

Effects of Tilt Test and Beta-Adrenergic Stimulation on the QT Interval in Normal Children and Pediatric Patients With Unexplained Syncope

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In normal children, any procedure that increases heart rate, such as the tilt test, may shorten the QT interval. The effect of the tilt test on QT interval in children with syncope remains unknown.

We analyzed the responses of RR and QT intervals during a tilt test in 3 groups of children: 28 healthy children (group 1), 26 with syncope of unknown etiology and negative tilt test results (group 2), and 17 with vasovagal syncope (group 3).

During the tilt test, RR and QT intervals were significantly shortened in groups 1 and 2. In group 3, the RR interval was lengthened during syncope whereas the QT interval remained constant.

QT interval lengthening during the tilt test is not a characteristic finding in normal children or in children with vasovagal syncope.

Key words: *Adrenergic. Autonomous nervous system.*

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INTRODUCTION

The electrocardiographic QT interval gives an indirect measure of the duration of the ventricular action potential, which includes depolarization and repolarization.¹ The duration of the ventricular action potential is influenced by many factors, particularly by the heart rate and its autonomic modulation. Sympathetic nervous system activity shortens the QT interval, whereas parasympathetic nervous system

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En niños normales, las maniobras que aumentan la frecuencia cardíaca acortan el intervalo QT. La prueba de la mesa basculante aumenta la frecuencia cardíaca y debería acortar el intervalo QT en niños sanos. Se desconoce el efecto de esta prueba en niños con síncope.

Se analizó el comportamiento de los intervalos RR y QT durante la prueba de la mesa basculante con isoproterenol en 3 grupos de niños: 28 sanos (grupo 1), 26 con síncope de etiología no precisada y prueba de la mesa basculante negativa (grupo 2) y 17 con síncope vasovagal (grupo 3).

Durante la prueba, los intervalos RR y QT se acortaron significativamente en los grupos 1 y 2. En el grupo 3, el intervalo RR se prolongó en el momento del síncope y el intervalo QT se mantuvo constante.

La prolongación del intervalo QT durante la prueba de la mesa basculante no es una característica de niños normales ni con síncope vasovagal.

Palabras clave: *Adrenérgico. Sistema nervioso autónomo.*

activity lengthens it.² Any imbalance between these two systems causes QT interval dispersion and eventually prolongs the QT interval, with consequent increases in the risks of arrhythmia and sudden death in individuals who suffer from congenital long QT syndrome.³ Adrenergic activity shortens the QT interval and increases the heart rate. In normal children and adolescents, any maneuver that increases the heart rate shortens the QT interval.^{4,5} Like other maneuvers that stimulate adrenergic activity, the tilt-table test, with or without the use of isoproterenol, increases the heart rate and shortens the QT interval in healthy children. In addition, it could prolong the QT interval in patients with congenital long QT syndrome.^{6,7} As well as having a role in the diagnosis of syncope, the tilt-table test could prove useful in evaluating autonomic nervous system function.

ABBREVIATIONS

TTT: Tilt-Table testing.
 SUE: syncope of unknown etiology.
 SUE-TTT: syncope of unknown etiology who had negative results on Tilt-Table
 VS: vasovagal syncope.

Our aim was to study changes in QT interval during tilt-table testing in: *a)* normal children; *b)* children with syncope of unknown etiology, and *c)* children with vasovagal syncope, all without congenital long QT syndrome.

PATIENTS AND METHODS

Study Population

A total of 28 healthy children (group 1), 26 children with syncope of unknown etiology who tested negative on the tilt-table test (group 2), and 17 children with vasovagal syncope (group 3) were studied. The general characteristics of the groups are shown in Table 1. Children with congenital long QT syndrome were excluded.⁸

Tilt-Table Test

Tilt-table testing was carried out using isoproterenol. The protocol used was as follows: period of rest in a reclining position (5 min); isoproterenol administration by infusion pump (0.25–1 g/min), during which the dose was raised every 3 min until the basal heart rate increased by 30%; and

inclination of the tilt-table by 70° (for 20 min maximum). Arterial pressure was measured every minute using an oscillometer and the electrocardiogram was recorded. The classification of hemodynamic responses proposed by the European Syncope Group in 1992⁹ was used to determine whether the test gave a positive result (i.e., vasovagal syncope). The criteria for a positive result were: systolic hypotension of less than 85 mm Hg accompanied by fatigue, imminent faint or loss of consciousness, sinus bradycardia, or a nodal rhythm less than 40 beats/min.

Measurement of QT and RR Intervals

Measurements were made manually using a compass by a cardiologist in a blinded manner. The QT interval was measured from the start of the QRS complex to the end of the T wave¹⁰ during the time when the RR interval was at a minimum. In patients who had a positive result on tilt-table testing, the QT interval was measured when the bradycardia was most severe (i.e., when the RR interval was at a maximum). The corrected QT interval (QTc), which is corrected for heart rate, was determined using Bazett’s formula.¹¹

Statistical Analysis

Results are expressed in terms of mean±standard deviation. Comparisons were made using an analysis of variance for repeated measurements or single-factor ANOVA. *P* values less than .05 were considered statistically significant.

RESULTS

Basal RR, QT and QTc intervals were similar and within normal limits in the 3 groups studied (Table 2).

TABLE 1. General Characteristics of the Groups Analyzed*

Variable	Group 1: Healthy Children (n=28)	Group 2: SUE-TTT(-) (n=26)	Group 3: VS (n=17)	<i>P</i>
Age, years	9.6±2	10.8±2.7	11±2.4	NS
Weight, kg	36.2±9.6	39.5±9.5	43±11.7	NS
Height, m	141±11.6	147±14	149±14.8	NS
Female sex	14 (50%)	19 (73%)	8 (47%)	NS

*SUE-TTT(-) indicates children with syncope of unknown etiology who had negative results on tilt-table testing; VS, children with vasovagal syncope; NS, not significant (*P*>.05). Results are expressed as mean±standard deviation. Between-group comparisons were made using ANOVA and the chi-squared test.

TABLE 2. RR, QT and QTc Intervals in the 3 Groups Studied*

Variable	Group 1: Healthy Children (n=28)	Group 2: SUE-TTT(-) (n=26)	Group 3: VS (n=17)	<i>P</i>
Basal RR, ms	719±29	698±26	735±42	NS
Final RR, ms	490±15 [†]	494±17*	844±72 [†]	
Basal QT, ms	364±7	356±6	354±8	NS
Final QT, ms	323±6 [†]	317±7 [†]	355±8	
Basal Qtc, ms	435±9	428±7	425±11	NS
Final Qtc, ms	464±9 [†]	454±10 [†]	393±12 [†]	

*SUE-TTT(-) indicates children with syncope of unknown etiology who had negative results on tilt-table testing; VS, children with vasovagal syncope; NS, not significant (*P*>.05). Results are expressed as mean±standard deviation. Between-group comparisons were made using analysis of variance. [†]*P*<.05 compared with basal value.

The RR interval shortened significantly during the tilt-table test in groups 1 and 2, by 32% and 29%, respectively ($P < .05$). The QT interval shortened significantly in groups 1 and 2, by 12% and 11%, respectively ($P < .05$), in a way that was consistent with the tachycardia induced during the test. In group 3, the RR interval lengthened by 13% during syncope but the QT interval did not alter during the period of maximum bradycardia. The QTc interval was significantly longer in groups 1 and 2 and significantly shorter in group 3.

DISCUSSION

The autonomic nervous system modulates ventricular repolarization. Tilt-table testing provides a means of analyzing physiological responses to orthostasis, in terms of both sympathetic and vagal activity.^{12,13} In healthy individuals, standing or being tilted upright on a tilt-table increases sympathetic activity, decreases parasympathetic activity, and raises plasma norepinephrine and renin levels.^{14,15} In healthy subjects, any maneuver that shortens the action potential in myocardial cells will also shorten the QT interval. This has been demonstrated during orthostatic maneuvers, adrenergic stimulation, and stimulation by atrial pacemakers.⁵

In our patient series, adrenergic stimulation and tilt-table testing shortened the QT interval in healthy children and in those with syncope of unknown etiology. In these subjects, there was no evidence of autonomic dysfunction characterized by shortening of the QT interval during increases in heart rate. They demonstrated appropriate responses.

In patients with vasovagal syncope, sympathetic hyperactivity causes reflex sympathetic suppression and vagal hyperactivity (i.e., the Bezold-Jarisch reflex), resulting in hypotension and bradycardia.^{12,13,16}

There is controversy about how adrenergic stimulation alters the QT interval in both children and adults with vasovagal syncope. According to the findings of Balaji et al,⁶ beta-adrenergic stimulation increases the heart rate and shortens the QT interval in normal individuals, but not in children with vasovagal syncope. In contrast, Salim and DiSessa failed to demonstrate QT interval prolongation in patients who were positive on the tilt-table test.¹⁷ Jaeger et al¹⁸ did not observe QT interval prolongation in adults with vasovagal syncope when bradycardia was at a maximum during tilt-table testing. They suggest that “paradoxical” modulation of the QT interval acts as an autonomic “buffer.”¹⁸ In our patients with vasovagal syncope, the autonomic activity that triggered bradycardia did not prolong the QT interval.

For decades, it has been suggested that the QT interval must be corrected according to heart rate, thereby giving the QTc value, so that different

individuals can be compared. To do this, Bazett’s formula is most often employed.⁸ It assumes that there is a fixed relationship between QT interval and heart rate, and that the way in which the former adapts to changes in the latter is identical in different individuals. In fact, it is known that the way in which the QT interval adapts to variations in heart rate can be influenced by numerous factors.^{1,2} Moreover, Bazett’s formula overcorrects the QT interval at high heart rates, which are common in children. The result is that the value of the denominator in the formula is reduced, thereby “falsely prolonging” the QT interval and leading to erroneous diagnoses of long QT syndrome.^{19–21} This may explain the significant variations in QTc interval that were found in groups 1, 2, and 3, which distorted our results (Table 2).

The tilt-table test is useful for evaluating autonomic nervous system modulation. Used in conjunction with isoproterenol administration, the test provides adrenergic stimulation and can help in the study of QT interval variations. In practice, we rarely administer isoproterenol and use it only when the test has not produced a clear diagnostic result or when there is an interest in investigating changes in QT interval.²²

CONCLUSIONS

The QT interval was not prolonged in any of the groups studied. Prolongation of this interval during testing was not a characteristic of either normal children or those with vasovagal syncope.

Prospective studies of patients with congenital long QT syndrome should be carried out to investigate QT interval variations. When there is a positive test result, the possibility that QT interval prolongation during tilt-table testing indicates the presence of congenital long QT syndrome should be considered and systematic measurement of the QT interval during pediatric tilt-table testing should be carried out.

It is essential that QTc interval measurements should be used with caution as false diagnoses of congenital long QT syndrome may be made.

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