

# Neurocardiogenic syncope and the elderly

Neurocardiogenic syncope is also known as neurally mediated syncope. It describes a transient failure of the brain to adequately regulate the body's blood pressure and heart rate. The exact reasons why this occurs are still unclear, but a basic understanding is evolving. In this article, **Drs N Obiechina, A Michael, A Ritch and PK Sarkar** discuss the clinical features and diagnosis of this condition.

**S**yncope is sudden transient loss of consciousness associated with loss of postural tone. It is caused by global impairment of blood flow to the brain. Neurocardiogenic syncope describes episodes of cerebral hypoperfusion in the absence of cardiac cause or vasovagal precipitants or situational triggers<sup>1</sup>.

Neurocardiogenic syncope was first described by Sir Thomas Lewis in 1931<sup>2</sup>. It is a frequent cause of unexplained syncope, and results from inappropriate and often excessive autonomic reflex activity and manifests as abnormalities in the control of vascular tone and heart rate<sup>2</sup>. It is also known as neurally mediated hypotension/syncope, vasodepressor syncope, and vasovagal syncope. All these terms describe an abnormality of blood pressure regulation characterised by the abrupt onset of hypotension with or without bradycardia<sup>3</sup>. It is a common disorder that affects at least 20 per cent of people at some time in their lives<sup>4</sup>. In about half of these patients, the symptoms are recurrent causing physical trauma, substantial reduction in quality of life, and difficulties with driving<sup>4</sup>. In elderly patients, it may lead to fractures and serious soft tissue injury such as subdural haematomas.

## Epidemiology

The precise incidence of this condition is unknown

but could account for a prevalence of about 25 per cent for patients seen in the accident and emergency setting with syncope and 11 per cent of patients seen in a tertiary centre<sup>5</sup>.

Data suggest that sex and age do not influence the likelihood of this condition being diagnosed on head-up tilt testing<sup>6,7</sup>. However, although it shows no age preponderance, the malignant form (recurrent syncope with prolonged asystole on head-up tilt testing) occurs more in patients over the age of 65 years.

The Westminster group's landmark study found that 67 per cent of patients with otherwise unexplained syncope demonstrated a vasovagal reaction during head-up tilt, compared to 10 per cent of healthy controls<sup>8</sup>.

## Pathophysiology

On assuming an upright posture, there is pooling of about 300 to 800mls of blood from the thorax to abdomen and lower extremities<sup>9</sup>. This leads to a 25 per cent drop in circulating volume, which in turn leads to reduced venous return. An attempt by the ventricles to increase stroke volume by contracting vigorously results in activation of C-fibers (mechanoreceptors in the ventricular walls that send afferent signals to the dorsal vagal nucleus) leading

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**Table 1.** Causes of syncope**Vascular causes (the most common)**

Anatomical (subclavian steal syndrome)  
 Orthostatic  
 Reflex-mediated causes (neurocardiogenic or vasovagal syncope) – vasovagal syncope, micturition or defecation syncope or carotid sinus syncope

**Cardiac causes**

Organic heart disease producing inflow (e.g., myxoma, constrictive pericarditis) or outflow obstruction (e.g. aortic stenosis, pulmonary stenosis and hypertrophic obstructive cardiomyopathy)  
 Brady or tachyarrhythmia.  
 Prolonged QT interval syndrome

**Neurologic/cerebrovascular causes**

Seizures  
 Transient ischaemic attacks  
 Migraines

**Metabolic causes**

Hyperventilation (hypocapnea)  
 Hypoglycaemia  
 Hypoxemia  
 Drugs  
 Alcohol

**Psychogenic causes**

Psychogenic syncope  
 Hysterical  
 Panic disorder  
 Anxiety disorder.

to inappropriate or paradoxical increase in vagal tone (Bezold-Jarisch reflex) with hypotension and/or bradycardia<sup>5</sup>.

In addition, central mechanisms may play a role; as sudden hypovolaemia has been shown to cause central flooding with serotonin, which is thought to cause sudden sympathetic withdrawal leading to hypotension and/or bradycardia<sup>9</sup>. It has also been suggested that Selective Serotonin Reuptake Inhibitors (SSRIs) such as fluoxetine may dampen this effect by down regulation of post-synaptic serotonergic receptors<sup>9</sup>.

**Clinical features**

Patients frequently, but not always, experience a prodromal phase, which may include lightheadedness, visual disturbances, tinnitus, yawning, diaphoresis, abdominal discomfort and vomiting<sup>9</sup>. This may last from a few seconds to a few minutes and may warn patients early enough for them to abort an attack (e.g by adopting a recumbent posture). However, syncope may occur more suddenly without typical prodromal

**Table 2.** Clinical clues in the differential diagnosis of syncope

- > Vascular causes are the most common causes of syncope, accounting for a third of episodes
- > Cardiac causes, generally arrhythmias, are the second most common cause accounting for more about a sixth of syncopal episodes. Ventricular tachycardia is the most common tachyarrhythmia that can cause syncope
- > Up to half of patients with unexplained syncope may fall into the category of neurocardiogenic syncope
- > Rapid loss of consciousness with no prodrome may occur with seizures or some arrhythmias
- > Palpitations during the prodrome may be due to vasovagal events or tachyarrhythmias
- > Syncope in the recumbent position is unlikely to be due to vasovagal or orthostatic aetiologies
- > Syncope that occurs during exercise is most probably due to a cardiac cause
- > Unconsciousness alone is not the initial sign in basilar artery transient ischaemic attack. Usually brain stem symptoms precede or accompany the syncope
- > Rapid recovery of consciousness on assuming the recumbent position suggests vasovagal syncope, especially if there is no post event confusion
- > After vasovagal syncope recovery of orientation occurs simultaneously. After cardiac syncope the recovery is rapid (seconds), however following seizures it may take up to 20 minutes
- > Incontinence does not necessarily mean seizure. Syncope, of whatever cause, with a full bladder can result in incontinence. Seizures with an empty bladder will not be associated with incontinence
- > In psychogenic syncope, the episodes are usually witnessed and usually not associated with injury.

symptoms mimicking Stokes-Adams syncope<sup>2</sup>. When syncope occurs, the patient may have amnesia for it<sup>9</sup>. Bystanders may observe pallor and an ashen complexion. Urinary incontinence may occur as may tonic-clonic muscular contractions<sup>9</sup>. These episodes may be misdiagnosed as true seizures and labelled as epilepsy. However, patients frequently come round quickly with no prolonged post-ictal phase. Patients may complain of fatigue afterwards, which may last for up to a day<sup>9</sup>.

**Diagnosis**

The differential diagnosis of syncope is wide and varied (*Table 1*). Detailed history of what happened

**Table 3.** Investigations not needed

An exercise tolerance test and cardiac catheterisation are unlikely to establish a diagnosis in the evaluation of syncope as myocardial ischaemia is an unlikely cause of syncope

Electroencephalogram testing is not helpful unless the history suggests seizures

Brain imaging is not indicated as structural brain diseases are rarely a cause of syncope

Doppler studies should be used judiciously. Carotid stenosis alone does not cause syncope.

before, during, and after the episode is important in elucidating the aetiology of syncope. Unfortunately, this is not always available because of the frequent absence of eye witnesses to the event. Examination may add further clues to the diagnosis, and investigations such as 24-hour electrocardiogram (ECG) monitoring and echocardiography should be tailored to the clinical situation. Some of the helpful clinical points in the evaluation of syncope are listed in (Table 2) and (Table 3).

The mainstay of diagnosis of neurocardiogenic syncope is a combination of the typical clinical features and a positive haemodynamic response to a head-up tilt test.

## Head-up tilt testing

Head-up tilt testing is a useful tool in the investigation of all patients with suspected neurocardiogenic syncope<sup>6</sup> and is the 'gold standard' for diagnosis of the condition. Head-up tilt testing should be considered in patients with recurrent syncope or presyncope, high risk patients with a single syncopal episode, and elderly patients with unexplained recurrent falls<sup>10</sup>.

Patients are fasted for at least two hours and baseline recordings of heart rate and blood pressure made in the supine position. Patients are, subsequently, tilted head upwards, using a motorised tilt table at an angle varying between 60° to 80° to the horizontal depending on which protocol is used. Heart rate and rhythm are recorded continuously by cardiac monitor and 12-lead electrocardiography respectively. Blood pressure is monitored non-invasively with an automatic sphygmomanometer, sometimes in conjunction with continuous blood pressure monitoring with digital plethysmography (e.g. finapres). The duration of tilt varies with the protocol adopted. The test may be terminated

**Table 4.** Summary of Newcastle protocols for head-up tilt table testing<sup>10</sup>

Tilt test description	Method
Passive drug free tilt	40 min at 70°
Isoproterenol (µg) tilt	5 min tilt, 5 min supine 5 min 1µg/min supine, 5 min 1µg/min at 70°, infusion discontinued, supine 2 min, 5 min 3µg/min supine, 5 min 3µg/min at 70°
Glycerol trinitrate tilt (GTN)	2 metered doses sublingual GTN spray supine, 5 min supine then 20 min at 70°

Patients should remain supine for 20 minutes before testing. Isoproterenol and GTN tilts should follow non-diagnostic drug free tilt. Tilt should be terminated if symptom reproduction with concomitant hypotension/bradycardia or adverse event develops.

prematurely with a rapid return to the supine position if it is positive. This is evidenced by syncope or presyncope (together with limiting symptoms) occurring in association with hypotension and/or bradycardia<sup>6</sup>.

Two main approaches are, currently, used: A passive tilt and a drug challenge tilt test that involves, in most cases, a shorter period of tilt followed by the intravenous administration of isoproterenol or nitroglycerin or sublingual nitroglycerin<sup>6</sup>. Drug challenge improves the sensitivity of the test but this is offset by reduction in specificity.

Newcastle Protocols are summarised in (Table 4)<sup>10</sup>. A modified version of this protocol incorporates carotid sinus massage at the end of the test as long as there is no contraindication and the test is negative. Here, five to 10 seconds of carotid sinus massage is carried out, first on the right and if there is no response after 30 seconds, on the left. Medical supervision of the test is usually required together with availability of full resuscitation facilities.

## Haemodynamic responses to head-up tilt testing

Three main positive haemodynamic responses are

recognised and for purposes of this article, the Westminster classification<sup>6</sup> is used:

- > Type 1 (mixed) – blood pressure falls before the heart rate which drops to no less than 40/min together with syncope or presyncope
- > Type IIA (cardioinhibitory) – blood pressure falls before the heart rate which drops to less than 40/min or greater than three second asystole
- > Type IIB (cardioinhibitory) – heart rate falls to less than 40/min or greater than three second asystole before blood pressure falls (if at all)
- > Type III (vasodepressor) – heart rate rises or does not drop more than 10 per cent of its peak but blood pressure drops at least 50mmHg with presyncope and/or syncope.

## Treatment

The treatment depends on the diagnosis that is established.

## General measures

This includes avoidance of triggers such as prolonged standing, contracting arms and/or legs and sitting or lying down at the onset of prodromal symptoms. Other measures include, where possible, stopping or reducing hypotensive agents, counter-pressure measures, e.g. compression stockings of at least thigh length, increased salt intake in young patients and in some cases, tilt training has been shown to reduce episodes of syncope.

## Specific measures

Where syncope continues to recur despite general measures, specific treatment is required and includes drug treatment and permanent pacemakers.

## Drug treatment

There are a range of drugs that can be used to treat this condition. One of which is fludrocortisone, which is a synthetic analogue of aldosterone that causes salt and water retention. It also improves sensitivity of the alpha receptors to circulating catecholamines. It is used in treatment of the vasodepressor type. It may cause hypertension and congestive cardiac failure especially in elderly patients with impaired left ventricular function. Although there is some anecdotal evidence and small uncontrolled trials suggesting that it is efficacious in this context, there are no randomised controlled trials demonstrating this<sup>11</sup>.

Another drug is midodrine, which is a prodrug whose active metabolite, desglymidodrine is an alpha-adrenergic agonist. It has been shown in small randomised controlled trials and observational trials to be effective, particularly in the vasodepressor type<sup>12</sup>. Other drugs such as beta blockers and SSRIs have been tried with varying degrees of success. There are no randomised controlled trials proving their efficacy<sup>11</sup>.

## Permanent pacemaker

Indicated in the cardioinhibitory type IIB group where the heart rate drops before the blood pressure. It is also beneficial in the mixed and cardioinhibitory type IIA group where the blood pressure drops before the heart rate.

The SYNPACE clinical trial of pacing in patients with neurocardiogenic syncope showed no significant difference in benefit between patients with cardioinhibitory and mixed haemodynamic responses<sup>13</sup>. It is, of course, possible that the lack of statistical significance may have been due to the small number of patients (29 in total) involved in the study. Dual chamber pacemakers with rate drop algorithms are preferable in this context.

## Key points

- > Neurocardiogenic syncope is an important differential diagnosis of recurrent syncope and unexplained falls in elderly patients.
- > Although, not life threatening in itself, it can result in serious injury and fractures.
- > Despite its limitations, head-up tilt testing, in conjunction with clinical characteristics of the syncopal episodes forms the main basis for diagnosis of this condition.
- > Non-pharmacological measures, e.g. avoiding triggers, full-length compression stockings should be tried initially.
- > Where these measures fail, an individualised approach of pharmacological interventions, e.g. vasoactive drugs such as fludrocortisone for vasodepressor responses or permanent pacemakers for cardioinhibitory responses, should be considered.

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## Prognosis

Syncope predicts a risk for recurrence of syncope. Patients with cardiac causes have a higher mortality than those with non-cardiac causes. Syncope due to a cardiac cause is associated with 30 per cent mortality at one year. Older patients may have co-existent coronary heart disease or heart failure and therefore the mortality may be higher in this group of patients particularly in those who develop asystole during the attacks. In addition, syncope results in recurrent falls especially in older patients and potentially serious injuries and fractures. It is important to make the diagnosis and manage it appropriately as it is potentially treatable.

## Conclusion

Neurocardiogenic syncope is an important cause of syncope and falls in elderly patients. It can result in serious injuries and fractures, with their attendant mortality and morbidity. It is also potentially treatable and should be considered as a differential diagnosis in any elderly patient with recurrent or unexplained syncope as well as unexplained falls ■ GM

**Conflict of interest: none declared**