

THE USE OF HEAD-UP TILT TESTING IN THE INVESTIGATION OF SYNCOPE

N Malik. MRCP

Specialist Registrar

S Allen. MD. FRCP

Consultant Physician.

Department of Medicine and Geriatrics, The Royal Bournemouth Hospital, Dorset, UK

J HK Geriatr Soc 2002; 11:33-37

Correspondence: D. Stephen Allen

Email: stephen.allen@rbch-tr.swest.nhs.uk

Abstract

The cause of syncope remains unknown in about 40% of cases after extensive investigations. Elderly patients are at increased risk of syncope because of the physiologic changes due to aging, higher incidence of chronic illness and the use of a greater number of medications that may contribute to hypotension. Syncope is common, difficult to evaluate and has a high morbidity and mortality. Head-up tilt-testing (HUT) has become an important part of the investigation of patients with recurrent unexplained syncope. There have been concerns about the specificity and the lack of standard methodology for tilt testing. The reproducibility of HUT is therefore open to question. The effectiveness of treatment is uncertain because of the paucity of randomised-controlled trials. Drug therapy should be tried in patients with recurrent syncope. The usefulness of cardiac pacing for treatment of recurrent vasovagal syncope remains incompletely understood. Further research is needed to define the pathophysiology and effective treatments of neurocardiogenic syncope.

Key words: syncope, tilt-testing, vasovagal

Introduction

Syncope is defined as a sudden, transient loss of consciousness due to temporary cerebral hypoperfusion with spontaneous and complete recovery. It is associated with loss of postural tone. A wide variety of benign and life-threatening conditions can cause syncope as shown in table 1¹. Syncope is common, difficult to investigate and has a high morbidity and mortality. Neurocardiogenic syncope is more frequent in older patients than is generally recognized². Causes of syncope can sometimes be identified by taking a detailed history from a witness, physical examination and specific investigations. Yet, patient's history may be inaccurate and witness accounts are frequently unavailable. Retrograde amnesia for the loss of consciousness often results in confusion between syncope and falls particularly in patients with

Table 1: Causes of Syncope

• Cardiac arrhythmia	Sick sinus syndrome, complete heart block Supraventricular and ventricular
• Neurocardiogenic syncope	Vasovagal syncope Situational syncope Micturition syncope Tussive syncope
• Orthostatic hypotension	
• Carotid sinus syndrome	
• Drug-induced syncope	
• Postprandial syncope	
• Syncope associated with low cardiac output	Myocardial infarction Pulmonary embolism Severe aortic or mitral stenosis Hypertrophic cardiomyopathy Any cause of severe low output cardiac failure

otherwise unexplained recurrent syncope or falls of uncertain cause². Unexplained falls in the elderly should be considered as syncopal episodes.

Syncope in the older patient may result in soft tissue injuries, fractures, subdural hematomas and aspiration pneumonia and can transform a fully independent elderly person into a severely dependent one¹. It also places a huge psychological burden upon patients and their carers. The cost burden to health services is high. Thus a reliable cost-effective approach to investigation is needed. Over the past 15 years, Head-up tilt testing (HUT) has become an integral part of the evaluation of patients with recurrent unexplained syncope since it was first described by Kenny et al in 1986³. HUT provides an orthostatic challenge that provokes vasovagal syncope and provides a high diagnostic yield⁴.

Pathophysiology of neurocardiogenic syncope

A number of investigators have attributed unexplained recurrent syncopal episodes to neuroautonomically mediated profound

hypotension and bradycardia causing loss of consciousness². In a normal person, upright posture results in increased venous pooling in the lower limbs causing a compensatory increase in peripheral resistance and heart rate. Because of reduced venous return to the right ventricle, the cardiac mechanoreceptors in both the ventricles are not stretched thereby decreasing their afferent impulses to the brain stem. This causes a reflex tachycardia, increased diastolic blood pressure and unchanged or decreased systolic blood pressure.

Sir Thomas Lewis coined the term vasovagal syncope in 1932². The exact sequence of events leading to neurocardiogenic syncope is not yet completely understood⁵. It appears that there is a sudden drop in venous return to the heart due to excessive venous pooling in the legs. The consequent fall in ventricular volume causes vigorous ventricular contraction. This leads to stimulation of mechanoreceptors (C-fibers) causing a sudden increase in afferent discharge to the brain

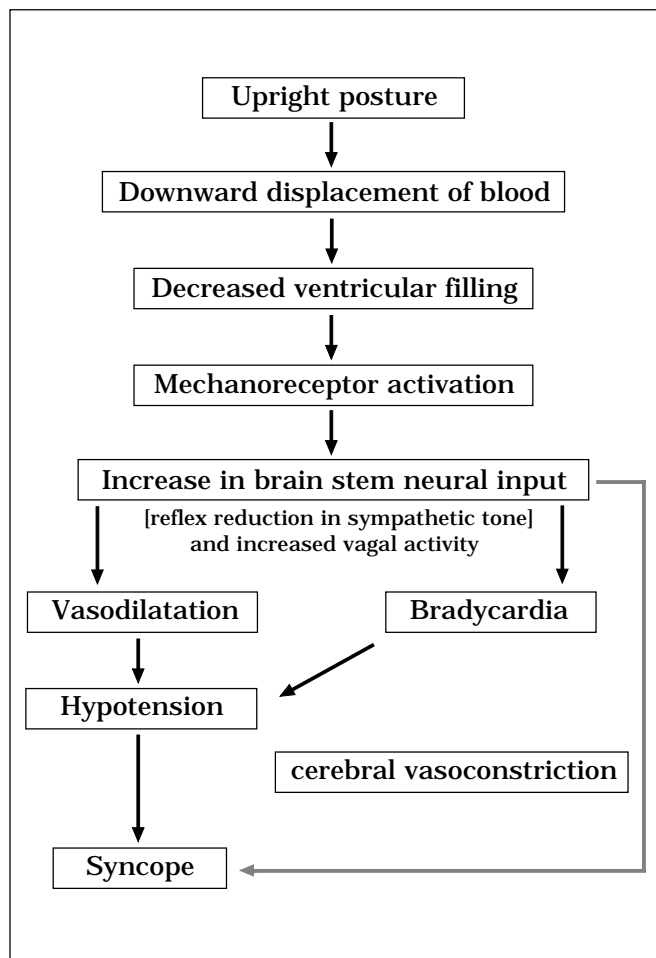


Figure 1. Proposed sequence of events in neurocardiogenic syncope.

stem. The efferent response is paradoxical with peripheral vasodilatation and bradycardia. Elam and Grubb have shown that depletion of serotonin stores blunts the hypotension and bradycardia^{6,7}. Bradycardia seen during syncope is thought to be due to parasympathetic stimulation but the exact mechanism by which vasodilatation occurs remains unclear³. Giller et al. have shown that there is a sudden increase in cerebral vasoconstriction in the face of systemic hypotension which may lower an already compromised cerebral blood flow and contribute to syncope⁸. (figure 1)

Using transcranial Doppler sonography it was demonstrated that during HUT induced syncope sudden cerebral vasoconstriction occurs in spite of increasing hypotension² Thus neurocardiogenic syncope is probably as much a manifestation of cerebral vasomotor control as it is of systemic vasodilatation.

Head-up Tilt Table Testing (HUT)

HUT has become an important diagnostic tool in the evaluation of patients with unexplained syncope⁴. It presents an orthostatic challenge that stimulates vasovagal syncope. In some studies, it established the diagnosis of syncope in 40-70% of patients⁴. Tilt table testing is also used to determine a patient's susceptibility to vasovagal syncope. Patients often describe symptoms of their spontaneous episodes as being closely reproduced by tilt-table testing.

Who needs a Tilt-Table Test?

- Patients with recurrent syncope or in high-risk patients after a single episode⁴ (airline pilots, commercial vehicle drivers, competitive athletes);
- Elderly patients with recurrent unexplained falls;
- Patients who have unexplained loss of consciousness and the test done to help differentiating convulsive syncope from seizures²;
- Patients with unexplained dizziness or presyncope;
- Some patients may have the psychological or emotional need to establish the diagnosis. The provocation of syncope during HUT can be reassuring and therapeutic in such patients, and help them adjust to their condition⁴.

Tilt-table testing is not warranted in the following:

- Single syncopal episode in a low-risk patient.
- In younger patients with a structurally normal heart who give a suggestive history with a long prodrome, a diagnosis of vasovagal syncope can be confidently made.

Method of HUT

There is no internationally agreed protocol for tilt testing and there are numerous variations in the methods used. However tilt-table testing is usually done in 2 stages: a prolonged period of head-up tilt in the drug-free state, followed by a shorter period of tilt after administration of provocative agents like IV isoprenaline or sublingual nitroglycerin⁹.

Tilt testing should be done in a quiet room with dimmed lights. Patients should fast for at least 3 hours before testing or overnight. There is continuous monitoring of blood pressure and ECG. It is essential to measure blood pressure with an automated beat to beat blood pressure monitor (Finapres or Portapres)⁴. There can be large fluctuations of blood pressure or transient periods of asymptomatic hypotension which are missed by 2-minute cuff measurements. Main determinants of a positive response appear to be the tilt angle and the duration of the test¹⁰. The angle of tilt varies between 60 and 80 degrees. Tilting patients to < 60 degrees is inefficient because the angle may not provide sufficient orthostatic stress⁴. The duration of test should be at least 30-45 minutes. The 45-minute tilt test captures 95% of patients who are likely to develop syncope⁴. The endpoint should be induction of syncope or presyncope associated with marked hypotension and bradycardia with reproduction of the patient's symptoms during a typical attack⁴. It is believed that the test should not be terminated for asymptomatic hypotension except in extreme hypotension (systolic blood pressure < 50mmHg). Every tilt-table laboratory must have resuscitation equipment readily available.

Isoprenaline is given as an intravenous infusion at the end of a negative drug-free tilt after the patient has been returned to supine position. Most investigators use 1-3µg /min dose. Some clinicians titrate the isoprenaline dose to an increase in supine heart rate of 20-25% above baseline. After the vital signs reach a steady state at a given dose, the patient is tilted head-up for 10-15 minutes⁴. When nitroglycerin is used as a provocative agent, it is given at the end of drug-free tilt while the patient is still upright (400 µg tablet or sublingual spray) and the patient remains tilted for an additional 20 minutes². Adding a provocative drug challenge increases the sensitivity and diagnostic yield. Various researchers have estimated the sensitivity of tilt testing between 67-83%⁵. Studies using isoprenaline have reported wide variability in specificity ranging between 35 and 100%¹⁰. The

reproducibility has also been widely variable, ranging from 65-85%¹¹. This wide range of specificity and reproducibility thus remain a potential limitation on wide spread use of HUT.

Patterns of collapse during Tilt-table Testing

Patients with vasovagal syncope have an abrupt fall in blood pressure accompanied by a degree of bradycardia that is thought to represent a manifestation of the Bezold-Jarisch reflex¹². Based on the blood pressure drop and degree of bradycardia, vasovagal syncopes are divided into several types. In *mixed vasovagal syncope (type 1)* a fall in blood pressure precedes a mild reduction in heart rate. In this type of vasovagal syncope, the heart rate does not fall below 40 beats / min for > 10 seconds⁴. Cardioinhibitory vasovagal syncope is characterised by significant bradycardia (<40 beats / min for >10 seconds or with an asystolic pause > 3 seconds) during collapse and is divided into 2 types based on the timing of the fall in blood pressure relative to bradycardia. In *type 2A vasovagal syncope* the blood pressure clearly falls before the decrease in heart rate. There is a brief period of asystole, which occurs after the fall in blood pressure. In *type 2B vasovagal syncope* there is a fall in blood pressure concurrently with a dramatic decrease in heart rate. A long asystolic pause associated with a concurrent fall in blood pressure is also recorded⁴. *Pure vasodepressor or type 3 vasovagal syncope* is relatively uncommon and refers to pure hypotension without bradycardia¹³. Vasodepressor syncope often occurs during a church service, in restaurants and cocktail parties and similar circumstances, and while waiting for food or standing in a hot overcrowded room where alcohol is consumed.

Patients with a *dysautonomic response (autonomic neuropathy)* demonstrate a gradual and progressive decrease in blood pressure, usually with a small change in heart rate. The dysautonomic pattern is associated with low levels of circulating catecholamines and such patients may have other signs of autonomic dysfunction such as impotence and postural hypotension⁴. These patients may benefit from stopping or reducing hypotensive medication as these drugs are often implicated as causal agents.

Patients with *postural orthostatic tachycardia syndrome (POTS)* demonstrate an early and sustained increase in heart rate, often associated with a progressive fall in blood pressure⁴. Some young females present with a prominent sinus tachycardia (> 120 beats / min) before a vasovagal

syncope with a fall in blood pressure, though not all patients become frankly hypotensive. It has been suggested that two types of POTS exist, one represents beta-receptor hypersensitivity and the other seems to represent a failing autonomic nervous system⁴.

Carotid Sinus Syndrome is a separate entity and is an important cause of syncope and presyncope in the older patient. Episodic bradycardia and / or hypotension resulting from carotid sinus hypersensitivity characterise this syndrome. Carotid sinus syndrome is diagnosed in patients with unexplained syncope or dizziness when a 5 second longitudinal massage of the carotid sinus produces asystole exceeding 3 seconds (cardioinhibitory), or a fall in systolic blood pressure > 50 mmHg in the absence of cardioinhibition (vasodepressor), or a combination of both (mixed)^{14,15}.

Treatment for Neurocardiogenic Syncope

The therapeutic approach to the older patient with syncope must be individually tailored. Every effort should be made to educate the patient and the carer as to the nature of the disease and to avoid precipitating factors. The medication should be reviewed and any drugs with a tendency to cause hypotension or syncope must be stopped if possible (diuretics, ACE-inhibitors, alpha blockers, phenothiazines, tricyclic antidepressants etc). The patient should be advised to lie down at the onset of any prodromal symptoms².

A number of different agents have been reported to be useful in preventing recurrence of vasovagal syncope. *Beta adrenergic receptor blockers* (such as metoprolol, pindolol and atenolol) are widely used². These agents decrease the force of ventricular contraction and reduce the degree of mechanoreceptor discharge. Transdermal scopolamine may be useful in some patients through its *anticholinergic* effects. Milstein et al. found disopyramide to be useful via its negative inotropic and *anticholinergic* effects¹⁶. *Fludrocortisone* causes fluid retention and an increase in circulating blood volume. It can be used as an adjunct to other forms of therapy². However, many of these agents could be relatively contraindicated or poorly tolerated in the older patients with syncope. Recent reports have shown that *selective serotonin re-uptake inhibitors* (like fluoxetine and sertraline) can be used with good effect in some patients with neurocardiogenic syncope⁷. Sudden sympathetic withdrawal resulting in vasodilatation and hypotension is a principal factor causing vasovagal syncope. *Peripheral alpha*

agonists were postulated to be able to diminish susceptibility to vasovagal syncope, etilefrine is widely used in Germany for the treatment of postural hypotension. Midodrine hydrochloride appears to be highly effective in preventing of all types of vasovagal syncope¹⁷. Midodrine was effective in the prevention of syncope during repeat tilt testing in the daily dose of 5 or 10 mg. Treatment with midodrine appears to be safe and adverse reactions are rare.

The usefulness of cardiac pacing for treatment of recurrent vasovagal syncope remains incompletely understood^{18, 19}. Various studies have shown that pacing may be beneficial in those patients whose recurrent intractable vasovagal symptoms are mainly caused by a cardioinhibitory mechanism. Dual chamber pacing is superior to ventricular pacing alone in the treatment of vasovagal syncope. Pacing alone will have little effect on the degree of vasodilatation. Future advances in sensor technology may thus make permanent pacing a more attractive treatment option for neurocardiogenic syncope.

Treatment of vasodepressor carotid sinus syndrome is less satisfactory due to its poorly understood pathophysiology¹³. Ephedrine may be of some use but is limited due to its adverse effects. Fludrocortisone is widely used with good results¹⁵. Atrio-ventricular sequential pacing is currently the treatment of choice in patients with symptomatic cardioinhibitory carotid sinus syndrome¹⁵. Ventricular pacing abolishes cardioinhibition but fails to alleviate symptoms due to a vasodepressor response. Dual chamber pacing has been shown to result in significantly less vasodepression than ventricular pacing alone¹⁵.

Non-pharmacological therapies may be helpful in some selected patients. Elastic support hose are effective but may be difficult and less practical for the older patient to use². Relaxation exercises, like biofeedback, can be used as an adjunct to other therapy. Increased sodium intake can be helpful in some patients.

Conclusion

Head-up tilt testing can be used to investigate unexplained recurrent syncope in the older patient. Since Kenny et al first described the technique in 1986, many different protocols have been described and their differences mainly are the angle of tilt, the duration of passive tilt and the use of provocative agents. The most common protocols use a tilt angle of 60-80 degrees for 30 to 45 minutes and use nitroglycerin or isoprenaline as provocative

agents. In patients with structural heart disease, cardiac arrhythmias should be excluded before referring for tilt testing. The response to tilt-testing should be interpreted in conjunction with the patient's symptoms.

The effectiveness of treatment is open to question because of the lack of randomised-controlled trials and the variable natural history of syncope, with spontaneous resolution of symptoms over time in many patients. The studies on reproducibility of tilt testing show a significant day-to-day variation in autonomic tone that may predispose patients to vasovagal syncope. The treatment should consist of patient reassurance and counselling on diagnosis, on the benign prognosis and on recognising their prodrome in order to take evasive postural actions to avoid syncope. Drug therapy should be reserved for patients with recurrent syncope as isolated episodes may not recur and efficacy of current treatment is not proven. Pacing should be reserved for patients with refractory recurrent symptoms who show cardioinhibitory response on tilt-testing. A great deal of research is needed to define pathophysiology and effective treatments of neurocardiogenic syncope.

References

- Kenny RA, Dey AB. Syncope. In Brocklehurst J, Tallis R, Fillit E (Eds) *Brocklehurst's Textbook of geriatric medicine and gerontology*. Churchill-Livingstone, Edinburgh 1998:455-473
- Grubb BP, Samoil D. Neurocardiogenic syncope. In Kenny RA (Ed) *Syncope in the older patient*. Chapman, London 1996:91-106.
- Kenny RA, Ingram A, Bayliss J. et al. Head-up tilt: A useful test for investigating unexplained syncope. *Lancet* 1986;**1**:1352-55.
- Sutton R, Bloomfield DM. Indications, Methodology and classification of results of Tilt Table testing. *Am J Cardiol* 1999;**84**:10-19.
- Wishwa N. Using a tilt table to evaluate syncope. *Am J Med Sci* 1999;**317**:117-23.
- Elam RF, Bergman Fand Feurstein G. The use of antiserotonergic agents for treatment of acute hemorrhagic shock in cats. *Eur. J. Pharmacol* 1985;**107**:275-8.
- Grubb BP, Wolfe DA, Samoil D. et al. Usefulness of fluoxetine hydrochloride for prevention of resistant upright tilt induced syncope. *PACE* 1993;**16**:458-64.
- Janosik D, Gomez C, Njemaze P. et al. Abnormalities in cerebral blood flow autoregulation during tilt induced neurocardiogenic syncope. *PACE* 1992;**15**:592.
- Kapoor WN, Smith MA, Miller NL. Upright tilt testing in evaluating syncope: a comprehensive literature review. *Am J Med* 1994;**97**:78-88.
- Ammirati F, Colivicchi F, Biffi A. et al. Head-up tilt testing potentiated with low-dose sublingual isosorbide dinitrate: a simplified time-saving approach for evaluation of unexplained syncope. *Am Heart J* 1998;**135**:671-6.
- Kapoor WN, Brant NL. Evaluation of syncope by upright tilt testing with isoproterenol. *Ann Int Med* 1992;**116**:358-63.
- Mark AL. The Bezold-Jarish reflex revisited. *J Am Coll Cardiol* 1983;**1**:90-2.
- Barbey JT. Vasodepressor syncope. *Cardiology Clinics* 1997;**15**:251-256.
- Strasberg B, Sagie A, Erdman S. et al. Carotid sinus hypersensitivity and the carotid sinus syndrome. *Prog Cardiovasc Dis* 1989;**31**:379-91.
- Kenny RA, McIntosh SJ. Carotid sinus syndrome. In Kenny RA (Ed) *Syncope in the older patient*. Chapman, London 1996:107-122
- Milstein S, Buetikofer J, Lesser J. et al. Usefulness of disopyramide for prevention of upright tilt induced hypotension and bradycardia. *Am J Cardiol* 1990;**65**:1339-44.
- Mitro P, Trejbal D and Rybar R. Midodrine hydrochloride in the treatment of vasovagal syncope. *PACE* 1999;**22**:1620-4.
- Benditt DG, Petersen M, Lurie KG. Et al. Cardiac pacing for prevention of recurrent vasovagal syncope. *Ann Int Med* 1995;**122**:204-9.
- Samoil D, Grubb BP, Brewster P. et al. Comparison of single and dual chamber pacing techniques in prevention of head-upright tilt induced vasovagal syncope. *Eur J Cardiac Pacing Electrophysiol* 1993;**1**:36-41.

Suggested further reading

Thach Nguen, Shiwen Wang, Vigay Dave et al: Syncope In: Thach Nguen (Ed) Management of Complex Cardiovascular Problems. Futura, Armonk NY, 1999, 89-111

LEARNING POINTS

- Unexplained falls in elderly people can be caused by cardioinhibitory and/or vasodepressor syncope**
- Head up tilt has been shown to be a useful investigation in this context**
- A substantial proportion of patients shown to have cardioinhibitory and/or vasodepressor responses can be treated successfully**