Pediatric Cardiology

Tilt Table Test in Children with Unexplained Syncope

Yu-Jan Lin,[1] Pi-Chang Lee,[1,2] Betau Hwang[1,2] and C.C. Laura Meng[1]

Background: Neurocardiogenic syncope is well known as the most frequent cause of syncope in childhood. The head-up tilt table test (HUTT) is now widely used to evaluate patients with unexplained syncope. Although many reports have reported on children associated with neurocardiogenic syncope, the relationship between the clinical characteristics of those patients and the results of the HUTT remains to be clarified. We therefore studied the children with unexplained syncope who underwent a tilt table test at our institution, to determine their clinical characteristics and the HUTT results.

Methods: From July 2001 to March 2006, a total of 17 pediatric patients with unexplained presyncope and syncope that underwent a HUTT at our institution were included. We divided those patients into two groups: Group 1 included five children who had a positive tilt table test, and Group 2 included 12 children who had a negative tilt table test. We compared the demographic, clinical and laboratory data between the two groups.

Results: There were no significant differences regarding the age, sex, syncopal episodes or duration of the syncopal history between the two groups. The children with a positive HUTT response often had predisposing factors of syncope and experienced prodromes (5/5 vs. 3/12, $p < 0.05$). A mixed hemodynamic response predominated (80%) in our positive tilt patients.

Conclusion: We concluded that the presence of predisposing factors or prodromes of syncope was closely associated with a positive HUTT.

Key Words: Children • Syncope • Tilt table test

INTRODUCTION

Syncope is a common clinical problem and is particularly prevalent in childhood and adolescence. Neurocardiogenic syncope, also referred to as neurally mediated syncope or vasovagal syncope, is well known to be the most frequent cause of pediatric syncope.[1] An appropriate clinical history in association with a positive head-up tilt test (HUTT) with or without pharmacological provocative agents currently provides the cornerstone for the diagnosis of vasovagal syncope in children and adolescents.[2-6] The purpose of this study was to investigate the relationship between the clinical characteristics and results of the HUTT in children with unexplained syncope.

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[1]Departments of Pediatrics, Taipei Veterans General Hospital; [2]National Yang-Ming University, Taipei, Taiwan.
Address correspondence and reprint requests to: Dr. Pi-Chang Lee, Division of Pediatric Cardiology, Department of Pediatrics, Taipei Veterans General Hospital, Taiwan.
Tel: 886-2-2875-7574; Fax: 886-2-2873-9019; E-mail: pichang_lee@yahoo.com, karenlin0612@ yahoo.com

METHODS

Patients

From July 2001 to March 2006, 17 pediatric patients who underwent a HUTT at our institution were included. All of these patients had one or repetitive episodes of syncope or presyncope, and all had normal physical findings. Their medical and family histories were thoroughly reviewed. The basic evaluation included a complete blood count, serum electrolyte level, blood sugar, orthostatic

blood pressure, 12-lead surface electrocardiogram (ECG), 24-hour Holter monitoring and echocardiography. A neurologist, psychiatrist and otolaryngologist were consulted if the clinical history suggested a non-cardiogenic cause. All of the 17 patients received a HUTT, and we divided these subjects into two groups according to their response. Group 1 included 5 children who had a positive result of the HUTT, and group 2 consisted of 12 children who had a negative result of the HUTT. We compared the demographic, clinical and laboratory data between these two groups.

Head-up Tilt Table Test Protocol

Informed consent for the 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 prior to the study. The studies were all performed in the post-absorptive state, and an intravenous access was obtained. Initially, the baseline heart rate (HR) and blood pressure (BP) were recorded in the supine position. Then we raised the table to 80 degrees for 30 minutes or until the occurrence of a positive response. In addition to continuous ECG monitoring, the HR and BP were recorded every two minutes. A positive result of the HUTT was defined as the presence of either presyncopal or syncopal symptoms associated with the sudden development of hypotension, bradycardia, or both. If no positive findings were observed, we flattened the table to the horizontal level until the patient's vital signs returned to the previous baseline. Then isoproterenol was continuously infused at a rate of 1-4 μg/min. A second tilt was performed after the patient's HR increased to at least 25% above the resting sinus rate. The supine position was regained immediately if positive responses occurred. Emergency medications were available at all times. If the patient remained asymptomatic for 20 minutes during the repeat tilt, the test was then discontinued and the results were considered negative.

Definitions

Presyncope was defined as the presence of any of the following symptoms: nausea, vomiting, dizziness, pallor, cold sweating, diaphoresis, blurred vision, or abdominal pain without the loss of consciousness. If loss of muscle tone and consciousness followed after the presyncope, the status was defined as syncope. A hypotensive response was defined as a fall in the systolic BP of ≥ 30% of the baseline value, whereas a bradycardic response was defined as a decrease in the HR of ≥ 40% of the baseline value.

Positive tilt table tests were categorized into three types according to the pattern of hemodynamic change. Type I was a mixed response: the HR rose initially and then fell, but the ventricular rate did not reach a bradycardic response for more than 10 seconds with or without asystole for ≥ 3 seconds. The BP rose initially and then fell before or after the HR fell. Type II was a cardioinhibitory response: the HR rose initially and then fell to reach a bradycardic response for ≥ 10 seconds or asystole occurs for ≥ 3 seconds. Type III was a pure vasodepressor response: the BP fell to reach a hypotensive response and caused syncope, but the HR did not fall > 10% from the peak at the time of syncope.

Orthostatic hypotension may sometimes mimic syncope. It was defined as a gradual decrease in the systolic BP of > 20 mmHg or diastolic BP of > 10 mmHg within 3 minutes of quiet standing. It is a physical sign, not a disease, and may be symptomatic or asymptomatic. If symptomatic, it is often associated with symptoms of cerebral hypoperfusion such as dizziness or lightheadedness. Symptomatic orthostatic hypotension is sometimes difficult to differentiate from neurocardiogenic syncope. Some believe it is part of neurocardiogenic syncope due to both having similar mechanisms.

Statistical Analysis

Data are expressed as the mean ± SD or percentage (number) of patients. Continuous variables were compared using the unpaired Student's t-test, and categorical variables were compared using the Fisher's exact test. *p* values of less than 0.05 were considered to indicate statistical significance.

RESULTS

The age of the patients was 13 ± 3 years old (range, 6-17 years old), and there were eight males and nine females. The comparative data related to the sex, age, number of previous syncopal episodes, duration of the history, and presence of predisposing factors and prodromes of syncope between the Group 1 and 2 patients

are listed in Table 1. The Group 1 patients more often experienced symptoms of presyncope or syncope under special circumstances, such as prolonged standing, sudden changes in the posture, especially from the supine or sitting to upright position, hot environment and/or dehydration, emotional stress or physical pain (e.g., needle phobia) (p = 0.02). They also had a higher incidence of prodromes such as dizziness, nausea, blurred vision or cold sweating before the syncopal attack (p = 0.02). However, the differences in the number of syncope episodes and duration of attacks exhibited no statistical significance between the two groups. Adolescents with an age between 13 and 18 years-old with unexplained syncope exhibited a trend toward a higher positive rate in the HUTT than those with an age younger than 13 years old. However the results did not have statistical significance.

In Group 1, four patients had a positive response in the HUTT (presyncope) during the initial stage, and one patient had a positive response (syncope) merely after an isoproterenol infusion. The times of the occurrence of the syncope or presyncope were 17 ± 5.3 minutes and 2 minutes into the initial stage and during the isoproterenol infusion, respectively. One patient needed a normal saline infusion to relieve the symptoms due to the discomfort persisting for more than 30 minutes after returning back to the supine position. The positive response included mixed-type in four patients and vasopressor-type in one patient. All of them were medicated with beta-blockers or alpha-agonists. We educated them to recognize their prodromal symptoms and avoid their predisposing factors, and emphasized the importance of hydration, salt intake and self-protection against trauma while near fainting.

In Group 2, 11 out of 12 patients received an isoproterenol infusion after an initial negative tilt test. The mean dose of isoproterenol used was 0.04 μg/kg/min. The mean follow-up time was 8.5 months in Group 1 and 5.3 months in Group 2. During the follow-up period, one patient who had a negative tilt result was diagnosed with epilepsy three months after the exam. No more convulsive syncopal events occurred after treatment with antiepileptic drugs. Alpha-agonists were prescribed in one patient in Group 2, who had frequent attacks and a long duration of syncope. However the efficacy of the treatment was unable to be evaluated due to loss to follow-up.

DISCUSSION

Syncope is a common clinical problem with a wide spectrum of etiologies. Although the underlying cause of pediatric syncope is usually benign, episodic attacks may cause body injury depending on the patient's activity. Before the cause of syncope is fully clarified, anxiety in the patients, family, friends and teachers can lead to a substantial psychosocial morbidity such as activity restrictions or missing classes. By using the HUTT, we were able to identify some patients with unexplained syncope that was neurocardiogenic syncope, when no abnormal findings were observed in the routine cardiac and neurological examinations.

The Association of the Prodromes of Syncope to the HUTT Response

Our study demonstrated that patients with prodromal symptoms were more likely to have a positive result of the HUTT than those without a prodrome. The findings are consistent with those of a previous study,[7] in which patients with a prodrome of syncope had 17.7 times higher possibility of a positive HUTT than those without

Table 1. Comparative data between the groups with a positive and negative HUTT

Variables	Group 1 Positive HUTT (n = 5)	Group 2 Negative HUTT (n = 12)	p value
Male/female	3/2	5/7	0.876
Age (years)	14.2 ± 0.9	11.7 ± 3.5	0.152
Syncopal episodes	2.2 ± 1.8	2.1 ± 2.96	0.348
Duration of history (months)	8.5 ± 10.8	5.3 ± 7.4	0.399
Presence of predisposing factors	100% (5/5)	25% (3/12)	0.02*
Presence of prodromes of syncope	100% (5/5)	25% (3/12)	0.02*

HUTT: Head-up tilt test. *: Statistical significance.

a prodrome. Richard et al.[8] found that most syncopal children could be empirically diagnosed with neurocardiogenic syncope if they had prodromal symptoms (dizziness, nausea, cold sweating, etc.) with normal findings in the cardiac or neurological examinations. By having an awareness of these "alarming factors", these patients are able to take actions (e.g. sit or lie in the supine position promptly) to prevent any bodily injury before the actual loss of consciousness.

The Association of Predisposing Factors of Syncope to the HUTT Response

The presence of any predisposing factors of syncope or presyncope is more likely to result in a positive result of the HUTT. In the present study, all of the patients with positive results experienced symptoms under particular circumstances such as during prolonged inactivity, hot environment, dehydration, emotional stress (e.g., needle phobia), or sudden arousal from a sitting or supine position. However, only 25% of the patients had predisposing factors before the syncope in the group with negative results. This may be related to the pathophysiology of vasovagal syncope. Some previous studies hypothesized that a significant increase in the sympathetic tone was triggered by vigorous contractions of an under-filled ventricle (due to pooling of blood in the lower half of the body) before the onset of the neurocardiogenic syncope.[9-11] Consequently, it would stimulate the mechanoreceptors in the left ventricle wall, as might normally occur in systemic hypotension. Activation of these "ventricular afferents" in the left ventricle might trigger an inhibitory response similar to the Bezold-Jarisch reflex, resulting in hypotension, bradycardia, and syncope. However, several studies challenged the preceding hypothesis.[12-15] Previous studies demonstrated that the cerebral blood flow and cortex might have a role in the initiation of bradycardia associated with neurocardiogenic syncope.[16,17]

Other Findings

In the present study, the age and sex of the syncopal children did not influence the HUTT result. Although the positive rate in the patients between 13 and 18 years of age was higher than that in those younger than 13 years of age (44.4% vs. 12.5%), it failed to reach statistical significance (p = 0.364), possibly due to the limited number of patients in our study. The same reason might also explain the female predominance in another study.[18] Among the patients with a positive result of the HUTT, the most common hemodynamic type of response was a mixed type (80%). This finding is consistent with the study report of Wolff and colleagues,[19] in which 50-80% of the patients had a mixed response.

Estimation of the Disease Severity and Significance of the HUTT Results

The frequency of the syncopal spells and duration of the history predict the clinical course of the illness, correlate with a reduction in quality of life, and determine which patients should be treated.[20,21] We assumed that patients with a worse clinical history were more likely to have a positive HUTT outcome, but the results of our study failed to support this hypothesis. Therefore, a HUTT can be useful in selected patients to help clarify the diagnosis, but it does not predict the outcome in those patients nor does it guide the treatment.[6] Since up to 87% of neurocardiogenic syncope can be clinically diagnosed without the benefit of a HUTT, the test may be an optional tool for evaluation to reassure anxious families of the diagnosis.[22]

CONCLUSION

We concluded that the presence of predisposing factors or prodromes of syncope was closely associated with a positive HUTT. Finally, the HUTT is only a method for diagnosing neurocardiogenic syncope; it cannot be used to determine whether patients should be treated or not.

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不明原因暈厥的兒童接受傾斜床檢查的結果

林鈺然[1] 黃碧桃[1,2] 李必昌[1,2] 孟春昌[1]
台北市 台北榮民總醫院 兒童醫學部[1]
台北市 國立陽明大學 小兒學科[2]

背景 神經心臟性暈厥是兒童時期最常見暈厥的原因。然而其機轉雖然被認為是自主神經功能的異常，但是在兒童身上卻未被完全瞭解。傾斜床檢查目前廣泛被用來評估不明原因的暈厥，雖然以前一些文獻曾經報告兒童時期的神經心臟性暈厥，但是臨床表徵與傾斜床結果之間的關係仍然未被釐清。這篇文章即在評估在本院接受傾斜床檢查的不明原因暈厥的病童，嘗試進一步瞭解兩者之間的關係。

方法 從 2001 年七月至 2006 年三月，在本院接受傾斜床檢查的不明原因暈厥病童總共有十七名。我們將這些病童分成兩組：第一組包括五位傾斜床檢查陽性的病童，而第二組則包括十二位傾斜床檢查陰性的病童。我們比較這兩組病童的基本資料、臨床表徵、與實驗室檢查的結果。

結果 兩組之間比較，關於性別、年齡、暈厥次數、與暈厥病史並無明顯不同。傾斜床檢查陽性的病童通常有較高比例的暈厥誘發因子與先驅症狀 (5/5 vs. 3/12, $p < 0.05$)，同時有百分之八十是屬於混合型。所有五位傾斜床檢查陽性，與一位傾斜床檢查陰性的病童，都接受藥物治療。同時教育病童與家屬瞭解暈厥的先驅症狀，如何避免誘發因子，強調喝水、攝取鹽分、與自我保護的重要性。

結論 我們認為暈厥病童的年齡及性別並不會影響傾斜床檢查的結果。發生暈厥的頻率與時間可能反應疾病的嚴重度；但是並不能以此預測傾斜床檢查的結果。如果不明原因暈厥的病童，有暈厥的誘發因子與先驅症狀，則通常有較高的比例傾斜床檢查是陽性的。

關鍵詞：兒童、暈厥、傾斜床檢查。