Implications of tilt-table induced faint time in patients with reflex syncope

Refleks senkoplu hastalarda tilt-masası ile indüklenen bayılma süresinin değerlendirilmesi

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ABSTRACT

Objective: The aim of this study was to determine whether patients who faint earlier in the course of a tilt table study represent a separate population with a poorer prognosis or different pathophysiology. We analyzed differences across patients with different syncopal times on the tilt-table study to answer this question.

Methods: This was a retrospective, approved, chart review. From our database of over 6000 patients, we identified 1222 patients with syncope. After excluding patients with orthostatic hypotension, postural tachycardia syndrome and diabetes, we were left with 131 patients with pure reflex syncope. We divided fainters into an early (<20 minutes) and late (>20 minutes) faint times. Along with the tilt table test all patients underwent heart rate response for deep breathing, Valsalva maneuver and quantitative sudomotor axon reflex tests.

Results: By 10 minutes in the tilt study, only 18% of subjects had fainted, 65% by 20 minutes, 92% by 30 minutes and 96% by 35 minutes. Age was evenly distributed across all syncopal times. Neither the 14 abnormal cardiac responses to deep breathing nor the 20 abnormal Valsalva maneuvers, nor the 28 abnormal axon reflex responses clustered with an early or late faint time.

Conclusion: A 10-minute tilt will miss 82% of syncopal episodes, while a 30- minute tilt increases the yield 10-fold, missing only 8%. Patients with early faint times did not differ from patients with late fainting times with regard to age or autonomic test abnormalities. Timing of syncope during the tilt table test does not associated with more severe dysautonomia. A prospective study is needed to confirm these observations. *(Anadolu Kardiyol Derg 2011; 11: 674-7)*

Key words: Reflex syncope, syncopal timing, tilt- table test, autonomic tests

ÖZET

Amaç: Bu çalışmanın amacı, tilt masası çalışmasında daha erken döneminde bayılan hastaların daha kötü prognoza veya farklı patofizyolojilere sahip olup olmadığını tanımlamaktır. Bu soruya cevap vermek için tilt masası testi sırasında farklı zamanlarda senkop geçiren hastalar değerlendirildi.

Yöntemler: Bu çalışma lokal etik kurulunca onaylanmış retrospektif bir çalışmadır. Altı bin hastalık arşivimizde, 1222 hastada senkop saptandı. Ortostatik hipotansiyon, postüral taşikardi sendromu ve diyabetli hastalar dışlandıktan sonra saf refleks senkoplu 131 hasta çalışmaya alındı. Bayılanları; erken (<20 dk) ve geç (>20 dk) olarak bayılma zamanlarına göre ayırdık. Tüm hastalara tilt masası testinin yanı sıra derin solunuma kalp hızı cevabı testi, Valsalva manevrası testi, kantitatif sudomotor akson refleks testleri yapıldı.

Bulgular: Tilt masası çalışmasında ilk 10 dakikada hastaların %18'i, 20 dakikaya kadar %65'i, 30 dakikaya kadar %96'sı ve 35 dakikaya kadar %96'sı bayıldı. Yaş dağılımı tüm senkop zamanlarına homojendi. On dört anormal derin solunuma kalp hızı cevabı testi, 20 anormal Valsalva manevrası testi, 28 anormal sudomotor akson refleks testi bayılma zamanına göre dağılımı benzerdi.

Sonuç: On dakikalık bir tilt testiyle senkopların %82'sini kaçırırken, 30 dakikalık tilt testi ile sadece %8 senkop vakası kaçırılabilecektir. Erken bayılan hastalar, yaş veya otonomik testlerdeki anormalliklere göre geç bayılan hastalardan farklı değildir. Prospektif çalışmalarla bu gözlemlerin doğrulanmasına ihtiyaç vardır. *(Anadolu Kardiyol Derg 2011; 11: 674-7)*

Anahtar kelimeler: Refleks senkop, senkop zamanı, tilt masası testi, otonomik testler

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Introduction

Reflex syncope (fainting) is defined by a sudden transient loss of consciousness and postural tone caused by changes in arterial blood pressure and cerebral hypoperfusion (1-4). Symptoms and signs of impending faint are the signs and symptoms of pre-syncopal state: pallor, nausea or stomach discomfort, headache, cold or warm feelings, and dizziness, which is often initially interpreted as a more ill-defined lightheadedness or cognitive loss. Symptoms accompanying reflex syncope are similar to those experienced by postural tachycardia syndrome patients (5, 6). Typical findings of reflex syncope on tilt table test include a rapid decrease in blood pressure and often a drop in heart rate resulting from inhibition of the sympathetic and activation of the parasympathetic nervous systems, which may be profound (7, 8).

Many studies have evaluated tilt-table testing. A large literature addresses the concurrent use of provocative agents such as isoproterenol or nitrates (9-12). In addition, others have examined the optimal duration of tilt table testing in the context of the syncopal population (13, 14). However, no study has examined whether the time of syncope during the tilt study (early vs late) has any pathophysiologic significance (for example earlier time reflecting a more severe dysautonomia) from a neurologic standpoint. In other words, do patients who faint earlier in the course of a tilt table study represent a separate population with a different pathophysiology?

The aims of this study were two fold; 1) Determine if timing of syncope during the tilt table test is associated with more severe dysautonomia, 2) Evaluate the optimal length of the tilt table test in subjects with syncope. We analyzed differences across patients with different syncopal times on the tilt-table study and also examined the proportion of patients who fainted during each time segment to estimate optimal tilt study duration.

Methods

Study population and inclusion criteria

This retrospective, Institutional Review Board approved review of the Autonomic Laboratory database of over 6000 patients included only patients with "pure" reflex syncope without other co-morbidities. Differentiating reflex syncope from delayed orthostatic hypotension can be difficult (15). However, a relatively rapid drop in blood pressure in an otherwise normal tilt study, or a concomitant drop in heart rate can be quite suggestive of "pure" syncope. Since neither the magnitude of bradycardia nor the definition of "rapid" drop in blood pressure have been established, we used the time frame of less than 3 minutes, thus reducing the possibility of misdiagnosing delayed orthostatic hypotension. Inclusion criteria therefore included an abrupt drop in pressure or were accompanied by a clear bradycardia while upright. Overall, 1222 patients with syncope of all types were identified.

In order to avoid a selection bias (created by including patients with known disorders of the autonomic nervous system referred to our laboratory for this reason), and to evaluate a pure population (that excluded patients who fainted due to orthostatic hypotension rather than reflex syncope) we excluded patients with associated orthostatic hypotension (OH), postural tachycardia syndrome (POTS), and diabetes, known small fiber neuropathy, Parkinson's disease or any disorder known to be associated with a dysautonomia. We were left with 131 patients with "pure" reflex syncope, with an age range of 8 to 73 (mean age=26.6±14) and 102 females (mean age=26.0±11.69), 29 men (mean age=32.3±19.07). We divided fainters into an early (<20 minutes) and late (>20 minutes) faint times.

Autonomic testing
The tilt table test

Subjects were initially asked to lie supine for a period of at least 5 min. Thereafter, they were tilted to an angle of 70 degrees using a motorized tilt table with footplate (UH systems). This was then sustained for a period of 40 min or until a syncopal or pre-syncopal event occurred. Beat-to-beat blood pressure and heart rate monitoring were recorded plethysmographically over the index finger by a non-invasive Finapres monitor (Finometer, Amsterdam, Netherlands) with external electrocardiograph tracing. All tests were performed without pharmacological provocation (since these add little to diagnostic yield). Subjects provided informed consent prior to all testing. Blood pressure was also monitored (in the contralateral arm) using a standard automated blood pressure monitor over the arm. The patient was actively questioned for symptoms and asked to provide a numeric rating for any symptom acknowledged such as feeling hot, nausea or dizziness. These symptoms are clinically correlated with any vital sign changes. We noted changes consistent with a diagnosis of reflex syncope and recorded time of onset in each subject.

Heart rate response to deep breathing

Heart rate response to deep breathing was performed in standard fashion, with the subject taking 5 deep breaths per minute while lying supine for 3 cycles separated by one minute. The response is calculated using the maximum heart rate minus the minimum heart rate (RR interval during inspiration compared to the RR interval during expiration) in the best 5 of 15 breaths.

Valsalva maneuver

The Valsalva maneuver was performed in standard fashion, the patient maintaining 40 mmHg for 15 seconds using an open glottis. Continuous HR and BP are measured throughout the study. The Valsalva ratio is computed from the longest RR interval after release divided by the shortest RR during pressure hold.

The Quantitative Sudomotor Axon Reflex Test (QSART)

QSART evaluates the postganglionic sudomotor (sympathetic cholinergic) nerve fibers. It consists of stimulating the

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sudomotor nerves under the outer chamber of a two-chambered capsule using a 2mA current across a solution of 10% acetylcholine and recording the sweat response under the inner chamber.

Data analysis

SPSS for Windows 15.0 (Chicago, IL., USA) was used for statistical analysis. The descriptive statistics were presented as frequency and percent. The autonomic testing for the 131 subjects was reviewed for abnormalities in each of the three autonomic tests other than tilt table testing. We examined differences in autonomic test findings and other discrete variables using Chi-square test for the group who fainted before 20' and those who fainted later. Pearson correlation test was used to determine the linear association between syncopal time and age. A p value of <.05 was accepted as statistically significant.

Results

The distribution of time of fainting is shown in Figure 1. By ten minutes into the tilt study less than 20% of patients had fainted, whereas more than 90% fainted by 30 minutes. Age was evenly distributed across all syncopal times (Figure 2; r^2=0.02; p=0.08), suggesting that neither youth nor age proffers a greater propensity to fainting early.

Neither the 14 abnormal cardiac responses to deep breathing (11%) nor the 20 abnormal Valsalva maneuvers (15%), nor the 28 abnormal axon reflex responses (21%) clustered with an early or late faint time, or specific age bracket (Table 1).

Discussion

This study shows that:

a. Abnormal autonomic tests did not cluster with an early or late faint time.

b. Age did not correlate with time of faint.

c. Tilt table testing carried out to verify a diagnosis of syncope would miss over 80% of cases if carried out for 10 minutes, but will only miss 8% if carried out for 30 minutes. Further extrapolation of our data suggests that we might pick up only 1 or 2 additional percent beyond 40 minutes, if the trend were to continue as shown in Figure 1.

The term "reflex syncope" refers to a heterogeneous group of functional disturbances characterized by episodic vasodilatation and/or bradycardia leading to loss of blood pressure and cerebral hypoperfusion (10, 15). A change in posture may be the inciting event, but other common settings exist, such as straining, dehydration, emotional or physical distress etc. A combination of several reflex and physical factors may induce the event (16-19). Syncope prevalence is higher in the younger age group and reflex syncope is the most common cause (7). In contrast, orthostatic hypotension (defined as a reduction of systolic or diastolic blood pressure within 3 minutes of assuming the erect

posture) occurs with greater frequency in the population aged 65 years and older (20). It is generally thought that more severe orthostatic hypotension results in a shorter standing time (21). We sought to determine if shorter tilt duration (i.e. a shorter standing time) would also imply a more severe disorder (which often harbors a poorer prognosis) or different pathophysiology in patients with syncope. No study has examined this question.

We hypothesized that patients who faint earlier during a tilt study could have more significant pathophysiology (hence the
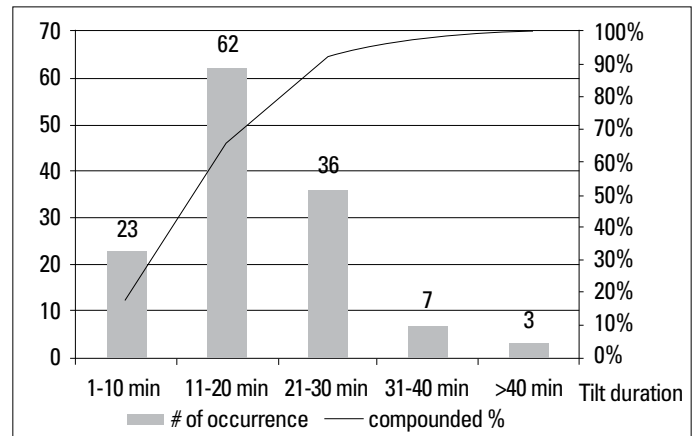

Figure 1. Tilt duration and number of occurrence ratio. Of 131 patients with "pure" reflex syncope, by ten minutes into the tilt study, only 18% of subjects had fainted, 65% by 20 minutes, 92% by 30 minutes, and 96% by 35 minutes
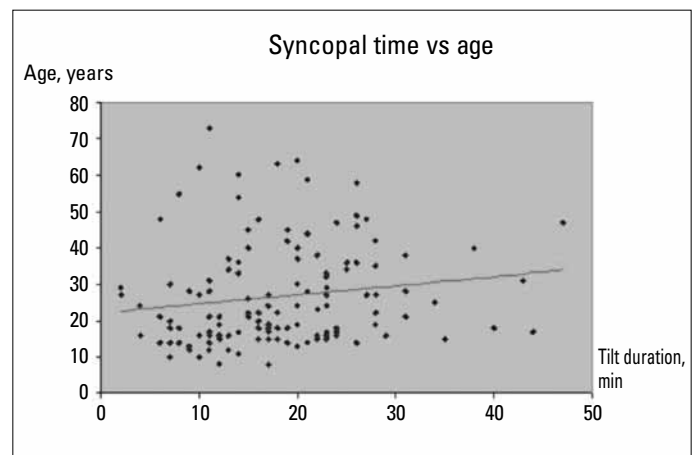

Figure 2. Age was evenly distributed across all syncopal times Pearson correlation analysis - r^2=0.02, p=0.078

Table 1. Autonomic tests results abnormality of 131 patients

Variables	Abnormal (n=131)	Abnormal autonomic testing <20 min	Abnormal autonomic testing >20 min	p*
VM, n (%)	20 (15)*	11	9	0.958
HRDB, n (%)	14 (11)*	7	7	
QSART, n (%)	28 (21)*	15	13	

*Chi-square test for TTT time < or >20 min
HRDB-heart rate response to deep breathing, QSART - the quantitative sudomotor axon reflex test, TTT - tilt -table test, VM- Valsalva maneuver

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shorter time upright), or have a younger age, since syncope occurs more frequently in a younger population (6).

Surprisingly, age did not correlate with time of faint as it was evenly distributed across all syncopal time (Fig. 2). This is an important finding. One explanation for these findings could be that the greater propensity to faint in the younger population is balanced by a more reactive baroreflex and vascular system, which prevents early syncope. Alternatively, syncopal timing may relate to other factors, such as concurrent emotional tone, or the effect of gravity on the vascular contents, whose timing is universal across all ages.

In addition, a similar finding related to the autonomic test data. These demonstrated no difference between patients with early faint times and those with late fainting times with regard to the degree or frequency of autonomic test abnormalities. Thus, our original hypothesis that patients with more evidence of dys-autonomia would faint earlier was not supported by our data. These findings imply that the primary central nervous system mechanisms of fainting bear little relationship to findings that assess peripheral autonomic nervous system function. These results are in keeping with those of Ojha et al. (13) who found that patients with orthostatic hypotension (who usually have highly impaired autonomic reflexes) faint less frequently than patients with postural tachycardia syndrome (who generally have preserved autonomic reflexes).

Study limitations

There are limitations to this study. First, its retrospective nature could have produced some bias in the selection of patients for study. However, the very objective nature of the data collected (the presence of absence of an observed faint on a tilt table study) militates against a selection bias, since all patients who fainted were included in the study. Second, we excluded all patients who had a known cause of dysautonomia in an attempt to select a very pure population of patients with reflex syncope only. As a result, these findings do not apply to patients with dysautonomias who happen to faint, but only to patients who experience syncope in the absence of an underlying autonomic disorder. Finally, since we do not perform tilt table tests for longer than 45 minutes, we do not know how many additional patients would have fainted in longer time frames. However, the clearly tapering frequency of syncopal occurrence (Fig. 1) with longer tilt duration suggests that very few patients would faint at later times, unless there is non-linear distribution of fainting.

Conclusion

We conclude that (1) in subjects with a history of syncope, the duration of the tilt table test should be of at least 30 minutes (2). It appears that "a faint is a faint" since age was evenly distributed across all syncopal times, and abnormal cardiac responses to deep breathing, Valsalva maneuvers and axon reflex responses did not cluster with an early or late faint time, or specific age bracket.

Conflict of interest: None declared.

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