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RESEARCH LETTER

Simona Maule
Mirko Tredici
Antonio Dematteis
Cristina Matteoda
Livio Chiandussi

Postprandial hypotension treated with acarbose in a patient with type 1 diabetes mellitus

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S. Maule · M. Tredici · A. Dematteis · L. Chiandussi
Autonomic Unit
San Vito Hospital, University of Turin
Turin, Italy

Dr. S. Maule (✉)
U. O. A. D. U. Medicina 4, Ospedale San Vito
Strada San Vito 34
10133 Torino, Italy
Tel.: +39-011/633-6997
Fax: +39-011/633-6931
E-Mail: simmaule@tin.it

C. Matteoda
Dept. of Diabetology
Martini Nuovo Hospital
Turin, Italy

Abstract Treatment of postprandial hypotension (PPH) is often unsuccessful. We report a case of a type 1 diabetic patient suffering from severely symptomatic PPH. The patient was treated with acarbose and showed definite improvement of both glycemic control and PPH.

Key words postprandial hypotension · acarbose · autonomic neuropathy · diabetic neuropathy

Introduction

Diabetic autonomic neuropathy may be symptomatic and cause severe postural and postprandial hypotension (PPH). It may be reversible in the early stages [2] or improved by strict glycemic control [13]. Pharmacological management of orthostatic and postprandial hypotension in diabetic patients is problematic. Such patients are at a high cardiovascular risk, and supine hypertension should be avoided in order to prevent congestive heart failure and renal damage. Treatment of PPH includes both dietary advice and pharmacological approaches. Less readily digestible carbohydrates or the addition of substances which impair the absorption of glucose may be of benefit in the treatment of PPH [7, 10]. In an interesting recent report, a diabetic patient with PPH was successfully treated with acarbose [11].

Case report

A 50-year-old female nurse was referred to our laboratory because of severely symptomatic PPH. Symptoms were more evident after the evening meal. Estimated calorie and carbohydrate contents of the meals were respectively: 207 Kcal and 35 g at breakfast, 788 Kcal and 55 g at lunch, and 956 Kcal and 127 g at dinner.

The patient had been affected by type 1 diabetes mellitus from the age of 28, treated with insulin (Regular 40 U daily, Intermediate NPH 10 U daily). Glycemic control was poor (hemoglobin A1c 11 %); glycemia was high after meals and not controlled by therapy. Patient was affected by proliferative retinopathy and autoimmune hyperthyroidism (under good control with tiamazole). The urine albumin-creatinine ratio was in the microalbuminuric range (39 μg/mg); mild signs of peripheral neuropathy had been confirmed by electromyography.

Findings on the first visit were: body mass index 27 Kg/m^2, pulse rate 88/min regular, supine blood pressure (BP) 150/90, standing BP 118/80. Laboratory findings: creatinine 0.9 mg/dl, fasting plasma glucose 200 mg/dl, sodium 139 mEq/l, potassium 3.9 mEq/l, hematocrit 40 %, hemoglobin A1c 11 %. Electrocardiogram was normal. Cardiovascular reflex testing (DAN Test Microlab, Padua, Italy) showed severe autonomic dysfunction (Deep Breathing ratio 1.09, Lying to Standing ratio 1.01, Valsalva ratio 1.05, Postural BP –50 mmHg). 24h-BP

monitoring (Spacelabs 90207, Redmond, USA) revealed that sitting systolic BP decreased by 52 mmHg 60 min after breakfast, 44 mmHg after lunch and 43 mmHg after dinner. Patient was asymptomatic for upper gastrointestinal symptoms (nausea, vomiting, early satiety, fullness, abdominal distension and epigastric pain) therefore gastric emptying status was not evaluated.

During follow-up 24h-BP monitoring, the patient was asked to consume meals analogous in composition to the pre-treatment one; the patient was also asked to maintain a sitting position for two hours after each meal.

The patient was treated with fludrocortisone (0.1 mg daily) and midodrine (15 mg daily), with mild improvement (reduced frequency of symptomatic hypotensive episodes). After one year, patient findings were: supine BP 160/90, standing BP 138/75, hemoglobin A1c 10 %; sitting systolic BP decreased by 45 mmHg 60 min after breakfast, 15 mmHg after lunch and 26 mmHg after dinner. Such a therapy was stopped because of supine hypertension (with reduced diastolic compliance at the echocardiography) and worsening of retinopathy (preretinal hemorrhage).

Based on a previous report [11], the patient was administered acarbose 150 mg/daily (50 mg tid 20 minutes prior to the meals). At the 3-month follow-up visit and BP monitoring, patient showed definite improvement in PPH (disappearance of symptoms at all meals and reduced BP fall after lunch and dinner) and absence of supine hypertension (Fig. 1). In Fig. 2, pre-prandial sitting systolic BP values are compared to values 60 min after meals, before any treatment, during fludrocortisone and midodrine and during acarbose. During acarbose treatment, systolic BP fall is reduced. Glycemic control was also clinically improved (HbA1c 9.7 %). Side-effects (abdominal fullness and flatulence) were well tolerated. Cardiovascular and metabolic improvement were maintained at 6- and 12-month follow-up visits.

Discussion

PPH is a postprandial decrease in systolic BP of at least 20 mmHg [12]. It is found in the elderly and in patients with primary autonomic failure and diabetic autonomic neuropathy. Prevalence is up to 30–40 % in type 2 diabetes [11], whereas no data are available in type 1 diabetes. PPH may cause somnolence, lightheadedness, fainting, falls, and transient ischemic attacks. PPH represents an independent risk factor for total mortality, coronary events and stroke [1]; in hypertensive patients, it is associated with asymptomatic cerebrovascular damage [5]. Pathogenetic mechanisms of PPH include impaired sympathetic response to splanchnic blood pooling [7], release of gastrointestinal vasodilatory peptides [7], and rapid gastric emptying in type 2 diabetes [10]. Treatment of PPH is often disappointing (dietary modifications, caffeine, sympathomimetic drugs) or expensive (octreotide). In a recent report, a type 2 diabetic patient with PPH was successfully treated with acarbose [11]. Acarbose inhibits intestinal α-glucosidases, thus reducing the rate of carbohydrate absorption. It decreases the peak postprandial plasma glucose rise in both type 1 and type 2 diabetic patients. The rationale for the use of acarbose in PPH may be: a) PPH is greater after glucose, rather than protein or fat intake [7]; b) large glucose oscillations impair BP control in diabetes [6]; c) guar gum and acarbose slow gastric emptying and reduce small intestine glucose absorption. Through such mechanisms it lowers blood glucose and attenuates the fall in BP after oral glucose in type 2 diabetic patients [9, 10]. By lowering postprandial blood glucose peaks,

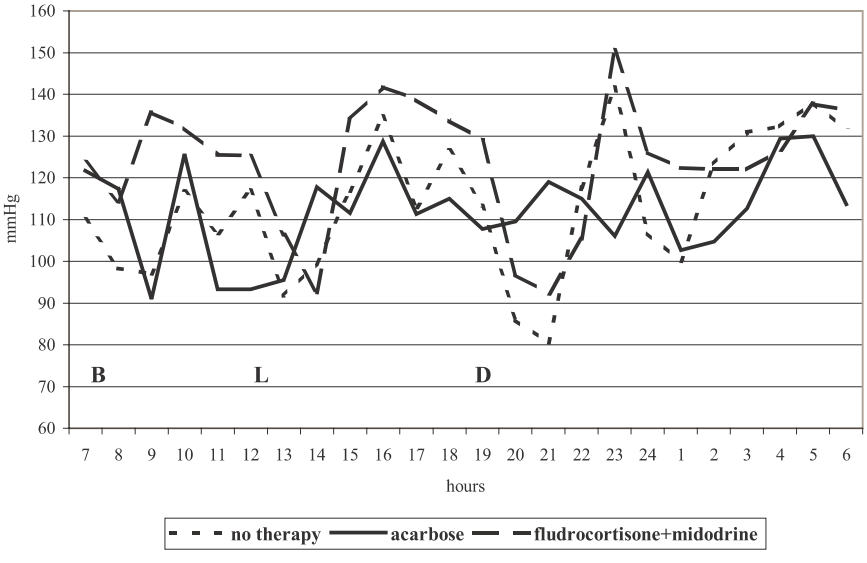

Fig. 1 Hourly blood pressure mean values before any treatment, during fludrocortisone and midodrine therapy, and during acarbose therapy (*B* breakfast; *L* lunch; *D* dinner)

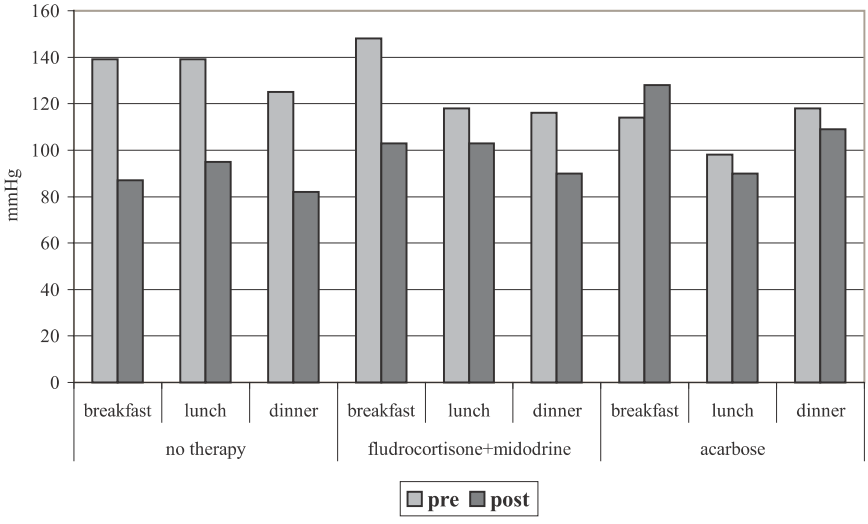

Fig. 2 Sitting systolic blood pressure values before and 60 min after meals, before any treatment, during fludrocortisone and midodrine therapy, and during acarbose therapy

acarbose may reduce the secretion of vasoactive gastrointestinal peptides. Improved glycemic control may, *per se*, ameliorate PPH [13].

In our report, compared to Sasaki [11], the patient was affected by type 1 diabetes and had poor metabolic control. During acarbose, BP fall was prevented especially after lunch and dinner, although pre-lunch BP values were lower compared to other periods and this might have overestimated the effects of acarbose. The BP fall still observed during acarbose therapy after breakfast (Fig. 1) was delayed and was possibly not related to food ingestion. Nevertheless, hypotensive symptoms significantly improved at all meals.

Acarbose may therefore be proposed in the treatment of both type 2 and type 1 diabetic patients with symptomatic PPH. This treatment seems to improve BP control without the development of supine hypertension. Controlled studies with standard meals are warranted to evaluate further the mechanisms of action and efficacy of acarbose in diabetic PPH.

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