between dCA determined using the Valsalva maneuver and systolic and mean daytime ambulatory BP was reliant on one outlying result.

Key Words: Cerebral Autoregulation, Hypertension, Transcranial Doppler Ultrasound

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PARALLEL MORNING AND EVENING SURGE IN STROKE ONSET, BLOOD PRESSURE AND PHYSICAL ACTIVITY

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Background and Purpose: A circadian variation with a morning peak upon waking and arising is known to occur in both blood pressure (BP) and cardiovascular event onset. A second peak in BP has been described to occur after an afternoon sleep (siesta). This study was designed to test the hypothesis that the two-peak diurnal variation of BP is dependent on physical activity and occurs in parallel with the diurnal variation of stroke onset.

Methods: The diurnal variation of stroke onset was compared to the diurnal variation of BP, pulse rate (PR) and physical activity in three independent groups of Greek hypertensives aged 50-80 years (633 stroke patients; 379 subjects with 24-hour ambulatory BP monitoring; 50 subjects with 24-hour physical activity monitoring using wrist devices).

Results: The diurnal variation of stroke onset, BP and PR all showed one morning and one evening peak with a decline in the afternoon and at night and occurred in parallel with the diurnal variation in physical activity (p<0.001 for differences among morning, afternoon, evening and nighttime intervals in BP, PR, activity and stroke). The afternoon decline in BP, PR and activity was significant only in subjects with a siesta.

Conclusions: The two-peak diurnal variation in stroke onset occurred in parallel with the variation of BP, PR and physical activity. These data support the hypothesis that an abrupt change in physical activity is not only a major determinant of the two-peak diurnal variation of BP, but also an important triggering factor for a cardiovascular event.

Key Words: Stroke Onset, Circadian Rhythm, Ambulatory Monitoring

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STROKE PREVENTION IN PATIENTS WITHOUT CORONARY HEART DISEASE: A LINK WITH ANGIOTENSIN AND SYMPATHETIC SYSTEMS ?

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HOPE trial has shown that in patients with a high prevalence of coronary heart disease (CHD = 80 %) an angiotensin converting enzyme inhibitor (ACEI) decreases the risk of stroke beyond what is expected from the BP-reduction. The objective of this study is to see whether suppression of the renin-angiotensin and/or sympathetic systems (RA/SS) by antihypertensive drugs also gives such a protection in primary or secondary stroke prevention trials in which patients have a low initial prevalence (<30 %) of CHD.

All the large randomized primary prevention trials in mild hypertension published since 1985 as well as the 2 recent large secondary stroke prevention trials (PATS and PROGRESS) were reviewed. The BP-independent stroke risk change was calculated by subtracting, from the stroke risk change observed in the trial, the risk change expected from the BP change. This latter was calculated from the log-linear relation between stroke risk and diastolic BP established by MacMahon in cohort studies of individuals without initial cardiovascular complications and from the relation established by Rodgers et al in the patients of the UKTIA trial showing that 10 mmHg SBP decrease is expected to reduce the stroke recurrence risk by 28 %. The trials were then classified as giving RA/SS-stimulation if diuretics or calcium antagonists were compared to placebo, beta blockers or ACEI (which decrease angiotensin II formation) or to alpha 1 blockers (which are neutral). When the reverse comparison was made the trial was considered as RASS-suppressing. Trials comparing associations of 2 drugs with opposite effect on RASS to placebo or to similar associations were considered as having a neutral effect on RASS. In hypertension primary prevention trials, median of DBP-independent stroke risk change was significantly higher in trials with RASS-suppression (+18 %; p=0.006) or with neutral effect on RASS (+10 %; p=0.02) than in trials with RASS-stimulation (-16 %).

In secondary stroke prevention trials the SBP-independent stroke risk change was significantly higher with perindopril alone (+9 %; p=0.01), or with the combination perindopril + indapamide (-9 %; p<0.05) than with indapamide alone (-15 %).

In patients without high prevalence of CHD, stroke prevention is worse when RASS are not activated by the antihypertensive treatment.

Key Words: Antihypertensive Drugs, Renin Angiotensin, Sympathetic System

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STROKE DEATH RATE ANNUAL DECREASE REVERSAL AND PRESCRIPTION DECREASE OF ANTIHYPERTENSIVE DRUGS STIMULATING THE ANGIOTENSIN II FORMATION

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Find an alternative explanation to the reversal in the age-adjusted stroke death rate annual decrease (DRAD) at the turn of the seventies to the eighties (from -4.9 % to -3.5 %) and its persistence in the early nineties (-0.7 %) observed in the USA while hypertension was better controlled (from 10 % to 29-27 %), smoking and cholesterol decreased and diabetes-obesity prevalence markedly increased only after 1994 whereas DRAD for coronary heart disease remained stable at -3.3, -3.1 and -2.7 % (Cooper. Circulation 2000;102:3137).

Since our review of hypertension primary prevention trials and stroke secondary prevention trials pointed out an inverse link between stroke risk change and the activation of the renin-angiotensin and/or sympathetic systems (RASS), we tested the hypothesis that a decrease in prescription of RASS-stimulating antihypertensive drugs could be a plausible explanation.

Thanks to a precise report on US office based antihypertensive drug visits (Nelson. Hypertension 2000;36-600) we calculated the prescription ratio between RASS-stimulating drugs (diuretics and calcium antagonists) and RASS-suppressing ones (beta blockers, ACEI, centrally adrenergic drugs), combination of drugs with opposite effects and alpha 1 blockers being considered as neutral.

This ratio decreased from 6 in 1980 to 1.36, 1.30 and 1.25 in 1985, 90 and 95, while the percentage of prescription of diuretics combined with RASS-suppressing drugs decreased from 35 to 24, 7.2 and 7.4 %.

There is a puzzling coincidence between the reversal of stroke DRAD at the turn of the seventies to the eighties and the decrease in the prescription of antihypertensive drugs stimulating RASS. Since in controlled trials stroke prevention is better when RASS are stimulated, a causal relationship between these 2 observations cannot be dismissed, in spite of their ecological nature.

Key Words: Sympathetic System, Antihypertensive Drugs, Renin Angiotensin