Diagnostic Relevance of the Carotid Sinus Massage During a Head Up Tilt Table Test (HUTT)

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Summary

Background: Syncope due to carotid sinus hypersensitivity (CSH) may be underdiagnosed due to a low level of diagnostic suspicion and fear of complications caused by massage of the carotid sinus.

Objective: To investigate the relevance of carotid sinus massage in the diagnosis of non-convulsive faints and unexplained falls.

Methods: Two-hundred and fifty-nine patients with a mean age of 50±24 years referred for the investigation of non-convulsive faints or unexplained falls were evaluated with a head up tilt table test (HUTT) without ("passive") and with pharmacological stimulation. Clinical and laboratory work-up did not reveal an obvious cause for the complaints. Fifty-five volunteers with a mean age of 57±21 years with no history of seizures, faints or falls were used as controls. All participants underwent a HUTT preceded by digital stimulation of each carotid sinus both at zero and 60°.

Results: Carotid sinus massage was positive in 4 controls. The relevance of CSH in the evaluation of syncope was supported by a positive response to carotid sinus massage at 60° in 28 patients, most of whom were elderly men. Carotid sinus massage was positive at 0° in only three of such patients. The results of the HUTT did not show statistical difference between patients with and without CSH.

Conclusion: Carotid sinus massage at 60° under controlled conditions should be included in the assessment of patients with non-convulsive faints or unexplained falls. Routine cardiovascular exams, including the HUTT, are not useful for the diagnosis in such cases. Further studies in normal individuals are needed to establish the significance of a positive response to carotid sinus massage in the absence of a history of fainting or falling. (Arq Bras Cardiol 2008; 90(4): 264-267)

Key words: Syncope; hypersensitivity; carotid sinus; tilt table test.

Introduction

The original description of convulsive syncope due to carotid sinus massage was also the first one to correctly interpret bradycardia and hypotension as abnormal *reflex* responses and its normalization by previous atropine use[1]. Currently, the carotid sinus *hypersensitivity* (CSH) is diagnosed in patients in whom the carotid sinus massage (CSM) induces asystole for more than 3 seconds (cardioinhibitory type) *or* systolic pressure decrease > 50 mmHg (vasodepressor type)[2]. Subsequent studies established the importance of CSM as the cause of fainting[3] and drop attacks[4], as well as the increase in the reflex reactivity of the carotid sinus that occurs with aging, mainly in men[5]. The inclusion of the Head-up Tilt Table Test (HUTT)[6] increased the extent of causes of neurocardiogenic syncopes, particularly those caused by CSH[7].

However, despite the increasing number of studies that used CSM under controlled positions, the clinical significance of CSH remains to be clarified, especially considering its unexpectedly high prevalence among individuals that have never fainted[8]. The main objectives of the present study were: (i) to report on a series of individuals referred to a HUTT to investigate non-convulsive faints or unexplained falls; (ii) to determine the prevalence of induced CSH induced by CSM in this series of patients and (iii) to determine the usefulness of the HUTT used in our Service based on a group of volunteers with no history of unexplained falls or fainting.

Methods

One hundred and seventy women and 89 men aged 10 to 96 years (mean age = 50 ± 24 yrs) were referred for the investigation of "fainting" or unexplained falls (drop attacks) of which the first episode had occurred several months before (mean period = 53 ± 100 months). Nineteen patients with +CSM had been regularly using benzodiazepines (n=2), anticonvulsants (n=3), hypotensive drugs (n=15), diuretics (n=5) and oral anticoagulants (n=1). The physical examination, ECG and echocardiogram were either normal or showed no association with the symptoms of interest. Fifty-five volunteers (32 women, 23 men) with no history of

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unexplained falls or fainting, aged 16 to 88 years (mean age = 57 ± 21 yrs) served as controls for the HUTT. There was no difference regarding age between men and women in the patients' group ($U = 5200$, $p > 0.56$) or controls ($U = 329$, $p > 0.98$). Additionally, there was no difference between the groups regarding the gender composition ($\chi^2 = 0.77$, $p > 0.38$). All patients and controls signed an informed consent form prior to enrollment in the study, which was approved by the Institutional Ethics Committee of *Hospital Universitário Gaffrée e Guinle*.

HUTT and CSM

The HUTT was performed between 2 and 5 PM[9] in a quiet room, under soft lights and comfortable room temperature, according to the broadly accepted technical recommendations[10]. The test table (Carci, São Paulo, Brazil), was equipped with a TEB system for continuous ECG monitoring and support for the feet and allowed 60 to 80° inclinations. Blood pressure was measured by an oscillometer and the levels were confirmed by a sphygmomanometer at regular intervals. A resuscitation tray was kept at hand throughout the test. Each individual was asked to fast for 12 hours and, if possible, to withdraw medications for 24 hours prior to the test. After 10 minutes of resting on dorsal decubitus, the examiner manually massaged the region of the neck where the carotid pulse attained maximum intensity, for 5 seconds, usually on the upper border of the cricoid cartilage, starting on the right side. Subsequently, the table was tilted at 60° and the maneuver was repeated on each side. Previous observations showed that the carotid sinus massage can be completely normal at 0° and become positive only after the tilting[11]. The HUTT consisted of two conditions[10]: (i) a "passive" condition (*i.e.*, without pharmacological intervention) and (ii) a pharmacologically "sensitized" condition that consisted in administering 1.25 mg of isosorbide dinitrate by sublingual route in order to cause unapparent symptoms in the passive condition. Each condition lasted 25 minutes or less, in case of pre-syncope. When the test was positive in the first phase, it was concluded without the need to perform the sensitized condition. The HUTT was normally performed in cases of positive CSM. The HUTT was considered abnormal ("positive") if syncopal or pre-syncopal symptoms mediated by neural mechanisms occurred due to hypotension, bradycardia or both, whether the individual attested or not the replication of symptoms that affected him/her in real life. The CSM was considered positive if there was a minimum decrease of 50 mmHg in the systolic blood pressure or bradycardia/asystole[2,10]. Carotid murmur, cerebrovascular accidents or acute myocardial infarction in the six months prior to the test or previous history of severe ventricular arrhythmia were contraindications for the test.

Statistical analysis of the results

The results are shown as means ± standard deviations. Possible associations between categorical variables were inferred by the Chi-square (χ^2) test. The significance of the differences between groups was measured by the Mann-Whitney test (*U*) and Fisher Exact test[12]. The relative contribution of age, sex, HUTT result and physiological indexes (blood pressure and heart rate) for the occurrence of CSH was inferred by Binomial Logistic Regression. The Binomial Logistic Regression is appropriate for dichotomous dependent variables (such as +CSM *vs* -CSM), to which a value equal to 1 is attributed to the main interest variable (for instance, +CSM) and zero to the other (for instance, -CSM). The size of the effect and the direction of the association between the independent variables are expressed as odds ratio (OR).

Each OR can vary from zero to 0.999 (in the case of an inverse relation) or from1.001 to infinite (in the case of a direct relation); when the OR = 1, the variables are statistically independent[13]. The size of the global effect of the logistic regression was measured by Nagelkerke's R^2, which, similarly to the multiple determination coefficient (R^2), varies from zero to 1. Statistical significance level was set at 0.05 (two-tailed), for all statistical tests. Calculations were carried out using the SPSS for Windows, v. 13.0 (SPSS Inc, 2004).

Results

The main results are shown in Table 1. Of the 259 patients referred to HUTT, 28 (11%) presented +CSM at 60° and only 3 at 0°. No participant presented complications caused by the CSM or HUTT, which is in agreement with the reported safety of the test[14].

Table 1 - Demographic characteristics and clinical and hemodynamic affiliations to the carotid sinus massage.

	Positive vagal maneuver (CSH) N=28	Negative vagal maneuver N=231
Age (yrs)*	71±11	47±23
Sex (M/F)*	20/8	69/162
Frequency of fainting episodes	4.4±3.4	3.7±2.7
Duration of symptoms (months)	59±88	52±94
Tilt test (positive/normal)	20/8	149/82
Passive (min)	22±8	24±4
Stimulated (min)	13±10	15±9
HR		
basal	67±8	72±12
maximum	88±15	101±18
during**	50±25	65±24
Systolic BP		
basal	131±28	121±21
maximum	137±28	123±26
during	65±21	70±17
Diastolic BP		
basal	80±14	74±13
maximum	84±14	80±15
during	34±13	40±13

** $p < 0.0001$, ** $p < 0.050$*

Patients

When compared to the –CSM patients, the +CSM group consisted mainly of elderly men. Although the HUTT was positive in more than two-thirds (71%) of the latter, this percentage did not statistically differ from that observed in –CSM patients ($p = 0.53$).

To explore the clinical associations of the CSH, the binomial logistic regressions were carried out, considering the CSM (+CSM *vs*. –CSM) as a dependent variable and age, sex, history of fainting (patients *vs*. controls), HUTT result (positive *vs*. normal) and hemodynamic indexes (blood pressure and heart rate) as independent variables. There was a significant correlation between the set of variables and the occurrence of CSH ($R^2 = 0.47$, $p < 0.001$). The CSH was predicted by male sex (OR = 5.19, $p < 0.02$), older age (OR = 1.10, $p < 0.001$), and lower heart rate during HUTT in the group with +CSM (OR = 0.96, $p < 0.04$). These results were not qualitatively modified after removing the controls from the calculation spreadsheets.

At a subsequent analysis, the result of the CSM was verified only in patients older than 60 years (n=138). In this subgroup, CSM was positive in 27 or 19% of the patients (20 men) and negative in 111 or 81% (32 men). As anticipated, there was no statistical difference regarding the age between the groups ($U = 1411$, $p > 0.64$), but the male predominance of CSH was confirmed ($\chi^2 = 19$, $p < 0.001$).

Controls

In the control group, the CSM at 60° was positive in four men with a median age of 70 years. The male predominance was significant in this group in relation to the other controls ($p = 0.02$) and, although there was no difference regarding the age ($U = 73$, $p > 0.45$), this group also showed a tendency to present lower basal heart rate during HUTT [medians: 62 bpm x 70 bpm ($U = 41.5$, $p < 0.07$)].

The HUTT was positive in only 3 controls (< 6%), none of which presented CSH. Regarding the controls, positivity at the HUTT was significantly higher in patients with CSH ($\chi^2 = 35$, $p < 0.001$).

Discussion

The main results of the study can be thus summarized: (a) among patients with a history of fainting, the HUTT did not differ between those with and without CSH; (b) statistically, the frequency of CSH did not differ between patients and controls; (c) the tendency to CSH in elderly men was statistically correlated with older age and male sex; (d) the CSM at 0° can be dispensed with in favor of the one at 60°.

Importance of CSM in the diagnosis of CSH

Our findings emphasize the importance of performing the CSM at 60° in the diagnosis of CSH: of 259 patients with a history of fainting or unexplained falls, 28 (11%) presented CSH at 60° inclination. Of these, only three presented a positive response at 0°. In contrast, only 4 controls presented CSH. Interestingly, CSH was not higher in the group with a history of fainting in relation to controls. Although the four individuals from the control group with CSH could present fainting episodes if followed for a sufficient period of time, we can, at the moment, only suggest that the diagnosis usefulness of the +CSM must be restricted to those individuals with a history of fainting clearly related to cervical manipulations. The relevance of the CSH is higher when it coincides with a history of fainting or falls that are precipitated by cervical manipulations in real life. Unfortunately, the causal nexus between head position and syncope becomes blurred due to the transient amnesia that affects some of these patients[15]. A recent study in 80 asymptomatic individuals older than 65 years demonstrated CSH in 28 (35%) of them[16]. The discrepancy between these findings and those of the present study is probably due to the lower mean age and higher prevalence of women among our controls. Although our results and those of several other studies agree that CSH is a relatively frequent occurrence among individuals that never fainted, the exact meaning of this phenomenon will only be clarified by further prospective studies that will determine the incidence of fainting with the passing of time. For the time being, the +CSM in the absence of fainting or falls has an unclear clinical significance[2,15].

HUTT and CSM

The HUTT positivity did not differ between patients with and without CSH; i.e., the HUTT did not substitute the CSM at 60° in the diagnosis of CSH. From a practical point of view, if the CSM had not been performed in the 8 individuals who presented fainting and negative HUTT, the diagnosis of CSH would have been missed. Additionally, the patients with CSH and negative HUTT demonstrate the existence of distinct physiopathological mechanisms in the syncope event.

In fact, the exact physiopathological mechanisms that lead to the intermittent failure of the cardiovascular reflexes in the daily life of patients with CSH have yet to be completely clarified. In this sense, a potentially relevant physiopathological observation was the lower HR *during* HUTT in patients with CSH, which is suggestive of baroreceptor reflex failure. These reflexes, of which physiology is currently well known[2], are integrated by fibers that reach, through the glossopharyngeal nerves, the vegetative nuclei of the reticular formation of the bulb, from where the vagal and reticulospinal fibers radiate to the sympathetic column of the thoracic spinal cord[17].

Further studies are necessary to clarify the altered segments of this circuit that impair the chronotropic response in patients with CSH.

Contribution of CSM to diagnostic economy

Most of the patients with CSH had been seen by general practitioners and specialists before the HUTT was requested. It is likely that the unpredictability and rarity of the faints contributed to delay the diagnosis of CSH. The mean of four fainting episodes, apparently low in absolute numbers, must not underestimate the high morbidity associated to a single fall, especially among elderly patients[18]. Additionally, the diagnosis delay implicates in frequently unnecessary costs. For instance, if the patients referred to a specialist's assessment (cardiologist or neurologist), electrocardiogram and echocardiogram,

Holter monitoring, EEG, echo Doppler of the carotid and vertebral arteries and at least one brain imaging assessment (computed tomography or magnetic resonance) had been initially submitted to CSM, the diagnostic cost would have been substantially lower. Apparently, such has not occurred due to the lack of diagnostic strategy guided by the hypothesis of CSH in these cases.

Also from an economical point of view, the CSH presents additional implications for automobile driving[19], considering that, due to the mechanism that triggers fainting in these cases, this type of syncope can affect the individual while driving, during head movements that compress one of the abnormally sensitive carotid sinuses.

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Potential Conflict of Interest

No potential conflict of interest relevant to this article was reported.

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Study Association

This study is not associated with any graduation program.

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