Volume expansion and vasodilators in the treatment of idiopathic postural hypotension

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Summary

A case is cited in which hydrallazine was used in conjunction with volume expansion as a novel approach to the improvement of orthostatic symptoms in a patient with idiopathic postural hypotension.

Introduction

Postural hypotension, whether isolated or associated with other neurological symptoms, such as the Shy-Drager syndrome, is a severely incapacitating and distressing condition. Therapy remains unsatisfactory and includes antigravity devices, α -adrenoceptor agonists with or without monoamine oxidase inhibitors, and volume expansion with mineralocorticoids. Recent reports have indicated an unpredictable response to tyramine with monoamine oxidase inhibitors, and the hazard of iatrogenic supine hypertension (Nanda, Johnson and Keogh, 1976; Davies, Bannister and Sever, 1978). A case is cited to illustrate the use of a therapeutic regime including the vasodilator hydrallazine which has provided subjective improvement in symptoms and objective evidence of enhanced orthostatic tolerance.

Case report

A 70-year-old man had experienced postural dizziness and blackouts for 4 years, and his BP had shown a marked postural drop with no change in heart rate. His therapy included elastic stockings, and oral administration of ephedrine and sustained release isoprenaline. There was no improvement in symptoms and signs; administration of fludrocortisone resulted in severe hypokalaemia (serum potassium 2.2 mmol/l). His symptoms became progressively worse and he was unable to leave his bed. Before investigation he had had several episodes of transient right hemipareses on standing. Severe morning headaches were experienced in the supine posture and dizziness and syncope occurred on standing. The addition of sodium supplements

caused peripheral oedema and exacerbated the supine hypertension.

Investigations showed no aetiology for the postural hypotension, but confirmed impaired cardiovascular reflexes (absent heart rate and pressor response to Valsalva's manoeuvre, cold pressor test, mental arithmetic and isometric handgrip exercise). Adrenocortical function was normal. Urinary catecholamine excretion was low at 8.1 $\mu\text{g/g}$ creatinine (normal range 19-54); plasma noradrenaline was also extremely low at 0.05 $\mu\text{g/l}$ (normal range 0.07-0.70) and did not rise on 70° head up tilt. Pressor sensitivity to i.v. noradrenaline (0.016 $\mu\text{g/kg/min}$ raised the systolic BP by 60 mmHg) was markedly increased. Intravenous atropine to a total dose of 2.4 mg failed to raise the heart rate above 64 beats/min.

Three therapeutic regimes were given to the patient in a single-blind manner. The patient continued to take 0.05 mg fludrocortisone and sodium chloride (80 mmol of sodium daily) in unchanged doses throughout the studies. The regimes comprised: (1) placebo; (2) 10 mg tyramine orally after pretreatment for 6 days with phenelzine 45 mg daily; and (3) hydrallazine 75 mg daily orally. Hourly measurements of pulse and BP were made following a morning dose of drug.

Tyramine and monoamine oxidase inhibition produced no improvement in orthostatic tolerance. Hydrallazine caused a small fall in the supine pressure and produced a small rise in the standing BP; it also caused an increase in the heart rate in both lying and standing positions. The BP and pulse rate are shown in the table.

The patient continued to wear elastic stockings during his stay in, and following discharge from, hospital. His drug therapy on discharge comprised fludrocortisone 0.05 mg daily, sustained release sodium chloride, and hydrallazine 75 mg daily. When reassessed 4 months later on the same regime, he had not experienced any further episodes of loss of consciousness, and was able to walk in and around his home. His BP and heart rate were

TABLE 1. Mean values of hourly BP and pulse recordings over a 6-hr period following drug administration

	Placebo	Tyramine + monoamine oxidase inhibitor	Hydrallazine
Supine			
BP (mmHg)	170/103	151/95	159/87**
pulse rate (beats/min)	55	59	69***
Standing			
BP	97/64	82/62	102/72*
pulse rate	60	61	65*

* $P < 0.05$; ** $P < 0.01$; *** $P < 0.001$.
Values compared with placebo.

unchanged from the recordings on hydrallazine in hospital.

Nine months following the patient's initial investigations he was readmitted to hospital for review of therapy and for single-blind substitution of the hydrallazine with placebo. On admission he was able to assume the standing position and to walk around without symptoms. Within 24 hr of placebo substitution, he experienced supine and postural headaches, and became weak and light-headed on standing and walking.

In view of favourable reports by Kochar and Itskovitz (1978) on the use of indomethacin in this condition, a trial of this drug in a dose of 100 mg daily was conducted. Tilt table measurements were attempted after 48 hr's treatment with indomethacin, but had to be abandoned because of severe postural symptoms and unrecordable BP after only one minute at a 35° tilt.

The patient was restarted on hydrallazine 100 mg daily. Within 24 hr his symptoms had improved, and by 48 hr he was able to walk around without postural symptoms.

Comment

Therapy in idiopathic postural hypotension has been directed towards increasing cardiac output by chronotropic agents, or by influencing the effective circulating volume by means of arteriolar constriction and/or volume expansion. These manoeuvres result in minimal subjective and objective improvement—and often exacerbate the not infrequent supine hypertension. The present case study investigates a novel approach to improve orthostatic tolerance—involving volume expansion in association with a reduction in cardiac afterload effected by a decrease in arteriolar resistance. Cohn and Franciosa (1977) have described hydrallazine as producing its effect almost exclusively in the arterial bed; in the

patient described, therefore, the reduced cardiac afterload, in conjunction with the increase in circulating volume produced by sodium supplementation and fluorocortisone, presumably results in improved cardiac output—but without producing supine hypertension. As a result of this increased output, venous return is increased, so that the tendency to a postural fall in BP is reduced. Hydrallazine (unlike some other vasodilators) does not cause venodilatation, and therefore does not have any adverse effect on cardiac preload. This indication for arteriolar vasodilator therapy is analogous to the role of vasodilators in the management of cardiac failure (Cohn and Franciosa, 1977).

This single-blind, crossover hospital study resulted in subjective and objective patient improvement which was maintained during longer term out-patient management. Further controlled trials of this regime are therefore indicated.

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