Carotid sinus syndrome

Carotid sinus syndrome is an important but frequently overlooked cause of syncope and presyncope in elderly people. It is characterized by episodic bradycardia and/or hypotension resulting from exaggerated baroreceptor-mediated reflexes or carotid sinus hyper-sensitivity. The syndrome is diagnosed in subjects with unexplained symptoms when 5 s of carotid sinus massage produces asystole exceeding 3 s (cardio-inhibitory), or a fall in systolic blood pressure exceeding 50 mmHg (6.6 kPa) in the absence of cardio-inhibition (vasodepressor), or a combination of the two (mixed).

The afferent limb of the carotid sinus reflex terminates at the nucleus of the tractus solitarius in the medulla. The efferent limb comprises the sympathetic nerves supplying the heart, the vasculature, and the cardiac vagus nerve. Physiological rises in arterial blood pressure generate the stretch necessary to activate the reflex. In health, the carotid baroreceptors in conjunction with those of the aortic arch play a major role in the neural control of blood pressure. In patients with carotid sinus syndrome, baroreflex sensitivity, which normally declines with increasing age, is enhanced compared with age-matched controls (Dehn *et al*. 1984). The site and mechanism of this hyper-sensitivity are not known, but may be central (O'Mahony 1995).

Atropine in a dose up to 700 μg can abolish bradycardia in all patients. Carotid sinus syndrome and sick sinus syndrome are two separate diagnostic entities, although up to 5 per cent of patients with carotid sinus syndrome can have abnormal intrinsic sinus node function (Morley *et al*. 1983). It is possible that carotid sinus syndrome results from a central abnormality of baroreflex gain. The frequent association of carotid sinus syndrome with atherosclerotic comorbidities has led to speculation that cerebral and/or cardiac ischaemia may play an important role in its pathogenesis (Morley *et al*. 1983).

The prevalence of carotid sinus reflex hypersensitivity in asymptomatic individuals is not known. However, it definitely increases with age and is rare in patients with syncope or falls who are aged less than 50 years. Recent studies suggest that it is not a feature of normal ageing. In a study of 25 healthy elderly subjects, none developed diagnostic or symptomatic cardio-inhibition or vasodepression during carotid sinus massage (McIntosh *et al*. 1994*a*). In another series, abnormal cardio-inhibition was reported in 2 per cent of 288 healthy subjects (age range 17–84 years) (Brignole *et al*. 1985). Carotid sinus hypersensitivity was demonstrated in 19 per cent of 1000 patients (aged over 50 years) who presented to an accident and emergency department with 'unexplained falls', and the prevalence increased to 21 per cent and to 35 per cent in fallers aged over 65 and over 80 respectively (Fig. 2) (Richardson *et al*. 1997). Abnormal responses to carotid sinus massage are more likely to be observed in asymptomatic individuals with coronary artery disease and those on vasoactive drugs known to influence reflex sensitivity (digoxin, β-blockers, and methyldopa). The prevalence of drug-induced carotid sinus hypersensitivity among elderly fallers is 11 per cent (Richardson *et al*. 1997). Although it is still

generally considered as a rare condition, referral centres which routinely perform carotid sinus massage in all older patients presenting with syncope and unexplained falls diagnose carotid sinus syndrome in up to 45 per cent (McIntosh *et al*. 1993*a*).

Carotid sinus reflex sensitivity is assessed by measuring heart rate and blood pressure responses to carotid sinus massage. In asymptomatic elderly subjects, the normal response is as follows: cardio-inhibition, 1038 ± 195 ms; vasodepression, of 21 ± 14 mmHg (2.8 ± 1.8 kPa) (McIntosh *et al*. 1994*a*).

Carotid sinus massage is a crude and unquantifiable technique and is prone to both intra- and interobserver variation. More scientific diagnostic methods employing neck chamber suction or drug-induced changes in blood pressure can be used for carotid baroreceptor activation, but neither of these techniques is suitable for routine use. A standardized 5- to 10-s stimulus has been accepted by most current investigators as safe and effective. Over 75 per cent of patients with cardio-inhibitory carotid sinus syndrome respond positively to right-sided carotid sinus massage either alone or combined with left-sided carotid sinus massage (McIntosh *et al*. 1993*b*).

Complications resulting from carotid sinus massage include cardiac arrhythmias and neurological sequelae. Fatal asystole or ventricular arrhythmias are extremely uncommon and have generally occurred in patients with underlying heart disease undergoing therapeutic rather than diagnostic massage. Digoxin toxicity has been implicated in most cases of ventricular fibrillation. Neurological complications are also uncommon (0.14 per cent) (Munro *et al*. 1994). In a retrospective analysis of 16 000 episodes of carotid sinus massage (Davies and Kenny 1998), only 12 patients developed neurological complications. These resolved within 24 h in eight patients and within 1 week in two patients; neurological deficits persisted in two patients.

It has been suggested that carotid sinus massage should not be performed in patients with known cerebrovascular disease or carotid bruits unless there is a strong indication. It should also be avoided immediately after myocardial infarction when reflex sensitivity may be increased. If there is a significant hypotensive response during the stimulus, it is prudent to rest patients for at least 10 min before allowing them to stand up for other tests. It is not possible to predict from either clinical characteristics or carotid Doppler studies which patients will develop neurological sequelae.

Carotid sinus syndrome should be diagnosed when carotid sinus hypersensitivity is documented in a patient with otherwise unexplained dizziness, falls, or syncope and in whom carotid sinus massage reproduces symptoms. As discussed previously, three subtypes of carotid sinus hypersensitivity or carotid sinus syndrome are currently recognized. The independent vasodepressor response can be confirmed by repeating carotid sinus massage after abolishing significant cardio-inhibition using either atrioventricular sequential pacing or intravenous atropine (Walter *et al*. 1978). Asystole exceeding 1.5 s should be considered ‘significant’ in this regard.

Symptom reproduction during carotid sinus massage was regarded by early investigators as essential in the diagnosis of carotid sinus syndrome, but it is not always justified in patients with reproducibly abnormal responses. Up to 15 to 30 per cent of patients with unexplained falls only have an abnormal response during upright carotid sinus massage (Kenny and Traynor 1991).

In carotid sinus hypersensitivity, recognized triggers for symptoms are head movement, prolonged standing, postprandial state, straining, looking or stretching upwards, exertion, defecation, and micturition. In a significant number of patients no triggering event can be identified. An abnormal response to carotid sinus massage may not always be reproducible necessitating repetition of the procedure if the diagnosis is strongly suspected.

Carotid sinus hypersensitivity is frequently associated with other hypotensive disorders such as vasovagal syncope and orthostatic hypotension (McIntosh *et al*. 1993*b*), indicating a common pathogenic process. Overlap of hypotensive disorders can make an attributable diagnosis difficult to identify, but every effort should be made as interventions may vary and assessment of response depends on the initial diagnosis. Approximately half of patients sustain an injury during symptomatic episodes; fractures, particularly of the femoral neck, had been sustained by 25 per cent of patients in one series (McIntosh *et al*. 1993*b*). In a prospective study of falls in nursing home residents, a threefold increase in the fracture rate was observed in those with carotid sinus hypersensitivity (Murphy *et al*. 1986). Indeed, it can be considered as a modifiable risk factor for fractures of the femoral neck (Ward *et al*., in press). Carotid sinus syndrome is not associated with an increased risk of death. The mortality in patients with carotid sinus syndrome is similar to that in patients with unexplained syncope and the general population matched for age and sex (Brignole *et al*. 1992). Mortality rates are similar for the three subtypes of the syndrome (Brignole *et al*. 1992).

Atrioventricular sequential pacing is the treatment of choice for patients with symptomatic cardio-inhibition (Morley *et al*. 1982). With appropriate pacing, syncope and unexplained falls are abolished in 75 to 90 per cent of patients with cardio-inhibition (Almquist *et al*. 1985). Treatment of vasodepressor carotid sinus syndrome is less successful owing to poor understanding of its pathophysiology. Fludrocortisone, a mineralocorticoid widely employed to treat orthostatic hypotension, is used with good results in the treatment of vasodepressor carotid sinus syndrome, but its longer-term use is limited by adverse effects (da Costa *et al*. 1993).