Autonomic nervous activity in elderly dipper and non-dipper patients with essential hypertension

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ABSTRACT. The pathogenetic mechanisms of the blunted nocturnal fall in blood pressure, frequently observed in elderly patients with essential hypertension, are unclear. The aim of this study was to evaluate the autonomic nervous system in elderly dipper and non-dipper hypertensive subjects. The study group consisted of twelve non-dipper and twelve dipper hypertensive patients (mean age 77.7 and 73.8 years, respectively). Non-dippers were defined as subjects whose nocturnal fall in systolic blood pressure (SBP), evaluated by means of Ambulatory Blood Pressure Monitoring, was less than 10% of diurnal SBP. All the patients underwent the following cardiovascular tests to explore autonomic function: Tilt Table, Valsalva Maneuver, Deep Breathing, Cough. The tests were performed under standard conditions, and heart rate and blood pressure were continuously recorded. Valsalva ratio (VR), Expiration/Inspiration Ratio (E/IR) and Cough Test Ratio (CTR) were calculated. Mann Whitney’s and $\chi^2$ tests were used for comparison between groups. Relationships were assessed by univariate and multivariate analyses. Non-dipper hypertensive subjects showed significantly lower scores in VR (11.1±0.08 vs 12.8±0.14), E/IR (1.11±0.07 vs 1.21±0.10), and CTR (1.07±0.02 vs 1.15±0.07). During the tilt test, a significant decrease in SBP and a late increase in heart rate were observed in non-dippers. The day-night difference in SBP was significantly related to VR, CTR and maximal SBP drop during tilting. The findings confirm that non-dippers show an impairment in autonomic nervous drive, which is characterized mainly by decreased parasympathetic activity. These observations may explain the increase in cardiovascular risk in non-dippers.

INTRODUCTION

Ambulatory Blood Pressure Monitoring (ABPM) studies have shown that the physiologic nocturnal fall in blood pressure in several patients with essential hypertension is blunted or even absent (1). Non-dipping is clinically relevant, because it is associated with a higher prevalence and incidence of cardio- and cerebrovascular events (2-7).

An impairment in autonomic nervous activity seems to play an important role in the pathogenesis of the non-dipping phenomenon; under physiologic conditions, the heart rate, cardiac output, peripheral resistances and plasma catecholamines (expression of sympathetic activity) are reduced during the night (8, 9); on the other hand, several conditions with abnormal autonomic activity, such as diabetes (10), heart failure (11), cardiac transplantation (12), orthostatic hypotension (13) and Shy-Drager Syndrome (14) are associated with a lack or attenuation of the day-night BP changes.

Only a few studies however, have addressed the problem of the autonomic nervous dysfunction in non-dipper subjects with essential hypertension. By means of spectral analysis of heart rate variability, Kohara et al. (15) found that circadian fluctuations in autonomic function are reduced in adult non-dipper hypertensives, who show an increased sympathetic activity compared to parasympathetic activity. Vaile et al. (16) observed that baroreflex sensitivity did not differ significantly between dippers and non-dippers, when they were either awake or asleep; however, by means of the sequence analysis technique, these workers found a reduction in the number of sequences in non-dippers (predominantly in the waking state), which may reflect an impairment in parasympathetic control of the heart.

Non-dipping is more frequent in elderly hyperten-
Autonomic function in non-dippers

SUBJECTS AND METHODS

Hypertensive subjects aged >65 years were recruited from our outpatient Center. Hypertension was diagnosed on the basis of the following criteria: 1) history of hypertension and treatment with antihypertensive drugs; 2) Systolic Blood Pressure (SBP) values >160 mmHg and/or Diastolic Blood Pressure (DBP) values >95 mmHg.

On the basis of history, physical examination, medical records and, if needed, supplementary investigations, the following conditions were excluded: 1) endocrine disorders (diabetes, pheochromocytoma, Cushing’s disease, hyperthyroidism, etc.); 2) other forms of secondary hypertension; 3) cardiovascular diseases (atrial fibrillation, valvular diseases, angina, myocardial infarction, heart failure); 4) cerebrovascular diseases (previous strokes or transient ischemic attacks); 5) other neurologic diseases (Parkinson’s disease, senile dementia, epilepsy, etc.); 6) psychiatric diseases; 7) severe chronic diseases, such as hepatic cirrhosis, respiratory failure, malignancy, anemia (Hb <10g/dL), etc.; 8) sleep disturbances (insomnia, sleep apnea syndrome); 9) every other illness or disability interfering with an active cooperation by the patient.

After a 3-week wash-out period, the patients underwent sphygmanometric recording and ambulatory monitoring of BP. Blood pressure was measured by the auscultatory method, with the patient sitting upright and the arm held in a horizontal position, using a random zero sphygmanometer. For each patient, at least three measurements were taken on two different occasions, and the mean was calculated.

ABPM was performed by means of a non-invasive automatic portable device (Spacelabs 90207). During the procedure, all the patients recorded their sleeping time in a diary. Automatic measurements were collected at 15-minute intervals from 6:00 a.m. to 10:00 p.m. (day-time), and at 30-minute intervals from 10:00 p.m. to 6:00 a.m. (night-time). Data obtained by ABPM were edited for artefacts, and day-time and night-time SBP and DBP values were computed. The nocturnal fall in SBP was calculated as (Day SBP-Night SBP) / Day SBP (23).

On the basis of ABPM data, 12 subjects with a blunted nocturnal BP fall (<10% of the mean SBP during the diurnal period), and whose amount and quality of sleep had been judged reasonably “normal”, were selected. For each non-dipper subject, a normally dipper subject (BP nocturnal fall >10% of day mean SBP) was consecutively enrolled in the study.

The patients then underwent the following cardiovascular tests: Tilt Table, Valsalva Maneuver, Deep Breathing, and Cough. All the tests were performed in a morning session, and in a temperature controlled, quiet room. Heart rate and BP were continuously measured throughout the study with a Nippon Colin monitoring apparatus. The reproducibility of the tests in our laboratory was satisfactory under these standard conditions (24-27). Short summaries of the tests follow.

Tilt Table

Patients were kept in the supine position for 30 minutes before postural change. After baseline data were obtained for 15 minutes, patients were passively placed in a 60° head-up tilting position for 4 minutes, and then returned to the supine position for 5 minutes. Means of systolic and diastolic BP and heart rate were obtained at baseline, computing 20 RR intervals, during the first 30 seconds and at 1-2-3 minutes of tilting. The maximal variations in the cardiovascular parameters with respect to baseline values were calculated. Patients were considered positive to tilting when the lowest standing systolic BP was more than 20 mmHg below that obtained in the supine position.

Valsalva Maneuver

The test was performed by having the patient blow into a mouthpiece attached to a mercury manometer to a pressure of 40 mmHg for 15 seconds. Heart rate was recorded throughout the test; the shortest RR interval during phase 2 and the longest RR interval during phase 4 (Valsalva Ratio) were computed.

Slow Deep Breathing

Inspiration and expiration, performed at a rate of one full cycle every 10 seconds, accentuates the normal respiratory sinus arrhythmia observed in most normal individuals.

The heart rate was monitored during 1 minute (6 cycles) of slow deep breathing. The difference between maximum and minimum heart rate, and the ratio of these two values (Expiration/Inspiration Ratio) were recorded.

Cough Test