LETTER

A new hope in the nightmare of diabetic orthostatic hypotension: the midodrine–fludrocortisone association

F. Andreelli, I. Plotton, C. Thivolet and J. P. Riou

Department of Endocrinology and Diabetes, Hospital E. Herriot, Pavilion X, Lyon, France

Received 1 April 1999; returned for revision 14 April 1999; revised version accepted 1 July 1999

To the Editor

Orthostatic hypotension is a severe chronic disease. Its treatment is difficult and sometimes ineffective. Midodrine (Gutrone, Nycomed SA, Paris, France) is an orally active dihydroergotamine-like α-1 adrenergic agonist. Recently the beneficial effects on orthostatic hypotension of midodrine alone or associated with octreotide were reported [1]. We report the case of a diabetic woman whose severe orthostatic hypotension was improved by the association of midodrine and fludrocortisone.

A 54-year-old woman was referred for management of severe orthostatic hypotension. Her insulin-dependent diabetes mellitus was discovered at 38 years of age and was complicated by retinopathy, nephropathy (treated by Ramipril, 1.25 mg/day) and asymptomatic peripheral polyneuropathy. She had experienced dizziness and orthostatic syncope since 47 years of age and had lost the confidence to walk alone. Autonomic neuropathy was confirmed by abnormal electrocardiographic R-R interval with deep breathing, by absence of increase of heart rate after rapid tilting and by a decrease of systolic blood pressure of >30 mm Hg after standing as according to the Zeigler criteria [2]. Gastroparesis was excluded by scintigraphic technique.

The orthostatic hypotension was resistant to increased salt intake, indomethacine, caffeine, fludrocortisone (150 μg/day) and octreotide (125 μg three times/day, 6 μg.kg.d) treatment either alone or in various combinations. The midodrine trial was started in October 1997 (7.5 mg/day) combined with fludrocortisone (100 μg/day). A dramatic improvement of orthostatic symptoms was rapidly noted with a complete disappearance of syncope episodes leading to an increase in quality of life. During 6 months of beneficial effect, the frequency of follow-up visits was monthly. At each visit, blood pressure was measure electronically with a Dinamap (Critikon®, Tampa, FL, USA) before and after the patient had stood for 5 min. Mean supine blood pressure (before and 6 months after midodrine–fludrocortisone association) increased from (mean + s.d.) 120 ± 50 mm Hg ($n = 15$) to 160 ± 70 mm Hg ($n = 60$) ($p < 0.05$). One min of upright blood pressure increased from 60 ± 20 mm Hg ($n = 15$) to 85 ± 20 mm Hg ($n = 60$) ($p < 0.05$). After 6 months of clinical improvement, midodrine was stopped and fludrocortisone was continued alone. Five days after this therapeutic modification, a relapse of orthostatic syncope episodes occurred. The reintroduction of the midodrine–fludrocortisone association was followed by clinical improvement maintained for 3 months of further follow-up. No potassium or sodium variations were noted on different blood samples analysis. No effect was observed on insulin requirement.

Midodrine is known to improve hypotensive circulatory disturbances of different conditions (e.g. neurogenic orthostatic hypotension [3] or intradialytic hypotension [4]). We showed that the combination of midodrine and fludrocortisone is a potent association for the therapeutic management of severe orthostatic hypotension in an insulin-treated diabetic patient. Indeed, in our patient, this asociation was more effective that fludrocortisone alone or than fludrocortisone combined with octreotide, or indomethacine or caffeine. Furthermore, the relapse of orthostatic symptoms after stopping midodrine contrasted with the rapid improvement observed after the reintroduction of this drug, suggesting the crucial role of midodrine in the management of orthostatic hypotension in our patient. Because a good quality of life was rapidly obtained when midodrine and fludrocortisone were combined we decided, for obvious ethical reasons, not to test the efficacy of midodrine alone. Even if a randomised trial with midodrine alone is needed to examine the blood pressure response in hypotensive diabetic patients, the fludrocortisone–midodrine combination seems to be very

Correspondence:
Fabrizio Andreelli, MD, Department of Endocrinology and Diabetes, Hospital E. Herriot, Pavilion X, 69437 Lyon cedex 03, France.

promising for the treatment of orthostatic hypotension in insulin-dependent diabetic patients and the improvement of their quality of life without metabolic consequence.

References

1 Hoeldtke RD, Gabriella Horvath G, Bryner KD, Hobbs GR. Treatment of orthostatic hypotension with Midodrine and Octreotide. J Clin Endocrinol Metab 1998; **83:** 339–343.

2 Ziegler D. Diabetic cardiovascular autonomic neuropathy: prognosis, diagnosis and treatment. Diabetic Metab Rev 1994; **10:** 339–383.

3 Wright RA, Kaufmann HC, Perera R, Opfer-Gehrking TL *et al*. A double-blind dose response stdy of midodrine in neurogenic orthostatic hypotension. Neurology 1998; **51:** 120–124.

4 Cruz DN, Mahensmith RL, Brickel HM, Perazella MA. Midodrine is effective and safe for intradialytic hypotension over 8 months of follow-up. Clin Nephrol 1998; **50:** 101–107.

