Different patterns of tilt-table test outcome in children and their response to medications

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Background Syncope is a common and often frustrating clinical problem encountered by pediatricians in outpatient or emergency room settings. Neurocardiogenic syncope is believed to be the most common cause of syncope in the absence of structural heart disease. In our study, we aimed to study different responses to tilting-table test among children and teenagers with suspected neurocardiogenic syncope.

Patients and methods We collected data from patients of Ain Shams Hospital who presented with more than two attacks of syncope and got positive tilt-table test findings. All the patients were subjected to thorough history taking, full cardiac examination, and a tilt-table test. Patients were later followed up for 2 months for recurrence.

Results Our study included data from 30 patients, of which 19 were females, and seven were on antiepileptic drugs. Approximately 20% of patients had a family history of epilepsy, and 10% had a family history of syncope. Prolonged standing especially in hot weather was the most common predisposing factor for their syncopal attacks. Palpitation and dizziness were the most common symptoms occurring before the attack, whereas palpitation and headache commonly affected these patients after syncope. Physical examination of these patients revealed no specific abnormality, and their hemoglobin level and random blood sugar level also revealed no specific abnormality. Tilt-table test was done to all the patients and revealed that ~75% showed a vasodepressor response; however, only ~23% showed a mixed response and no patients demonstrated cardioinhibitory response. No complications were reported during the test. The study revealed a significant negative correlation between the frequency of the attacks and initiation-response lag (r=–0.676, P<0.001), meaning that the more the attack numbers of syncope, the earlier the occurrence of positive response in tilt-table test. All patients in the study received midodrine tablets together with diet modification and tilt training for 2 months. They were followed up for recurrence of syncope and only ~16% of these patients showed recurrence. On asking patients with recurrence, they stated that they were noncompliant neither to the treatment nor to the exercise.

Conclusion It is evident that tilt-table test is a safe and effective test to diagnose neurocardiogenic syncope in children and teenagers and that vasodepressor response is more common than both mixed and cardioinhibitory responses in children and teenagers. Midodrine, diet modification, and tilt training are effective management of neurocardiogenic syncope in children and teenagers.

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Introduction

Syncope is a relatively frequent symptom in children, and its evaluation is an important aspect in pediatric medical practice. Although the incidence of pediatric syncope is difficult to assess, it appears to peak around the age of 15 years, with 20–50% of females reporting to have experienced at least one syncopal episode by the age of 20 years [1].

Aim

The aim of the work was to study the different responses to tilting-table test among children and teenagers with suspected neurocardiogenic syncope.

Patients and methods

This =is a prospective study that included 30 patients with positive tilt-table test result after exclusion of 42 patients with negative tilt-table test result. All these patients were referred to Ain Shams Specialized Hospital owing to recurrent attacks of syncope during the period between March 2009 and April 2010. The study was conducted at the Cardiology Department at Ain Shams Specialized Hospital.

The inclusion criteria for these patients in this study were as follows:

(1) All the patients were under the age of 18 years old.
(2) All the patients who chiefly complained of syncope (>two attacks) were referred for tilt-table testing.
(3) Those patients with positive tilt-table test result were included in the study.
(4) Those patients with negative tilt-table test result were excluded from the study.

These patients were subjected to the following:

(1) Careful history taking including age; sex; full analysis of the attacks; number of attacks per week; symptoms before, during, and after the attack; family history of epilepsy; syncope and sudden death; precipitating factors; and history of antiepileptic drug intake and any trauma during the attack.
(2) Meticulous physical examination including supine and erect systolic and diastolic blood pressure (BP) measurement.
(3) Twelve-lead surface ECG.
(4) Continuous 24-h Holter monitoring ECG.
(5) Baseline laboratory workup.
(6) Echocardiography examination: colored echo-Doppler examination was carried out in all patients with M-mode guided by two-dimensional views and Doppler study to exclude congenital or acquired cardiac diseases.
(7) Electroencephalogram was done to exclude any underlying neurological cause of syncope.
(8) Tilting-table test with the following criteria:
    (a) Tilt angle is 80°.
    (b) Potentiating drug is sublingual nitroglycerine.
    (c) Tilt duration is 45 min with potentiating drug

Head-up tilt-table test protocol

Informed consent for the head-up tilt-table test (HUTT) was obtained from the parents of the patients who were younger than 18 years old. All drugs were discontinued for at least five half-lives before the study. The study used motorized tilt table with a foot plate support and patients were supported by two belts and trunk and legs. Elevation or lowering of the table was achieved at speed of 40°/s directly to the final angle of tilt [2].

The studies were all performed in the postabsorptive state, and an intravenous access was obtained. Initially, the baseline heart rate (HR) and BP were recorded in the supine position. Then we raised the table to 80° for 15 min or until the occurrence of a positive response. In addition to continuous ECG monitoring, the HR and BP were recorded every 2 min. A positive result of the HUTT was defined as the presence of symptoms of presyncope or syncope associated with the sudden development of hypotension, bradycardia, or both [9].

Head upright till test includes two consecutive stages

(1) Stage I: patient was tilted to 80° for 15 min without provocation, followed by rest for 5 min.
(2) Stage II: patient was tilted to 80° for 15 min after giving 5 mg isosorbide dinitrate sublingually, and rest for 5 min is allowed.

The supine position was regained immediately if positive responses occurred. Emergency medications were available at all times. BP, HR, ECG, and symptoms were monitored throughout the procedure. The data for each patient were recorded on tilt-table test operation sheet [10].

Follow-up was done for 2 months after giving treatment.

End point of the test

(1) Positive response is defined as the development of syncope or presyncope recognized by the patient as identical to its clinical spells in association with sudden and marked hypotension and/or a decrease in HR occurring in less than 5 min [3].
(2) Negative response included the following:
    (a) Exaggerated response is defined as the gradual development of symptoms such as dizziness and fatigue not recognized by the patient as similar to the spontaneous ones and resulting from progressive and steady (occurring in >5 min) decrease in systolic BP with concomitant compensatory tachycardia or with only slight decrease in HR occurring after a prolonged period of marked hypotension [3].
    (b) Completion of test: with the absence of symptoms and significant hypotension or bradycardia [2].

According to vasovagal syncope international study classification, the positive response is classified into the following.

Mixed response (type 1)

(1) HR rises initially and then decrease by greater than 10% but not decreases to less than 40 bpm for less than 10 s.
(2) BP rises initially and then decrease (systolic BP <90 mmHg or decrease >20%) before HR decrease.

Cardioinhibitory (type 2A)

(1) HR rises initially and then decreases to less than 40 bpm for greater than 10 s or systole for greater than 3 s.
(2) BP rises initially and then decrease before HR decrease.

Cardioinhibitory (type 2B)

(1) HR initially rises and then decrease to less than 40 bpm for greater than 10 s or asystole for greater than 3 s.
(2) BP rises initially and decreases after HR decreases.

Vasodepressor (type 3)

(1) HR rises initially and then does not fall greater than 10% from the maximum HR observed during tilt.
(2) BP drops dramatically trigging the syncope [4].

Statistical methods

Data was analyzed by the 10th version of SPSSS software (SPSS Inc., Chicago, Illinois, USA). Quantitative variable were presented as mean±SD, whereas qualitative variable were presented as frequencies and percentage, and the prevalence was presented as a percentage of the total population.

Comparison of qualitative variables between various groups was done using χ^2–test, and the comparison of quantitative variables between two independent groups was done using Student *t*-test.

For all tests, *P* value less than 0.05 was considered statistically significant, and values less than 0.01 were considered highly significant.

Results

The 30 patients enrolled in the present work have an average age of 12±4.4 years old (ranging from 6 to 18 years old). There were 16 children (<12 years) and 14 adolescent (>12 years), representing 53.3% and 46.7%, respectively. Nineteen of the studied patients were females (63.3%) and the remainders were males (36.7%). Regarding the children, there were eight (50%) females and eight (50%) males. However, adolescents represented 11 (78.6%) females and only three (21.4%) males. These demographic data are demonstrated clearly in Table 1.

The study also revealed that there were six (20%) patients with family history of epilepsy and only three (10%) patients with family history of syncope. Seven (23.3%) patients were taking antiepileptic drugs. The studied population experienced an average of 3.5 attacks per week, with each attack ranging from 1- to 3-min (average 2 min) duration. These comparative data are present in Table 1.

The commonest predisposing factor (PF) of Neuro Cardiogenic Syncope (NCS) in the study population was prolonged standing, which present in 14 (46.7%) patients. Other PFs included exertion occurring in 10 (33.3%) patients and emotions (e.g. Fear) in five (16.7%) patients.

Regarding the symptoms of NCS occurring before, during, and after the attack, the study revealed that dizziness and palpitation were the commonest premonitory symptoms occurring in 25 (83.3%) patients, whereas 20 (67%) and nine (30%) patients experienced headache and flushes, respectively. Pallor was the most frequent sign occurring during the attack affecting 13 (43.3%) patients. Other symptoms such as convulsions and trauma occurred in three (10%) and six (20%) patients, respectively. Only two (6.7%) patients experienced incontinence. No one experienced cyanosis. During the period following syncope, headache was the most frequent symptom accounting for 11 (36.7%) patients, whereas palpitation occurred in six (20%) patients of the studied group (Fig. 1).

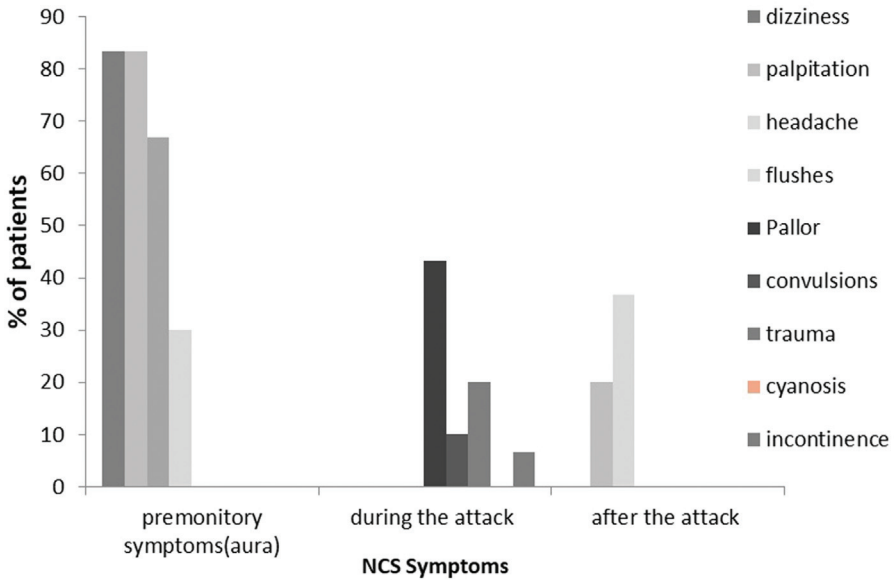
Table 1 demonstrates the clinical data obtained from examination of studied patients. These data revealed that the average BMI was 19.2±3.3, whereas the

Table 1 Demographic characteristics of studied patients

Parameters	Measure [*n* (%)]
Age (mean±SD) (years)	12.0±4.4
Age groups	
Children (<12 years)	16 (53.3)
Adolescent (>12 years)	14 (46.7)
Sex	
Female	19 (63.3)
Male	11 (36.7)
Sex in children	
Female	8 (50.0)
Male	8 (50.0)
Sex in adolescent	
Female	11 (78.6)
Male	3 (21.4)
Family history	
Present	9 (30.0)
Syncope	3 (10.0)
Epilepsy	6 (20.0)
Antiepileptic intake	
Present	7 (23.3)
Attack rate/week [median (IQ range)]	3.5 (1–7)
Attack duration [median (IQ range)]	2 (1–3)
Anthropometric weight (mean±SD) (kg)	42.0±16.6
Height (mean±SD) (cm)	144.0±19.2
BMI (mean±SD)	19.2±3.3
Pulse and blood pressure (mean±SD) (bpm)	3.5±10.0
SBP supine (mean±SD) (mmHg)	104.7±9.4
DBF supine (mean±SD) (mmHg)	69.7±8.5
SBP erect (mean±SD) (mmHg)	103.0±10.2
DBF erect (mean±SD) (mmHg)	68.6±8.3

IQ, interquartile range; SBP, systolic blood pressure.

Figure 1



Symptoms of neurocardiogenic syncope illness in studied patients.

Table 2 Tilt test of studied patients

Parameters	*n* (%)
Tilt test of studied patients	
Provocation	
Yes	23 (76.7)
Response	
Vasodepressor	23 (76.7)
Mixed	7 (23.3)
Initiation-response lag [median (IQ range)] (min)	30 (20–35)
Response to midodrine in studied patients	
Recurrent syncope	
Yes	(16.7)
Syncope free duration in recurrent patients [median (IQ range)] (months)	3 (1–4.5)

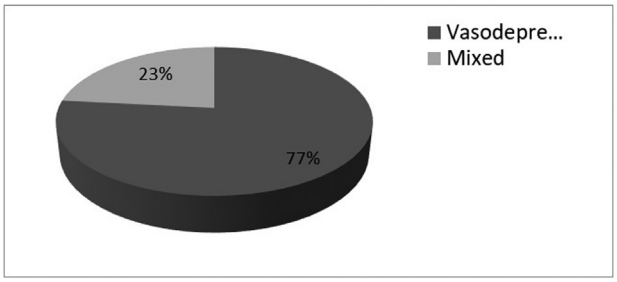
IQ, interquartile range.

examination of pulse and BP revealed an average pulse of ~83 beat per minute (bpm) and an average supine BP of ~104/70 mmHg and that of erect BP of ~103/69 mmHg. Moreover, there were no significant statistical findings regarding cardiac examination.

The study showed that only seven (23.3%) patients showed a positive tilt-table test result without provocation. Regarding the response of that test, most showed a vasodepressor (VD) response (23 patients), and only seven patients demonstrated mixed response. No patient showed cardioinhibitory response. The time between the beginning of the test and the positive response – initiation-response lag – was ~30 min on an average. These results are expressed in Table 2.

VD response was more frequent than that of mixed type in the present study as demonstrated in Fig. 2.

Figure 2



Tilt-test response of studied patients.

Follow-up of the patients after medical treatment

Only five patients experienced recurrent syncope after taking midodrine with an average syncope-free duration of ~3 months, putting in mind that on asking these patients and their relatives or parents, we discovered that they were noncompliant to neither the pharmacological treatment nor the nonpharmacological therapy (Table 2).

The study revealed a significant negative correlation between the frequency of the attacks and initiation-response lag (r=–0.676, P≤0.001), meaning that the more the attack numbers of syncope, the earlier the occurrence of positive response in the tilt-table test (Table 3 and Fig. 3).

Discussion

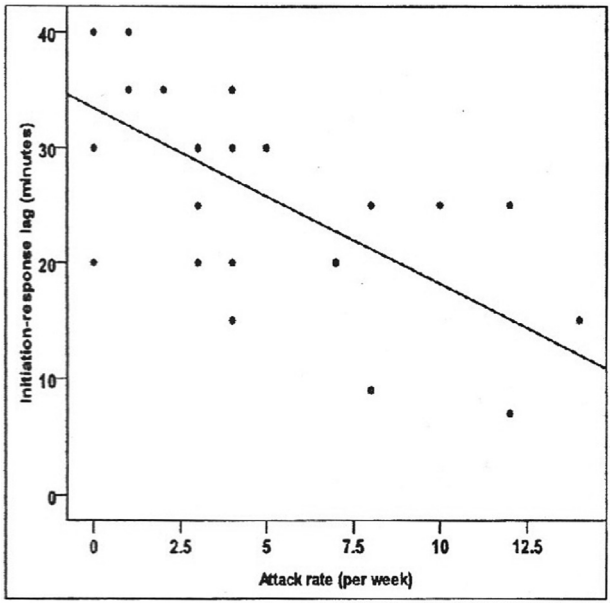
In the present study, we found that family history of epilepsy was reported in 20% of the study population whereas that of syncope was 10%; these findings coincided with the findings of Udani *et al.* [5],

Table 3 Correlation between attack rate and initiation-response lag

Groups	*r* value	*P* value
All sample	−0.676[£]	<0.001*
Vasodepressor	−0.575[£]	0.004*
Mixed	−0.972[£]	<0.001*

[£]Spearman ρ correlation test. *Significant.

Figure 3



Correlation between attack rate and initiation-response lag in all sample.

who recruited 20 patients with a strong clinical suspicion of syncope. These patients were between 5.5 and 18 years old. The HUTT was then carried out at baseline and after provocation and found that family history of epilepsy and syncope was reported in 18 and 12% of patients with positive HUTT, respectively [5].

Predisposing factors

In the present study, we found that the whole study population had PFs for NCS, and these results are in agreement with the data reported by Jan Lin and colleagues, who recruited 17 pediatric patients with unexplained presyncope and syncope and who underwent HUTT. They divided those patients in two groups, group I with positive HUTT result and group II had negative HUTT result, and found that group I showed 100% PFs for NCS [6].

In the current study, we found that prolonged standing triggered syncope in 53% of the study population, whereas exercise and emotions triggered 33 and 16% of the study population, respectively.

These data disagree with what was reported by Hegazy *et al.* [7], who collected the clinical charts of 234 pediatric patients presenting with a primary complaint of syncope, with their age ranging from 3.5 to 16 years, which were reviewed by investigators, and found that the commonest trigger for syncope in the study population was early following exercise, whereas emotions and hot weather accounted for ∼12 and 9%, respectively [7].

This disagreement was owing to those authors recorded all patients presenting with a primary complaint of syncope regardless of the cause of this syncope, whereas in our study, we recorded neurocardiogenic syncope only.

Characteristics of the syncopal attack aura

In our study, we found that dizziness and palpitation accounted for 83% of the premonitory symptoms, whereas headache and flushing accounted for 66 and 50%, respectively.

These results are in agreement with Lin and colleagues who reported that there was a higher incidence of prodromes such as dizziness, nausea, blurred vision, or cold sweating before the syncopal attack [6].

In the present study, we found that palpitation and dizziness were the most common prodrome, and this finding coincided with the findings of Hegazy *et al.* [7] who reported that the commonest prodrome was palpitation.

During the attack

In the current study, there were a number of signs reported by witness of the syncopal attack such as pallor, trauma, convulsions, and incontinence; pallor was the most common sign accounted for 43% of population.

These results are in agreement with Udani *et al.* [5] who reported that pallor was the most common sign representing 39% of the population study.

In the present study, we found that urinary incontinence occurred in 6.7% of our study population, but this finding was in contrast to what was found by Udani *et al.* [5] who recorded no urinary incontinence reported during the attack.

Postattack

Our results agree with Udani *et al.* [5], who reported headache as the most common sign following syncope. In our study, headache and palpitation accounted for 36 and 20%, respectively [5].

Tools to diagnose neurocardiogenic syncope

Physical examination

In our study, all patients were subjected to physical examination including HR recording, systolic and diastolic BP measurement in both supine and erect position, and cardiac auscultation and revealed that no abnormality was detected.

These results coincided with the findings reported by Udani *et al.* [5] who reported that there were no abnormalities detected during examination of the patients with positive HUTT result.

Tilt-table test

We found that 23.3% of the study population showed a positive HUTT result without provocation, whereas 76.7% of the study population showed a positive HUTT result with provocation.

Our results agree with the results reported by Udani *et al.* [5] who found that 31.2% of the patients with a positive HUTT result were without provocation, whereas 68.8% only showed a positive HUTT result after provocation.

The present study reported that VD response represented 76.7% of patients with positive tilt-table test result, whereas mixed response represent 23.3%; however, no patients showed cardioinhibitory response.

Those results coincided with El-Fakharany *et al.* [8], who recruited 20 patients with an average age of 39.35 ±19.14 years old with unexplained syncope and presyncope, where they were underwent HUTT, which revealed a VD response of ~70% and mixed response of ~10%, yet they reported 5% of patients with cardioinhibitory response.

On the contrary, our results were in contrast to what was found by Udani *et al.* [5], who reported a VD response of ~12.5%, mixed response of ~75% and cardioinhibitory response of ~12.5%.

This disagreement is probably owing to genetic and environmental factors, where our study and the study by El-Fakharany *et al.* [8] were conducted in Egypt, whereas the study by Udani *et al.* [5] was conducted in India.

Conclusion

It is evident that tilt-table test is a safe and effective test to diagnose neurocardiogenic syncope in children and teenagers, and VD response is more common than both mixed and cardioinhibitory response in children and teenagers. Midodrine, diet modification, and tilt training are effective management of neurocardiogenic syncope in children and teenagers.

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Nil.

Conflicts of interest

There are no conflicts of interest.

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