation. The mean difference is significant at the 0.05 level.

Outpatient clinic files recorded by the pediatric cardiologist were also screened. Fifty healthy, age- and body mass index-matched children who had normal cardiovascular examination were included in the study as the control group. Only children who had standard 12-lead ECG information were included in the study.

Children with a known history of cardiovascular disease, arrhythmias, diabetes, hypertension, obesity, hyperlipidaemia, metabolic disorders, significant blood chemistry abnormalities, smoking, congenital or acquired heart disease, renal failure, chronic inflammatory disease, and those under medical treatment, especially taking arrhythmogenic medication, were excluded. A detailed cardiac examination, including ECG evaluation, in healthy controls and migraine patients, was normal. All the patients had sinus rhythm in ECG measurement.

Electrocardiography

The patients' routine ECG records were screened from the outpatient clinic files. A standard 12-lead ECG is defined as the ECG that is obtained in supine position at a paper speed of 25 mm/second and an amplitude of 10 mm/mV (NihonKohden ECG 1250K, Tokyo, Japan). All of the measurements were performed by the same pediatric cardiologist, and only the beats with normal sinus rhythm morphology were used. We used magnifying glass and compasses to increase sensitivity.

The beginning of the P-wave is defined as the first elevation from the isoelectric line for the positive waves and depression from the isoelectric line for the negative waves. The point of return to the isoelectric line is defined as the end of the P-wave. The longest P interval is defined as P maximum (milliseconds), and the shortest P interval is defined as P minimum (milliseconds). The difference between P-max and P-min durations on the ECG is defined as P-wave dispersion. For P-wave dispersion, at least three P-wave durations are averaged.

The distance from the beginning of the Q-wave to the last point where the T-wave returned to isoelectric line is defined as the QT interval (milliseconds). If U-waves are present, the shortest points between the T- and U-waves are accepted as the end of the T-wave. Biphasic T-waves are measured as the time of final return to baseline. The longest QT interval is defined as QT maximum (milliseconds), and the shortest QT interval is defined as QT minimum (milliseconds). QT dispersion is defined as the difference between QT maximum and QT minimum on a standard 12-lead ECG. QTc intervals (milliseconds) are calculated using Bazett's formula (QTc = QT interval/$\sqrt{}$RR interval). Patients whose QTc interval could be calculated in at least eight leads were included.

All measurements were done by the same experienced pediatric cardiologist. The durations of the P-wave, QT, and QTc intervals and dispersion values and heart rate (beats/minute) were compared between the patient and control groups.

Statistical analysis

Statistical data were evaluated using the Statistical Package for the Social Sciences for Windows software package (version 15.0; SPSS Inc., Chicago, IL, USA). Descriptive statistical methods (mean ± standard deviation) were used for the assessment of data. Student's t-test for the comparison of dual groups and chi-square test for the comparison of qualitative data were employed. P values <0.05 were considered statistically significant.

Results

Sixty children diagnosed with migraine (23 males, 37 females; mean age 147.93 ± 38.14 months; range 76–204 months) (patient group) and 50 healthy children (20 males, 30 females; mean age 148.86 ± 33.27 months; range 77–205 months) (control group) were enrolled. None of the subjects in both the patient and control groups reported a family history of arrhythmias. Transthoracic echocardiography and 12-lead ECG were normal in all children. None of the patients were receiving any treatment. No significant difference was detected between the patient and control groups in terms of age, sex, and body mass index. The demographic features of the patient and control groups are presented in Table 1.

P-wave, QT, and QTc interval durations and dispersion parameters, and heart rate values (beats/minute) were compared between the patient and control groups (Table 2).

P maximum was significantly higher and P minimum was significantly lower in the patient group compared with the control group ($p < 0.001$ and < 0.001, respectively). P-wave dispersion was significantly higher in the patient group as well ($p < 0.001$).

QT and QTc maximum were significantly higher, and QT and QTc minimum were significantly lower in the patient group ($p < 0.001$, <0.001; and $p < 0.001$, $p = 0.005$, respectively). QT and QTc dispersions were significantly higher in the patient group as well ($p < 0.001$, <0.005, respectively).

Resting heart rate (beats/minute) was found to be significantly higher in children with migraine as well ($p < 0.001$).

Discussion

It has been suggested that both sympathetic and parasympathetic dysfunctions play a role in migraine pathophysiology.[2] Disturbed

https://doi.org/10.1017/S1047951119000088 Published online by Cambridge University Press

Table 2. Comparison of ECG parameters between the patient and control groups

	Control group	Patient group	p
Heart rate/minute	76.80 ± 14.65	104.49 ± 20.44	<0.005
P duration (minimum), ms	70.31 ± 7.35	62.21 ± 8.84	<0.001
P duration (maximum), ms	95.35 ± 8.09	110.33 ± 6.09	<0.001
P dispersion, ms	23.851 ± 12.06	48.26 ± 9.86	<0.001
QT (minimum), ms	314.19 ± 9.49	307.68 ± 10.44	<0.001
QT (maximum), ms	347.68 ± 8.31	358.37 ± 16.37	<0.001
QT dispersion, ms	33.62 ± 6.55	50.72 ± 10.11	<0.001
QTc (minimum), ms	337.65 ± 11.79	361.61 ± 11.65	<0.005
QTc (maximum), ms	389.60 ± 14.61	400.75 ± 13.8	<0.001
QTc dispersion, ms	37.57 ± 14.6	48.13 ± 12.04	<0.005

ms, millisecond; QTc, corrected QT.
Values are presented as mean ± standard deviation. The mean difference is significant at the 0.05 level.

autonomic innervation of the heart may cause possible ECG changes in patients with migraine, and changes in these parameters appear to correlate with the severity of the autonomic dysfunction.[3–6]

Previous studies on adults[11] have reported ECG changes, such as sinus bradycardia, ventricular extrasystoles, and non-specific ST-T segment changes, during migraine attacks and migraine-free period. Aygun et al.[14] reported prolonged QTc interval during migraine attacks. A study by Appel et al.[15] showed increased sympathetic activity and decreased parasympathetic activity in patients with migraine.

To the best of our knowledge, there are no studies evaluating the ECG aspects of pediatric patients with migraine during attack-free period.

It has been shown that QT dispersion is an ECG parameter that reflects the physiological variability of ventricular repolarisation, and prolonged QTc interval and QTc dispersion have been reported to be an indicator of risk for ventricular arrhythmias and sudden cardiac death in several studies.[7,8] Also, P-wave dispersion has been shown to be related with inhomogeneous and discontinuous propagation of sinus node impulses and atrial fibrillation.[9,10]

In our study, during the attack-free period, mean QT and mean QTc dispersion (50.72 ± 10.11, 48.13 ± 12.04 ms, respectively) in children with migraine were significantly higher compared with the control group. QT dispersion >40 ms was reported to have 88% sensitivity and 57% specificity for the development of ventricular repolarisation heterogeneity and is considered a marker for the prediction of inducibility of sustained ventricular tachycardia.[16] In our study we found a significant decrease in the minimum (QT and QTc) intervals and increase in the maximum (QT and QTc) intervals in the migraine group. We assumed that these findings are related to sympathetic hyperactivity that can be seen even during the attack-free period in migraine patients. Heart rate values were significantly higher in the migraine group. This finding also represents sympathetic hyperactivity, which is known to be a factor affecting changes in QT and QTc intervals.[16]

In our study, children with migraine showed significantly lower duration of P minimum and significantly higher duration of P maximum and P dispersion compared with the control group. It has been shown that P dispersion >40 ms is a marker of the risk of atrial arrhythmias.[17] So, we thought that these patients have increased sympathetic activity and impaired sympathovagal balance even during an attack-free period, and these changes can suggest a risk for atrial arrhythmias.

Limitation

Long-term follow-up of patients with migraine for arrhythmias is needed.

Conclusion

According to our findings, although the patient group was asymptomatic and no arrhythmias were detected in their surface ECG, sympathovagal balance disrupted in favour of the sympathetic system continued even during the attack-free period, and we should be careful in terms of serious arrhythmias that may develop in these patients.

Author ORCIDs. Oyku Tosun 0000-0003-1031-273X

Financial Support. The authors received no financial support for the research and/or authorship of this article.

Grant support and financial disclosures. None.

Conflict of interest. The authors declared no conflicts of interest with respect to the authorship and/or publication of this article.

Ethical Standards. The local ethical committee of our hospital approved this retrospective study on 18 July, 2018 with 2018/0276 report number. As the study was retrospective and the patients' routine ECG data were screened, informed consent was not applicable.

References

1. Lipton RB, Bigal ME. Migraine: epidemiology, impact and risk factors for progression. Headache 2005; 45: 3–13.
2. Havanka-Kanniainen H, Tolunen U, Myllyla VV. Autonomic dysfunction in migraine: a survey of 188 patients. Headache 1988; 28: 465–470.
3. Koçer A, Eryılmaz M, Tutkan H, Ercan N, Küçükbayrak ZS. Higher P-wave dispersion in migraine patients with higher number of attacks. Sci World J 2012; 2012: 791460.
4. Bellavere F, Ferri M, Guarini L, et al. Prolonged QT period in diabetic autonomic neuropathy: a possible role in sudden cardiac death? Br Heart J 1998; 59: 379–383.
5. Yılıdırır A, Aksoyek S, Calguneri M, et al. QT dispersion as a predictor of arrhythmic events in patients with ankylosing spondylitis. Rheumatology 2000; 39: 875–879.
6. Galinier M, Vıalette JC, Fourcade J, et al. QT interval dispersion as a predictor of arrhythmic events in congestive heart failure. Importance of aetiology. Eur Heart J 1998; 19: 1054–1062.
7. Barr CS, Naas A, Freeman M, Lang CC, Struthers AD. QT dispersion and sudden unexcepted death in chronic heart failure. Lancet 1994; 343: 327–329.
8. Zabel M, Klingenheben T, Franz MR, Hohnloser SH. Assessment of OT dispersion for prediction of mortality or arrhytmic events after myocardial infarction: results of prospective, long-termfollow-up study. Circulation 1998; 97: 254–350.
9. Dilaveris PE, Gialafos EJ, Sidesis S, et al. Simple electrocardiographic markers for prediction of paroxysmal idiopathic atrial fibrillation. Am Heart J 1998; 135: 773–778.
10. Dilaveris PE, Gialafos EJ, Andrikopoulos GK, et al. Clinical and electrocardiographic predictors of recurrent atrial fibrillation. Pacing Clin Electrophysiol 2000; 23: 352–358.

https://doi.org/10.1017/S1047951119000088 Published online by Cambridge University Press

11. Jhee SS, Salazar DE, Ford NF, et al. Monitoring of acute migraine attacks: placebo response and safety data. Headache 1998; 38: 35–38.
12. Duru M, Melek I, Seyfeli E. Q Tc dispersion and P-wave dispersion during migraine attacks. Cephalalgia 2006; 26: 672–677.
13. Headache Classification Committee of the International Headache Society (IHS). The international classification of headache disorders, 3rd edition (beta version). Cephalalgia 2013; 33: 629–808.
14. Aygun D, Altıntop L, Doganay Z, Guven H, Baydın A. Electrocardiographic changes during migraine attacks. Headache 2003; 43: 861–866.
15. Appel S, Kuritzky A, Zahavi I, Zigelman M, Akselrod S. Evidence for instability of the autonomic nervous system in patients with migraine. Headache 1992; 32: 10–17.
16. Diedrich J, Jordan JR, Shannon D, et al. Modulation of QT interval during autonomic nervous system blockade in humans. Circulation 2002; 106: 2238–2243.
17. Dilaveris E, Gialafos JE. P wave dispersion: a novel predictor of paroxysmal atrial fibrillation. Ann Noninvasive Electrocardiol 2001; 6: 159–165.

https://doi.org/10.1017/S1047951119000088 Published online by Cambridge University Press