

## **PUTATIVE BLOOD PRESSURE OVERSWINGING, CIRCADIAN HYPER-AMPLITUDE-TENSION (CHAT), IN TYPE 2 DIABETES**

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### **A b s t r a c t**

Within the scope of an international project of the Biosphere and the Cosmos (BIOCOS) focusing on stroke prevention, a population of Mexican patients was screened. Each subject's blood pressure and heart rate were measured around the clock by ambulatory monitoring for 24 h. The subject group primarily consisted of patients with non-insulin-dependent diabetes mellitus (NIDDM). Each profile was assessed by sphygmochron, consisting of a parametric approach wherein a 2-component model was fitted to the data, complemented by a non-parametric approach wherein the patient's profile was compared by computer with reference limits specified as a function of time, gender and age. CHAT (circadian hyper-amplitude-tension), a condition characterised by an excessive circadian amplitude of blood pressure, was found.

### **Key words**

Blood pressure overswinging, Circadian hyper-amplitude-tension (CHAT), Type 2 diabetes mellitus

### **INTRODUCTION**

In laboratory experiments (1) and in a series of clinical studies (2-5), the incidence of CHAT has been associated with the largest known risk of cerebral ischaemic disease and also with a high risk of myocardial infarction, nephropathy and retinopathy. Diabetes is a serious medical and financial burden on Western societies. It is the seventh leading cause of death in the United States and Canada. The disease is due to a primary defect in glucose tolerance and carbohydrate metabolism resulting from either a deficiency of insulin (insulin-dependent diabetes mellitus) or a state of insulin resistance (non-insulin-dependent diabetes mellitus, NIDDM). NIDDM accounts for more than 80% of the total diabetic cases. Associated with the primary metabolic defects are equally deleterious secondary complications affecting the renal, ocular, nervous and cardiovascular systems (6). In particular, the cardiovascular complications account for a major proportion of diabetic mortality (6, 7). NIDDM has been reported to be responsible

for a high risk of coronary heart disease death in both men and women, independently of other risk factors (8). The diagnosis of NIDDM at 55 years of age is thought to reduce life expectancy by about 5 years, notably because of an increased death rate from coronary heart disease (8). Careful monitoring of cardiovascular risk factors and microalbuminuria, combined with optimal metabolic control, has been shown to substantially reduce mortality of NIDDM patients (9). Since abnormal circadian patterns of blood pressure and heart rate are predictors of cardiovascular problems, and timely chronotherapeutic interventions may help reduce the incidence of morbid obesity (10), this study aimed at monitoring the blood pressure and heart rate of NIDDM patients in Mexico.

#### MATERIALS AND METHODS

In a Mexican population, 116 time series of automatically ambulatorily monitored blood pressure (BP) and heart rate (HR) at 60-minute intervals, each covering 24 h, were analysed by a two-component model, consisting of cosine curves with periods of 24 and 12 h (11, 12). The rhythm characteristics of the circadian component were compared with 90% prediction limits derived from clinically healthy Caucasian subjects matched by gender and age. Each series was also compared by computer with time-, gender- and age-specified reference limits (13) to assess any excess and/or deficit. Results were obtained from each subject in the form of sphygmochron, an easily interpreted record prepared by a computer (14).

#### RESULTS

In 10 patients with systolic (S) and/or diastolic (D) CHAT, only transient or likely CHATs were diagnosed. In three of them, the circadian amplitude of both SBP and DBP was excessive, whereas in the other seven patients only the amplitude of either SBP or DBP was excessive, while the other variable was „high normal“. In another eight patients, both SBP and DBP peaked during night or in the morning instead of in the afternoon, i.e., they had circadian ephasia. One patient diagnosed with SBP-CHAT also had ephasia. By comparison with the lower 5% prediction limit of healthy peers matched by gender and age, 22 patients were found to be MESOR-hypotensive, including three patients with CHAT. Only three patients with CHAT were found to be MESOR-hypertensive.

#### DISCUSSION

The foregoing assessments are based on reference values from Caucasians. They will have to be revised when reference values for Mexicans become available. The restriction of the record to 24 h constitutes a limitation, perhaps less severe in the case of group studies on 116 subjects than in assessing the individual patient. For the latter aim, it should be realised that individuals can have circadian abnormality, e.g., CHAT or MESOR-hypertension, for 5 or more days, but have acceptable records for spans of months and years thereafter (15). International consensus has been reached on requiring 7-day monitoring at the

outset (16), as now implemented within the scope of the Biosphere and the Cosmos (BIOCOS) project, with an opportunity for interested participants to benefit from a 90% reduction in price of monitors and from analyses at the University of Minnesota. The CHAT found in almost 10% of the population of NIDDM patients may suffice to urge the implementation of screening for CHAT precisely not only because CHAT is the largest risk factor among all those examined so far, including old age or blood pressure over 130/80 mm Hg (wherein the low values during rest and/or sleep are included), but also because it constitutes a risk independent of an elevated 24-hour average in the absence of diabetes (2–6). CHAT can be treated by non-pharmacological (17) or pharmacological (10) intervention. In prospective studies, the probable double jeopardy from CHAT and diabetes remains to be assessed, notably in view of added risks related to age, MESOR-hypertension and ecphasia, which may reflect autonomic neural dysfunction associated with a reduced heart rate variability. Clinical studies are under way to check on these issues.

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#### VELKÉ CIRKADIÁNNÍ KOLÍSÁNÍ KREVNÍHO TLAKU („OVERSWINGING“) – ZVÝŠENÁ CIRKADIÁNNÍ-AMPLITUDA KREVNÍHO TLAKU U DIABETIKŮ 2. TYPU

##### S o u h r n

V souladu s řešením projektu biosféry a kosmu (BIOCOS) s cílem prevence výskytu cévních mozkových příhod, jsme vyšetřili populaci pacientů z Mexika. Pacienti byli vyšetřováni 24-hodinovým monitorováním krevního tlaku a srdeční frekvence. Jednalo se o pacienty s diabetem mellitem 2. typu (NIDDM). 24-hodinový profil krevního tlaku a srdeční frekvence byl hodnocen pomocí parametrických a neparametrických statistických metod a srovnán s referenčními hodnotami dle pohlaví, věku a denní doby. CHAT (circadian hyper-amplitude-tension), charakterizovaná excesivně zvýšenou cirkadiánní amplitudou krevního tlaku, byla nalezena u velkého množství nemocných.

##### A c k n o w l e d g e m e n t s

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