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Short Versus Long Head-up Tilt Test Protocols to Evaluate Vasovagal Syncope in Children

Çocuklarda Vazovagal Senkopu Değerlendirmek için İki Farklı Eğik Masa Testi Protokolünün Karşılaştırılması

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ABSTRACT

Objective: Vasovagal syncope is a common clinical problem in children and adolescents, for which the head-up tilt test (HUTT) is the standard diagnostic procedure. In this study, we evaluated sublingual nitroglycerine-stimulated HUTT protocols, comparing the results with passive phases of 20 minutes versus 45 minutes.

Method: A total of 293 patients aged 6 to 18 years with a history of recurrent syncope were studied. Physical examination, laboratory parameters, and echocardiographic examination were normal in all. The patients underwent standard HUTT with sublingual nitroglycerin used in the active phase. A short protocol was used for one group (n=143) with a passive phase of 20 minutes, while testing in the others (n=150) comprised a long protocol, with a passive phase of 45 minutes.

Results: There were no significant differences between the two groups in terms of age, sex, and length of time between the first syncope and the tilt test. In the short protocol group, HUTT results were positive in 43(30.1%) in the passive phase, 40(28%) in the active phase, and 83(58%) overall, compared with 65(43.3 %), 32(21.3%), and 97(64.7%), respectively, in the long protocol group. Among those in the long protocol group, 26 of 32 (81.5%) who had a positive response in the passive phase developed syncope within the first 20 minutes.

Conclusion: The HUTT protocol with a short passive phase has the advantage of saving time while providing results comparable with the long protocol, which might be preferable in children and adolescents.

Keywords: children, head-up tilt test, vasovagal syncope

ÖZ

Giriş: Vazovagal senkop, çocuklarda ve ergenlerde hayat kalitesini bozan yaygın bir problemdir. Tanı aşamasında eğik masa testi (HUTT) standart tanı prosedürüdür. Günümüze kadar farklı protokoller kullanılmıştır. Bu çalışmamızda 20 dakika veya 45 dakika pasif faz sonrası sublingual nitrogliserin ile provakasyon uygulanan iki ayrı eğik masa testi protokolü karşılaştırıldı.

Yöntem: Tekrarlayan senkop öyküsü olan 6-18 yaşları arasında toplam 293 hasta incelendi. Fizik muayene, laboratuvar parametreleri ve ekokardiyografik incelemeleri normal olan hastalar çalışmaya dahil edildi. Grup 1'de (n =143) 20 dakikalık pasif fazlı kısa bir protokol kullanılırken, grup 2'de (n =150) 45 dakikalık pasif fazlı uzun bir protokol kullanılmıştır. Aktif Fazda tüm hastalara sublingual nitrogliserin uygulandı.

Bulgular: İki grup arasında yaş, cinsiyet ve ilk senkop ile tilt testi arasında geçen süre açısından anlamlı fark yoktu. Kısa protokol grubunda, 43'ünde (% 30,1) pasif fazda, 40'ında (% 28) aktif fazda olmak üzere hastaların %58'inde test pozitif saptandı. Uzun protokol grubunda ise pasif fazda 65 (%43,3), aktif fazda 32 (%21,3) toplamda 97 (%64,7)hastada test pozitif saptandı. Uzun protokol grubunda pasif fazda senkop gelişen 32 hastadan 26'sında (% 81,5) senkop ilk 20 dakika içinde gelişti.

Sonuç: Kısa pasif fazlı HUTT protokolü, çocuklarda ve ergenlerde uzun protokolle kıyaslanabilir sonuçlar verirken zamandan da tasarruf etme avantajı sunar.

Anahtar Kelimeler: çocuk, eğik masa testi, vazovagal senkop

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INTRODUCTION

Syncope is a sudden, transient loss of consciousness and postural tone, which is usually preceded by a short period of symptoms and signs called presyncope with a spontaneous, rapid, complete recovery (1). Syncope is a common problem among children and adolescents, with up to 15% of that age population reporting at least one episode by early adulthood. Although most of patients with syncope have a benign etiology, syncope is a leading cause of referral to pediatric cardiologists, and results in considerable excessive testing and expense (2).

Vasovagal syncope (VVS) is the eventual diagnosis for the vast majority of children referred to pediatric cardiologists for syncope (3). One of the widely used tools is the head-up tilt test (HUTT) for diagnosing syncope in children. It is an orthostatic stress test to evaluate vasovagal response to a postural change from a supine to a standing position. Since HUTT came in to use in 1986, different protocols have been reported to increase to the sensitivity of the test. Variations in tilt methodology, with different tilt angles, test duration, and pharmacologic stimulation, have been introduced in an attempt to define optimal protocols for specific patient populations (4-7). Most HUTT protocols include a passive phase and an active drug-provocation phase.The latest guidelines for the diagnosis and management of syncope endorsed by European Society of Echocardiography recommend nitroglycerin (NTG) or isoproterenol for provocation in the active phase, following a passive phase lasting at least 20 min to 45 min (7). One of the most commonly used HUTT protocol is the İtalian with 20-minute passive phase and 400 µg of nitroglycerin provocation. However, there are no specific HUTT protocol recommendations for children and adolescents. In this study, we aimed to evaluate the results of two HUTT protocols in pediatric patients, comparing short passive phase of 20 minutes with long passive phase of 45 minutes, followed in both cases by an NTG-stimulated active phase.

MATERIAL AND METHODS

Patient Characteristics

Patients younger than 18 years of age presenting to our outpatient pediatric cardiology clinic for evaluation of a principal complaint of syncope were enrolled in the study. Demographics and clinical characteristics including signs, symptoms, and consequences of the syncopal event as well as relevant past medical and family history were recorded. All the patients with syncope in our study experienced at least one episode of syncope and/or presyncope. Patients who had a history of structural heart disease, arrhythmia, seizure, or systemic disease were excluded from the study. Physical examination, 12-lead electrocardiogram, transthoracic echocardiography, and 24-hour Holter monitoring were normal in all of the patients.

Head-up Tilt Test

Oxygen, suction, and resuscitative equipment was immediately available in the HUTT lab. A physician and registered nurse accompanied toall patientsduring the procedure. To avoid potential interference from diurnal autonomic variability, all tests were performed between 8 a.m. and 10 a.m. The patients were tested in a quiet room maintained at an appropriate temperature after at least a 4-h fast. Arterial blood pressure measurements weredone using an ambulatory blood pressure monitor. Heart rate and 12-lead electrocardiography were monitored throughout the procedure. We used a tilt table with footboard support. A baseline electrocardiogram and blood pressure were recorded when the patients were in the supine position for 5 min.

We compared two HUTT protocols differing only in the length of the passive phase. The 193 patients in the study were randomly assigned to a short protocol with a 20-min passive phase (n = 143) or a long protocol with a 45-min passive phase (n = 150). In all other respects, the HUTT procedures were the same. The test sequence comprised a resting phase in the supine position for 5 min, a drug-free 70º-tilt passive phase for the designated length of time in each group, and a 70º-tilt active phase for 15 min after administration of 400 µg of sublingual NTG.

Patients who developed syncope or presyncopal symptoms at any point were immediately returned to the supine position and allowed to recover. Positive responses were reported using the modified VASIS classification (8-10). A prominent drop in systolic arterial blood pressure without a marked decrease in heart rate during symptoms was denominated as vasodepressor response. A sudden decrease in heart rate with or without asystole was designated as cardioinhibitory response. A mixed response was defined as reductions in both blood pressure and heart rate.

Patients with orthostatic hypotension and paroxysmal orthostatic tachycardia syndrome were not included into the study as HUTT with passive phases of 3 min and 10 min are sufficient for diagnosis of these conditions.

Statistical Analysis

Data are expressed as the mean ± standard deviation for continuous and normally distributed variables and the median (range) for variables with a skewed distribution. Data was analyzed with the t-test, chi-square test, or Mann-Whitney U test as appropriate. IBM SPSS 20.0 (SPSS Inc., Chicago, IL, USA) was used to analyze the data, and a p value ≤0.05 was considered to indicate a significant difference.

RESULTS

A positive HUTT response to was observed in 83 patients (58%) with the short protocol and 97 patients (64.7%) with the long protocol. There were no significant differences between the two groups in terms of age, sex, age at first syncope, and length of time between the first syncope and HUTT (Table 1).

For the short protocol group, HUTT results were positive for 43 (30.1%) in the passive phase, 40 (28%) in the active phase, and 83 (58%) overall, compared with 65 (43.3%), 32 (21.3%) and 97 (64.7%) in the long protocol group, respectively (Table 2). There is no statistically significant difference between the two protocols (p = 0.060). According to the modified VASIS classification, a mixed response was the most prevalent type in both groups (Table 3).

Table 1: Demographic and Clinical Characteristics of Patients Undergoing Head-up Tilt Table Testing

	Short protocol (n = 143)		Long protocol (n = 150)		p
	n	&	n	&	
Age (Months)	155 ± 38		148 ± 34		0.115
Sex (Female)	83	58	100	66	0.128
Number of syncopes	3.2 ± 3.7		3.8 ± 4.7		0.288
Onset of symptoms before testing (Months)	12 ± 15		8.5 ± 10.6		0.055
Age at first syncope (Months)	140 ± 40		140 ± 36		0.981

**p = 0.060 by Pearson chi-square test*

Table 2: Positive Head-up Tilt Table Test Responses in the Passive or Active Phase*

	Passive Phase		Active Phase		Total	
	n	%	n	%	n	%
Short protocol	43	30.1	40	28	83	58
Long protocol	65	43.3	32	21.3	97	64.7

Table 3: Type of Response During Head-up Tilt Table Testing*

	Negative		Cardioinhibitory		Vasodepressor		Mixed	
	n	%	n	%	n	%	n	%
Short protocol	60	42	16	11.2	19	13.3	48	33.6
Long protocol	53	35.3	15	10	30	20	52	34.7

**p* = 0.403 by Pearson chi-square test

During the passive phase, the median time to syncope was 9 min (1–20 min) in the short protocol group and 11 min (1–42 minutes) in the long protocol group (Figure 1). In the latter group, syncope occurred within the first 20 minutes of the passive phase in 81.5% (26 of 32) of those with a positive response in this phase. During the active phase, the median time to syncope in the short protocol group was 7.5 min (1–15 min) and 6 min (1–15 min) in the long protocol group (Figure 2).

DISCUSSION

Syncope characterized by a rapid onset and spontaneous complete recovery is a temporary loss of consciousness and results from transient cerebral hypoperfusion (7). About 15% of children experience a syncopal episode during thechildren and adolescence period, with VVS being the most common cause of syncope (11,12).

A syncopal episode typically is preceded by a precipitating factor and prodromal stage. Precipitating events include physical or emotional stress, long standing although certain activities (such as swallowing, hair grooming, or micturition) have also been reported to precipitate syncope (13). Contributing factors include dehydration, heat, crowding, stress, illness, anemia, and high basal vagal tone (1). Patients typically have at least oneprodromal symptom, such as lightheadedness, dizziness, reducedvisual acuity, nausea, pallor, and diaphoresis. Vasovagal syncope is more frequent in adolescents than in younger children and in girls when compared to boys (14). In our study, the demographics were as expected, with an average age of 13.21 ± 3.08 years and the majority of patients being girls (Table 1).

HUTT is a safe and recommended method for diagnosis of VVS. There has been no reported death during the test. Minor side effects commonly seen in the procedure include palpitations with isoproterenol administration and headache with NTG. However, even though the risk is low, it is recommended that resuscitation equipment be available (7).

We observed no complications during either the passive or active phase, for which we used NTG. HUTT creates blood pooling together with a decrease in venous return due to orthostatic stress and immobilization, which results in reproduction of a neurally mediated reflex leading to VVS in a laboratory setting. It is thought that abnormal cardiac autonomic reflexes occurring during the test lead to inappropriate vasodilatation (vasodepressor syncope), inappropriate bradycardia (cardioinhibitory syncope), or both (mixed response)(15). Our positivity rate for NTG-provoked HUTT in children was similar to that seen in adult studies, where it ranges from 51% to 78%. Among our study children with positive NTG-provoked HUTT, the mixed response was the most prevalent.

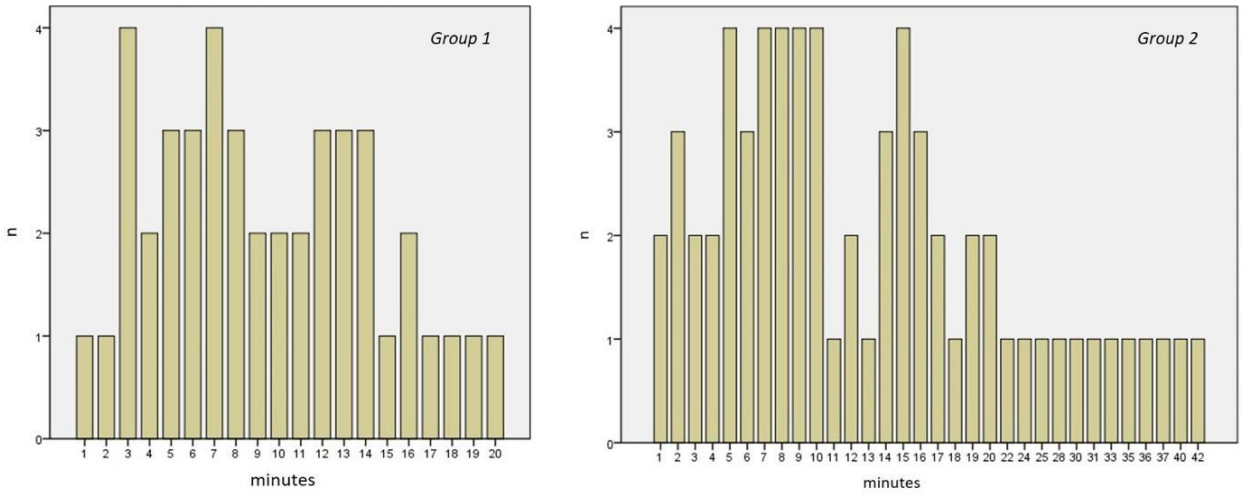

Figure 1: Numbers of patients developing syncope at each minute during the passive phase of had-up tilt table testing with a short (left) versus long (right) passive phase.

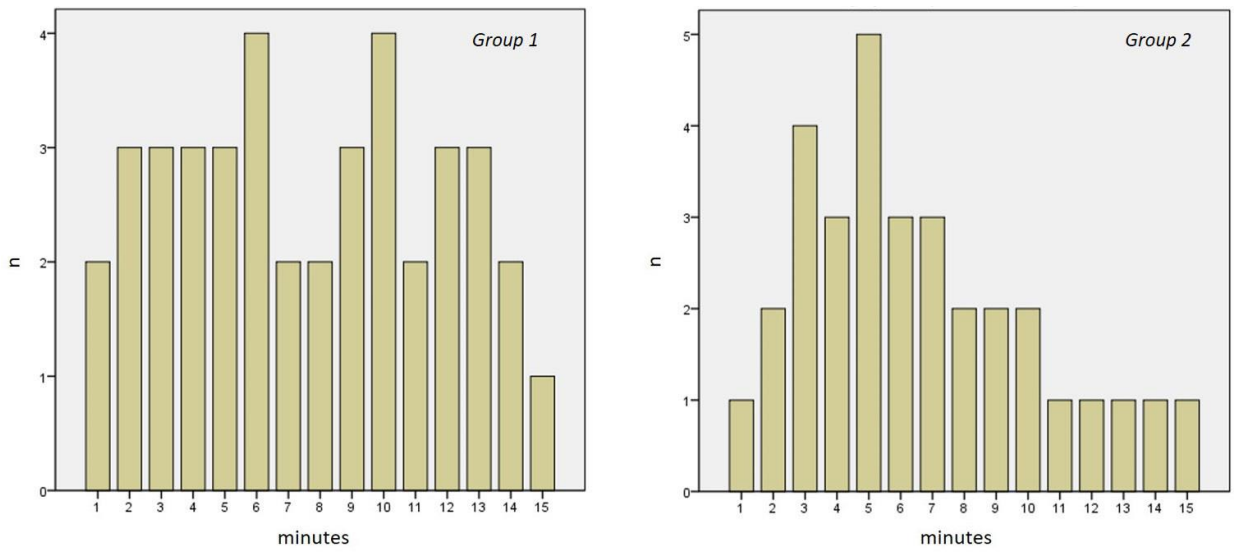

Figure 2 : Numbers of patients developing syncope at each minute during the active (drug-provoked) phase of head-up tilt table testing after a short (left) versus long (right) passive phase.

Kenny et al. introduced HUTT in 1986 to the clinical practice for the evaluation of patients with syncope of unknown origin (16). Since then, diverse protocols have been used applying differenttest duration and type of support, various pharmacologic provocations and tilt angle. The sensitivity and specificity of various protocols have been reviewed in detail (7).

There is no consensuson the optimal duration of the drug-free passive phase or the active phase with pharmacologic stimulation.As noted by Moya, et al, a longer passive phase increases the positivity rate during that phase but is prone to decrease the proportion of patients who fainted during the active phase. On the other hand, different test durations have no significant influence on the sensitivity of tilt testing. HUTT with a shorter passive phase could underestimate the number of patients with a positive response, but then a greater number of syncopal episodes could be detected during the active phase. Based on these data, an overlap is seen between the positive results from the passive and active phases of the test. A passive phase lasting from a minimum of 20 min to a maximum of 45 min is recommended by the current syncope guidelines (7).

The Westminster Hospital in London was performed one of the first HUTT protocols without any provocation agents, which solely used a footboard and a table set at 60°. This protocol called the basal or Westminster protocol was reported to have a sensitivity of 75% and specificity of 93% (4). During the Westminster protocol patients was supported at an angle of 60° for 45 min. Because the HUTT takes a long time, the duration of the test was questioned by Stein et al., who analyzed results from 11 published studies of results using the Westminster protocol (17). They compared the results in those studies with those from 213 patients for whom they performed HUTT for 30 to 60 min. The authors found that diagnostic accuracy did not significantly improve when a test lasted for more than 30 min.

The route of administration of nitrates (intravenous NTG, sublingual NTG in tablets or aerosol, and isosorbide dinitrate), the dose and angle of inclination (60º or 70º), duration of tilting before and after administration of the drug show differences between several protocols (18). Shortening the duration of the test could reduce tilt-related time and cost, but it might also underestimate the rate of positivity. Extending the duration of the test can improve the positivity rate, but it is unsuited for weaker patients who may not be able to achieve the test end-point (19). Therefore, an appropriate duration is an important factor, both of the test as a whole and of each phase.

The 2009 European Society of Cardiology Syncope Guideline recommends a minimum of 20 minutes of passive tilt before the administration of isoproterenol or NTG. In order to increase the diagnostic yield of HUTT, several provocative agents have been proposed. The purpose of the active phase is to increase the yield of the test beyond what might be achieved with passive tilt only. These pharmacologic agents increase the effect of tilt-induced orthostatic stress and precipitate neurally mediated syncope by rising sympathetic stimulation and/or increasing venous pooling(7).A meta-analysis conducted by Forleo et al. demonstrated that provocative protocols in comparison to the ones of unmedicated were associated with increased sensitivity but decreased specificity (6). However, when pharmacologic protocols were assessed by multivariate analysis, NTG significantly raised the diagnostic yield with a specificity similar to that achieved with isoproterenol.

Because the patient´s salivation and mastication capacity has not an effect on aerosol formulations of NTG, these agents have better bioavailability with more homogeneous absorption (18). A recent study compared the two protocols (with and without a 5-min rest period before NTG administration in the supine position) reported no differences in the positivity rates (61% versus 60%) or in specificity (92% versus 90%) (20).

Due to the widespread use of HUTT as a diagnostic tool for VVS, the use of different tilt protocols leads to high heterogeneity in test outcomes. Protocols including pharmacologic provocation are more sensitivity and less specific than passive protocols. NTG-stimulated HUTT reportedly has greater diagnostic capability than protocols using isoproterenol (6). Sublingual NTG appears to be timesaving and is better tolerated, avoiding placement of an intravenous catheter, which makes it preferable for children (21).In our study, sublingual NTG for HUTT was safe and well tolerated.

A critical point in the methodology is identifying the optimal tilt angle to maximize the number of true positive responses while minimizing the number of false positives leading to an incorrect diagnosis of VVS. Recent guidelines recommend the performance of HUTT with a table angle between 60° and 70°(7). We used 70°in our study.

CONCLUSION

Tilt testing is a safe and well tolerated procedure which may provide a diagnosis for unexplained syncope. Our study in children and adolescents supported the use of a protocol with a passive phase of only 20 minutes, which has the advantage of being timesaving. Thus, it may be preferable to longer protocols. However, it should be remembered that a longer passive phase may produce a higher rate of positivity in that phase. More number of subjects are diagnosed with VVS by HUTT potentiated with sublingual NTG. Larger studies in diverse populations and longer-term follow-up are needed to clarify the effectiveness of the proposed abbreviated HUTT protocol in the assessment of patients with suspected VVS.

Study Limitations

The results of this study were compared with those from other published studies using various protocols. There was no control group of patients without a history of syncope with which to evaluate false positive rates for the short or long passive phase. To avoid the potential risks and costs of repeated HUTT, we did not include a crossover study, testing both methods in each patient.

Conflict of Interest

The authors declare that there is no conflict of interest.

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Ethic Committee Approval

The study was approved by the ethics committee of Kocaeli University Research and Application Hospital (KÜ GOKAEK/2019/306). Written informed consent forms were obtained from the parents and/or relatives of all the patients in the study.

Informed Consent

Written informed consent forms were obtained from the parents and/or relatives of all the patients in the study.

Authors Contributions

The authors' contribution rates in the study are equal

REFERENCES

1. Sapin SO. Autonomic syncope in pediatrics: a practice-oriented approach to classification, pathophysiology diagnosis and management. Clin Pediatr. 2004;43:17-23.
2. Johnson ER, Etheridge SP, Minich LL, Bardsley T, Heywood M, Menon SC. Practice variation and resource use in the evaluation of pediatric vasovagal syncope: are pediatric cardiologists over-testing? Pediatr Cardiol. 2014;35:753-58.
3. Paris Y, Toro-Salazar OH, Gauthier NS, Rotondo KM, Arnold L, Hamershock Ret al. Regional Implementation of a Pediatric Cardiology Syncope Algorithm Using Standardized Clinical Assessment and Management Plans (SCAMPS) Methodology. J AmHeartAssoc. 2016;5:e002931.
4. Fitzpatrick AP, Theodorakis G, Vardas P, Sutton R. Methodology of head-up tilt testing in patients with unexplained syncope. J AmCollCardiol. 1991;17:125-30.
5. Bartoletti A, Alboni P, Ammirati F, Brignole M, Del Rosso A, Foglia Manzillo Get al. 'The Italian Protocol': a simplified head-up tilt testing potentiated with oral nitroglycerin to assess patients with unexplained syncope. Europace. 2000;2:339-42.
6. Forleo C, Guida P, Iacoviello M, Resta M, Monitillo F, Sorrentino Set al. Head-up tilt testing for diagnosing vasovagal syncope: a meta-analysis. Int J Cardiol. 2013;168:27-35.
7. Moya A, Sutton R, Ammirati F, Blanc JJ, Brignole M, Dahm JB et al. TheTask Force forthe Diagnosis and Management of Syncope of the European Society of Cardiology (ESC). Developed in collaboration with, European Heart Rhythm Association, Heart Failure Association, and Heart Rhythm Society. EurHeart J.2009;30:2631-71.
8. Brignole M, Menozzi C, Del Rosso A, Costa S, Gaggioli G, Bottoni Net al. New classification of haemodynamics of vasovagal syncope: beyond the VASIS classification. Analysis of the pre-syncopal phase of the tilt test without and with nitroglycerin challenge. Vasovagal Syncope International Study. Europace. 2000;2:66-76.
9. Macedo PG, Asirvatham SJ, Maia L, Ferreira Neto E, Zanatta A, Sobral Neto Jet al. Comparison of a shortened isosorbide dinitrate-potentiated head-up tilt testing with the conventional protocol: tolerance and diagnostic accuracy. PacingClinElectrophysiol. 2012;35:1005-11.
10. Parry SW, Reeve P, Lawson J, Shaw FE, Davison J, Norton Met al. The Newcastle protocols 2008: an update on head-up tilt table testing and the management of vasovagal syncope and related disorders. Heart. 2009;95:416-20.
11. Vlahos AP, Tzoufi M, Katsouras CS, Barka T, Sionti I, Michalis L Ket al. Provocation of neurocardiogenic syncope during head-up tilt testing in children: comparison between isoproterenol and nitroglycerin. Pediatrics. 2007;119:e419-25.
12. Massin MM, Bourguignont A, Coremans C, Comté L, Lepage P, Gérard P. Syncope in pediatric patients presenting to an emergency department. J Pediatr. 2004;145:223-8.
13. Strieper MJ. Distinguishing benign syncope from life-threatening cardiac causes of syncope. Semin Pediatr Neurol. 2005;12:32-8.
14. Driscoll DJ, Jacobsen SJ, Porter CJ, Wollan PC. Syncope in children and adolescents. J AmCollCardiol. 1997;29:1039-45.
15. Teodorovich N, Swissa M. Tilt table test today - state of the art. World J Cardiol. 2016;8:277-82.
16. Kenny RA, Ingram A, Bayliss J, Sutton R. Head-up tilt: a useful test for investigating unexplained syncope. Lancet. 1986;1:1352-5.
17. Stein KM, Slotwiner DJ, Mittal S, Scheiner M, Markowitz SM, Lerman BB. Formal analysis of the optimal duration of tilt testing for the diagnosis of neurally mediated syncope. AmHeart J. 2001;141:282-8.
18. Lacunza Ruiz J, García Alberola A, Sánchez Muñoz JJ, Martínez Sánchez J, Llamas Lázaro C, Barnés Martínez Jet al. Head-up tilt test potentiated with nitroglycerin. What is the optimal duration of the test after administration of the drug? RevEspCardiol. 2002;55:713-7.
19. Liu J, Fang P, Liu Y, Lu G, Li Z, Li Xet al. Duration of head-up tilt test for patients with suspected vasovagal syncope. Europace. 2011;13:576-80.
20. Alasti M, Nikoo MH, Jadbabaei MH, Seyedian M, Payami B, Taghavianpour Set al. RandomizedProspectiveComparison of Two Protocols for Head-up Tilt Testing in Patients with Normal Heart and Recurrent Unexplained Syncope. IndianPacingElectrophysiol J. 2013;13:203-11.
21. Foglia-Manzillo G, Giada F, Fteita N, Nessi I, Santarone M, Raviele A. Tilt testing potentiated with sublingual nitroglycerin in children with unexplained syncope. EurHeart J. 2007;28:2605-9.