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DAY-TO-DAY VARIABILITY PROMPTS SEVEN-DAY AND 24 –HOUR BLOOD PRESSURE PROFILES

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A b s t r a c t

In order to analyse the dynamics of blood pressure measured in periods shorter than a week, we evaluated the results of measurements in a 68-year-old man with benign prostatic hypertrophy and hypertension. During the period of investigation between September and November 1999, he changed his drinking habits and the time of Hytrin intake. In three 7-day periods, he monitored his blood pressure and heart rate around the clock. The results showed that alcohol consumption was related to an increase in circadian-hyper-amplitude-tension regardless of medication.

K e y w o r d s

Blood pressure variability, Circadian rhythm, Circaseptan rhythm

INTRODUCTION

From a conventional perspective, there is abundant evidence of a relationship between lifestyle and the onset of hypertension. A consistent relationship between the consumption of alcohol and increased blood pressure has been reported (*1).* In laboratory rats, chronic alcohol consumption has also been associated with an increase in blood pressure (*2*). It has been shown that wine has a lesser effect on blood pressure than beer (*3).* In normotensive workers aged 45 to 54 years, habitual alcohol consumption reportedly increases blood pressure linearly, but light consumption does not affect blood pressure in those aged 40 to 44 years (*4*).

The circadian amplitude of blood pressure, computed by cosinor analysis (*5,6*), was found to be larger when subjects drank 40 g Ballantine whisky (Scotland) in the evening for 5 days than when they drank orange juice (*7,8).* In a case study (*9*) and in a study on 297 patients (*10*), the circadian amplitude of blood pressure was found to be significantly larger among subjects who consumed ethanol regularly than among those who did not. Circadian hyper-amplitude-tension (CHAT) was found to be associated with a 720% increase in

the risk of cerebral ischaemia, notably stroke, but ethanol intake was also shown to increase this risk by 150% (*11–16*).

MATERIAL AND METHODS

A clinically healthy man, 68 years of age at the time of study, was diagnosed with 24-hour CHAT based on an incomplete, i.e., too short, blood pressure profile covering 70 hours (*Table 1*). In this case, in order to determine the course of action and the need for any medication, an inquiry into the subject's daily habits had revealed the consumption of ethanol and the use of terazosin (Hytrin®), a drug indicated for the treatment of both benign prostatic hypertrophy and hypertension. In order to see whether these factors could be manipulated to bring the CHAT under control without any added antihypertensive medication, the subject monitored himself at 30-minute intervals during spans in which he abstained from ethanol and then when he resumed drinking alcohol but changed the timing of taking Hytrin from evening to morning (*Table 1*). In a systematic near-3-week study, the response of the circadian blood pressure amplitude to ethanol was investigated (*Table 2)*. During the first week, the subject consumed about eight ounces of liquor each evening; in the second week, he took four ounces, and in the third week he cut back to two ounces. The data were evaluated by a 24-hour cosinor analysis (*6*).

RESULTS

In the subject investigated, a 4-day profile with complete ethanol withdrawal seemed to normalise the circadian amplitude of both systolic and diastolic blood pressure (*Table 1*). As apparent from *Table 2,* the differences in circadian blood pressure characteristics between the periods of alcohol intake and alcohol abstinence were significant in most of the parameters evaluated. Circadian heart rate characteristics differed only in the rhythm-adjusted mean MESOR.

The relationships among the amount of alcohol consumed, the time of Hytrin administration and circadian characteristics of heart rate and blood pressure in the periods of the study are shown in *Tables 3, 4* and *5*.

DISCUSSION

Although we cannot exclude the usual day-to-day variability in blood pressure, as well as variability in emotional factors, conflict and grief documented elsewhere (*12, 13*), we consider the results of blood pressure monitoring (from September 20 to November 30, 1999) in our subject reliable enough to evaluate them in relation to alcohol consumption and antihypertensive treatment.

A reduction of alcohol intake has been associated with a decrease in blood pressure in randomised clinical trials (*17*). *Okubo et al*. (*18*), however, reported that daily alcohol consumption was associated non-linearly with changes in blood pressure, with a threshold effect at 18 ml of ethanol per day, in middle-aged Japanese workers and *Nakanishi et al*. (*19*) found a dose-dependent increase in the risk of hypertension with an increase in alcohol intake also in middle-aged Japanese men. In a similar population, *Okubo et al.* (*20*) failed to observe a nonlinear association of blood pressure with ethanol consumption, a result that

Table 1

Effect of ethanol consumption on circadian blood pressure characteristics

Starting date	N	Duration (hours)	Ethanol consumed (oz)	Time of Hytrin (mg) administration	SBP (mm Hg)		DBP (mm Hg)	
					M	2A	M	2A
20 Sep 99	142	70	4	2 (PM)	123.6	48.2	84.8	39.8
23 Sep 99	198	99	0	2 (PM)	125.1	27.1	87.3	24.7
28 Sep 99	138	71	4	2 (AM)	116.5	31.1	80.4	24.5

N, number of measurements; M, MESOR (rhythm-adjusted mean); 2A, double amplitude; SBP, systolic blood pressure; DBP, diastolic blood pressure; underlined values for 2A indicate overswinging (CHAT).

Table 2

Circadian blood pressure characteristics related to alcohol intake

Blood pressure characteristics	1999 Sep 20–23 (N=142)	1999 Sep 23–27 (N=198)	Comparison	
	4 oz alcohol/day	No alcohol	F	(*P*)
SBP (mm Hg)				
M ± SE	123.6 ± 1.1	125.1 ± 0.8	1.034	(0.310)
2A ± SE	48.2 ± 3.0	27.0 ± 2.2	26.305	(<0.001)
ϕ ± SE	-177° ± 4	-211° ± 5	26.277	(<0.001)
(A,ϕ)			28.808	(<0.001)
DBP (mm Hg)				
M ± SE	84.8 ± 0.8	87.3 ± 0.6	5.248	(0.023)
2A ± SE	39.8 ± 2.4	24.8 ± 1.8	23.220	(<0.001)
ϕ ± SE	-176° ± 3	-210° ± 4	32.462	(<0.001)
(A,ϕ)			30.136	(<0.001)
HR (beats/min)				
M ± SE	74.3 ± 0.6	69.3 ± 0.6	31.927	(<0.001)
2A ± SE	17.2 ± 1.8	20.4 ± 1.6	1.626	(0.203)
ϕ ± SE	-190° ± 6	-199° ± 5	1.634	(0.202)
(A,ϕ)			1.697	(0.185)

N, number of measurements; M, MESOR (rhythm-adjusted mean); 2A: double amplitude; ϕ, acrophase; (A,ϕ), statistical evaluation of the two components; F, Fischer's test; *P*, level of statistical significance.

Table 3

Effect of ethanol consumption and Hytrin treatment on circadian blood pressure characteristics

Start Date	N	Duration (hours)	Ethanol consumed (oz)	Hytrin dose (mg) & time	SBP (mm Hg)		DBP (mm Hg)	
					M	2A	M	2A
1 Oct 99	140	71	4	4 (AM)	123.2	26.7	84.9	24.0
4 Oct 99	92	47	2	1 (AM)	128.7	35.5	89.4	27.1
6 Oct 99	92	47	0	0	126.1	38.7	88.9	32.1

N, number of measurements; M, MESOR (rhythm-adjusted mean); 2A: double amplitude; SBP, systolic blood pressure; DBP, diastolic blood pressure; underlined values for 2A indicate overswinging (CHAT).

Table 4

Dose-response of circadian amplitude of systolic and diastolic BP to ethanol

Start Date	N	Duration (hours)	Ethanol consumed (oz)	Time of Hytrin (mg) administration	SBP (mm Hg)		DBP (mm Hg)	
					M	2A	M	2A
16 Nov 99	322	168	8	2(AM)	126.1	27.1	83.8	21.7
23 Nov 99	322	168	4	2(AM)	127.8	17.6	84.0	15.9
30 Nov 99	235	125	2	2(AM)	124.5	15.9	81.6	14.9

N, number of measurements; M, MESOR (rhythm-adjusted mean); 2A: double amplitude; SBP, systolic blood pressure; DBP, diastolic blood pressure.

Table 5

Comparison of circadian pattern of blood pressure and heart rate in relation to alcohol consumption in various amounts

	1999 Nov 16 (N=322)	1999 Nov 23 (N=322)	1999 Nov 30 (N=235)	Comparison	
	8 oz/day	4 oz/day	2 oz/day	F	(P)
SBP (mm Hg)					
MESOR (M) ± SE	126.1 ± 0.7	127.8 ± 0.7	124.5 ± 0.9	4.822	(0.008)
24-h double amplitude (2A) ± SE	27.0 ± 1.8	17.6 ± 2.0	15.8 ± 2.6	7.841	(<0.001)
24-h acrophase (ϕ)_ SE	-177° ± 4	-203° ± 7	-209° ± 9	8.932	(<0.001)
(A,ϕ)				8.356	(<0.001)
DBP (mm Hg)					
M ± SE	83. ± 0.5	84.0 ± 0.6	81.6 ± 0.7	4.871	(0.008)
2A ± SE	21.8 ± 1.6	15.8 ± 1.6	14.8 ± 2.0	4.802	(0.009)
ϕ ± SE	-172° ± 4	-201° ± 6	-208° ± 8	12.796	(<0.001)
(A,ϕ)				8.623	(<0.001)
HR (beats/min)					
M ± SE	74.5 ± 0.5	71.2 ± 0.5	72.9 ± 0.6	9.095	(<0.001)
2A ± SE	15.2 ± 1.6	19. ± 1.4	23.0 ± 1.8	6.298	(0.002)
ϕ ± SE	-203° ± 6	-203° ± 4	-202° ± 5	0.014	(0.956)
(A,ϕ)				3.158	(0.014)

N, number of measurements; M, MESOR (rhythm-adjusted mean); 2A: double amplitude; ϕ, acrophase; (A,ϕ), statistical evaluation of the two components; F, Fischer's test; *P*, level of statistical significance.

must be viewed in the light of a great variability in blood pressure (*21–23*). In chronobiological studies, which assess dynamic circadian characteristics of blood pressure, data are based on 24-hour blood pressure monitoring.

The first rational step in a non-pharmacological approach to the treatment of circadian hyperamplitude tension (CHAT) was to stop alcohol drinking. Our results provide evidence that alcohol consumption induces CHAT.

Endogenous endocrine mechanisms are known to be responsible for controlling human blood pressure before we wake up every day. *Cornélissen et al.* showed that blood pressure in adults has prominent circadian rhythms (*5*). In hypertension, circadian rhythms may be altered and, sometimes, CHAT can be manifested. The understanding of CHAT as a risk factor for stroke or heart attack may be important in terms of prevention and treatment of these conditions (*12, 24*).

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

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DENNÍ VARIABILITA KREVNÍHO TLAKU VYŽADUJE SEDMIDENNÍ A DVACETIČTYŘHODINOVÉ PROFILY KREVNÍHO TLAKU

S o u h r n

Abychom mohli analyzovat dynamiku krevního tlaku v periodách kratších než 7dní, hodnotili jsme výsledky měřené u 68 let starého muže s benigní hypertrofií prostaty a hypertenzí. V období vyšetřování mezi zářím a říjnem 1999, pacient měnil zvyklosti konsumace alkoholu a čas podání Hytrinu. Ve třech periodách po 7 dnech byly srdeční frekvence a krevní tlak monitorovány po 24 hodin. Výsledky ukázaly, že konzumace alkoholu vede k výskytu cirkadiánní hyperamplitudové tenze bez ohledu na hypotensní medikaci.

REFERENCES

1. *Dickey RA, Janick JJ*. Lifestyle modifications in the prevention and treatment of hypertension. Endocr Pract 2001; 7: 392–399.
2. *Utkan T, Yildiz F, Ilbay G et al.* Blood pressure and vascular reactivity to endothelin-1, phenylephrine, serotonin, KCl and acetylcholine following chronic alcohol consumption in vitro. Fundamental & Clin Pharmacol 2001; 15: 157–165.
3. *Marques-Vidal P, Montaye M, Haas B et al.* Relationships between alcoholic beverages and cardiovascular risk factor levels in middle-aged men: the PRIME Study. Prospective Epidemiological Study of Myocardial Infarction Study. Atherosclerosis 2001; 157: 431–440.
4. *Schoppet M, Maisch B.* Alcohol and the heart. Herz 2001; 26: 345–352.
5. *Cornélissen G, Halberg F.* Impeachment of casual blood pressure measurements and the fixed limits for their interpretation and chronobiologic recommendations. In: Portaluppi F, Smolensky MH, editors. Time-dependent Structure and Control of Arterial Blood Pressure. Ann NY Acad Sci 1996; 783: 24–46.
6. *Halberg F.* Chronobiology. Ann Rev Physiol 1969; 31: 675–725.
7. *Kumagai Y, Cornélissen G, Halberg F.* Lessons learned from human circadian amplitude-hypertension associated with alcohol consumption in the evening. In: Otsuka K, Cornélissen G,

Halberg F, eds. Chronocardiology and Chronomedicine: Humans in Time and Cosmos. Tokyo: Life Science Publishing, 1993: 79–89.
8. *Kumagai Y, Shiga T, Sunaga K et al.* Repeated alcohol intake changes circadian rhythm of ambulatory blood pressure. Chronobiologia 1993; 20: 77–85.
9. *Watanabe Y, Cornélissen G, Otsuka K et al.* Effect of alcohol intake and treatment with calcium antagonist on blood pressure and heart rate assessed by ambulatory monitoring. Abstract from the MEFA Symposium, Brno, Czech Republic, 1999, No. 16.
10. *Otsuka K, Cornélissen G, Halberg F, Oehlert G.* Excessive circadian amplitude of blood pressure increases risk of ischemic stroke and nephropathy. J Med Eng & Technol 1997; 21: 23–30.
11. *Halberg F, Cornélissen G, Halberg J et al.* Circadian Hyper-Amplitude-Tension, CHAT: a disease risk syndrome of anti-aging medicine. J Anti-Aging Med 1998; 1: 239–259.
12. *Halberg F, Cornélissen G, Halpin C et al.* Fleeting "monitor", "conflict" or "grief-associated" blood pressure disorders: MESOR-hypertension and circadian hyper-amplitude-tension (CHAT). EuroRehab 1996; 6: 225–240.
13. *Cornélissen G, Halberg F, Wall D et al.* How long to screen: ice hockey game and transient circadian hyper-amplitude-tension, CHAT. Scripta Med 1997; 70: 189–198.
14. *Schaffer E, Cornélissen G, Rhodus A et al.* Outcomes of chronobiologically normotensive dental patients: a 7-year follow-up. J Am Dent Assoc 2001; 132: 891–899.
15. *Halberg F, Cornélissen G,* International Womb-to-Tomb Chronome Initiative Group: Resolution from a meeting of the International Society for Research on Civilization Diseases and the Environment (New SIRMCE Confederation), Brussels, Belgium, March 17–18, 1995: Fairy tale or reality ? Medtronic Chronobiology Seminar No.8, April 1995, 12 pp.
16. *Otsuka K.* Interview with Franz Halberg: Quo vadis basic and clinical chronobiology: chronoastrobiology, chronoecology and chronotherapy. Proceedings, 1st International Symposium, Workshop on Chronoastrobiology & Chronotherapy (Satellite Symposium, 7th Annual Meeting, Japanese Society for Chronobiology), Kudan, Chiyodaku, Tokyo, 11 Nov 2000: 140–167.
17. *Cushman WC.* Alcohol consumption and hypertension. J Clin Hypertens 2001; 3: 166–170.
18. *Okubo Y, Suwazono Y, Kobayashi E, Nogawa K.* Alcohol consumption and blood pressure change: 5-year follow-up study of the association in normotensive workers. J Hum Hypertens 2001; 15: 367–372.
19. *Nakanishi N, Yoshida H, Nakamura K et al.* Alcohol consumption and risk for hypertension in middle-aged Japanese men. J Hypertens 2001; 19: 851–855.
20. *Okubo Y, Miyamoto T, Suwazono Y et al.* Alcohol consumption and blood pressure in Japanese men. Alcohol 2001; 23: 149–156.
21. *Zadek I.* Die Messung des Blutdrucks am Menschen mittels des Bauschen Apparates. Z Klin Med 1881; 2: 509–551.
22. *Janeway TC.* The Clinical Study of Blood Pressure. New York: D. Appleton & Co., 1904, 300 pp.
23. *Bartter FC.* Periodicity and medicine. In: Scheving LE, Halberg F, Pauly JE, eds. Chronobiology. Tokyo: Igaku Shoin Ltd., 1974: 6–13.
24. *Cornélissen G, Sothern RB, Wendt HW et al.* Statistical significance without biologic signification is not enough: illustrative example. Chronobiologia 1994; 21: 315–320.