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CONSENSUS STATEMENT

Consensus statement on the definition of orthostatic hypotension, neurally mediated syncope and the postural tachycardia syndrome

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Introduction

In 1996, following a multi-specialty Consensus Conference sponsored by the American Academy of Neurology and the American Autonomic Society, a brief definition of orthostatic hypotension was published. This definition has been widely used and has withstood the test of time. Fifteen years later, advances in the understanding of orthostatic hypotension and disorders of orthostatic tolerance have made it necessary to clarify and expand the earlier definition. In this updated consensus statement, endorsed by the American Autonomic Society, the European Federation of Autonomic Societies, the Autonomic Research Group of the World Federation of Neurology and the Autonomic Disorders section of the American Academy of Neurology, we refine and update the definition, pathophysiology and clinical features of orthostatic hypotension. We also add the definitions of two highly prevalent disorders of orthostatic tolerance, neurally mediated (reflex) syncope and the postural tachycardia syndrome. This update is the product of a group of experts in the field but is not an evidence based clinical guideline.

Orthostatic hypotension

Definition

Orthostatic hypotension is a sustained reduction of systolic blood pressure of at least 20 mmHg or diastolic blood pressure of 10 mmHg within 3 min of standing or head-up tilt to at least 60° on a tilt table. Orthostatic hypotension is a clinical sign and may be symptomatic or asymptomatic. In patients with supine hypertension, a reduction in systolic blood pressure of 30 mmHg may be a more appropriate criterion for orthostatic hypotension because the magnitude of the orthostatic blood pressure fall is dependent on the baseline blood pressure.

Pathophysiology

Immediately after standing, there is gravitationally mediated redistribution of the blood volume, and a pooling of 300–800 ml of blood in the lower extremities and splanchnic venous capacitance system. As a consequence, venous return to the heart falls and cardiac filling pressure is reduced. This results in diminished stroke volume and cardiac output. In response, sympathetic outflow to the heart and blood vessels increases and cardiac vagal nerve activity decreases. These autonomic adjustments increase vascular tone, heart rate and cardiac contractility, and stabilize arterial pressure. During standing, contraction of lower body skeletal muscle prevents excessive pooling and augments venous return to the heart.

Orthostatic hypotension is caused by an excessive fall of cardiac output or by defective or inadequate vasoconstrictor mechanisms. The focus of this consensus statement is neurogenic orthostatic hypotension, i.e., orthostatic hypotension due to inadequate release of norepinephrine from sympathetic vasomotor neurons leading to vasoconstrictor failure.

Epidemiology

Orthostatic hypotension occurs in patients with neurodegenerative disorders such as multiple system atrophy,

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Parkinson's disease and pure autonomic failure and in individuals with peripheral neuropathies and ganglionopathies that affect autonomic nerves. The prevalence of orthostatic hypotension increases with age. Orthostatic hypotension is more common in institutionalized (up to 70%) than community dwelling elderly ($\sim$6%).

Clinical features

Characteristic symptoms include lightheadedness, dizziness, pre-syncope and syncope. Loss of consciousness is usually of gradual onset but may occur suddenly. Some patients present with more general complaints such as weakness, fatigue, cognitive slowing, leg buckling, visual blurring, headache, neck pain, orthostatic dyspnea or chest pain.

Confounding variables

Several confounding variables may influence the extent of the orthostatic blood pressure fall.

Supine hypertension

Many patients with neurogenic orthostatic hypotension have supine hypertension even before treatment of hypotension is initiated. Some of these patients have blood pressure falls on standing that fulfill criteria for orthostatic hypotension although blood pressure remains at or above normal range. The clinical significance of this phenomenon is not known.

Diurnal variability

Orthostatic hypotension is more common and more severe in the morning. This phenomenon is most likely due to high supine nocturnal blood pressure which causes a pressure diuresis and results in intravascular volume depletion over night. Redistribution of intravascular volume also may contribute to diurnal variability.

Food ingestion

Patients with autonomic failure and the elderly are susceptible to significant falls in blood pressure associated with meals. This is exacerbated by large meals, meals high in carbohydrate, and alcohol intake.

Age

The orthostatic blood pressure fall increases with age in many elderly individuals. This is due to several factors including supine hypertension, age associated changes in baroreflex function, inadequate vasoconstrictor responses, reduced cardiac and vascular compliance, decreased blood volume and lesser efficiency of the skeletal muscle pump.

Medications

Diuretics, sympatholytic agents and other vasodilators may increase the postural blood pressure fall. Such medications include blood pressure lowering medications, antidepressants (particularly tricyclic agents) and certain anti-Parkinsonian agents.

Other variables

The orthostatic blood pressure fall is also influenced by hydration, cardiac and vascular stiffness, ambient temperature, gender, prolonged recumbency and deconditioning.

Variants

Initial orthostatic hypotension

An exaggerated transient fall in blood pressure may occur shortly upon standing accompanied by symptoms of hypoperfusion. Initial orthostatic hypotension is defined as a transient blood pressure decrease (>40 mmHg systolic blood pressure and/or >20 mmHg diastolic blood pressure) within 15 s of standing. This blood pressure fall, which occurs in both old and young subjects, is observed with continuous beat-to-beat blood pressure monitoring. It may occur during active standing and to a lesser degree with passive tilting. This may be a common unrecognized cause of syncope. The underlying pathophysiology is thought to be a transient mismatch between cardiac output and peripheral vascular resistance that occurs with rapid postural change.

Delayed orthostatic hypotension

Some patients present with symptomatic orthostatic hypotension that occurs beyond 3 min of standing. The clinical significance of delayed orthostatic hypotension is unknown. These delayed falls in blood pressure may be a mild or early form of sympathetic adrenergic failure. This disorder may be revealed in patients with suspected orthostatic hypotension by extending the period of orthostatic stress (head-up tilt or stand) beyond 3 min.

Neurally mediated (reflex) syncope

Definitions

Syncope and transient loss of consciousness

There are several different mechanisms that result in transient loss of consciousness. Causes may be traumatic or nontraumatic; the latter include syncope, epileptic seizures, metabolic disorders, and very rarely a transient ischemic attack in the posterior circulation. The term syncope indicates a specific pathophysiology and should only be used to describe a transient loss of consciousness and postural tone resulting from global cerebral hypoperfusion with spontaneous and complete recovery and no neurological sequelae. When the cause of unconsciousness is not clear the episode should not be called syncope.

Neurally mediated syncope

Neurally mediated (reflex) syncope, e.g., vasovagal, situational (cough, swallowing, micturition) or carotid sinus syncope refers to a heterogeneous group of conditions in which there is a relatively sudden change in autonomic nervous system activity leading to a fall in blood pressure, heart rate and cerebral perfusion. Neurally mediated syncope is best understood as a reflex with afferent, central and efferent pathways. The term 'neurocardiogenic syncope' is frequently used to describe reflex syncope but it should be abandoned because the origin of the reflex is rarely in the heart.

Clinical features

Neurally mediated syncope is typically preceded by prodromal symptoms and signs that may occur up to 60 s prior to loss of consciousness. Prodromal features include pallor, diaphoresis, nausea, abdominal discomfort, yawning, sighing, and hyperventilation. These are followed by the features of cerebral and retinal hypoperfusion such as visual and auditory disturbances, concentration difficulties and cognitive slowing.

Pathophysiology

During neurally mediated syncope, efferent sympathetic vasoconstrictor nerve activity decreases leading to a loss of vasoconstrictor tone and parasympathetic (vagal) outflow increases causing heart rate slowing. The range of bradycardia varies widely in reflex syncope, from a small reduction in peak heart rate to several seconds of asystole.

The trigger for reflex syncope can be central (e.g., emotions, pain, blood phobia) or peripheral (e.g., prolonged orthostasis, increased trigeminal or carotid sinus afferent activity), but the precise afferent nerve pathways and central nervous system mechanisms involved in reflex syncope are largely unknown.

In addition to reflex-mediated neural changes, other environmental or physical factors frequently contribute to lower blood pressure and diminish cerebral blood flow during reflex syncope. For example, heat exposure leading to peripheral vasodilatation may contribute to hemodynamic stress; straining with a closed glottis reduces venous return and increases intracranial pressure; and hyperventilation-induced hypocapnia reduces cerebral blood flow and induces vasodilatation in skeletal muscle. In some instances, these factors may be the main reason for loss of consciousness.

As reflex syncope requires a reversal of the normal autonomic outflow, it usually occurs in people with a functional autonomic nervous system. Reflex syncope should be distinguished from syncope due to neurogenic orthostatic hypotension in patients with chronic autonomic failure.

Epidemiology

The prevalence of syncope in the general population is high. The vast majority of syncope is caused by reflex syncope. The frequency of reflex syncope increases during adolescence and in those over 55 years. Many adults with reflex syncope have had similar episodes in their youth. In the young, orthostatic and emotional vasovagal faints accompanied by characteristic prodromal symptoms are common, while in the elderly, typical prodromal symptoms are less frequent. Carotid sinus hypersensitivity, cough and defecation syncope occur almost exclusively in the elderly.

Postural tachycardia syndrome

Definition

The postural tachycardia syndrome (POTS) is characterized by a sustained heart rate increment of $\geq$30 beats/minute within 10 min of standing or head-up tilt in the absence of orthostatic hypotension. The standing heart rate for all subjects is often $\geq$120 beats/minute. These criteria may not be applicable for individuals with low resting heart rates. For individuals aged 12–19 years the required increment is at least 40 beats/minute. The orthostatic tachycardia may be accompanied by symptoms of cerebral

hypoperfusion and autonomic overactivity that are relieved by recumbency.

Pathophysiology

The etiology and pathophysiology of POTS are unknown but are likely to be heterogeneous. The syndrome is associated with deconditioning, recent viral illness, chronic fatigue syndrome and a limited or restricted autonomic neuropathy.

The differential diagnosis includes conditions that cause tachycardia, such as thyrotoxicosis, inappropriate sinus tachycardia and other cardiac rhythm abnormalities, pheochromocytoma, hypoadrenalism, anxiety, dehydration, and medications (e.g., vasodilators, diuretics, and β-agonists).

Epidemiology and clinical features

The prevalence of POTS is not known. The syndrome is more common in women. The orthostatic symptoms consist of lightheadedness, visual blurring or tunnel vision, palpitations, tremulousness, and weakness (especially of the legs). Other symptoms include fatigue, exercise intolerance, hyperventilation, shortness of breath, anxiety, chest pain, nausea, acral coldness or pain, concentration difficulties and headaches.

On clinical examination, in addition to the heart rate increment, pulse pressure may be reduced and acral coldness may be present. Continued standing may lead to venous prominence, cyanosis and foot swelling. A hyperadrenergic state is present in some patients who have a resting tachycardia, sweating, and tremulousness.