Unusual causes of severe orthostatic hypotension

M Abu Nasar, Shaku Murty

INTRODUCTION

Two elderly female patients presented with severe refractory orthostatic hypotension, one of which was an isolated case and the other as a part of multisystem atrophy (MSA; Shy–Drager syndrome). Both patients showed significant improvement in blood pressure (BP) and postural symptoms following administration of midodrine, a peripherally acting α-adrenergic agonist.

CASE REPORT 1

A 73-year-old woman presented with a short history of recurrent dizziness on standing, tiredness and difficulty in walking with a tendency to falls. She was on no regular medication. Clinically, she was not anaemic or dehydrated. She had expressionless facies and shuffling gait with tremor of both hands, more apparent on the left. On examination, her pulse was 78/min regular, her blood pressure (BP) was 160/100 mmHg (lying) and 90/0 mmHg (on standing). The patient had to be supported to stand.

Full blood count, random glucose, liver function test, thyroid function tests and electrolytes were within the normal range, but urea and creatinine were mildly elevated. Serum cortisol was not measured. A provisional diagnosis of Shy–Drager syndrome was made and she was given full-length elastic stockings and, at the same time, commenced fludrocortisone at 50 μg daily increasing gradually to 150 μg daily. There was a slight improvement in standing BP, but the patient experienced severe headaches and developed signs of cardiac failure. The fludrocortisone was discontinued. Midodrine was commenced at an initial dose of 2.5 mg daily increasing to a maximum dose of 5 mg three times daily. Her BP improved (lying 140/70 mmHg and standing 130/70 mmHg). Benzhexol was introduced to treat her mild tremor and excess salivation.

Her BP remained stable for about 16 months, after which her neurological symptoms worsened. The dose of midodrine was increased to 20 mg daily in divided doses, and other measures, such as head-up tilt, slow sodium and ephedrine, were also tried, with very little benefit. She was transferred to a specialist unit where a magnetic resonance imaging scan and autonomic tests confirmed the diagnosis of multisystem atrophy. Her condition continued to deteriorate, and she died about 2 years after the initial presentation.

CASE REPORT 2

An 89-year-old woman presented with an 8-month history of recurrent falls preceded by dizziness and episodic faintness. She had been diagnosed with non-insulin dependent diabetes over 13 years ago. She had undergone recent surgery for carcinoma of the sigmoid colon.

Clinically, she was pale, apathetic and appeared depressed. On examination, her pulse was 86/min regular, and her blood pressure (BP) was 143/77 mmHg (lying) and 78/43 mmHg (standing). On multiple occasions, a postural drop in BP greater than 50 mmHg was recorded. There were no signs or symptoms of Parkinson's disease or of any other neurological disorder. Her gait was unsteady, however, and she needed assistance with walking because of constant dizziness. A diagnosis of orthostatic hypotension was made, probably secondary to autonomic neuropathy caused by diabetes mellitus.

Fludrocortisone was commenced at the maximum dose of 150 μg daily. Her BP improved, but she developed marked bilateral leg oedema. Fludrocortisone was stopped, and she was started on midodrine 2.5 mg daily increasing to 2.5 mg three times a day as her orthostatic hypotension improved. There was no dizziness, and she was walking with one stick. Her BP averaged 180/80 mmHg (lying) and 170/80 mmHg (standing). The dose of midodrine was reduced and maintained at 2.5 mg twice daily.

DISCUSSION

Orthostatic hypotension is a disabling disorder associated with advanced age (Robbins and Rubenstein, 1984) as well as with a variety of disease states and medications, such as diuretics, antihypertensive drugs, antiparkinsonian drugs and benzodiazepines. It is defined as a drop in systolic BP of more than 20 mmHg or a drop in diastolic BP of more than 10 mmHg at least 1–2 minutes after standing (Stumpf and Mitrzyk, 1994). The most common presenting symptoms are light-headedness and/or syncope.

The treatment includes non-pharmacological and pharmacological measures and is aimed at improving standing BP and relieving symptoms (Fouad-Tarazi et al, 1995).

MSA is a neurodegenerative disorder in which degeneration in diverse brain regions leads to problems in the control of movement, balance, BP and urinary tract function. It is often accompanied by Parkinsonian symptoms, which are sometimes initially the most prominent symptoms. In patients in whom changes in autonomic function dominate the initial presentation, particularly changes in BP regulation, MSA is often called Shy–Drager syndrome.

The disease may progress rapidly. Patients survive on average 9 years following the onset of illness (National Parkinson Foundation, 1998). Current treatment is symptomatic. The most valuable agents to increase BP are fludrocortisone and midodrine. Other autonomic symptoms include impotence and urinary

Dr M Abu Nasar is Consultant Physician and **Dr Shaku Murty** is Staff Physician in the Department of Medicine for the Elderly, Bridlington & District Hospital, Bridlington, East Yorkshire YO16 4QP

Correspondence to: Dr M Abu Nasar
Manasar001@aol.com

incontinence, and in later stages some patients develop breathing problems, including stridor and sleep apnoea, that may require tracheotomy as a life-saving measure.

The drug of choice is fludrocortisone which acts mainly by expansion of plasma volume secondary to sodium retention with increased sensitivity of the vasculature to the effects of norepinephrine. For severe or refractory cases, newer agents are available, one of which is midodrine. This is a peripherally acting α-adrenergic agonist that induces arterial and venous vasoconstriction.

Fouad-Tarazi et al (1995) carried out a trial in patients with refractory idiopathic orthostatic hypotension and Shy–Drager syndrome which showed improvement in symptoms and standing BP. The effects of midodrine appear to be related to the function of the autonomic system, with those who improve having less severe dysfunction. It can also be combined with fludrocortisone with additive effect.

The recommended initial dose is 2.5 mg 2–3 times per day, the usual maintenance dose is 30 mg/day and the maximum dose 40 mg/day (McTavish and Goa, 1989). The most prevalent adverse effects are pilomotor reactions, e.g. nausea, heartburn, tachycardia, supine hypertension, headache and irritability. Most of these are mild and transient, responding to a decrease in dosage (McTavish and Goa, 1989).

Both these patients had a good response to midodrine with an increase in standing BP and improvement in symptoms and quality of life. This may be an effective drug in cases of severe refractory orthostatic hypotension and is worthy of a larger scale trial and clinical use. **HM**

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