Effectiveness of acarbose in treating elderly patients with diabetes with postprandial hypotension

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ABSTRACT

Postprandial hypotension (PPH) is a common condition that occurs primarily in elderly patients with type 2 diabetes mellitus (T2DM). This study aimed to assess the effectiveness of acarbose for PPH; it also investigated possible mechanisms behind PPH development. This single-blind, randomized controlled trial included 91 elderly patients with T2DM, aged between 60 and 80 years, who were inpatients at Beijing Hospital between March 2012 and November 2014. The patients were included into one of three groups: Group A, patients with T2DM without PPH; Group B, patients with T2DM with PPH receiving placebo; and Group C, patients with T2DM with PPH receiving acarbose. After an overnight fast, patients received a single dose of acarbose (100 mg) or placebo and then consumed a standardized 450 kcal meal. Blood pressure, glucose levels, heart rate (HR), and catecholamine levels were evaluated. Acarbose ameliorated PPH as determined by significant improvements in the duration and maximal fall in blood pressure (both $p<0.001$); however, no differences in HR and blood glucose levels were observed. In patients with PPH, blood pressure was correlated with blood glucose and HR variability values ($p<0.05$). Correlations between epinephrine and glucagon-like peptide-1 with blood pressure in groups A and C were largely lost in group B. Acarbose reduced postprandial blood pressure fluctuations in elderly patients with diabetes. PPH may be related to impaired autonomic nervous system function, reduced catecholamine secretion, and postprandial fluctuations in blood glucose levels.

Trial registration number Chinese Clinical Trial Registry ChiCTR-IPR-15006177.

Significance of this study

What is already known about this subject?

- Postprandial hypotension (PPH) is a common condition that occurs primarily in elderly patients with type 2 diabetes mellitus (T2DM).
- Although the exact mechanism is not clear, the pathogenesis of PPH in patients with diabetes mellitus is likely multifactorial.
- Diabetic autonomic failure, abnormal rate of gastric emptying, hyperglycemia, and abnormal vasoactive hormones (eg, insulin, glucagon-like peptide-1, or catecholamines) may each play a role.

What are the new findings?

- Acarbose reduced postprandial blood pressure fluctuations in elderly patients with diabetes.
- PPH may be related to impaired autonomic nervous system function, reduced catecholamine secretion, and postprandial fluctuations in blood glucose levels.
- Heart rate variability was associated with blood pressure, but only in patients with PPH.

How might these results change the focus of research or clinical practice?

- PPH may be related to impaired autonomic nervous system function.
- Acarbose attenuates the falling magnitude and shortens the duration of PPH.
- Acarbose reduces the fluctuation of blood pressure in elderly patients with T2DM.

INTRODUCTION

Postprandial hypotension (PPH) is an under-recognized disease that is especially common in elderly patients with diabetes mellitus. PPH is classically defined as a decrease in systolic blood pressure (SBP) of ≥20 mm Hg or a decrease below 90 mm Hg from a pressure of ≥100 mm Hg within 2 hours after a meal.[1] The prevalence of PPH among patients with type 2 diabetes mellitus (T2DM) was 37%,[2] increasing to 93.3% in elderly patients with diabetes.[3] However, no data are yet available on the prevalence of PPH among older adult patients with T2DM in China.

Although the exact mechanism is not clear, diabetic autonomic failure,[4] abnormal rate of gastric emptying,[5] hyperglycemia,[6] and abnormal vasoactive hormones[7–9] may play a role. Moreover, acarbose attenuates postprandial hyperglycemia and diminishes the postprandial fall in blood pressure in patients with T2DM,[3 4 8 10–12] even in those with symptomatic PPH.[13] The purpose of the present study

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was to assess the effectiveness of acarbose treatment on PPH in elderly patients with diabetes. To investigate possible mechanisms behind PPH in this population, continuous glucose monitoring and heart rate variability (HRV) monitoring were also evaluated.

MATERIALS AND METHODS

Study population

For this single-blind, randomized controlled trial, we recruited 124 elderly patients with T2DM, aged between 60 and 80 years, who were inpatients at Beijing Hospital between March 2012 and November 2014 for routine monitoring of blood glucose levels and analysis of T2DM complications. In total, 91 patients who had a T2DM diagnosis according to 1999 WHO criteria, were ≥60 years, were inpatients undergoing routine T2DM monitoring, and received insulin but not oral antidiabetic drugs were enrolled. Glycated hemoglobin (HbA1c) values were 7–11%. Sixty-one patients had a PPH diagnosis.[1] The extent of diabetic complications was determined by a Diabetic Complications Score that comprised as follows: screening for diabetic peripheral neuropathy, diabetic retinopathy, neck and lower extremity diabetes macrovascular disease, and diabetic nephropathy. The sum of all the complications of each patient is the comorbidity score.

Individuals were excluded if they had one of the following exclusion criteria: a history of renal disease with a plasma creatinine concentration of ≥133 μmol/L (1.5 mg/dL); severe gastrointestinal diseases; severe cardiac diseases; hepatic diseases, or an aspartate aminotransferase or alanine aminotransferase concentration at least twice as high as the upper limit of the normal range; endocrine diseases; uncontrolled hypertension (SBP ≥160 mm Hg or diastolic blood pressure (DBP) ≥95 mm Hg) or use of drugs that can affect the blood pressure or heart rate, acute illness; or a history of intestinal surgery, mental disorders, diabetic ketoacidosis, or hyperosmolar non-ketotic coma.

This study was carried out in accordance with the Declaration of Helsinki. The research ethics committee at Beijing Hospital reviewed and approved the study protocol. Each subject provided signed informed consent before participating in this study. The registry number of this study on Chinese Clinical Trial Registry is ChiCTR-IPR-15006177.

Study design

Randomization codes were generated with SAS V.9.10 software (SAS., Cary, North Carolina, USA). Patients with diabetes with PPH were randomly assigned into two treatment groups (1:1): a single dose of acarbose (100 mg; Bayer Healthcare, Beijing, China) and placebo. All patients involved in the study were blinded to their treatment allocation, and all received insulin on the day of testing. The study was conducted in the morning following an overnight fast. After taking either acarbose or placebo, patients received a standardized 450 kcal meal containing 9.1 g of protein (10%), 10 g of fat (31.85%), and 50.05 g of carbohydrate (55%). They were requested to eat for ∼15 min in a sitting position. Then, the subjects were asked to remain quietly in their beds for the next 120 min during which SBP, DBP, and mean arterial blood pressure (MBP) were monitored at 15 min intervals. Heart rate (HR) was monitored at 5 min intervals, and GLU levels were monitored by a continuous glucose monitoring system (CGMS).

Blood pressure assessment

All patients underwent an initial blood pressure examination at enrollment. SBP and DBP were continuously measured using an automated oscillometric blood pressure monitor. Measurements were initiated before the standard meal and continued for 120 min after the meal at 15 min intervals. Blood pressure variation from baseline was assessed by coefficient of variation (CV) and SD.

Autonomic function tests

Autonomic function tests over a 24-hours period, from 9:00 the first day to 9:00 the next day were performed with a Holter ECG. Parameters for HRV, including frequency-domain and time-domain parameters, were assessed as the following: mean of all R-R intervals, SD of the R-R intervals (SDNN), root mean square of successive differences of adjacent R-R intervals (RMSSD), and percentage of differences between adjacent R-R intervals >50 ms (PNN50). The frequency-domain analyses included total power (0.003–1 Hz), very low frequency (VLF, <0.04 Hz), low frequency (LF, 0.04–0.15 Hz), high frequency (HF, 0.15–0.5 Hz), and LF:HF ratio.

Continuous glucose monitoring

A CGMS (Medtronic, Northridge, California, USA) was used to detect intercellular glucose concentrations every 11 s. The mean electric signals were calculated within 5 min and stored, totaling 288 measurements of glucose concentration over 24 hours. The patients' blood glucose was also measured before and 2 hours after each meal and before sleep via collecting blood through a finger prick.

Blood glucose levels were also determined at 1 day before and after therapy to evaluate the following parameters: (1) mean blood glucose (MBG) in 24 hours; (2) the difference between maximum and minimum blood glucose concentrations (BGdiff); (3) the mean amplitude of glucose excursion (MAGE) over the 24-hours period as calculated between peaks and troughs, and an amplitude of glucose excursion (AGE) larger than 1 SD was regarded effective fluctuation (the number of glucose excursions (NGE) was determined); (4) TBG >7.8 mmol/L and TBG >11.1 mmol/L, the proportion of times at which the blood glucose was higher than 7.8 mmol/L and 11.1 mmol/L over 24 hours; (5) the area under the curve (AUC) of high blood glucose >7.8 mmol/L × day and AUC of high blood glucose >11.1 mmol/L × day; (6) the MBG over 2 hours before a meal (MBG1); (7) the MBG over 2 hours after a meal (MBG2); (8) BGdiff measured at 2 hours before a meal (BGdiff1); (9) BGdiff measured at 2 hours after a meal (BGdiff2); (10) the maximum postprandial blood glucose (max PBG) within 2 hours after a meal; and (11) the peak time at which max PBG was detected within 2 hours after a meal.

Analysis of plasma insulin, C-peptide, GLP-1, and catecholamine concentrations

A 21-gauge catheter was inserted into an antecubital vein for blood sampling. Venous blood samples (5 mL) were obtained immediately before the meal and at 120 min following the meal. Blood samples for plasma insulin, C

peptide, and GLP-1 were collected in EDTA-untreated tubes; samples for the serum catecholamines were collected with tubes using suitable EDTA plasma as an anticoagulant. All plasma and serum samples were stored at −70°C for subsequent analysis. Insulin, C peptide, GLP-1, and catecholamine concentrations were measured by ELISA following the manufacturer's instructions (Beijing Winter Song Boye Biotechnology Co., Beijing, China).

Statistical analysis

The primary outcome of the study was change in blood pressure. Regarding sample size, we assumed the difference of the primary end point between the acarbose and placebo groups was 15 mm Hg with a SD of 13.2 mm Hg.[14] In order to analyze the data of the primary end point, each group needs 17 patients, $\alpha=0.05$, $\beta=0.1$. We assumed a drop-off rate of 30%; therefore, a sample size of 25 was required for each group. A sample size of 30 among the three groups was required when enrolling group A considering a drop-out rate of 15% (based on the sample size of 25 for each group). Therefore, the total sample size was 90 patients.

Data represent mean±SD for continuous variables and n (%) for categorical variables in each group. Differences among groups were compared using the Pearson χ^2 test for categorical variables; Kruskal-Wallis tests with Mann-Whitney U tests were also performed for age as for the post hoc pair-wise comparisons for continuous variables without normal distributions. One-way analysis of variance with Bonferroni tests were used for the post hoc pair-wise comparisons for continuous variables with normal distributions between two groups. Spearman correlation analysis was applied for identifying the correlation between the lowest blood pressure and the change in glucose, HRV parameters, and serum catecholamine parameters. All statistical assessments were two-tailed, and $p<0.05$ was considered significant. An adjusted significance level of 0.0167 was applied for the post hoc pair-wise comparisons. All statistical analyses were carried out with IBM SPSS statistical software V.22 for Windows (IBM Corp., New York, USA).

RESULTS

A flow chart describing participant enrollment is shown in online supplementary figure S1. A total of 91 patients with a mean age of 66 years (range, 60–83 years) and a mean diabetes duration of 13.2 years (range, 0.042–38 years) were enrolled for evaluation. The patients' baseline demographics and characteristics, including those for patients without PPH (Group A, treated with insulin only), with PPH treated with placebo (Group B), and with PPH treated with acarbose (Group C), are represented in table 1. The only demographic variable that was significantly different between the groups was age ($p=0.013$).

Effects of acarbose on blood pressure and HR in PPH

The mean change in SBP (figure 1A), DBP (figure 1B), MBP (figure 1C), and HR (figure 1D) before consumption of the standard meal to 2 hours postprandial are shown for each group. Online supplementary table S1 shows the mean SBP, DBP, and MBP for each group at time 0 (ie, immediately following the meal). Analysis of the mean change in blood pressure showed significant differences among the three groups (all $p\leq0.004$). Post hoc pair-wise analysis showed significantly greater decreases in SBP, DBP, and MBP in control patients with PPH as compared with those treated with acarbose (all $p\leq0.003$; figure 1A–C). No differences in HR were detected among the three groups (figure 1D).

Online supplementary table S2 represents the post-treatment measurements in blood pressure, SD and CV of blood pressure, and HR at 2 hours postprandial by group. For the lowest value during measurement, significant differences among the three groups in SBP and MBP were detected ($p=0.043$ and $p=0.041$, respectively). However, no differences between any two groups were detected by post hoc pair-wise analysis. In addition, control patients with PPH had significantly greater falls in DBP and MBP than observed for patients with PPH treated with acarbose as well as control T2DM patients (both $p\leq0.002$). Control patients with PPH also had a longer duration of fall >20 mm Hg in blood pressure (all $p<0.001$). There was no significant difference in time of max fall of blood pressure.

With the exception of the CV value for DBP and HR, significant differences in all of the SD and CV values of blood pressure and HR at 2 hours postprandial were observed (all $p\leq0.033$; online supplementary table S2). Untreated patients with PPH had the highest values (all $p\leq0.015$). The HRV data were summarized in online supplementary table S3, which showed that no differences were detected among the three groups (all $p>0.05$).

Effects of PPH on glucose levels

Online supplementary table S4 shows the measurements obtained through the CGMS among the three groups. The BGdiff1 and peak time values were significantly different among three groups ($p=0.042$ and $p<0.001$, respectively). The BGdiff2 for acarbose-treated patients was significantly lower than that observed for placebo-treated control patients ($p=0.004$). Patients treated with acarbose also had a lower peak time than the placebo group ($p<0.001$; online supplementary table S4).

The mean change in GLU levels from the preprandial period to 2 hours postprandial (120 min in total) is shown in figure 1E. However, no significant differences were observed between the groups ($p=0.452$; figure 1E).

Effects of PPH and acarbose on serum catecholamine, C-peptide, and GLP-1 levels

Although significant differences among the three groups in C peptide ($p=0.045$) and GLP-1 levels ($p=0.002$) at 120 min were detected (figure 2B and C), post hoc pair-wise comparisons detected that only GLP-1 levels were significantly increased in the acarbose group at 120 min as compared with control patients with T2DM without PPH ($p=0.001$). No differences in serum insulin, epinephrine, norepinephrine, and dopamine were observed between the groups (figure 2A, D–F).

Correlation between postprandial blood pressure and CBGM parameters

The average DBP and MBP were correlated with MAGE (coefficient of $r=0.397$, and 0.402, respectively) in group A (table 2). In group B, the lowest DBP value was positively correlated with TBG >11.1 mmol/L and

Table 1 Patients' demographics and characteristics by group

Variables	A group (n=30)	B Group (n=30)	C group (n=31)	p Value
Sex†				
Males	15 (50)	20 (66.7)	19 (61.3)	
Females	15 (50)	10 (33.3)	12 (38.7)	
Age‡, y	66.67±6.49	64±5.55§	69.35±8.15	0.013*
Diabetes duration**, y	14.22±8.8	12.21±8.37	14.42±9.19	0.560
SBP‡, mm Hg	137.17±17.22	138.53±16.1	135.52±18.03	0.612
DBP‡, mm Hg	78.53±10.66	83.93±9.21	79.94±8.27	0.035
Weight‡, kg	67.52±10.65	69.52±10.63	68.47±10.97	0.798
BMI**, kg/m^2	24.32±2.78	24.77±3.42	25.13±3.51	0.624
FPG**, mmol/L	9.06±3.16	8.56±3.87	8.45±3.47	0.774
FINS‡, mmol/L	30.64±38	26.49±39.65	71.78±208	0.834
$Hb_{A1}c$‡, %	9.46±2.06	8.82±1.84	9.2±2.03	0.379
HOMA-IR‡	12.97±15.6	11.2±17.27	36.8±129.23	0.687
HOMA-β‡, %	211.16±747.95	108.05±197.09	398.91±1177.17	0.676
Diabetic complications index‡	2.4±0.81	2.33±0.96	2.45±0.99	0.964
UAER‡, μg/min	32.61±41.33	20.73±25.89	39.53±62.03	0.537
Uric acid**, μmol/L	258.8±81.18	300.23±93.72	290.26±75.34	0.140
TC‡, mmol/L	5.92±8.78	4.24±0.97	4.2±1.33	0.740
TG‡, mmol/L	1.68±0.97	1.87±1.69	1.71±1.04	0.901
HDL-C‡, mmol/L	1.06±0.29	1.24±0.62	1.1±0.34	0.748
LDL-C**, mmol/L	2.56±1.05	2.42±0.78	2.56±0.96	0.791

Data were presented as mean±SD for each group.
A Mann-Whitney U test was also performed for age as for the post hoc pair-wise comparisons.
*p<0.05, significantly different among three groups.
†Differences among groups were compared using Pearson χ^2 test for categorical variables.
‡Kruskal-Wallis test for continuous variables without normal distribution.
§p<0.05, compared with group A.
¶p<0.01, compared with group B.
**One-way ANOVA for continuous variables with normal distribution.
BMI, body mass index; DBP, diastolic blood pressure; FINS, fasting insulin; FPG, fasting plasma glucose; HDL-C, high-density lipoprotein cholesterol; HOMA-IR, homoeostatic model assessment insulin resistance; HOMA-β, homoeostatic model assessment of β-cell function; LDL-C, low-density lipoprotein cholesterol; SBP, systolic blood pressure; TC, total cholesterol; TG, triglyceride; UAER, urinary albumin excretion rate.

hyperglycemia AUC >11.1 mmol/L × day; the max fall in SBP was also positively correlated with BGdiff2 (table 2). In addition, the max fall in DBP and MBP were negatively correlated with TBG >11.1 mmol/L in group B; the SBP SD was positively correlated with BGdiff2 and MAGE. Furthermore, the DBP SD was negatively correlated with hyperglycemia AUC >7.8 mmol/L × day, and the CV value for SBP was positively correlated with BGdiff2. Finally, the CV value for DBP was positively correlated with MBG[1], but negatively correlated with hyperglycemia AUC >7.8 mmol/L × day. In group C, the SD value for DBP was positively correlated with BGdiff1 and TBG >7.8%, and the CV value for DBP and MBP were positively correlated with BGdiff1 (table 2).

Correlation between blood pressure with HRV parameters in each group

The lowest SBP value in the placebo group was positively correlated with LF/HF and negatively correlated with the max fall value as well as the SD value and CV value for SBP (table 3). The lowest DBP value was also negatively correlated with all the HRV parameters except LF/HF; the lowest value of MBP was negatively correlated with ASDNN[i], rMSSDN[ii], pNN50[iii], BB50[iv], VLF, HF and positively correlated with LF/HF in the placebo group. The max fall SBP and MBP values were negatively correlated with LF/HF; the average DBP value was negatively correlated with all of the HRV parameters except SDNN, SDANN,[v] BB50, and LF/HF in the placebo group. The average value of MBP was negatively correlated with pNN50 and VLF, and the SD value of SBP and the CV value of DBP and MBP were positively correlated with rMSSD, pNN50, and BB50. The SD value of SBP was also positively correlated with HF, and the CV value of SBP was positively correlated with pNN50.

In the acarbose group, the lowest DBP value was negatively correlated with NN[vi], SDNN, SDANN, pNN50 and positively correlated with LF/HF (table 3). In addition, the lowest MBP value was negatively correlated with SDNN and SDANN and positively correlated with LF/HF. The

[i]The average of the standard deviation of all R-R intervals for all 5-minute segments in the 24-hour recordings.
[ii]Square root of mean of the sum of squares of successive N-N interval difference.
[iii]Number of successive N-N intervals differing by >50ms divided by the total number of successive N-N intervals.
[iv]Number of successive N-N intervals differing by >50ms.
[v]SD of all 5min average N-N intervals.
[vi]The average of all normal R wave (N-N) intervals.

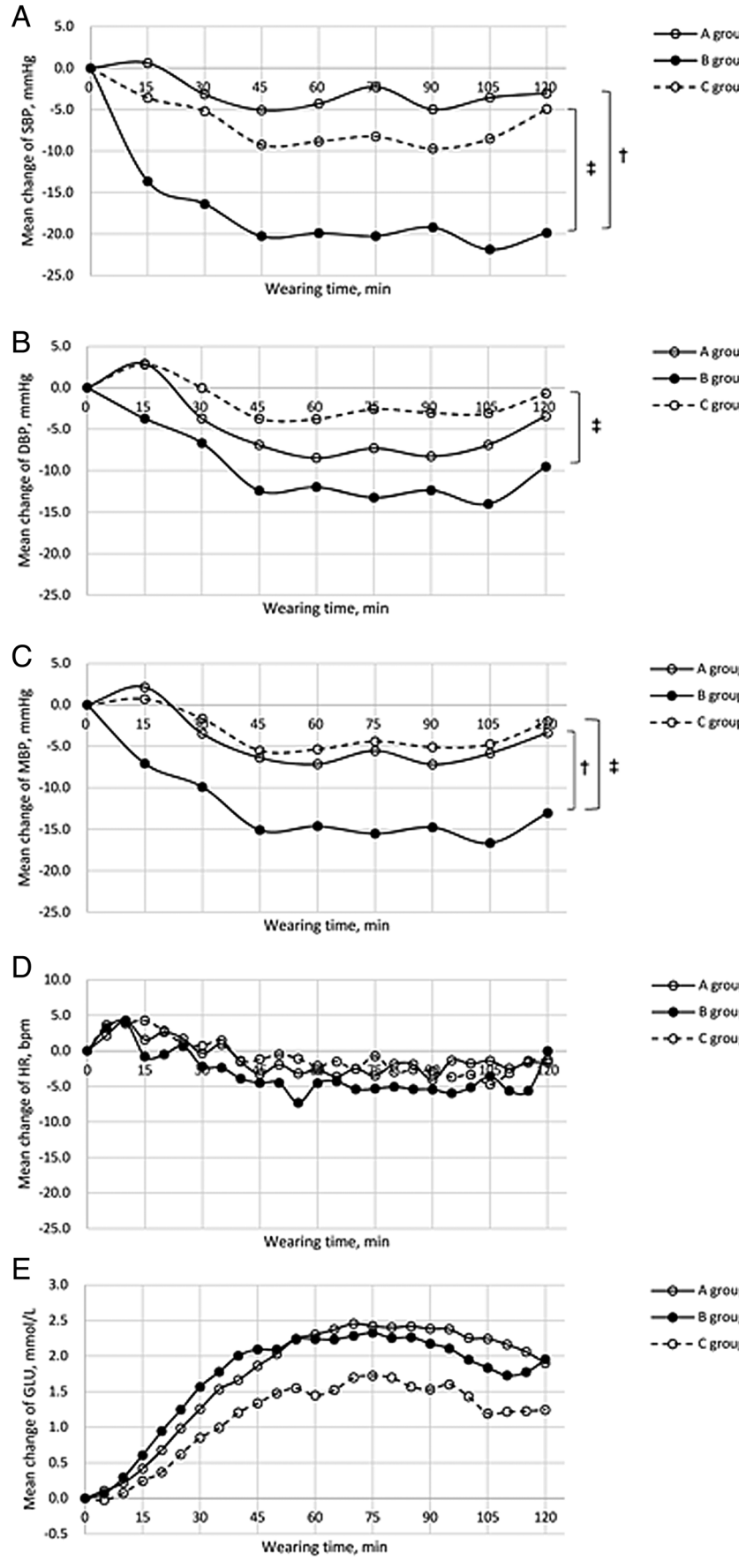

Figure 1 Effects of acarbose on blood pressure, heart rate (HR) and glucose (GLU) levels. The mean change in SBP (A), DBP (B), MBP (C), HR (D), and GLU (E) from before the standard meal to 2 hours postprandial for each group. Data were shown as mean for given time point in each group. Differences in the mean change in blood pressure over the wearing times among three groups were compared using repeated measurements ANOVA with post hoc pair-wise comparisons, Bonferroni test. Significant differences among three groups were derived from the repeated measurements ANOVA ($p<0.001$ for SBP and MBP; $p=0.004$ for DBP), but not in HR ($p=0.263$) and GLU ($p=0.452$). †,‡ $p<0.0167$, significantly different as compared with groups †A and ‡C. ANOVA, analysis of variance; DBP, diastolic blood pressure; GLU, glucose; HR, heart rate; MBP, mean blood pressure; SBP, systolic blood pressure.

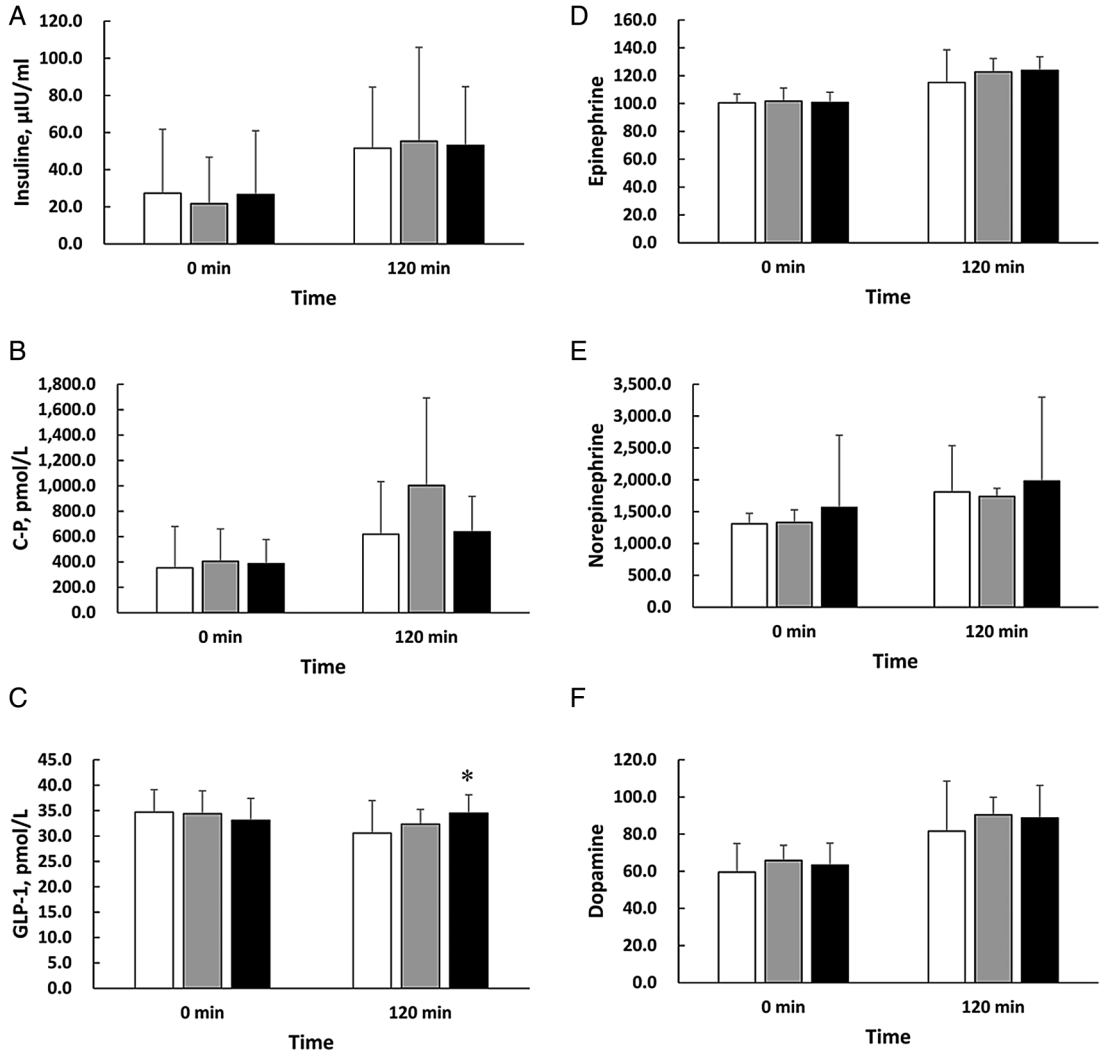

Figure 2 Glucose metabolism and serum catecholamine parameters for each group. Data represent the mean±SD by group. Differences among groups were compared using the Kruskal-Wallis test with a post hoc pair-wise comparison, Mann-Whitney U test for data without normal distribution. A significant difference among three groups in C peptide at 120 min (p=0.045) and GLP-1 at 120 min (p=0.002) was observed. However, the post hoc pair-wise comparisons only identified a significant difference in GLP-1 between groups A and C at 120 min (*p=0.001). C peptide, connecting peptide; GLP-1; glucagon-like peptide-1.

average DBP and MBP were negatively correlated with SDANN, and the average DBP was also negatively correlated with SDNN but positively correlated with LF/HF. Finally, the CV value of SBP was negatively correlated with LF/HF, and the CV value of DBP was positively correlated with rMSSD (table 3).

Correlation between blood pressure and serum catecholamine parameters within each group

In the placebo group, the max fall in SBP and MBP were negatively correlated with the change in GLP-1 (table 4). In the acarbose group, the average SBP value was negatively correlated with the change in epinephrine; the SD value of DBP and MBP were negatively correlated with the change in GLP-1. In addition, the CV value of SBP was negatively correlated with the change in C peptide, and the CV values of DBP and MBP were negatively correlated with the change in GLP-1 (table 4).

DISCUSSION

The present study evaluated the effects of acarbose treatment for PPH in elderly patients with T2DM; it also investigated possible mechanisms behind PPH in this population. We showed that acarbose attenuates the falling magnitude, shortens the duration, and reduces the fluctuations in blood pressure; it also controls glycemia status, which is consistent with previous studies.[3 4 8 10–12] In addition, HRV was associated with blood pressure, but only in patients with PPH, which may be due to the large fluctuations observed. Finally, correlations between hormones and blood pressure shown in patients with T2DM without PPH and those with PPH treated with acarbose were largely lost in the placebo control group.

The reduced falling magnitude, duration, and blood pressure fluctuations observed in the present study with acarbose are similar to previous case reports and

Table 2 Correlation of blood pressure after treatments with the outcomes from continuous glucose monitoring system

	Lowest value			Max fall value			Average value			SD value			CV value		
	SBP	DBP	MBP	SBP	DBP	MBP	SBP	DBP	MBP	SBP	DBP	MBP	SBP	DBP	MBP
A group															
MBG, mmol/L	0.077	−0.009	0.076	0.031	0.189	0.101	−0.060	0.032	0.009	−0.131	−0.058	−0.108	−0.169	−0.112	−0.161
SD, mmol/L	0.058	0.284	0.273	0.185	−0.031	0.047	0.037	0.268	0.314	0.199	−0.111	−0.001	0.205	−0.201	−0.108
Bgdiff, mmol/L	−0.212	0.092	−0.073	−0.170	−0.067	−0.070	−0.213	0.184	0.101	0.086	0.042	0.058	0.235	−0.004	0.032
MBG*, mmol/L	−0.030	−0.143	−0.164	0.023	0.119	0.159	−0.175	−0.041	−0.150	−0.021	0.094	0.085	−0.032	0.103	0.081
MBG†, mmol/L	−0.116	0.000	−0.171	0.226	0.253	0.339	−0.211	0.133	−0.070	−0.027	−0.067	−0.021	−0.006	−0.107	−0.047
Max PBG, mmol/L	−0.105	−0.030	−0.134	0.370	0.267	0.369	−0.287	0.050	−0.154	−0.127	−0.082	−0.120	−0.124	−0.114	−0.137
BGdiff*, mmol/L	−0.121	−0.143	−0.133	0.211	−0.123	−0.024	−0.222	−0.108	−0.200	−0.107	−0.012	−0.036	−0.103	0.017	−0.062
BGdiff†, mmol/L	0.178	0.189	0.205	0.105	0.174	0.173	0.207	0.269	0.362	0.335	0.212	0.294	0.257	0.109	0.189
TBG >7.8 mmol/L, %	0.028	−0.064	0.012	0.075	0.135	0.063	−0.113	−0.038	−0.075	−0.208	−0.097	−0.175	−0.262	−0.126	−0.210
TBG >11.1 mmol/L, %	0.162	0.110	0.152	0.169	0.268	0.256	0.068	0.187	0.202	0.087	−0.050	0.025	0.033	−0.140	−0.077
Hyperglycemia AUC >7.8 mmol/L × day	0.132	0.019	0.123	0.072	0.157	0.087	0.026	0.058	0.098	−0.055	−0.075	−0.102	−0.101	−0.141	−0.185
Hyperglycemia AUC >11.1 mmol/L × day	0.098	0.144	0.155	0.193	0.203	0.221	0.008	0.203	0.198	0.080	−0.049	0.021	0.052	−0.137	−0.085
MAGE, mmol/L	0.032	0.332	0.297	0.278	0.278	0.333	0.036	0.397‡	0.402‡	0.078	−0.106	0.014	0.102	−0.227	−0.108
NGE, time/days	0.009	−0.295	−0.273	−0.095	−0.187	−0.247	−0.005	−0.352	−0.306	−0.147	0.028	−0.133	−0.172	0.164	−0.076
B group															
MBG, mmol/L	0.075	0.267	0.194	0.151	−0.355	−0.257	0.149	0.075	0.086	0.124	−0.167	−0.063	0.021	−0.143	−0.059
SD, mmol/L	−0.244	0.186	0.047	0.279	0.034	0.136	−0.234	−0.119	−0.228	0.288	−0.156	0.010	0.257	−0.185	0.044
Bgdiff, mmol/L	−0.353	0.124	−0.038	0.288	−0.005	0.092	−0.337	−0.085	−0.257	0.331	−0.118	0.033	0.327	−0.146	0.088
MBG*, mmol/L	−0.041	−0.126	−0.131	0.119	0.160	0.115	−0.008	0.151	0.088	0.089	0.358	0.338	0.059	0.380‡	0.326
MBG†, mmol/L	−0.048	−0.058	−0.100	0.171	−0.045	0.038	−0.001	−0.051	−0.088	0.288	0.146	0.226	0.193	0.167	0.222
Max PBG, mmol/L	−0.143	−0.007	−0.099	0.249	−0.071	0.049	−0.084	−0.062	−0.156	0.357	0.111	0.221	0.285	0.098	0.215
BGdiff*, mmol/L	−0.080	−0.256	−0.195	−0.017	0.291	0.196	−0.050	−0.169	−0.102	0.096	0.237	0.238	0.084	0.302	0.301
BGdiff†, mmol/L	−0.359	0.061	−0.140	0.408‡	0.035	0.191	−0.293	−0.135	−0.251	0.526§	0.055	0.240	0.507§	0.039	0.297
TBG >7.8 mmol/L, %	0.116	0.180	0.156	0.002	−0.429‡	−0.392‡	0.114	0.051	0.076	−0.018	−0.194	−0.165	−0.089	−0.139	−0.139
TBG >11.1 mmol/L, %	0.115	0.431‡	0.330	0.201	−0.233	−0.144	0.180	0.202	0.179	0.162	−0.199	−0.035	0.045	−0.239	−0.059
Hyperglycemia AUC >7.8 mmol/L × day	0.041	0.286	0.181	0.181	−0.266	−0.115	0.116	0.013	−0.003	0.043	−0.416‡	−0.273	−0.028	−0.417‡	−0.255
Hyperglycemia AUC >11.1 mmol/L × day	0.035	0.420‡	0.299	0.237	−0.255	−0.157	0.090	0.169	0.113	0.225	−0.204	−0.024	0.124	−0.243	−0.038
MAGE, mmol/L	−0.319	0.072	−0.097	0.344	0.173	0.296	−0.138	0.061	−0.071	0.376‡	0.005	0.183	0.316	0.002	0.219
NGE, time/days	0.115	−0.225	−0.101	−0.257	−0.252	−0.330	−0.012	−0.298	−0.182	−0.048	0.006	−0.085	−0.061	0.076	−0.023
C group															
MBG, mmol/L	−0.185	−0.209	−0.163	0.048	0.224	0.062	−0.158	−0.029	−0.177	0.046	0.323	0.128	0.103	0.308	0.260
SD, mmol/L	−0.085	−0.039	−0.074	−0.021	0.203	0.154	−0.090	0.025	−0.080	−0.119	0.113	0.037	−0.090	0.124	0.071
Bgdiff, mmol/L	−0.148	−0.123	−0.158	−0.048	0.299	0.201	−0.137	−0.046	−0.141	−0.044	0.216	0.137	−0.019	0.219	0.184
MBG*, mmol/L	0.047	−0.070	0.078	−0.214	−0.003	−0.233	0.036	0.081	0.034	−0.077	0.334	0.038	−0.047	0.239	0.137
MBG†, mmol/L	−0.082	−0.124	−0.016	−0.245	−0.066	−0.238	−0.174	−0.084	−0.175	−0.309	0.257	−0.063	−0.249	0.234	0.080
Max PBG, mmol/L	−0.039	−0.106	0.010	−0.214	0.003	−0.161	−0.102	−0.041	−0.113	−0.270	0.309	0.011	−0.236	0.270	0.135

Continued

Table 2 Continued

	Lowest value			Max fall value			Average value			SD value			CV value		
	SBP	DBP	MBP	SBP	DBP	MBP	SBP	DBP	MBP	SBP	DBP	MBP	SBP	DBP	MBP
BGdiff*, mmol/L	−0.138	−0.263	−0.221	−0.122	0.299	0.113	−0.079	−0.067	−0.114	0.158	0.446‡	0.337	0.146	0.408‡	0.367‡
BGdiff†, mmol/L	0.007	0.177	0.132	0.060	0.004	−0.012	−0.050	0.243	0.059	−0.220	−0.083	−0.191	−0.221	−0.119	−0.144
TBG >7.8 mmol/L, %	−0.134	−0.198	−0.116	−0.048	0.146	−0.072	−0.098	−0.010	−0.115	0.107	0.362‡	0.152	0.139	0.309	0.274
TBG >11.1 mmol/L, %	−0.123	−0.188	−0.132	0.093	0.282	0.224	−0.112	−0.038	−0.144	−0.062	0.231	0.125	−0.027	0.259	0.213
Hyperglycemia AUC >7.8 mmol/L·day	−0.155	−0.204	−0.136	0.109	0.270	0.171	−0.121	−0.012	−0.137	0.032	0.283	0.128	0.082	0.285	0.233
Hyperglycemia AUC >11.1 mmol/L × day	−0.168	−0.274	−0.210	0.149	0.308	0.296	−0.136	−0.089	−0.185	0.032	0.306	0.236	0.075	0.345	0.312
MAGE, mmol/L	−0.128	−0.091	−0.130	−0.081	0.108	0.108	−0.131	−0.049	−0.113	−0.084	0.155	0.071	−0.062	0.179	0.099
NGE, time/days	−0.153	−0.129	−0.119	−0.131	0.076	−0.108	−0.144	−0.231	−0.223	0.163	0.218	0.116	0.190	0.211	0.177

Results were presented as the coefficient (r) of correlation of blood pressure after treatments with the outcomes from continuous glucose monitoring system.
*At 2 hours before the meal.
†At 2 hours after the meal.
‡p<0.05, indicated significant correlation.
§p<0.01, indicated significant correlation.
AUC, area under the curve; BGdiff, difference between maximum and minimum blood glucose concentrations; CV, coefficient of variation; DBP, diastolic blood pressure; MAGE, mean amplitude of glucose excursion; MBG, mean blood glucose; MBP, mean blood pressure; NGE, number of glucose excursions; PBG, postprandial blood glucose; SBP, systolic blood pressure; TBG, the proportion of times at which the blood glucose was higher than set levels over 24 hours.

randomized controlled studies of acarbose in elderly patients with diabetes.[3 8 11 15] Furthermore, the attenuation of PPH by acarbose was also observed in patients with severe autonomic failure.[16] α-Glucosidase inhibitors diminish the decreased postprandial blood pressure before inhibiting carbohydrate digestion at the level of the brush border in the small intestine. As all of the patients were treated with insulin, we were unable to determine the effects of insulin in the present results. However, the correlation of blood glucose and blood pressure shown in table 2 suggests that hyperglycemia may cause PPH, and blood glucose control may reduce the incidence of PPH in patients with T2DM. Acute and chronic hyperglycemia can induce a relaxation response in the aorta that may be mediated by factor secreted by perivascular adipose tissue through a mechanism that is independent of the endothelium, but may involve H_2O_2 produced from superoxide.[6] However, further studies are necessary to determine the precise mechanism by which acarbose influences PPH.

As compared with young patients, elderly patients exhibit increased HRV and impaired catecholamine response following a meal.[17] HRV is also significantly impaired in patients with T2DM.[18] In the present study, the SDs and CVs of blood pressure were positively correlated with HRV, catecholamines, and blood glucose values. Thus, a blunted sympathetic response, possibly due to autonomic diabetic neuropathy, may be responsible for the compensatory failure. In a separate analysis of autonomic nerve function in elderly patients with PPH, impairments in baroreceptor signaling were observed.[19] In a study that included 10 patients with diabetes with PPH and 10 healthy volunteers, the postprandial LF and LF/HF of the healthy controls increased slightly but significantly and HR increased; these values remained almost constant in the patients with diabetes.[4] Similarly, Smits *et al*[20] reported that a meal-related increase in the LF:HF ratio observed in the control group was absent in patients with T2DM. Thus, a lack of compensatory sympathetic activation is likely a factor contributing to PPH in patients with diabetes.

Although positive correlations between the SDs and CVs of SBP, MBP, and HRV in patients with diabetes with PPH were observed in the present study, there was no obvious difference in HRV between the three groups during meals in the same time period. We consider that the long course of disease (average of 12.55 years), accompanied by autonomic neuropathy, short time of treatment (ie, single dose), and short observation time may be responsible for the failure in detecting differences in HRV between the groups.

The HRV and hormonal changes observed in the present study suggest that autonomic nervous dysfunction (ie, impaired sympathoadrenal activation following a meal) may be one factor that induces PPH. This is consistent with Mitro *et al*,[9] in which a marked decline in postprandial SBP was observed, which was associated with lower postprandial levels of norepinephrine, epinephrine, and dopamine in patients with PPH. In contrast, Sasaki *et al*[2] found no significant differences in the norepinephrine response pattern during 75 g oral glucose tolerance test (OGTT) between normal subjects and patients with diabetes with and without PPH. Furthermore, Harris *et al*[3] showed that administration of acarbose as a single-dose treatment in older adults with T2DM had no significant effect on

Table 3 Correlation of blood pressure after treatments with the HRV parameters

	Lowest value after treatment			Max fall value after treatment			Average value after treatment			SD value after treatment			CV value after treatment		
HRV parameters	**SBP**	**DBP**	**MBP**	**SBP**	**DBP**	**MBP**	**SBP**	**DBP**	**MBP**	**SBP**	**DBP**	**MBP**	**SBP**	**DBP**	**MBP**
Group															
A group															
NN	0.190	−0.323	−0.252	−0.191	−0.035	−0.050	0.157	−0.347	−0.131	0.079	0.090	0.062	0.095	0.173	0.115
SDNN	−0.127	−0.055	−0.128	0.016	−0.179	−0.162	−0.036	−0.088	−0.080	0.168	0.045	0.019	0.147	0.056	0.013
SDANN	−0.112	−0.089	−0.130	0.007	−0.105	−0.128	−0.013	−0.109	−0.089	0.144	0.140	0.068	0.120	0.141	0.061
ASDNN	−0.052	−0.036	−0.101	0.037	−0.149	−0.101	0.021	−0.037	0.014	0.291	0.013	0.064	0.261	0.007	0.033
rMSSD	−0.008	−0.078	−0.110	−0.146	0.004	0.022	−0.005	−0.026	−0.031	0.092	−0.045	−0.062	0.032	−0.024	−0.029
pNN50	−0.072	−0.161	−0.176	−0.292	−0.197	−0.208	−0.040	−0.118	−0.115	0.091	0.013	−0.067	0.047	0.068	−0.008
BB50	−0.055	−0.141	−0.148	−0.279	−0.172	−0.190	−0.016	−0.082	−0.079	0.090	0.036	−0.048	0.036	0.082	0.004
VLF	−0.082	−0.061	−0.122	−0.066	−0.176	−0.161	−0.027	−0.071	−0.034	0.254	−0.026	0.031	0.246	−0.014	0.011
LF	−0.023	−0.045	−0.103	0.028	−0.105	−0.096	0.053	−0.052	−0.005	0.190	0.040	0.060	0.124	0.029	0.042
HF	−0.040	−0.119	−0.143	−0.195	0.030	0.007	−0.053	−0.082	−0.107	0.008	−0.040	−0.081	−0.026	−0.007	−0.032
LF/HF	0.024	0.061	0.068	0.267	−0.302	−0.267	0.124	−0.019	0.108	0.341	0.059	0.155	0.270	−0.014	0.058
B group															
NN	−0.188	−0.453*	−0.340	0.217	−0.117	0.024	−0.154	−0.434*	−0.311	0.254	0.132	0.151	0.228	0.240	0.234
SDNN	−0.111	−0.505†	−0.353	−0.076	−0.046	−0.076	−0.032	−0.263	−0.173	0.191	0.307	0.285	0.157	0.422*	0.332
SDANN	−0.022	−0.420*	−0.251	−0.020	−0.082	−0.099	0.068	−0.175	−0.063	0.055	0.274	0.235	0.014	0.356	0.273
ASDNN	−0.218	−0.527†	−0.430*	0.006	−0.101	−0.078	−0.207	−0.427*	−0.347	0.243	0.189	0.171	0.239	0.327	0.272
rMSSD	−0.307	−0.543†	−0.483†	0.256	−0.028	0.045	−0.205	−0.433*	−0.356	0.394*	0.222	0.253	0.360	0.371*	0.372*
pNN50	−0.372*	−0.547†	−0.523†	0.311	0.033	0.102	−0.252	−0.421*	−0.379*	0.476†	0.267	0.319	0.439*	0.413*	0.438*
BB50	−0.297	−0.446*	−0.421*	0.200	0.006	0.005	−0.183	−0.337	−0.285	0.397*	0.244	0.278	0.350	0.393*	0.393*
VLF	−0.249	−0.551†	−0.455*	0.005	−0.101	−0.067	−0.242	−0.444*	−0.373*	0.223	0.182	0.156	0.234	0.318	0.261
LF	−0.128	−0.455*	−0.352	−0.039	−0.178	−0.162	−0.149	−0.402*	−0.295	0.186	0.134	0.091	0.187	0.262	0.185
HF	−0.286	−0.478†	−0.427*	0.218	−0.085	0.001	−0.188	−0.378*	−0.329	0.380*	0.107	0.166	0.338	0.250	0.266
LF/HF	0.503†	0.310	0.429*	−0.496†	−0.287	−0.401*	0.340	0.204	0.327	−0.407*	−0.069	−0.189	−0.438*	−0.142	−0.259
C group															
NN	−0.168	−0.361*	−0.294	0.148	−0.097	0.026	−0.124	−0.298	−0.243	0.152	0.109	0.137	0.166	0.212	0.193
SDNN	−0.226	−0.465†	−0.437*	−0.024	0.047	0.096	−0.266	−0.359*	−0.342	−0.027	0.192	0.168	−0.021	0.259	0.235
SDANN	−0.261	−0.473†	−0.442*	0.010	0.023	0.109	−0.305	−0.442*	−0.416*	0.008	0.162	0.127	0.023	0.249	0.200
ASDNN	−0.103	−0.250	−0.244	−0.038	0.044	0.027	−0.124	−0.150	−0.149	−0.009	0.137	0.188	−0.012	0.178	0.207
rMSSD	−0.220	−0.381*	−0.325	0.041	0.046	−0.025	−0.194	−0.244	−0.246	0.092	0.315	0.248	0.122	0.357*	0.352
pNN50	−0.218	−0.285	−0.270	0.016	−0.006	−0.087	−0.196	−0.196	−0.214	0.090	0.266	0.191	0.119	0.299	0.289
BB50	−0.263	−0.295	−0.301	0.035	0.046	−0.054	−0.233	−0.195	−0.231	0.112	0.298	0.219	0.151	0.316	0.323
VLF	−0.068	−0.190	−0.183	−0.004	0.086	0.082	−0.079	−0.063	−0.071	0.031	0.139	0.226	0.007	0.148	0.204

Continued

Table 3 Continued

HRV parameters	Lowest value after treatment			Max fall value after treatment			Average value after treatment			SD value after treatment			CV value after treatment		
	SBP	DBP	MBP	SBP	DBP	MBP	SBP	DBP	MBP	SBP	DBP	MBP	SBP	DBP	MBP
LF	0.067	−0.043	−0.052	−0.240	0.092	−0.048	−0.023	0.028	0.013	−0.315	0.085	0.064	−0.341	0.072	0.069
HF	−0.132	−0.342	−0.276	0.044	0.105	0.061	−0.121	−0.198	−0.184	−0.001	0.250	0.203	0.014	0.287	0.278
LF/HF	0.299	0.396*	0.363*	−0.328	0.086	−0.068	0.210	0.430*	0.349	−0.309	−0.040	−0.076	−0.388*	−0.156	−0.188

Results were represented as the coefficient (r) of correlation of blood pressure after treatments with the HRV parameters.
*Correlation is significant at the 0.05 level (2-tailed).
†Correlation is significant at the 0.01 level (2-tailed).
CV, coefficient of variation; DBP, diastolic blood pressure; MBP, mean blood pressure; SBP, systolic blood pressure.

postprandial rise in plasma norepinephrine. Although no obvious differences in catecholamines were found between the three groups in the present study, we found negative correlations between the CVs of DBP and MBP and postprandial epinephrine in patients without PPH; the maximum fall in SBP was also positively correlated with SBP in this group. In addition, epinephrine was negatively associated with the average SBP in patients with diabetes treated with acarbose. Thus, further studies are required to fully examine whether sympathetic response deficiencies might be responsible for PPH in patients with diabetes.

The relationship between glucose levels and postprandial blood pressure is not fully known as previous studies have produced inconsistent results. In Sasaki *et al*,[2] plasma glucose levels from 0 to 120 min during a 75 g OGTT were not significantly different between patients with diabetes with PPH and those without PPH. Similarly, no significant differences in glucose levels over the 120 min test period were observed between the groups in the present study. However, positive correlations between the CVs of DBP with MBG and BGdiff1 in patients with PPH were observed. Also, in the patients with PPH treated with acarbose, the postprandial blood glucose peak time was delayed and BGdiff 2 was smaller than in those in the placebo group, suggesting that the acarbose attenuation of PPH may be relevant to reducing the blood pressure fluctuation and delaying the peak time of blood glucose levels.

In the progression of diabetes, the insensitivity to GLP-1 by β-islet cells plays an important role. In patients with PPH, postprandial GLP-1 secretion was greater as compared with those without PPH.[21] Moreover, administration of exogenous GLP-1 attenuated the fall in SBP and DBP in older patients with T2DM.[21] Acarbose can increase the level of GLP-1 sensitivity by increasing stimulation of L-cells through delayed absorption and altered transit of dietary carbohydrates.[22] In our study, we also found that the postprandial GLP-1 was higher in the patients with PPH treated with acarbose. Similarly, 100 mg of acarbose prolonged GLP-1 release significantly from 210 to 360 min,[22] which is similar to results reported for the MARCH (Metformin and AcaRbose in Chinese as the initial Hypoglycaemic treatment).[23] However, in another study of patients with hyperglycemic T2DM, ingestion of acarbose with a mixed test meal failed to enhance GLP-1 release.[24] As Fukushima *et al*[21] reported that acarbose decreased GLP-1 secretion in patients with multiple system atrophy, further studies are necessary to determine the role of this gastrointestinal vasoactive peptide in PPH.

We speculate that acarbose inhibits the digestion of carbohydrates, improves abnormal splanchnic pooling, which plays an important role in PPH.[25 26] Acarbose also modulates the rate of gastric emptying, which is related with PPH.[5 26 27] Furthermore, acarbose reduces small intestinal glucose absorption and hence, reduces postprandial glycemia, stabilizing blood pressure. Finally, acarbose can increase GLP-1 levels,[21 22] which may enhance satiety, delay gastric emptying and also attenuate PPH.

The main limitation of our study is that the sample volume was small, and it was not a multicenter study. In addition, it was a single-blind study, which increases the potential for bias. Another limitation is that the acarbose treatment was a single dose, and the results for only one

Table 4 Correlation of blood pressure after treatments with the glucose metabolism and serum catecholamine parameters

	Lowest value after treatment			Max fall value after treatment			Average value after treatment			SD value after treatment			CV value after treatment		
Parameters.	**SBP**	**DBP**	**MBP**	**SBP**	**DBP**	**MBP**	**SBP**	**DBP**	**MBP**	**SBP**	**DBP**	**MBP**	**SBP**	**DBP**	**MBP**
Group															
Group A															
Insulin	−0.137	−0.206	−0.233	0.232	−0.080	0.060	−0.181	−0.151	−0.178	−0.103	−0.261	−0.232	−0.012	−0.216	−0.204
C-P	−0.051	−0.265	−0.162	−0.214	0.214	0.034	−0.098	−0.079	−0.050	−0.008	0.427*	0.395*	0.088	0.404*	0.425*
GLP1	0.010	0.094	0.098	0.652†	0.124	0.241	0.101	0.105	0.117	0.035	−0.001	0.035	0.010	−0.030	−0.010
Epinephrine	−0.071	0.269	0.181	.521†	0.001	0.160	−0.053	0.178	0.061	−0.119	−0.453*	−0.384*	−0.135	−0.469†	−0.392*
Norepinephrine	−0.135	0.007	−0.154	0.006	0.246	0.289	−0.174	0.137	−0.011	−0.033	−0.008	0.016	−0.081	−0.065	0.017
Dopamine	−0.236	0.056	−0.030	0.216	0.039	0.070	−0.195	−0.027	−0.107	−0.103	−0.087	−0.111	−0.090	−0.072	−0.143
Group B															
Insulin	0.203	−0.021	0.088	−0.269	0.052	−0.100	0.184	0.022	0.092	−0.226	0.053	−0.031	−0.247	0.035	−0.079
C-P	−0.015	0.096	0.050	−0.136	−0.148	−0.241	−0.057	0.167	0.090	−0.027	0.029	−0.003	0.024	0.049	0.003
GLP1	0.112	−0.016	0.047	−0.379*	−0.263	−0.364*	0.023	0.015	0.045	10.195	−0.233	−0.310	−0.189	−0.189	−0.275
Epinephrine	0.096	0.020	0.070	−0.085	−0.075	−0.099	0.165	0.154	0.196	−0.024	−0.086	−0.069	−0.070	−0.044	−0.023
Norepinephrine	−0.336	−0.182	−0.294	0.112	0.041	0.109	−0.257	−0.154	−0.238	0.169	0.217	0.266	0.270	0.307	0.306
Dopamine	0.429*	0.199	0.341	−0.249	−0.195	−0.247	0.239	0.066	0.194	−0.205	−0.169	−0.207	−0.270	−0.209	−0.232
Group C															
Insulin	0.136	0.234	0.126	0.225	−0.001	0.192	0.145	−0.032	0.076	−0.054	−0.166	−0.082	−0.119	−0.182	−0.145
C-P	0.351	−0.059	0.198	−0.104	0.154	0.132	0.273	0.079	0.212	−0.283	0.155	−0.079	−0.386*	0.022	−0.133
GLP-1	−0.194	0.325	0.068	0.267	−0.160	−0.058	−0.184	0.122	−0.027	−0.088	−0.533†	−0.424*	−0.013	−0.480†	−0.379*
Epinephrine	−0.360*	0.035	−0.195	0.055	0.047	−0.012	−0.363*	−0.083	−0.242	−0.161	−0.158	−0.121	−0.095	−0.119	−0.024
Norepinephrine	−0.022	0.023	−0.074	0.122	0.332	0.312	0.076	0.008	0.057	0.260	0.272	0.318	0.235	0.184	0.266
Dopamine	0.068	0.129	0.113	0.075	0.038	0.024	0.086	0.096	0.063	−0.018	−0.054	0.007	−0.028	−0.034	0.018

Results were presented as the coefficient of correlation (r) of blood pressure after treatments with the glucose metabolism and serum catecholamine parameters.
*Correlation is significant at the 0.05 level (2-tailed).
†Correlation is significant at the 0.01 level (2-tailed).
CV, coefficient of variation; DBP, diastolic blood pressure; GLP-1, glucagon-like peptide-1; MBP, mean blood pressure; SBP, systolic blood pressure.

meal were examined. Also, the study did not assess the role of other gut hormones in addition to GLP-1 that could be affected by acarbose, especially gastric inhibitory peptide. Further investigations are also needed to evaluate the mechanism of acarbose treatment in attenuating PPH in elderly patients with T2DM. Finally, adjustments for multiple comparisons between the groups and correlations between all of the variables in the HRV analysis were not performed.

In conclusion, acarbose attenuated the magnitude of fall, shortened the persistence, and reduced the fluctuation of postprandial blood pressure in patients with T2DM. Fluctuation of postprandial blood pressure was positively correlated with HRV, catecholamines, and blood glucose.

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