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Original

Head-Up Tilt Test: Lessons Learned from 564 Consecutive Cases.

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Abstract

Introduction. Syncope is a frequent reason for medical consult; the most common mechanism is reflex syncope, that includes neurocardiogenic syncope (NS), orthostatic hypotension, carothid sinus hypersensitivity among others. These variants are evaluated with head-up tilt test with or without pharmacological stimulus with nitroglycerine. This study assessed our experience for the last 8 years with this complementary test.

Material and method. It is a retrospective study; we analyzed the results of head-up tilt test performed to patients consecutively referred to our centre between july 2003 – august 2010. Data was obtained from an electronic database and from an interrogatory about symptoms that prompted the exam.

Results. We included 565 performed head-up tilt test: mean age was 36,33±18,4 years old (6-89), with a female predominance (373) over male (191). The reason it was indicated was history of syncope (67%), lipothymia (26%) and others. The test was abnormal in 470 patients (negative in 92, sensibility 83,6) and diagnosis were: NS of vasodilator type 118 (25%), NS of cardioinhibitory type 112 (24%) and 157 NS of mixed type (33%); 60 patients presented postural orthostatic tachycardia (12%) and 24 orthostatic hypotension (5%), 9 of whom were taking antihypertensive pharmacological treatment; their mean age was 64 years old. In 11 patients (2,3%) carotid sinus hypersensitivity was documented, 9 of whom had also another form of NS; mean age 60,63 years old.

Conclusion. Head-up tilt test is a sensitive tool for evaluation of patients with syncope, especially in young people without cardiac disease. NS is the most frequent disautonomia and it is more prevalent in women, but more severe in men. Otherwise, orthostatic hypotension and carotid sinus hypersensitivity are predominant in older ages.

Keywords: tilt test, syncope, neurocardiogenic syncope, orthostatic hypotension, carothid sinus Hypersensitivity

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Syncope is a frequent reason for medical consults in emergency rooms and outpatient medical centers. Approximately one out of three people will experience it during their lives[1], many of whom will not seek medical attention because it does not occur on a frequent basis. In other cases, low intensity episodes, which resemble most intense ones, including prodromal (pro=forward, drom=race) symptoms such as palpitations, weakness and intolerance to upright position. The biggest challenge for the physician is to differentiate between patients with a reflex syncope, lacking structural heart disease, from those in which it is a symptom of bradyarrhythmia or tachyarrhythmia that may be the prelude to sudden death. This subgroup should undergo a cardiological assessment in order to assess the presence of structural heart disease, such as aortic stenosis or coronary artery disease, and to detect channelopathies such as Long QT syndrome or Brugada syndrome.[2]

In most patients with reflex syncope, the mechanism is neurocardiogenic.[1] In essence; stimuli such as prolonged upright position or a rapid change in position generate an initial and

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often disproportionate (hypertension and tachycardia) adrenergic discharge that excites afferent information from the myocardium and arteries to the brain stem. Consequently, after a period that is usually of several minutes, a reflex response of sympathetic inhibition and parasympathetic excitation (hypotension and bradycardia) appears resulting in cerebral hypoperfusion, loss of postural tone and syncope. Once the supine position is adopted again,the patient awakensand prodromal symptoms disappear. In some patients bradicardia[3] predominates ("cardioinhibitory" response), in others, hypotension ("vasodepressor" response) and in others, a combination of the two of them. It usually occurs in young people with no structural heart disease and with a history of similar episodes characterized by rapid recovery and no significant consequences in their general condition. This is a feature that differentiates it from seizures that occur due to a loss of postural tone, without drop-attacks. It should be noted, however, that some patients with neurocardiogenic syncope present seizures due to bradycardia or extreme hypotension. Thus, these two conditions must be carefully diagnosed. In some patients the symptoms appear in relation to micturition, coughing and even laughing or swallowing.[1]

There is another group of patients that shows identical prodromal symptoms, but rarely suffer from syncope: "postural orthostatic tachycardia"[4], which usually occurs with swift and unmotivatedpalpitations, accompanied by sweating and faintness; also triggered by postural changes. Palpitations are usually accompanied by dyspnea and sometimes-oppressive chest pain, which can be triggered by physical effort and relieved through repose. Hence, although occurring in very young individuals, a remarkable feature in some cases is intolerance to exercise. This entity is different from "inappropriate sinus tachycardia," from which it should be distinguished.[5-7] Other less common forms of reflex syncope exist, such as carotid sinus hypersensitivity and orthostatic hypotension,[7] which are rather observed in people of older age that use antihypertensive drugs and in some cases with coexisting conditions that affect the autonomic nervous system, such as diabetes mellitus and Parkinson's disease.[7-9]

The head-up tilt test is a supplementary test widely used for the evaluation of these dysautonomic syndromes.[8, 10-12] It was initially used by physiologists and its clinical effectiveness was established by the various pathological responses to postural change. However, in this test there is no "gold standard" against which to compare its sensitivity and specificity. Somepatients with no history of syncope could develop it during the test if we wait long enough, and many patients with a history of syncope may only show minor hemodynamic changes that fall within normality's broad spectrum. In these cases, provocative pharmacologic agents such as intravenous isoproterenol and sublingual nitroglycerin are used to increase sensitivity[10-12]. The first is a beta-adrenergic whose objective is to increase stimuli so as to trigger the subsequent paradoxical autonomic reflex. The second also aims at increasing the adrenergic tone, but as a vasodepressor response and the subsequent reduction in venous return produced. It is generally accepted that the presence of bradycardia and hypotension after an adrenergic stimuli such

Table 1. Different dysautonomic syndromes shown by the head-up tilt test.[10,11]

1. Nerocardiogenic syncope of "cardioinhibitory" type:
Fall in heart rate to less than 40 bpm or asystole longer than 3 s. The fall in blood presure concurs with that of heart rate.
2. Nerocardiogenic syncope of "vasodepressor" type:
Fall in blood pressure without a fall in heart rate (no more than 10% of the peak rate experienced).
3. Nerocardiogenic syncope of "mixed" type:
Fall in blood pressure before a fall in heart rate, but the latter in not less than 40 bpm.
4. Postural orthostatic tachycardia:
Increase in heart rate of more than 30 bpm in relation to the baseline heart rate or greater than 130 bpm, together with instability of blood pressure, without experiencing syncope.
5. Orthostatic hypotension (part of the "autonomic insufficiency" syndrome):
It may be "classic": fall in blood pressure (20mmHg in the systolic and 10 in the diastolic) within 3 minutes of upright position; or deferred: the absence of hypertension and tachycardia in response to the upright position (less than 10% of baseline rate)
6. Carotid sinus hypersensitivity:
Fall in blood pressure by more than 50mmHg or ventricular pause of more than 3 s after the compression of the carotid during 5-10 s.

Table 2. Drugs taken by the group of patients studied		
No drugs		399
Vasodilators or other cardiotonic drugs:		49
Angiotensin receptor antagonist	28	
Angiotensin converting enzyme inhibitor	16	
Calcium channel blocker	3	
Diuretics	2	
Drugs acting on the autonomic nervous system:		28
Beta-blocker	23	
Salbutamol or other inhaled bronchodilator	3	
Etilefrine	1	
Hyoscine	1	
Psychoactive drugs: (antidepressant, anxiolytic and antipsychotic)		2
Other drugs (antacids, anti-inflammatories and statins)		71

as the orthostatic challenge is a pathological response, and thus it is established that the patient suffers from one of these dysautonomic disorders. Treatment in most cases is preventive and includes hydration, regular exercise and use of compression stockings.[13] Some recurring cases require prescription of fludrocortisone[13] (a mineralocorticoid) or a beta-blocker[14] or other drugs. Cardiac pacing should only be considered in special cases when symptomatic bradycardia occurs and it does not respond to other non-invasive measures. [13]

This study reports the experience with this supplementary test performed in our medical center during the last 8 years in order to identify the characteristics of the population studied and the results obtained.

Materials and methods

This is a retrospective study that analyzed the results of head-up tilt tests performed in a sequential order and by a single operator to patients referred to the Cardiology Department during the period July 2003- August 2010. The information was obtained from the database (electronic records) of our medical center. The database records on a regular basis and in consecutive order the patients' personal data, the main symptom for which the test was requested and the drugs taken at that moment, as well as the data obtained during the study and its result.

All patients were interrogated about their symptoms in order to determine the reason for the test request. Basically, the protocol used for the test is as follows: after a 15 minute rest period in supine position, the patient is placed in passive upright position at 70-80 degrees by using a tilt table and through continuous electrocardiographic recording, heart rate and blood pressure are logged every 3 minutes. If after 20 minutes in passive upright position the patient has not experienced any hemodynamic symptoms or changes, 5-10 µg of sublingual nitroglycerin are administered while similar vital signs and electrocardiographic controls are performed. If after 12 minutes the patient has not presented any symptoms or hemodynamic changes, the test is considered to be over. Conversely, if during the test the patient experiences hemodynamic symptoms or signs, such as hypotension or bradycardia, the procedure is considered to be over at that moment. Table 1 shows the definitions used to describe the study's results.

The tests were requested mainly by the Internal Medicine, Emergencies, Cardiology and Neurology departments of our and other medical centers. The vast majority of patients had been assessed through other supplementary tests to rule out a structural heart disease or neuropathies and then was referred under such condition to take the test. Simple statistical calculations were performed and subgroups were compared, using a value of $p < 0.05$ as a statistically significant difference.

Results

The data included was that of 564 head-up tilt tests performed on the same number of patients in a consecutive order. The mean age was 36.33 ± 18.4 years (range 6-89, median 32), predominantly females (373 females, 191 males). The reason for performing the test was: history of syncope (67%), lipothymia (26%) and others, which included vertigo, orthostatic intolerance, palpitations, and bradycardia. In 399 of the patients the test was performed without prior pharmacologic treatment and 23 patients were taking a beta-blocker or other drugs acting on the autonomic nervous system (Table 2).

Table 3. Hemodynamic results, according to diagnosis obtained

Diagnosis	n	%	Mean age	Mean baseline HR	Immediate HR*	HR during the symptom
Neurocardiogenic syncope	387	82	34,2	75,9		56,8 and 71**
Mixed	157	33				
Vasodepressor	118	25				
Cardioinhitory	112	24				
Postural orthostatic tachycardia	60	12	31,1	83,8	98,1 (Δ18%)	130
Orthostatic hypotension	24	5	64	86,42		
Carotid sinus hypersensitivity	11	2,3	60,63	14,55		
ALL	565		36,39	72,8 ± 14 (41-141)	82,2 (Δ14%)	80,58 (m) 65,9 (h)

n: absolute number; HR: heart rate; *: in passive upright position; **: without nitroglycerine and with nitroglycerine; Δ: variation with respect to baseline; m: mate; f: female

The test was abnormal in 470 patients (negative in 92, overall sensitivity 83.6). Diagnoses were (Table 3): 112,neurocardiogenic syncope of cardioinhibitory type (24%, Fig 1); 118, neurocardiogenic syncope of vasodepressor type (25%) and 157 of mixed type (33%). The three of them amounted to a total of 387 patients (82%); 60 patients presented postural orthostatic tachycardia (12%) and 24 orthostatic hypotension (5%). This group had a mean age of 64 years (as opposed to 36 years for the group as a whole); 8 took an antagonist of the renin-angiotensin-aldosterone system and 1 a beta-blocker. In 11 patients (2.3%) carotid sinus hypersensitivity was recorded, 9 of which also suffered from some form of neurocardiogenic syncope. The mean age of this group was 60.63 years and only 1 patient was taking an antagonist of the renin-angiotensin system. When selected according to the prescription reason, in patients with a history of syncope, the test result was abnormal in 317 out of 378 (sensitivity=84%), while in those whose symptom was lipothymia or other, the test result was abnormal in 152 out of 182 (sensitivity=83%).

In the group of patients with induced neurocardiogenic syncope without provocative pharmacologic agent (n=31), the mean time of symptom onset was 10.6 minutes; heart rate (HR) was 56.8 beats per minute (bpm, range 6-145) and mean blood pressure 26.3 mmHg at the time of symptom. In the group in which a pharmacological provocative agent with nitroglycerin was used (n=356), said variables were 5.3 minutes, 71 bpm (4-156) and 48.68 mmHg, respectively. Two cases presented complete atrioventricular block (Figure 2).

Fig 1. Female patient, 32 years old, presented severe bradycardia 14 minutes after upright position began, preceded by classical prodromal symptoms such as nausea, blurry sight and sweating. Notwithstanding extreme bradycardia, these patients do not require a pacemaker because their sinus dysfunction is reversible.

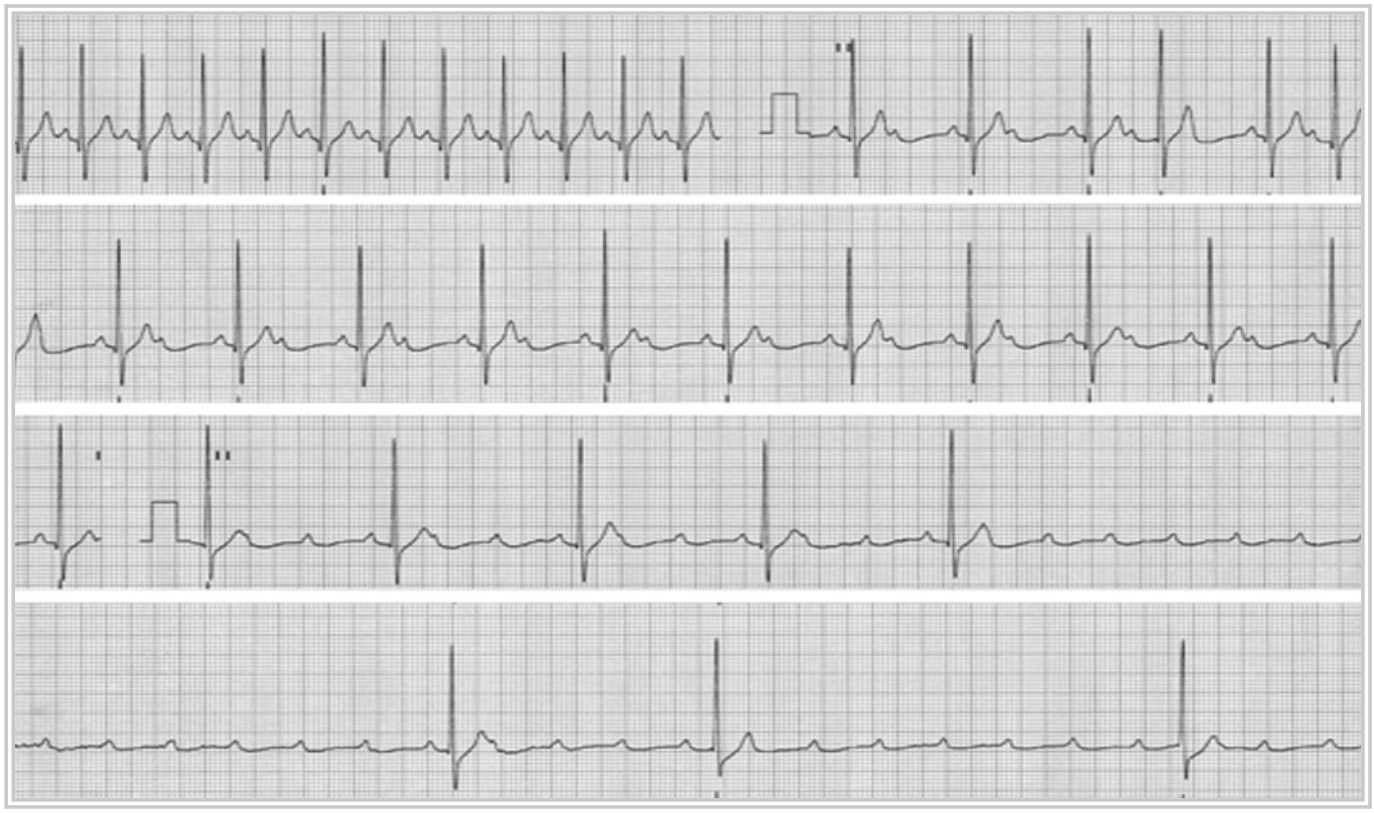

Fig 2. Male patient, 30 years old, soccer player; presented symptoms and signs compatible with neurocardiogenic syncope of cardioinhibitory type and complete atrioventricular block during the head-up tilt test, which reverted with the supine position (authorized use from ref. 3).

In the group that was diagnosed with postural orthostatic tachycardia, the meanbaseline HR was 83.8±15.3 bpm, the immediate HR in passive upright position was 98.11±19.8 (a variation of 15±4 bpm or 18%) and the mean HR reached in the second stage was 130 bpm (range 74-177 bpm); while in the group as a whole, these values were 72.8±14 (41-141), 82.2±16.7 (variation of 10±2 bpm or 14%) and 80.58 (in females) - 65.9 (in males, p=<0.05). Systolic blood pressure in the group reached mean maximum values of 138.12±20.6 and the diastolic one, 96.56±13.6.

Discussion

As reported by the literature, most patients with dysautonomies examined through this test are young people, mainly female[1,2,10-12]. The most frequent diagnosis resulting from this test was neurocardiogenic syncope, mostly of a mixed type. Although the mean age was similar in males and females, mean heart rate was significantly different among them: in men syncope is less frequent but more severe. Although this test is more sensitive in people with a history of syncope than with other symptoms such as lipothymia or palpitations, in this series sensitivity was similar because many patients with test requests due to lipothymia or palpitations had a previous history of syncope at some point of their lives. It is also important to point out that this supplementary test does not have a "gold standard" with which to determine its capacity[10-12]. Postural orthostatic tachycardia is also a common reason to seek medical attention, in many cases it is attributed by the patient to cardiac origin and is often confused with paroxysmal supraventricular tachycardia; however, the non-paroxysmal beginning and end rule out this possibility. In this series high blood pressure values were also found during the test (the so-called "orthostatic hypertension"), which is compatible with the initial adrenergic activation that occurs in these disorders. In addition, it was observed that in several young patients the neurocardiogenic syncope coexisted with their hypertensive debut.

On the other hand, orthostatic hypotension and carotid sinus hypersensitivity are much less frequent causes (5 and 2.3% respectively) and affect older people (64 and 60 years, respectively), compared to the mean age of 33.6 years in the group studied for lipothymia or syncope in this series[12]. It is noteworthy that 10 out of 24 patients with orthostatic hypotension were taking an antihypertensive drug, thus, a pharmacologic cause must be though of when studying the origin of syncope in these type of patients. This age group also has increased risk of morbidity from trauma related to syncope episodes and higher probability of coexistence of other conditions affecting the autonomic nervous system.

From the results obtained, it is important to observe that the sub classification of the different dysautonomic syndromes not only provides diagnostic information, but it also guides the selection of the type of drug therapy, once this course of action is decided. Since the results of different studies with drug therapy have not clearly demonstrated its benefits, always the recommendation is to first prescribe preventive measures such as regular exercise, hydration, increased salt

intake, use of compression stockings, orthostatic training and to avoid triggering situations that may be identified[14]. The use of pacemakers is more controversial; even in cases in which bradycardia prevails, since this is a reversible condition[14].

In conclusion, this retrospective study shows that the head-up tilt test, with or without pharmacologic provocative agent is adequately sensitive for the assessment of patients with syncope (more than with other symptoms), in particular, in young patients without evidence of structural heart disease. Neurocardiogenic syncope is the most frequent dysautonomy and is more prevalent in women (but more pronounced in men), while orthostatic hypotension and carotid sinus hypersensitivity prevails in older people, many of them in relation to antihypertensive drug therapy.

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