# EFFECT OF ALCOHOL INTAKE AND TREATMENT WITH CALCIUM ANTAGONIST ON BLOOD PRESSURE AND HEART RATE ASSESSED BY AMBULATORY MONITORING

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#### Abstract

The study was aimed at investigating the effect of alcohol intake and treatment with calcium antagonist on blood pressure and heart rate assessed by ambulatory monitoring. The large circadian amplitude is a testable mechanism possibly underlying the increase in the incidence of morbid events among drinkers.

Key words

Essential hypertension, Ambulatory blood pressure monitoring, Cosinor analysis, Alcohol intake

### INTRODUCTION

Adverse vascular events are associated with an elevated mean value of blood pressure (1). An excessive circadian variation gauged the amplitude of blood pressure, also warning of an increase in vascular disease risk. This amplitude can be computed by the fit of a 24-hour cosine curve (2,3). The present study was aimed at evaluating longitudinally (over several months) changes in blood pressure (BP) and heart rate (HR) of a patient presenting as a heavy sake drinker, monitored around the clock. His alcohol intake was stepwise decreasing, treatment with a calcium antagonist started and its effects were assessed.

## MATERIALS AND METHODS

A 70-year-old man with MESOR-hypertension drank 7–8 bottles of sake per day (1 bottle = 180 ml). To avoid problems often associated with alcohol withdrawal, he was advised to cut his alcohol intake gradually, first to 50% of the usual intake, then to one-third of usual intake, and finally to quit alcohol intake. After the patient had withdrawn from alcohol consumption, treatment was started with felodipine (5 mg/day; 2.5 mg in the morning and evening). Ambulatory monitoring started on July 19, 1999, while the patient consumed his usual dose of alcohol daily.

After two days, the amount of alcohol was cut to 50%, and two more days later it was further cut

to one-third of his usual daily consumption. After two more days, drinking stopped, monitoring was continued from July 26 to August 12, 1999, and thereafter, on August 13, treatment with felodipine started, and monitoring continued until August 19, 1999. The data were analyzed in each span by cosinor, to obtain estimates for the MESOR (rhythm-adjusted mean) and for the circadian amplitude and acrophase (measures of the extent and timing of predictable change of BP and HR during a day). Parameter tests compared changes in BP and HR characteristics from one stage to another.

## **RESULTS**

Without treatment, the circadian amplitude of BP slowly decreased with no difference in overall mean value, whereas HR slowly decreased as alcohol consumption decreased, *Table 1*.

Stage	PR P	MESOR ± SE	Amplitude $\pm$ SE $\Phi$ $\pm$ SE	
1	56 < 0.001	SBP (mm Hg) 163.5 ± 1.8	$26.0 \pm 2.6$	-189 ± 6
2	39 < 0.001	$164.9 \pm 2.0$	$+19.6 \pm 2.7$	$-184 \pm 8$
3	29 < 0.001	$160.7 \pm 1.6$	$+12.9 \pm 2.2$	$-163 \pm 11$
4a	31 < 0.001	$164.8 \pm 1.7$	$13.7 \pm 2.2 \#$	$-162 \pm 11$
4b	13 < 0.001	$*172.4 \pm 0.7$	$*7.9 \pm 1.0$	$-176 \pm 8$
5	14 < 0.001	$*154.4 \pm 0.8$	$7.4 \pm 1.1$	-178 ( 9
		—— DBP (mm Hg) —		
1	48 < 0.001	$94.3 \pm 0.9$	$10.9 \pm 1.3$	$-216 \pm 7$
2	24 < 0.001	$95.0 \pm 1.0$	$*7.2 \pm 1.4$	$-215 \pm 11$
3	8.032	$93.6 \pm 1.0$	$+3.7 \pm 1.4$	$-210 \pm 22$
4a	26 < 0.001	$95.4 \pm 0.9$	$6.7 \pm 1.3 \#$	$-191 \pm 12$
4b	11 < 0.001	$96.0 \pm 0.4$	$+4.0 \pm 0.6$	$-215 \pm 8$
5	14 < 0.001	$*89.9 \pm 0.6$	$5.3 \pm 0.8$	$-194 \pm 9$
		— HR (beats/min) ——		-
1	38 < 0.001	$73.7 \pm 0.9$	$9.4 \pm 1.3$	$-280 \pm 8$
2	27 < 0.001	$71.4 \pm 1.0$	$8.1 \pm 1.5$	$-269 \pm 10$
3	29 < 0.001	$69.0 \pm 1.0$	$8.2 \pm 1.4$	$-291 \pm 10$
4a	32 < 0.001	$67.2 \pm 0.9 \#$	$8.2 \pm 1.3$	$-273 \pm 8$
4b	28 < 0.001	$*61.6 \pm 0.4$	$6.8 \pm 0.5$	$-264 \pm 4$
5	40 < 0.001	$*67.0 \pm 0.4$	$8.1 \pm 0.6$	$-263 \pm 4$

Stage 1: no Rx, usual daily alcohol intake; Stage 2: no Rx, alcohol intake 50% of usual; Stage 3: no Rx, alcohol intake 33% of usual; Stage 4: no Rx, no alcohol; stage 5: Rx, no alcohol. Test of equality of MESOR and circadian amplitude between consecutive stages: +P<0.10; \*P<0.05; #P<0.05 in comparison with Stage 1.

#### DISCUSSION

The significance of this study lies in the fact that it evaluates the dynamics of variables such as blood pressure rather than relying on casual measurements. The circadian amplitude of systolic and/or diastolic blood pressure contributes valuable clinical information, to be considered in deciding on a treatment plan for the given patient (4). Heavy alcohol drinking is reportedly associated with an increased incidence of morbid cardiovascular events thought to be mediated by changes in BP, yet there is no consensus on the effect of alcohol intake on BP. This situation may stem at least in part from the fact that the major alcohol effect on BP is that on the circadian amplitude, with very little change in the MESOR. Several previous studies relying on longer than 24-hour ambulatory BP monitoring support this finding. A one-time intake of alcohol (vs. orange juice) tested on healthy volunteers was associated with an increased circadian amplitude, while the MESOR did not change. In another study of 297 patients, those who reported regular alcohol drinking also had a larger circadian amplitude as compared to those who were not alcohol drinkers. An increase in the circadian amplitude of BP is also associated with a large increase in the risk of adverse vascular events, notably ischemic strokes. The large circadian amplitude is a testable mechanism possibly underlying the increase in the incidence of morbid events among drinkers.

The antihypertensive medication facilitates the incorporation of chronobiological monitoring of blood pressure and heart rate in everyday care and for screening as a public service (5). The increase in risk was also shown not to depend on the presence or absence of other known risk factors such as obesity, high cholesterol, gender, age, familial antecedents, smoking and alcohol consumption (6,7,8). The long lasting monitoring in this study brought very important results. We could prove the direct influence of alcohol consumption on development of hypertension with an increase in circadian amplitude.

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# ZMĚNY KREVNÍHO TLAKU A SRDEČNÍ FREKVENCE ZJIŠŤOVANÉ AMBULANTNÍM MONITOROVÁNÍM PŘI POŽÍVÁNÍ ALKOHOLU A LÉČBĚ KALCIOVÝM ANTAGONISTEM

#### Souhrn

Cílem této studie bylo vyšetření vlivu požívání alkoholu a léčení kalciovými antagonisty na krevní tlak a srdeční frekvenci měřené ambulantním monitorováním. Velká cirkadiánní amplituda je testovatelným mechanismem, který je pravděpodobně příčinou zvýšení mortality mezi alkoholiky.

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