

Comparison of short head-up tilt test with conventional protocol after omission of nonmedicated phase in children and young adults

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Abstract

Background: Syncope is an important and common clinical condition, and the neurally mediated syncope is the most frequent type of syncope. Tilt testing is considered as a first-line diagnostic test.

Materials and Methods: We conducted the conventional and modified tilt test on 200 subjects in the age range of 5-20 years. In conventional protocol, the patient was tilted for up to 15 min without medication. If syncope did not develop, the patient received 0.1 mg/kg sublingual isosorbide dinitrate. Then, the patient was continued to be tilted for another 15 min. In modified tilt test, before starting the test, the patient received 0.1 mg/kg isosorbide dinitrate sublingually in supine position. Then, the table was tilted for a maximum of 25 min or until the test became positive.

Results: In conventional tilt test group 79.13% and in modified tilt test group 87.06% of subjects showed positive results. In conventional tilt test, the mean of response time was 17.67 ± 4.74 min. The mean of the total time of conventional tilt test was 49.81 ± 5.57 min. In modified tilt test, the mean of response time was 7.24 ± 4.83 min. The mean of the total time of modified tilt test was 35.09 ± 7.58 min. Furthermore, the means of both response and total times between two groups were significantly different ($P < 0.001$).

Conclusions: Our study showed that we can save about 15-20 min in total test time which may increase the cooperation and compliance of young patients and decrease their anxiety with this new protocol.

Key Words: Neurally mediated syncope, nitrates, tilt table testing

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INTRODUCTION

Syncope is defined as the sudden transient loss of consciousness and postural tone with spontaneous recovery. It results from a reduction of blood flow to the reticular activating system in the brainstem. Syncope is an important and common clinical condition which accounts for 1% of hospital admissions and 3% of emergency department visits

with a reported major complication rate of over 7%.^[1] Up to 15% of children will experience at least one episode of syncope before adolescence. The incidence reaches a peak at 15–19 years of age and is more common in females.

In a population-based study, neurally mediated syncope (NMS) was the most frequent type of syncope (75%) recorded.^[2] NMS is characterized by

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peripheral vasodilation and hypotension along with bradycardia. This leads to loss of consciousness if sufficiently severe, to presyncope if less severe or if the patient is lying down. These changes in heart rate and blood pressure result from an increase in parasympathetic tone and concurrent inhibition of sympathetic tone. Related circumstances include situational fainting, coughing, micturition, defecation, diving, sneezing, and swallowing syncope, carotid sinus syncope (shaving syncope), and autonomic conditions including hyperadrenergic and hypoadrenergic states.^[3]

NMS is classified according to the response to tilt table testing. Tilt testing is considered as a first line diagnostic test, particularly in pediatric patients with unexplained syncope. Tilt table testing is achievable in children as young as 6 years of age. One trouble in young children is anxiety, which may occur when safety belts are applied.^[4] Sutton's law suggests the following causes: (i) Vasodepressor type, reflecting mainly a drop in blood pressure at the time of syncope without changes in heart rate; (ii) cardioinhibitory type with a decrease in heart rate and/or asystole; and (iii) mixed type reflecting both a decrease in heart rate and blood pressure.

Significant reasons for misdiagnosis of epilepsy include a failure to acquire a complete medical history from the patient and undue emphasis on a positive family history for seizure. The head upright tilt (HUT) test is a simple, noninvasive diagnostic method for differentiating syncope from epilepsy in children. It should be considered early in the diagnostic plan and when determining a management program for patients with convulsive-like attacks.^[5] The positive predictive value of a positive response to the head-up tilt is 93%, and the negative predictive value is 43%.^[6]

There is yet no standard protocol for the HUT testing, but most studies administered the test in two sequential stages. In the first or "passive" stage, a patient who has not taken medication is tilted 60–70° for up to 45 min. If syncope does not develop, the second "active" phase begins. The patient receives a provocative medication such as sublingual isosorbide dinitrate (ISDN), nitroglycerin, or isoproterenol and continues to be tilted for another 15 min. If syncope occurs during the test, the tilt table is rapidly returned to the supine position and the test is terminated. A cardiologist and a technician are present during the entire procedure, and the patient is closely observed for 15 min after the test.^[7-10]

The latest published protocol for tilt testing by the European Society of Cardiology in 2009 recommends

a supine pretilt phase of at least 5 min without venous cannulation and of at least 20 min with cannulation. The tilt angle is 60–70° and the passive phase lasts a minimum of 20 min and a maximum of 45 min. In the active phase, it is recommended to increase the average heart rate by 20–25% over baseline using nitroglycerin administered sublingually at a fixed dose of 300–400 µg in an upright position or isoproterenol administered at an incremental infusion rate of 1–3 µg/min.^[11] In older patients, omission of the passive stage to begin testing with administration of nitroglycerin may be more effective and improve compliance.^[11] This study proposes shortening of the HUT test by omitting the passive nonmedicated phase to decrease patient anxiety and fatigue and save time.

MATERIALS AND METHODS

This study was approved by the Local Ethics Committee, and all subjects (or their parents) provided written informed consent before the procedure was initiated. The study was cross-sectional and used the proposed modified tilt table test protocol on 85 patients (40 males and 45 females) with a history of unexplained syncope and a mean age of 13.16 ± 4.84 . The results were compared with the results of tilt tests performed using the routine and conventional protocol on 115 children (47 males and 68 females) with a mean age 12.81 ± 4.16 year (5–20 years) having a history of unexplained syncope. All subjects in both groups were matched for age, gender, and body mass index.

All patients had been referred to the cardiology outpatient clinic of Shahid Chamran Hospital of Isfahan University of Medical Sciences between March 2011 and February 2014 for evaluation of syncope. After a complete medical history was obtained and physical examinations were completed, all patients in both groups participated in the HUT table test. Patients with a history of true neurally mediated syncope or seizure, an abnormal physical exam, abnormal electrocardiogram (ECG), electroencephalogram or echocardiography, psychological problems, or those with diseases that could influence their diagnoses were excluded.

Tilt test

HUT testing was carried out on a mechanical tilt table with a footboard for weight-bearing and safety belts at a 65° tilt. The test was performed by a pediatric cardiologist in a quiet standard room at 21–25°C with the lights dimmed.

The patients in both groups initially fasted for 6 h. They were placed in a supine position, and an open vein with 5% dextrose in water was established. ECG

monitoring was carried out and base line vital signs for body temperature, respiratory rate, heart rate, and blood pressure were taken and recorded. After 10 min of patient preparation in the conventional protocol, the patient was tilted to 65° for up to 15 min without medication. If syncope did not develop, the tilt table was returned to a supine position for 5 min and the patient received 0.1 mg/kg ISDN as provocative medication. The patient was again tilted for 15 min. If syncope occurred during the test, the tilt table was rapidly returned to the supine position and the test was terminated.

In the second group, the proposed modified protocol for HUT testing began with omission of the nonmedicated phase. After 10 min in a supine position for preparation, the patient received 0.1 mg/kg ISDN sublingually in a supine position before tilting was initiated. The table was then tilted to 65° for a maximum of 25 min or until the test became positive. Patients in each group were allowed a recovery phase of at least 10 min in a supine position at the end of testing.

During the tilt period, patient vital signs and ECGs were taken and reported at 3-5 min intervals. A cardiologist and a technician were present during the entire procedure. All patients were closely observed for 15 min in the clinic after completion of testing.

Statistical analysis

Statistical analysis was carried out using the descriptive statistic and independent sample *t*-tests using SPSS version 20 software (IBM, USA). The results were considered significant at $P \leq 0.05$.

RESULTS

The conventional and modified tilt tests were performed on a total of 200 subjects. Table 1 shows the characteristics of the 115 subjects selected for the conventional tilt test and 85 subjects selected for the modified tilt test also Table 2 shows the distribution of the types of hemodynamic positive response to head up tilt test.

The mean response time in the conventional tilt test was 17.67 ± 4.74 min. The mean total test time for the conventional tilt test was 49.81 ± 5.57 min. In this group, the tilt test became positive during the passive phase in 25.6% of patients. In other participants, it became positive during the medicated phase after patients had received ISDN.

In the modified tilt test, the mean response time was 7.24 ± 4.83 min. The mean total test time for the modified tilt test was 35.09 ± 7.58 min. The means of

the response times and total test times between groups were significantly different at $P < 0.001$.

Two patients in each group showed positive responses at the beginning of the test during preparation phase with needling. Figure 1 shows the distribution of the test response time for both groups.

DISCUSSION

The results showed that omission of the passive phase of tilt test saved time and improved patient compliance by decreasing anxiety and discomfort. Several studies support these results in adult patients.

In 1999, Shen *et al.* conducted a study on 111 patients with a history of syncope (mean age 55 ± 20 years) by a single-stage isoproterenol tilt testing at 0.05 mg/kg/min and for 10 min and compared it with the passive tilt table test. Each patient subject underwent both tilt table testing protocols. Of the total, 56% had a positive vasovagal response during isoproterenol tilt table testing and 32% during passive tilt table testing. The mean procedural times of the study population were 11.7 ± 3.6 min

Table 1: Data of subject enrolled in conventional and modified tilt test

| | Conventional tilt test (n=115) | Modified tilt test (n=85) | P |
|----------------------|--------------------------------|---------------------------|--------|
| Age (year) | 12.81±4.16 | 13.16±4.84 | NS |
| Male/female | 47/68 | 40/45 | NS |
| Positive results (%) | 91 (79.13) | 74 (87.06) | 0.043* |

All variables reported in mean±SD. * $P < 0.05$ set as significant, SD: Standard deviation, NS: Not significant

Table 2: Distribution of the types of hemodynamic positive responses to head-up tilt test

| Type of positive response | Cardioinhibitory | Vasodepressor | Mixed response |
|---------------------------|------------------|---------------|----------------|
| Conventional group (%) | 7 | 30 | 63 |
| Modified group (%) | 9 | 21 | 70 |

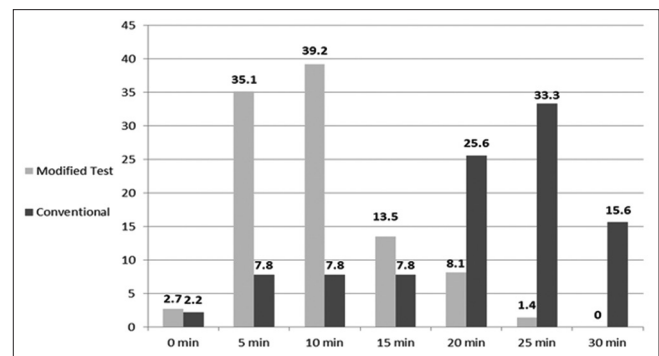


Figure 1: Distribution of test response time of conventional and modified tilt test (data shows in percent)

and 36.9 ± 13.3 min for isoproterenol and passive tilt table testing. They concluded that the single stage isoproterenol tilt testing was more effective in inducing a vasovagal response than “standard” tilt table testing in adult patients.^[12] Similarly, to our results, there was a significant difference between the duration of total times in single stage isoproterenol tilt test and the passive protocol.^[12]

Aerts and Dendale^[13] performed tilt testing after direct administration of sublingual nitroglycerin spray in an erect posture on 38 patients (mean age 46 ± 16) and 31 control subjects. In the patient group 31 (82%) and in controls 5 (16%) had a positive test. Sensitivity, specificity, and accuracy at test end were 82%, 84%, and 83%, respectively. They concluded that testing without administration of the initial passive tilt phase provided an accurate, sensitive, and specific method to provoke vasovagal reactions in subjects with clinically suspected vasovagal syncope; however, they did not compare their results with those for conventional tilting also none of these two studies were performed in children.

Khan *et al.*^[14] performed HUT testing on 100 patients with orthostatic intolerance and compared the conventional and short duration HUT protocols. The conventional protocol had a passive tilt phase of 30 min and a drug provocation phase of 20 min. The short duration protocol had both phases with durations of 15 min, which reduced the total test duration by 20 min. All patients underwent short duration HUT. Patients having negative short duration HUT underwent conventional HUT after 1 week. Diagnostic yield of short duration and conventional HUT was 53% and 63%, respectively, with no statistically significant difference between the two protocols. They concluded that short duration HUT can be substituted for conventional HUT to save time.

Sabri and Maghjian^[8] conducted a large study on 172 patients referred for evaluation of unexplained syncope with ages ranging from 6 to 18 years (43 patients in the case group and 129 patients in the control group). The patients in the case group were tilted for 20 min (nonmedicated phase). If the test results were negative, the patient received 0.1 mg/kg ISDN sublingually in a supine position and the table was then tilted for a maximum of 20 min or until the test became positive (medicated phase). The patients in the control group were tilted to an angle of 65° for 40 min (conventional HUT test protocol). The results showed that in 39.5% of the case group in the nonmedicated phase and 44% in the medicated phase had a positive response and 62% of the control group had a positive response. As in the results of this

study, the distribution of positive response was greater during the medicated phase.

Parry *et al.*^[15] compared a shortened front-loaded 20-min glyceryl trinitrate-provoked HUT with the standard 40-min passive tilt as the first line of investigation for 149 adult patients (18–90 years of age) with unexplained syncope and 83 asymptomatic controls. They subjected all participants to both methods at 1 week intervals. The number of positive results increased 24.8% using the front-loaded glyceryl trinitrate HUT than using the passive HUT. The controls group showed an increase of 16.8% in significant hemodynamic changes using front-loaded glyceryl trinitrate HUT than using HUT. They concluded that the front-loaded GTN protocol provides a higher diagnostic rate than the passive tilt test and is a rapid alternative to conventional methods.

Sabri and Maghjian^[8] reported a mean duration for developing symptoms in the nonmedicated phase of 11 ± 6 min (2–20 min) and in the medicated phase of 9 ± 3 min (4–17 min). They concluded that the use of sublingual 0.1 mg/kg ISDN as a provocative agent in children and adults is safe and has no major complications. This study used ISDN as the most feasible medication, and all patients tolerated it well and showed good compliance.

The results of this study indicate a savings in 15–20 min in total test time using the proposed modified protocol. During the follow-up period under appropriate monitoring, no patient with a positive test in either group experienced a recurrence of syncope. This modified protocol simply omitted the passive phase. Because patients with a negative passive phase under conventional protocols continued their test with provocation, it appears that change in the test protocol had no influence on the test results nor did it increase the rate of false positive cases.

It should be noted that a less steep tilt angle of 65° was used; a steeper angle may have produced a higher number of positive responses. A higher positive rate using a steeper tilt angle has been previously demonstrated in passive and isoproterenol protocols.^[16]

CONCLUSIONS

This study tested a short HUT test protocol that omitted the preceding passive phase. This new protocol offers a practical and easy-to-perform method of diagnosis of neurally mediated syncope. By reducing the burdensome nature of the test, its accessibility and usage increases and provides a positive alternative to the current diagnosis of patients with syncope.

Study limitations

The results of this study were compared with the results of different protocols. There was no control group of patients without a history of syncope with which to evaluate false positive rates of both methods. To avoid the potential risks and costs of repeated HUT testing, the patients were not tested using both methods.

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Conflicts of interest

There are no conflicts of interest.

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