DIURNAL VARIATIONS IN BLOOD PRESSURE AND THEIR RELATION WITH CAROTID ARTERY INTIMA-MEDIA THICKENING

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Abstract

INTRODUCTION: Hypertension is a very common cardiovascular disease with extensive effects on body organs. This study was conducted to compare the extent of target organ damage in hypertensive patients with and without significant nocturnal fall in blood pressure (dippers and non-dippers, respectively).

METHODS: One-hundred patients with recently diagnosed hypertension underwent 24-hour ambulatory blood pressure monitoring and carotid Doppler ultrasonography. They were divided into patients with nocturnal fall in blood pressure (dippers) and without nocturnal fall in blood pressure (non-dippers).

RESULTS: Sixty-five patients with nocturnal systolic blood pressure fall greater than 10% (dippers) were matched for age, sex, body mass index (BMI) and body mass area (BMA) with 35 patients with less than 10% fall in nocturnal blood pressure (non-dippers). The two groups were not different in terms of ambulatory and mean 24-hour blood pressure. Assessments showed significantly greater carotid intima-media thickening in the non-dipper group.

DISCUSSION: This study suggests that a reduced nocturnal fall in blood pressure may play a pivotal role in the development of some features of target organ damage such as carotid intima-media thickening, despite similar clinical findings and no significant difference in mean 24-hour blood pressure.

Keywords • Hypertension • Ambulatory blood pressure monitoring • Carotid intima-media thickness • Carotid color Doppler sonography

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Introduction

Ambulatory blood pressure measurement at the physician's office has long been the basis of diagnosis and treatment of hypertension. However, studies have demonstrated that whole-day BP and the circadian pattern of changes in blood pressure are closely linked to target organ damage, affecting mortality and morbidity associated with hypertension.[1] Forty-five percent of all cardiovascular mortality in the Framingham study had occurred against a backdrop of left ventricular hypertrophy (LVH), with five-year mortality rate in male LVH patients measuring 35% compared to 10-15% in men without LVH.[2]

Development in 1962 of ambulatory blood pressure monitoring systems[3] enabled the assessment of circadian variations in blood pressure.[4,5] Nocturnal fall in blood pressure normally occurs in normotensive and hypertensive patients.[6,7] However, studies have showed that nocturnal blood pressure does not decrease, or decreases bluntly in some patients; these patients are referred to as non-dippers.

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The none-dipper phenomenon was for the first time introduced by O'Brien and colleagues in 1988 in Lancet.[8]

This was followed by extensive studies on the non-dipper phenomenon and its outcomes, as well as comparison of the so-called dippers and non-dippers.

Results of 24-hour blood pressure monitoring have demonstrated that mean circadian blood pressure may be higher or lower than ambulatory blood pressure readings at the physician's office.[9] Two main patterns of blood pressure variation have been described:

1. *Dipper*: characterized by a decrease of about 10% in nocturnal and sleeping blood pressure.
2. *Non-dipper*: characterized by absence of any notable fall in nocturnal blood pressure.

The dipper pattern is predominant, occurring in nearly two-thirds of normotensive and hypertensive individuals.[6,10] The non-dipper pattern, the exact mechanism of which has yet to be understood, is associated with disease conditions such as diabetes, renal failure, primary aldosteronism, pregnancy toxemia, malignant hypertension, sleep apnea, and autonomous neuropathies, as well as old age, lifestyle factors and behavioral traits.

The association of the non-dipper phenomenon (which also remains unexplained) with some conditions and diseases has been reported, nonetheless, studies have suggested that non-dippers are at greater risks due to their exposure to higher hemodynamic pressure.[11,12] Cross-sectional studies have also proposed a higher likelihood of target organ damage in non-dippers, compared to dippers.[13-15]

The significance of the dipper and non-dipper phenomena is still being studied. For example, a recent meta-analysis has questioned the suggestion that LVH is more strongly linked to nocturnal blood pressure than mean 24-hour blood pressure.[16]

Moreover, some recent cross-sectional studies have not demonstrated any significant difference between the extent of cardiovascular damage in hypertensive dippers and non-dippers with similar mean 24-hour blood pressure.[15,16] Circadian blood pressure variations seem to be an important determinant of target organ damage. If this link is confirmed, treatment of hypertension will require specific therapeutic plans which take account of the patients' circadian blood pressure variations. Given that some studies have cast doubt on the proposed link,[15-17] the present study was undertaken to compare target organ damage in dippers and non-dippers.

Materials and methods

Patients with short-term history of irregularly treated hypertension (<2 years) and no history of diabetes, secondary hypertension, congestive heart failure, myocardial infarction, valvular heart disease, or coronary graft were included in the study.

The patients underwent 24-hour blood pressure monitoring, routine blood tests, and carotid ultrasonography.

Blood pressure measurement in clinic: Blood pressure was measured after 5-10 minutes in resting state using a mercury sphygmomanometer. The readings corresponding to the first and fifth Korotkov sounds were recorded as systolic and diastolic blood pressure, respectively.

24-hour blood pressure monitoring: Ambulatory blood pressure measurement was conducted on the patients' non-dominant arm every half hour in daytime (6 AM-11 PM) and every hour during the night (11 PM- 6 AM).

The patients were asked to continue performing their normal routines but remain still during the measurements and go to bed at 11 PM.

Blood pressure measurement was performed for all patients on all days of the working week. Mean daily, nocturnal, and 24-hour blood pressure and pulse rate of patients were analyzed.

Dipping (i.e. nocturnal blood pressure fall) was defined as a reduction of more than 10% in mean systolic nocturnal blood pressure compared to mean daily values.

24-hour blood pressure monitoring was conducted using a Sunny system operating on software developed by Biomedical Systems.

End-diastolic intima-media thickness, i.e. the distance between the anterior borders of the first and second echogenic lines was measured on the posterior wall of both carotid arteries at distances of 0, 5, 10 and 15 millimeters from the bulb.

Plaques were defined as local thicknesses greater than one-third of a millimeter in any of the carotid artery segments; thicknesses greater than 0.8 millimeters were considered as intima-media thickening.

Statistical analysis: The values were expressed as mean ± standard deviation. Mean values corresponding to dippers and non-dippers were compared using Student's t-test for independent samples. Significance level was set at 0.05.

TABLE 1. Characteristics of dippers and non-dippers

Variable	Dipper	Non-dipper	P value
Sex (M/F)	36/29	19/16	P>0.05
Age	45±12	47±14	P>0.05
BMI	26.35±3.2	26.46±4.1	P>0.05
FBS	92.5±7	96.2±9	P>0.05
Cholesterol	217±37	226±41	P>0.05
TG	131.5±13	127.1±11	P>0.05

TABLE 2. Systolic and diastolic blood pressure and pulse rate in dippers and non-dippers

Variable	Dippers	Non-dippers	P value
Systolic BP* (mmHg)			
Physician's office	145±12	146±8	NS
Mean 24-hour BP	138±10	139±12	NS
Mean diurnal BP	145±10	140±11	S
Mean nocturnal BP	122±8	132±10	S
Diastolic BP (mmHg)			
Physician's office	93±6	95±7	NS
Mean 24-hour BP	90±8	90±8	NS
Mean diurnal BP	95±8	92±9	NS
Mean nocturnal BP	76±8	81±7	S
Pulse rate			
Physician's office	77±12	75±10	NS
Mean 24-hour BP	78±9	76±9	NS

*BP: Blood pressure
**S: Significant, NS: Non-significant

TABLE 3. Comparison of carotid artery damage in dippers and non-dippers

Variable	Dippers	Non-dippers	P value
Common carotid artery intima-media thickness	0.7±0.8	0.8±0.3	S
Common carotid artery diameter (millimeter)	57±0.9	59±0.7	NS
Plaque prevalence	32%	34%	NS

*S: Significant, NS: Non-significant

Results

Some demographic and biochemical characteristics of the study populations are demonstrated in Table 1.

A significant difference was seen between means of diurnal and nocturnal blood pressure between the study groups (Table 2). Mean intima-media thickness on the posterior wall of the common carotid artery and the prevalence of thickening in non-dippers was slightly but significantly greater than in dippers. Arterial thickness was nearly equal in the two groups. The prevalence of plaques in the two groups was not significantly different (Table 3).

Carotid intima-media thickness was significantly related to diurnal and nocturnal blood pressure.

Discussion

This study was conducted on patients with and without nocturnal fall in blood pressure (dippers and non-dippers, respectively). The results showed that the nocturnal fall in blood pressure can play an important and independent role in the development of some of the signs of damage in target organs.

Roman and colleagues[16] studied 183 hypertensive patients comprising 140 dippers and 79 non-dippers, with a mean age of 55 years and history of antihypertensive treatment in 60% of cases. They reported a higher prevalence of carotid artery plaques in non-dippers (41% vs. 27%). However, this difference lost its significance when the age factor was considered (non-dippers had a higher mean age than dippers).

In a case-control study, Pierdomenico and colleagues[18] found the prevalence of LVH, carotid intima-media thickening and carotid artery plaques in dippers to be higher than non-dippers. However, mean 24-hour systolic and diastolic blood pressure in non-dippers in the latter study was 7 and 3 mmHg higher than in dippers, respectively, showing a significant difference between the two groups.

Ferrera and colleagues[19] studied left ventricular structure, diastolic function and carotid morphology in 56 patients with recently diagnosed hypertension.

They showed the diastolic dimensions of the left ventricle and the atrial contribution in left ventricular filling in non-dippers to be slightly, but significantly higher than in dippers, whereas carotid intima-media thickness was similar in the two groups.

However, in the latter study too, blood pressure readings at the physician's office and mean 24-hour systolic blood pressure were 7 and 5 mmHg higher in non-dippers, respectively.

The current study is distinct from others in that it found personal and metabolic characteristics, as well as office and mean 24-hour blood pressure readings in dippers and non-dippers to be similar.

Earlier studies have suggested that the higher prevalence of LVH reported in non-dippers by some studies may not be due to the non-dipping phenomenon; rather it may be related to higher circadian blood pressure levels.[20] The same might be true of carotid artery involvement.[21]

The present study suggests that carotid intima-media thickening in non-dippers is probably independent of the overall blood pressure load (which was similar in the two groups) and is related to reduced nocturnal fall in blood pressure. This phenomenon may be due to reduced activity of the sympathetic nervous system, increased vagal drive and dilation of peripheral vessels which cause the difference between nocturnal and diurnal blood pressure.[22] It may also emanate from the preponderance of hypertensive factors (e.g. angiotensin, catecholamines) relative to those which lower blood pressure and regulate the nocturnal dip. The role of changes in vascular structure should also be heeded.

Given the link between target organ damage and the circadian variations of blood pressure, even a single hypotensive episode in 24 hours may suffice to prevent target organ damage.[23]

Finally, it can be concluded that the non-dipping phenomenon within the context of essential hypertension is capable of predisposing to structural changes in the heart and large vessels.

Reduced circadian variations of blood pressure can be regarded as an important factor that can lead to end-organ damage.

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