

## WHEN WEEK-LONG MONITORING IS NOT ENOUGH: CASE REPORTS

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### Abstract

The aim of the present study was to document the changed blood pressure profile on blood pressure monitoring lasting 222 days. We examined an untreated 27-year old asymptomatic woman. The data were analyzed using cosinor analysis. As illustrated in our case report, there can also be large day-to-day changes in the circadian characteristics of blood pressure and heart rate in some people.

### Key words

Chronobiology, Circadian rhythm, Blood pressure

### INTRODUCTION

There is a growing body of evidence suggesting that time structures in us and around us are intricately interwoven. Most if not all components of variation found in biota are also found in the environment, and vice versa (1). For instance, about daily changes are seen in almost every biological variable under 24-hour synchronized conditions. It has also long been known that the phase of circadian rhythms can be manipulated by changing the phase of the environmental cycles (2). At least for the case of circadian rhythms, their genetic inheritance has been demonstrated on a molecular basis (3, 4), suggesting that the influence from the environment has been acquired genetically during the course of evolution.

Several studies (5, 6) comparing the classification of patients based on single office blood pressure measurements with that based on ambulatory monitoring for one to seven days suggest that the incidence of misdiagnosis is around 40%, in keeping with the 48% response to placebo in the Australian Therapeutic Trial (7, 8). Comparison of circadian characteristics from day to day in records spanning at least two days further indicates the shortcomings of monitoring limited to a single 24-hour span (9, 10, 11). Prolonging the monitoring from one to two days

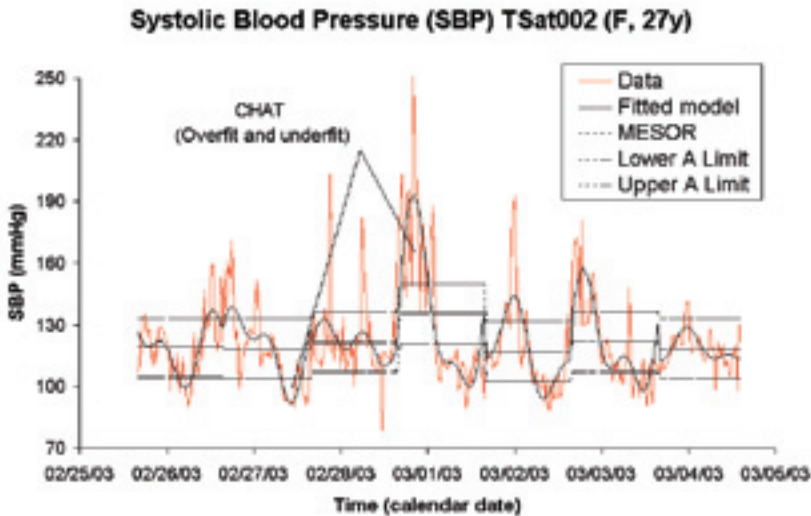
reduces the uncertainty in the estimation of circadian parameters by about 35% (12), whereas further information on the biological week (13, 14) requires monitoring for at least 7 days, the current recommendation of BIOCOS for everybody at the outset (15). It is now widely accepted that prognosis of target organ damage is by far superior when it is based on around the clock monitoring than on single office measurements (16, 17, 18). The aim of the present study was to document the changed blood pressure profile on blood pressure monitoring lasting 222 days.

## METHODS

We examined an untreated 27-year old asymptomatic woman. Ambulatory blood pressure monitoring was carried out 222 days. The data have been analyzed for each day separately by the least squares fit of a model consisting of cosine curves with periods of 24 and 12 hours. The daily MESORs (middle horizontal line segments) are bracketed by the 90% prediction limits for the 24-hour amplitude determined for each day separately (upper and lower horizontal line segments).

## RESULTS

Seven-day profile of systolic blood pressure of an untreated 27-year old asymptomatic woman illustrates how variable blood pressure can be from one day to another as shown in *Fig. 1*. The daily MESORs (middle horizontal line segments) are bracketed by the 90% prediction limits for the 24-hour amplitude determined for



*Fig. 1*

Seven-day profile of systolic blood pressure of an untreated 27-year old asymptomatic woman illustrates how variable blood pressure can be from one day to another. Systolic blood (SBP, mmHg).

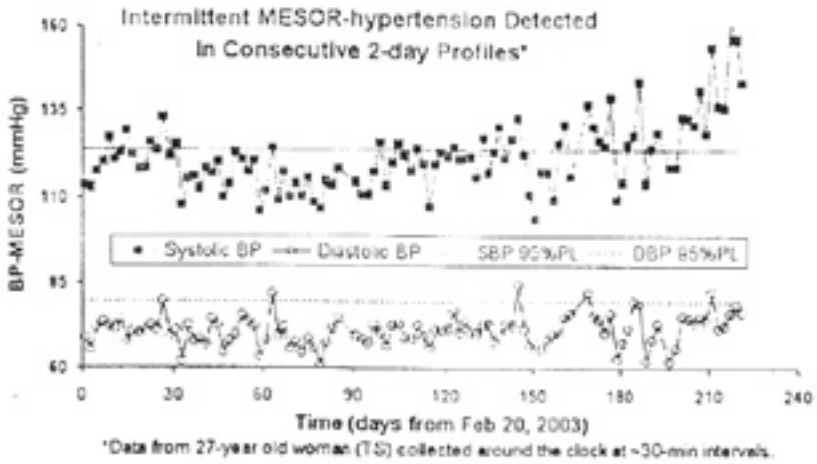


Fig. 2

Intermittent MESOR- hypertension of the same untreated 27-year old asymptomatic woman detected in consecutive 2-day profile.

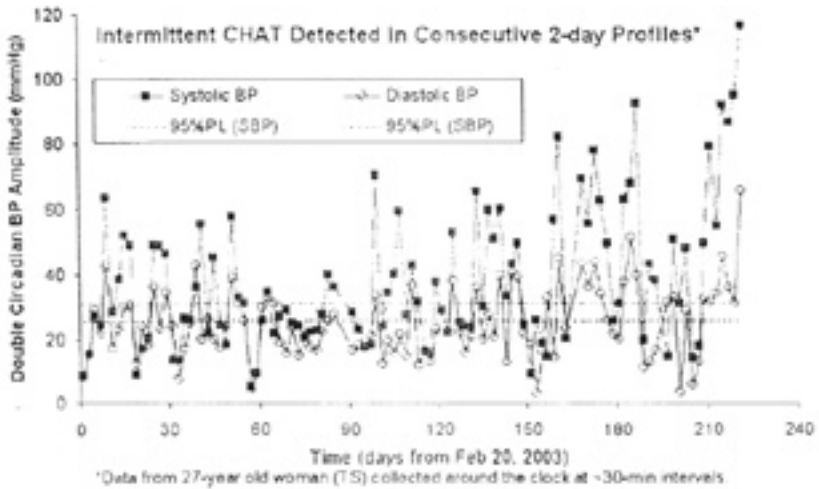


Fig. 3

Data from 27-year old women, collected around the clock at 30-min intervals. Intermittent CHAT (Circadian-Hyperamplitude-Tension) detected in consecutive 2-day profile.

each day separately (upper and lower horizontal line segments). Whereas all parameters can be within acceptable limits on some days, large deviations are seen to occur on other days, when CHAT (circadian hyper-amplitude-tension) is diagnosed in the absence or in the presence of MESOR-hypertension. The day-to-day variability can be so large in some case that a perfectly acceptable profile observed on one day may repeal MESOR-hypertension complicated with CHAT on another day. Results from analysis of 30-min data on consecutive 2-day intervals for 222 days in *Fig. 2,3* show that the absence of anti-hypertensive treatment, MESOR-hypertension (*Fig. 2*) and CHAT (*Fig. 3*) can occur on some days but not on others. The device can rightly be suspected, but it was changed three times.

## DISCUSSION

There can also be large day-to-day changes in the circadian characteristics of blood pressure and heart rate in some people, as illustrated in our case report. Evidence from longitudinal records suggests that circadian characteristics can vary greatly from one day to another in some patients. These data cast doubt on the wisdom of using 24-hour profiles for diagnosis and fixed-dose 24-hour formulations of anti-hypertensive drugs for treatment.

The mistaken impression that the circadian variation in blood pressure and heart rate is sufficiently stable to be approximated by a single 24-hour profile stems in large part from the use of statistical methods on groups of subjects rather than focusing on the individual patient.

Correlation analyses applied to large groups of subjects with a wide range of average values emphasize similarity. Statistical analyses focusing on individual differences observed from one profile to another, however, yield information more likely to help the patient in need of treatment (21). Several case reports document this point (21, 22, 23, 24). Continued monitoring is the most logical solution. Feasible today by telemetry for the lifetime of laboratory animals, it still awaits industrial developments for application in human beings.

Longitudinal monitoring does not need to be costly. The high cost of ambulatory blood pressure monitoring prevailing today stems in large part from the practice to limit the procedure to special cases. Should the recommendation to screen every citizen be embraced, the cost of monitors would drop drastically as was the case for many commodities (such as the ball pen, the wrist watch, and the pocket calculator) when they became widely accessible. Self-measurements taken 5 to 8 times a day during waking, preferably with at least occasional nightly readings (which could be taken by a family member so as not to interrupt sleep), have been successful to help the treatment of patients with malignant hypertension (25). Manual measurements have also been successful to separate children with or without familial antecedents of high blood pressure and/or related cardiovascular disease and to predict outcomes (25, 26) by the assessment of the circadian amplitude of blood pressure

interpreted in the light of reference values derived specifically for self-measurements (12).

Taking serial measurements a few times each day is important to greatly reduce the error associated with single measurements. The assessment by cosinor (2, 27) of the circadian amplitude and acrophase in addition to the MESOR further reduces the error term since blood pressure and heart rate are usually characterized by a circadian variation of large extent. Taking only one or two measurements a day, always at awakening and/or at bedtime may fail to reveal abnormalities seen only at other times of day, or abnormalities that apply only to the variability in blood pressure or heart rate.

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#### KDE TÝDENNÍ MONITOROVÁNÍ KREVŇÍHO TLAKU NENÍ DOSTATEČNÉ: KAZUISTIKA

##### Souhrn

Cílem předložené práce bylo dokumentovat změny 24-hodinové křivky krevního tlaku monitorované po dobu 222 dní. Vyšetřili jsme dvacetisedmiletou ženu bez léčby a bez známek onemocnění. Data byla analyzována kosinorovou analýzou. Jak ukazuje naše kazuistika, u některých osob můžeme nalézt změny cirkadiánní charakteristiky den po dni v krevním tlaku a srdeční frekvenci.

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