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The usefulness of the head-up tilt test in patients with suspected epilepsy

Inês Rangel [a,c,*], João Freitas [a,c], Ana Sofia Correia [a,c], Alexandra Sousa [a,c], Ana Lebreiro [a,c], Carla de Sousa [a,c], Maria Júlia Maciel [a,c], Elsa Azevedo [b,c]

[a] Cardiology Department, São João Hospital Center, Porto, Portugal
[b] Neurology Department, São João Hospital Center, Porto, Portugal
[c] Faculty of Medicine of Porto University, Porto, Portugal

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ABSTRACT

Purpose: It is estimated that approximately 20–30% of patients diagnosed with epilepsy have been misdiagnosed, and neurocardiogenic syncope (NCS) might frequently be the real cause of transient loss of consciousness (TLOC) episodes.

We assessed the role of the head-up tilt test (HUTT) in patients previously diagnosed with refractory epilepsy to evaluate the ability of this test to correctly diagnose patients with NCS.

Method: We retrospectively analysed the clinical records of 107 consecutive patients with a previous diagnosis of refractory epilepsy that were taking antiepileptic drugs and who were referred for HUTT between January 2000 and December 2010. During the subsequent follow-up, we recorded the treatments performed and the recurrence of symptoms.

Results: Complete follow-up data were available for 94 (88%) patients, and the mean follow-up period was 80 ± 36 months. The HUTT was positive in 54% of patients. Thirty-one (33%) patients were misdiagnosed with epilepsy, and 20 (21%) patients had a dual diagnosis of NCS and epilepsy. The recurrence of TLOC was reported in 55% of the patients, but it was significantly lower in the misdiagnosed group (42% versus 64%; $P = 0.039$).

Conclusion: NCS is an important cause of epilepsy misdiagnosis. The HUTT is often critical for making an accurate diagnosis and subsequently selecting the appropriate treatment for patients presenting with TLOC. The diagnostic overlap between epilepsy and NCS is not uncommon, suggesting that electroencephalographic monitoring during a HUTT may play an important role in diagnosing patients with recurrent, undiagnosed TLOC episodes.

1. Introduction

Epilepsy and syncope, two prevalent clinical conditions, are frequently initially diagnosed incorrectly.[1,2] Transient loss of consciousness (TLOC) associated with involuntary motor activity is sometimes mistaken for epilepsy and, consequently, antiepileptic drugs (AEDs) are often prescribed in these circumstances.[3,4] It is estimated that 20–30% of patients diagnosed with epilepsy have been misdiagnosed, and neurocardiogenic syncope (NCS) might be the most frequent cause of this mistake.[4,5] An incorrect diagnosis of epilepsy can lead to inadequate therapeutic treatments and prognostic deductions, which can subsequently cause refractory therapy, adverse secondary effects of the AED, symptom recurrence, and a delayed identification of the real TLOC cause.

When differentiating between syncope and epilepsy, it is extremely helpful to carefully and methodically analyse the patient's history.[6] However, a complete and accurate history may not be sufficient to differentiate between the two clinical entities, and the head-up tilt test (HUTT) has already proven to be a valuable diagnostic tool when investigating unexplained TLOC.[7] Nonetheless, it is not well established how prevalent a dual diagnosis of NCS and epilepsy is or how a systematic performance of the HUTT and an electroencephalogram (EEG) test in patients with TLOC might help to achieve a more accurate diagnosis. In patients with refractory TLOC, we aimed to assess the role of the

* Corresponding author at: Alameda Prof. Hernâni Monteiro, 4200-319 Porto, Portugal. Tel.: +351 966462512.
E-mail address: inesrang@gmail.com (I. Rangel).

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HUTT in the diagnosis of NCS, the prevalence of a dual diagnosis of NCS and epilepsy, and the frequency of symptom recurrence in a long-term follow-up for each group.

2. Methods

In this study, we retrospectively analysed the clinical records of 107 patients with a prior diagnosis of refractory epilepsy that were taking AEDs and who were consecutively referred to an Autonomic Clinic for HUTT between January 2000 and December 2010. Exclusion criteria included patients without an available EEG.

Refractory epilepsy was defined as a failure to achieve a sustained absence of seizures following two trials of tolerated and appropriately chosen AED regimens of either mono- or combination therapy.[8] The diagnosis of refractory epilepsy was established by the patient's neurologist and was based on symptom recurrence, which was occasionally associated with dubious clinical manifestations. The epileptiform activity on EEGs was defined as characteristic waves or wave complexes, distinct from the background activity, and resembling those recorded in a group of human subjects suffering from epileptic disorders.[9]

When the patients underwent the HUTT, they completed a questionnaire to obtain clinical details including pre- and post-TLOC symptoms. The HUTT was performed according to the guidelines of the European Society of Cardiology, which involves a 70° upright head-up tilt in an electric tilt table with footplate support and body straps for up to 40 min. Blood pressure was monitored using digital photoplethysmography (Finapres®), and an electrocardiogram was continuously recorded throughout the study. When no syncopal event was observed during the tilting phase (baseline), sublingual nitrates were administered. Patients over 40 years of age were also examined with bilateral carotid massage, which was performed in the supine position and after a prolonged orthostasis whenever there was no contraindication. A positive HUTT required the presence of syncope or pre-syncope, associated with the reproduction of usual clinical symptoms, and a significant sudden drop in blood pressure and/or heart rate.

A final clinical diagnosis was supported by a consensus between a neurologist and a cardiologist and was based on the patient's clinical features and the results of the HUTT and the EEG (Table 1):

- Epilepsy alone: negative HUTT and symptoms and EEG consistent with epilepsy.
- NCS alone: typical clinical reproduction of symptoms during the HUTT and symptoms and EEG not consistent with epilepsy.
- Dual diagnosis of epilepsy and NCS: typical clinical reproduction during the HUTT of some of the patients' symptoms, but coexistence of other episodes, symptoms and EEG consistent with epilepsy.
- TLOC of unknown cause: unspecific symptoms, negative HUTT and EEG not consistent with epilepsy.

The patients' subsequent follow-up was performed via a telephone interview to evaluate their clinical evolution, including treatments performed and symptom recurrence. Clinical records for each patient were carefully reviewed to complete the information regarding symptom recurrence as well as type and date of clinical outcomes. We considered clinical outcome a recurrence of sudden spontaneous TLOC, which presented with the same characteristics of the previous episodes.

2.1. Statistical analysis

We calculated the mean of continuous variables and the frequency of categorical variables. Comparisons were made using ANOVA (Scheffe's F test) for continuous variables, and the chi-square test was used for categorical variables. The cumulative proportion of TLOC recurrence was estimated via the Kaplan–Meier method by plotting proportion recurrences as a function of time. The survival curves according to the final diagnosis (NCS versus epilepsy/dual diagnosis) were compared using the log-rank test. Two-tailed P-values < 0.05 were considered statistically significant. Statistical analysis was performed using SPSS Statistics version 19.0 (SPSS Inc., Chicago, IL).

Table 1
Clinical characteristics according to final clinical diagnosis.

Variables	Total (N = 94; 100%)	Epilepsy (N = 39; 41%)	NCS (N = 31; 29%)	Dual (N = 20; 21%)	P value
Age (years), mean (SD)	39 (17)	40 (15)	33 (16)	41 (18)	0.160
Female, N (%)	67 (71)	27 (69)	22 (71)	15 (75)	0.898
Episode frequency					
Weekly	3 (3)	2 (5)	1 (3)	0 (0)	0.457
Monthly	28 (30)	14 (36)	7 (23)	5 (25)	
Bi-annually	31 (33)	9 (23)	14 (45)	7 (35)	
Annually	32 (34)	14 (36)	9 (29)	8 (40)	
Prodromal/associated signs and symptoms					
Visual symptoms	50 (53)	21 (54)	18 (58)	9 (45)	0.657
Dizziness and light-headedness	62 (66)	26 (67)	21 (68)	12 (60)	0.835
Diaphoresis	34 (36)	13 (33)	13 (42)	8 (40)	0.742
Palpitations	33 (35)	17 (44)	7 (23)	7 (35)	0.185
Nausea/vomiting	17 (18)	8 (21)	7 (23)	2 (10)	0.198
Pallor	33 (35)	13 (33)	11 (35)	7 (35)	0.981
Asthenia	49 (52)	22 (56)	17 (55)	9 (45)	0.693
Myoclonic movements	71 (76)	34 (87)	22 (71)	15 (75)	0.098
Sphincter incontinence	18 (19)	12 (31)	3 (10)	3 (15)	0.074
History of trauma	32 (34)	19 (49)	7 (23)	6 (30)	0.064
Precipitated by standing position	59 (63)	20 (52)	23 (74)	14 (70)	0.111
Comorbidities					
Hypertension	10 (11)	3 (8)	4 (13)	2 (10)	0.253
Diabetes mellitus	4 (4)	1 (3)	0 (0)	2 (10)	0.142
Cardiac disease	2 (2)	2 (5)	0 (0)	0 (0)	0.516
Psychiatric disease	4 (4)	2 (5)	0 (0)	0 (0)	0.920

* Statistical significance for p value < 0.05.