Uncontrolled Hypertension is Associated with Postprandial Hypotension

La hipertensión no controlada se asocia con hipotensión posprandial

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ABSTRACT

Background: In a previous study that incorporated post-lunch measurements to the conventional scheme of home-based blood pressure monitoring, we detected postprandial hypotension in about a quarter of hypertensive patients.
Objectives: The aim of this study was to compare the postprandial change of systolic blood pressure, and the corresponding chronotropic response, associated to the control of hypertension.
Methods: We prospectively evaluated 140 treated hypertensive patients, aged over 40 years, with home-based blood pressure monitoring. The control of hypertension was based on the average morning and evening blood pressure, considering 135/85 mmHg as cutoff value. Postprandial hypotension was defined as a drop in systolic blood pressure equal to or greater than 20 mmHg with respect to the preprandial value in at least one of three lunches.
Results: Postprandial hypotension was found in 13.2% (n=10) of patients with controlled hypertension and in 42.2% (n=27) with uncontrolled hypertension (p<0.001). After lunch, the average decrease of systolic blood pressure was 9.5±10.5 mmHg (6.4%±7.8%) in patients with uncontrolled hypertension and 3.2±7.8 mmHg (2.6%±6.5%) in those with controlled hypertension (p<0.001), with no significant difference in the chronotropic response. After stratifying the patients by hypertension control, the postprandial response of heart rate and systolic blood pressure showed a significant inverse correlation in controlled hypertensive patients (r = -0.24; p = 0.035), and a not significant correlation in uncontrolled patients. On the multiple linear regression analysis, lack of blood pressure control (beta=0.26, p=0.002) and female gender (beta=0.22; p<0.001) were significant predictors of a postprandial drop in systolic blood pressure, without a significant influence of age or number of antihypertensive drugs.
Conclusion: Lack of blood pressure control was associated with an abnormal postprandial circulatory response that predisposes to hypotension.

Key words: Home-based Blood Pressure Monitoring - Hypotension - Postprandial Period - Hypertension

RESUMEN

Introducción: En un estudio previo que incorporó mediciones posalmuerzo al esquema convencional de monitoreo domiciliario de la presión arterial hemos detectado hipotensión posprandialen alrededor de la cuarta parte de nuestros pacientes hipertensos.
Objetivos: Comparar el cambio posprandial de la presión arterial sistólica, y la correspondiente respuesta cronotrópica, en relación con el control de la hipertensión.
Material y métodos: Se evaluaron prospectivamente con monitoreo domiciliario de la presión arterial 140 pacientes hipertensos tratados, mayores de 40 años. El control de la hipertensión se basó en el promedio de la presión arterial matinal y la vespertina, tomando como valor de corte 135/85 mm Hg. Se consideró hipotensión posprandialcuando la presión arterial sistólica disminuyó 20 mm Hg o más respecto del valor preprandial en al menos uno de tres almuerzos.
Resultados: Se detectó hipotensión posprandial en el 13,2% (n = 10) de los hipertensos controlados y en el 42,2% (n = 27) de los no controlados (p < 0,001). Después de los almuerzos, la presión arterial sistólica disminuyó en promedio 9,5 ± 10,5 mm Hg (6,4% ± 7,8%) en los hipertensos no controlados y 3,2 ± 7,8 mm Hg (2,6% ± 6,5%) en los controlados (p < 0,001), sin diferencia significativa en la respuesta cronotrópica. Al estratificar a los pacientes por el control de la hipertensión se observó una correlación inversa entre la respuesta posprandial de la frecuencia cardíaca y la presión arterial sistólica en los controlados (r = -0,24; p = 0,035), sin relación significativa en los no controlados. En el análisis de regresión lineal múltiple, la falta de control de la hipertensión (beta = -0,26; p = 0,002) y el sexo femenino (beta = 0,22; p < 0,001) fueron predictores significativos de la caída posprandial en la presión arterial sistólica, sin influencia significativa de la edad o del número de fármacos antihipertensivos.
Conclusión: La falta de control de la hipertensión se asoció con una respuesta circulatoria posprandial anormal que favorece la hipotensión.

Palabras clave: Monitoreo domiciliario de la presión arterial - Hipotensión - Período posprandial - Hipertensión

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Abbreviations

BP	Blood pressure	**HBPM**	Home-based blood pressure monitoring
BMI	Body mass index	**SBP**	Systolic blood pressure
HR	Heart rate		

INTRODUCTION

Postprandial hypotension, defined as a decrease in systolic blood pressure (SBP) of 20 mm Hg or more, can cause syncope, falls, dizziness, weakness, angina, and stroke (1). The episodes of postprandial hypotension are usually asymptomatic and only suspected in a syncopal event. (2, 3)

In a previous study that incorporated postprandial measurements to the conventional scheme of home-based BP monitoring (HBPM), we diagnosed postprandial hypotension in approximately one quarter of hypertensive patients evaluated, identifying old age, high office SBP, low body weight and history of stroke as independent risk predictors. (4) Systolic hypertension interferes with sympathetic reflex response predisposing to postprandial hypotension (5).

The coexistence of hypertension with hypotension poses a therapeutic dilemma in which priority is given to reduce the doses of antihypertensive drugs to prevent hypotension (6). However, it has also been suggested that control of hypertension might reduce orthostatic and postprandial hypotension. (7, 8) In this study we compared posprandial change in SBP, and the corresponding chronotropic response related to the degree of hypertension control.

METHODS

This is a cross-sectional study of consecutive patients referred to the Hypertension Section of the Hospital Italiano de Buenos Aires to assess HBPM. The original sample consisted of 230 patients. (4) Twenty untreated patients, 29 who did not complete the scheme of measurements, 2 who were aged under 40 years, 2 with extrapyramidal disease, 2 with renal artery stenosis, 5 with arrhythmias, 2 with pacemaker, 1 with HIV, and 1 with a history of deep vein thrombosis were excluded from the study. The final sample included 140 treated hypertensive patients over 40 years of age.

Home-based blood pressure monitoring consisted of automatic measurements duplicated during 4 days (OMRON 705 CP, Omron, Tokyo, Japan). In addition to morning and evening conventional measurements, patients were instructed to obtain measurements immediately after lunch and 1 measurement after 3 hours, without changing their eating habits. Measurements obtained during the first day of monitoring were not considered for the analysis. Control hypertension was defined as average morning and evening blood pressure, considering 135/85 mmHg as cutoff value. (9) The postprandial SBP and heart rate (HR) changes express the absolute (mmHg) or relative (%) difference between pre- and post-lunch values. A drop in SBP>20 mmHg with respect to the previous lunch value was defined as postprandial hypotension.

Statistical analysis

Data are expressed as mean and standard deviation or percentage. Student's t-test for continuous variables and the chi-square test for categorical variables were used for comparisons.

A multiple linear regression analysis was performed with postprandial SBP change as dependent variable. The following independent variables were included: hypertension control (0 = controlled and 1 = uncontrolled), age (≤ vs > 74 years), diabetes (0 = no, 1 = diabetic), gender (0 = female, 1 = male), body mass index (BMI- kg/m2), beta blockers (0 = no, 1 = yes), diuretic (0 = no, 1 = yes), calcium blocker (0 = no, 1 = yes), ACE inhibitor or AT1 antagonist (0 = no, 1 = yes), alpha blocker (0 = no, 1 = yes), and number of antihypertensive drugs (1 = 1 drug, 2 = 2 drugs, 3 = 3 drugs or more).

Because patients with uncontrolled hypertension were older than those with controlled hypertension, a two-way ANOVA was used to compare postprandial SBP changes between controlled and uncontrolled patients divided by age (≤ vs > 74 years). The Kolmogorov-Smirnov test and Levene's test were used to assess normality and homogeneity, respectively.

Repeated measures ANOVA was used for to compare SBP and HR between the morning, preprandial, postprandial and evening periods.

The association between HR and postprandial SBP changes was assessed using Pearson's correlation coefficient, stratifying patients by the degree of hypertension control.

Ethical considerations

The study was approved by the Ethics Committee of our institution and patients signed a written informed consent form.

RESULTS

Patient characteristics

Table 1 compares patient characteristics according to hypertension control. Uncontrolled hypertensive patients were significantly older than controlled hypertensive ones. The proportion of men and women, anthropometric characteristics, as well as the proportion of diabetic patients were similar between groups. The proportion of patients with postprandial hypotension was 4 to 5 times higher in uncontrolled than in controlled hypertensive patients (see Table 1).

There were no significant differences in the proportion of patients treated with monotherapy or combination therapy. There were no significant differences in the proportion of patients treated with diuretics, beta-adrenergic blockers, calcium channel blockers and angiotensin inhibitors. Only uncontrolled hypertensive patients received some type of alpha-adrenergic blocker (doxazosin, terazosin and tamsulosin).

Table 2 compares the average SBP and HR by periods (morning, preprandial, postprandial and evening) in controlled and uncontrolled hypertensive patients.

In the postprandial period SBP and HR reached their lowest and highest level, respectively (p<0.001 for both parameters; repeated measures ANOVA).

The postprandial drop in SBP [9.5±10.5 mmHg vs. 3.2±7.8 mmHg (p<0.001) or 6.4±7.8% vs. 2.6±6.5% (p=0.002)] was significantly higher in uncontrolled than in controlled hypertensive patients. Two-way ANOVA showed significant differences in postprandial SBP changes related with hypertension control (p <0.001), but not with age, without interaction between both factors.

The postprandial increase in HR was lower in uncontrolled hypertensive patients than in controlled patients, although the difference did not reach statistical significance (2.8±4.6 bpm vs. 4.1±4.6 bpm; p=0.08 or 4. 1±8.9% vs. 7.0±9.1%; p=0.054). Figure 1 shows the correlation between postprandial HR and SBP changes according to hypertension control. Controlled hypertensive patients showed an inverse correlation between postprandial HR and SBP changes (r=-0.24; p<0.035). In contrast, in uncontrolled hypertensive patients, the correlation between both parameters was not significant (r=0.019; p=0.87).

Multiple regression analysis showed that postprandial SBP drop was significantly higher in patients with poorly controlled hypertension (beta=-0.315; P <0.001) and in female gender (beta=0.217; p<0.001), and significantly lower in patients treated with calcium channel blockers (beta=0.207; p <0.05) and diuretics (beta=0.17; p<0.05). The remaining predictors (age, diabetes, BMI, beta-blocker, alpha blocker and angioten ininhibitor therapy, and the number of antihypertensive drugs) were excluded from the model. The adjusted R^2 was 0.17

DISCUSSION

By incorporating postprandial measurements to the HBPM conventional protocol, we detected SBP drops greater than 20 mmHg in 13% of patients with controlled hypertension and in 42% of patients with uncontrolled hypertension (defined according to the average morning and evening HBPM). This indicates that poorly controlled hypertension increases the risk of postprandial hypotension and suggests that improved hypertension control could restore circulatory homeostasis. In this sense, previous reports have shown a lower prevalence of orthostatic and postprandial hypotension in patients with better hypertension control. (7, 8) In addition, it can be interpreted that the ability to control hypertension is an indemnity marker of BP regulating mechanisms.

Patients with uncontrolled hypertension were significantly older than those with controlled hypertension. However, a multivariate analysis showed that the

Table 1. Patient characteristics

	Controlled	Uncontrolled	p
N	76	64	
Age, years	68.9 ± 10.8	77.3 ± 8.9	<0.001
Female, n (%)	57 (75)	45 (70.3)	0.53
Weight, kg	72.5 ± 14,7	70.5 ± 15	0.46
Height, m	1.6 ±0.9	1.6 ± 0.9	0.51
BMI, kg/m2	28.5 ± 5	27.7 ± 4	0.39
Diabetics, n (%)	6 (7.9)	6 (9.5)	0.48
Number of drugs, n (%)			0.06
1	26 (34.2)	11 (17.5)	
2	26 (34.2)	23 (36.5)	
3 or more	24 (31.6)	29 (46.0)	
Diuretics, n (%)	26 (34.2)	30 (48.0)	0.08
Calcium channel blockers, n (%)	36 (47.4)	34 (54.0)	0.27
ACEI/ARA II, n (%)	59 (77.6)	47 (74.6)	0.41
Betablockers, n (%)	32 (42.1)	34 (54.0)	0.11
Alphablockers, n (%)	0 (0)	6 (9.5)	NA
PPH, n (%)	10 (13.2)	27 (42.2)	<0.001
PPH episodes, n (%)			0.001
1	4 (5.3)	11 (17.2)	
2	4 (5.3)	8 (12.5)	
3	2 (2.6)	8 (12.5)	

Data are expressed as mean and standard deviation or percentage. N: Number of patients. BMI: Body mass index. ACEI: angiotensin converting enzyme inhibitors. ARA II: Angiotensin II receptors antagonists. NA: Not applicable. PPH: Postprandial hypotension.

	Controlled	Uncontrolled	p
SBP, mm Hg			
Morning	122.9 ± 9	151.4 ± 16	<0.0001
Preprandial	118.5 ± 8	139.7 ± 14	<0.001
Postprandial	115.3 ± 9*	130.2 ± 13*	<0.001
Evening	122.5 ± 9	146.4 ± 14	<0.001
HR, bpm			
Morning	66.0 ± 9	64.8 ± 10	0.46
Preprandial	67.0 ± 8	66.8 ± 9	0.87
Postprandial	71.7 ± 10*	69.4 ± 11*	0.20
Evening	69.5 ± 10	66.8 ± 10	0.12

Table 2. Average systolic blood pressure and heart rate by day periods according to hypertension control defined by home-based blood pressure monitoring

Data are expressed as mean and standard deviation. SBP: Systolic blood pressure. HR: Heart rate. bpm: Beats per minute. * p<0.001 vs. the remaining periods (repeated measures ANOVA).
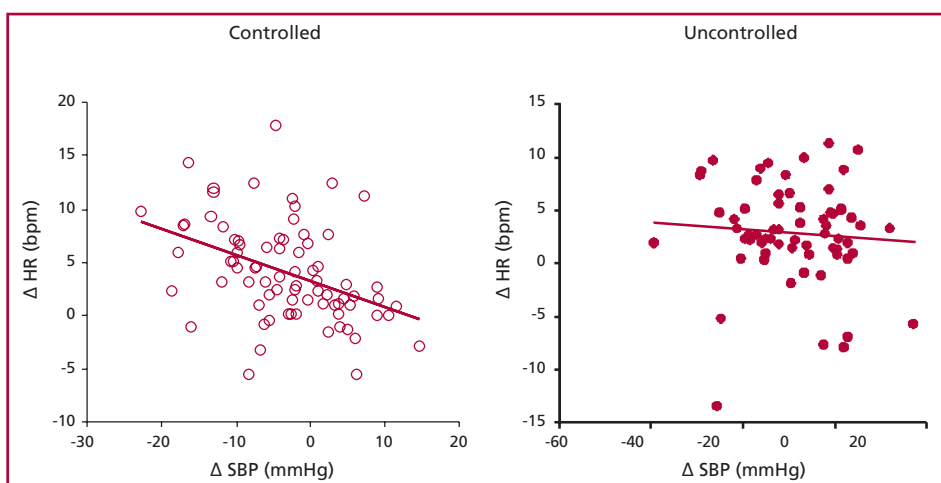

Fig. 1. Heart rate response (Δ HR) was inversely correlated with postprandial systolic blood pressure change (Δ SBP) in controlled hypertensive patients (r= -0.24; p=0.035) (r = 0.42; p <0.001). This relationship was absent in uncontrolled hypertensive patients(r= -0.08; p=not significant).

association between poorly controlled hypertension and exaggerated postprandial BP drop was independent of age. This indicates that posprandial hypotension is more related with the increase in SBP than age per se. Posprandial circulatory response showed no significant relationship with the number of antihypertensive drugs received. The significant association between female gender and greater postprandial SBP drop was an unexpected finding. So was the significant association between lower postprandial SBP drop and treatment with calcium channel blockers or diuretics.

The largest postprandial SBP drop observed in uncontrolled hypertension could be explained by increased preprandial SBP. However, the persistence of the difference expressing changes as percentage of preprandial values eliminates this possibility. Furthermore, poor chronotropic response in relation to greater postprandial SBP drop indicates a qualitative abnormality of BP regulation associated with poorly controlled hypertension.

Morning hypertension is associated with increased risk of cardiovascular events; therefore its detection and control represent a therapeutic target (10). Morning hypertension may contribute to increased arterial stiffness and reduced baroreflex sensitivity. (11) Bet-

ter hypertension control may improve arterial compliance and therefore restore reflex circulatory response. However, when hypertension coexists with severe hypotension, we recommend reducing antihypertensive treatment during daytime (6).

The decrease in BP associated with food intake can mask morning hypertension when the medical consultation schedule matches posprandial time (12). The extended scheme of measurements allowed us to detect the coexistence of morning hypertension and postprandial hypotension, posing the dilemma of whether to intensify or not antihypertensive treatment.

There are a number of HBPM advantages over ambulatory monitoring to assess postprandial BP.

One advantage of HBPM is the possibility of surveying morning hypertension in successive days. The inclusion of measurements after food intake can detect the coexistence of uncontrolled hypertension with postprandial hypotension. In addition, the patient must be awake for postprandial measurements, ruling out the confounding effect of napping. Finally, better patient compliance to repeat HBPM represents an additional advantage over ambulatory monitoring when assessing the effect of antihypertensive treatment adjustment on hypertension and

postprandial BP control.

The design used does not allow us to conclude whether strengthening treatment for hypertension control restores BP homeostasis and reduces the risk of postprandial hypotension. Furthermore, the relative flexibility of the interval after lunch (between 1 to 3 hours) and the lack of dietary standardization represent variability sources of postprandial change. However, assessment of the postprandial phenomenon at home, without changing eating habits, provides representative information of this phenomenon in the individual patient.

CONCLUSIONS

Our data show an association between lack of hypertension control and abnormal postprandial circulatory response predisposing to hypotension. These results suggest that the review of postprandial hypotension should be included in the scheme of HBPM and pose the dilemma of whether to reinforce the treatment in uncontrolled hypertensive patients with asymptomatic episodes of hypotension.

Conflicts of interest
None Declared
(See author´s conflicts of interest forms in the web / Supplementary Material)

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