The effect of alcohol consumption on the circadian control of human core body temperature is time dependent

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Received 18 September 2000; accepted in final form 6 March 2001

Danel, Thierry, Christian Libersa, and Yvan Touitou. The effect of alcohol consumption on the circadian control of human core body temperature is time dependent. Am J Physiol Regulatory Integrative Comp Physiol 281: R52–R55, 2001.—The few controlled studies dealing with the action of alcohol on core body temperature in humans have focused on the effect of a single dose of ethanol and reported that it has a hypothermic effect. No studies report the effects of repeated ethanol intake over a 24-h period, a pattern of consumption much closer to the clinical condition of chronic alcoholism. We therefore designed a trial in which alcohol was repeatedly and regularly administered, with a total dose of 256 g. Nine healthy male volunteers (mean age 23.3 ± 2.9 yr; range 21–30) each served as his own control. The circadian temperature rhythm was studied by a single-blind, randomized, crossover study that compared a 26-h alcohol session to a 26-h placebo session. The trial controlled for so-called masking effects known to affect temperature. The volunteers were in bed; the ambient temperature was maintained between 20 and 22°C. Meals were standardized. And light was controlled during the night. All sessions took place between November and April. The two sessions were separated by 2 to 5 wk. Rectal temperature was monitored every 20 min throughout the trial. We found the standard hypothermic effect of alcohol in the early hours of the trial, during the daytime, but our principal result is that alcohol consumption induced a very significant hyperthermic effect (+0.36°C) during the night and thereby reduced the circadian amplitude of core body temperature by 43%. The dramatic decrease of the amplitude of circadian temperature rhythm that we observed may explain, at least in part, some clinical signs observed in alcoholic patients, including sleep and mood disorders. We suggest that jet lag, shift work, and aging, which are known to alter body temperature, are aggravated by alcohol consumption.

alcoholism; circadian rhythm

ALCOHOL IS THE MOST COMMON psychoactive drug in Western countries and leads to somatic, psychic, and social disorders. The chronobiological aspect of alcohol-related diseases has not been examined; however, if alcohol alters biological rhythms, some complications such as sleep or depression disorders, which are frequently associated with alcohol and are also known to have a strong chronobiological determinant, may be partly explained by a chronobiological approach. The circadian temperature rhythm is one of the main indexes of 24-h synchronization and is essential for the adaptation of humans to their environment. Only a few controlled studies deal with the effect of alcohol on core body temperature (12–14), and they examine single doses of ethanol. No published studies report the effects of a 24-h consumption period, of the type found in heavy drinkers. Two major problems arise in performing such a study. First, it is difficult to monitor temperature in alcoholics during the course of the disease because of their poor compliance. Second, giving alcoholic beverages to abstinent patients is not ethically acceptable. We therefore conducted a trial based on a 26-h alcohol consumption period with healthy volunteers. The total dose reached the amount generally ingested by alcoholic patients, i.e., 256 g/day (corresponding roughly to 2.5 l of wine at 12° per cent, 700 ml of whisky at 40° per cent, or 6 l of beer at 4.5° per cent), administered at regular intervals during the trial. Rectal temperature was monitored throughout the trial to study the circadian temperature cycle during alcohol consumption compared with that during a control session.

METHODS

Subjects. Nine healthy men (Table 1) between the ages of 21 and 30 yr (23.3 ± 2.9 yr) were included after obtaining their informed written consent. Lifestyle, physical health, and clinical status were assessed by routine clinical and laboratory examinations to determine eligibility for the study. All subjects were synchronized with diurnal activity and nocturnal rest. Subjects had no physical abnormalities at the time of examination. Body mass index ranged from 20 to 25. No subject had a current or past diagnosis of alcohol, tobacco, or other substance abuse or dependence. They took no medication, worked no rotating shifts, took no transmeridional flights, and had no infection or disease for at least 1 mo before the session. No subject had a current or past depressive disorder or psychosis. All scores on the Montgom-
ery and Asberg (10) depression-rating scale were lower than 18, which ruled out any current depressive disorder. No subject had a current diagnosis of delayed or advanced phase or hypernyctohemeral syndrome. Horne and Ostberg (7) scores ranged from 39 to 59 (mean 49.5 ± 6.8), a criterion that excluded those who were “definitely morning” or “definitely evening” types. Routine blood counts and blood chemistry were in the normal range, and HIV and hepatitis B and C tests were negative.

Experimental protocol. The Ethics Committee of Lille, France, approved the study. The circadian rhythm of core body temperature was studied in nine healthy male volunteers during a single-blind, randomized, crossover study comparing a 26-h alcohol session and a 26-h placebo session. In the alcohol session (Table 2), 256 g of ethanol were administered between 1000 the first day and 1200 on the second day to obtain blood alcohol concentrations between 0.5 and 0.7 g/l throughout the session. To obtain a significant blood alcohol concentration (BAC) at the beginning of the data collection (1200), 20 g of ethanol were administered orally at 1000, 1100, and 1200; then 10 g/h were administered from 1300 to 2100 and from 0700 to 1100 on the second day. The alcohol administered was mixed with fruit juice. In the placebo session, only fruit juice was administered. To enable subjects to sleep while simultaneously maintaining a sufficient BAC, 7 g/h of alcohol (Curethyl®, AJC Pharma, Chateauneuf, France) in saline solution were administered intravenously during the night (between 2200 and 0600) in the alcohol session and saline solution only in the control session. A rectal probe (Squirrel Logger Equipment, Grant Instruments, Cambridge, UK) for recording core temperature was inserted at 1200 and left in place throughout the monitoring period. Rectal temperature was recorded every 20 min throughout the 26-h experimental period. All the sessions took place between November and April. For each subject, the two sessions were separated by 2 to 5 wk. Subjects were admitted to the Clinical Investigation Center at 0800. During observation from 1000 on the first day to 1500 on the second day, subjects were in bed, reading and watching television; they ate standardized meals at 0800, 1200, and 1900 on the first day and at 0800 and 1200 on the second day. They left at 1500. Lights were off between 2200 and 0600. Ambient temperature ranged from 20 to 22°C during the session. Blood samples were collected every 6 h (1200, 1800, 2400, 0600, and 1200) for blood alcohol determination. When the blood samples were collected at 2400, the room was illuminated by light with an average intensity of 50 lx.

Statistical analysis. All statistical analysis was performed with SAS software (SAS Institute, Cary, NC). Statistically significant differences between the alcohol and control sessions were determined with two-way, repeated-measures ANOVA. A general linear mixed model for repeated data (9) was used to assess the variations of temperature over time and group. Then, statistical comparisons for each point of the circadian temperature pattern were performed with the paired Wilcoxon’s rank sum test.

RESULTS

Figure 1 displays typical temperature patterns in the volunteers. Figure 2 reports the temperature patterns for the group during the control and alcohol sessions, and Fig. 3 reports the BACs at five points during the day, corresponding to the experimental protocol. Interaction (ANOVA) between the time factor and group factor was significant ($P < 0.0001$). Each point time of the temperature pattern during the alcohol session was compared with the corresponding point in the control session by paired Wilcoxon’s rank sum test. This comparison showed that the temperature during the alcohol session was significantly higher at night ($P$ value ranging from 0.046 to 0.007 from 0300 to 0820) and significantly lower in the daytime, at the beginning of the trial ($P$ value ranging from 0.047 to 0.007 from 1240 to 1400). Before, between, and after these hours, temperature did not differ significantly. The mean lowest temperature was 0.36°C higher in the alcohol session ($P$ value ranging from 0.046 to 0.047) than in the control session ($P$ value ranging from 0.007 to 0.006). The peak temperature in the alcohol session was significantly higher at 0600 ($P$ value ranging from 0.0001 to 0.0002) than in the control session ($P$ value ranging from 0.002 to 0.007). The peak temperature in the alcohol session was 0.17°C higher than in the control session ($P < 0.0001$) at 0800, and 0.18°C higher at 1200, and 0.22°C higher at 1800 and 2400. The mean lowest temperature was 0.36°C higher in the alcohol session ($P < 0.0001$) than in the control session ($P < 0.0001$). The peak temperature in the alcohol session was 0.17°C higher than in the control session ($P < 0.0001$) at 0600, and 0.22°C higher at 1200, and 0.20°C higher at 1800.

Table 1. Subjects’ characteristics

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<td>1</td>
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<td>70</td>
<td>21.6</td>
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<td>2</td>
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<td>78</td>
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<td>54</td>
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<td>9</td>
<td>26</td>
<td>68</td>
<td>21.5</td>
<td>52</td>
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<tr>
<td>Mean</td>
<td>23.3±2.9</td>
<td>70.8±5.9</td>
<td>22.5±1.6</td>
<td>49.6±6.8</td>
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Table 2. Experimental protocol

<table>
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<th>Alcohol Administration</th>
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<th>2200–0600</th>
<th>0700–1100</th>
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<td>Oral</td>
<td>Oral</td>
<td>Intravenous</td>
<td>Oral</td>
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</table>

Fig. 1. Individual circadian patterns of core body temperature. ●, Alcohol session; ○, control session. Top, subject 4; bottom, subject 7.
circadian temperature rhythm between the two sessions (43%) is due to the higher low point during the alcohol session, compared with the control session. Seven of nine volunteers experienced a hyperthermic effect at night.

DISCUSSION

Controlled studies of humans and other animals that have dealt with the action of alcohol on core body temperature focused on the effect of a single dose of ethanol and considered it for a few hours after administration. These studies all concluded that alcohol has a hypothermic effect. In humans, Reinberg et al. (13) found that the circadian 24-h mean value of oral temperature decreased when a single dose of 0.67 g/kg was administered at 0700 but was unaffected by the same single dose when it was administered at 1100, 1900, or 2300. O’Boyle et al. (12) recorded oral temperature for 3 h after consumption of 0.8 ml/kg of alcohol at either 0800 or 1600. They observed an alcohol-induced decline in oral body temperature during the 0800 session and no effect during the 1600 session. Yap et al. (14) found a hypothermic effect during the 2 h following the administration of 0.75 g/kg of alcohol at 0900, 1500, 2100, and 0300. Reports about rodents state that alcohol administration decreases body temperature (2), and it has been hypothesized that ethanol induces a downward shift of the set point for temperature control (1, 5). Another suggested mechanism is that alcohol suppresses thermoregulation (11).

Our study of the effects of alcohol on core body temperature is, to our knowledge, the first circadian study performed. It uses a standardized and sustained administration to obtain experimental conditions close to those experienced by alcoholic patients. So-called masking effects known to affect temperature (6) have been controlled throughout the trial. Volunteers were in bed, ambient temperature was maintained from 20 to 22°C, meals were standardized, and light was controlled at night. All these parameters were similar in both sessions. We found that alcohol consumption led to a decrease in core body temperature at the beginning of the trial, in the daytime (between 1240 and 1400), a finding consistent with the standard hypothermic effect of alcohol reported in the literature, as described above. The principal finding of our study, however, is that alcohol consumption increased nocturnal core body temperature. Indeed, in this study, we clearly show that alcohol consumption dramatically affected the circadian core body temperature by inducing its nocturnal increase (average increase of 0.36°C); this resulted in an ~43% decrease in the amplitude of the circadian temperature rhythm. Our data, obtained on a circadian basis, strongly suggest that the effect of alcohol on core body temperature is time dependent and ultimately reduces the amplitude of the rhythm.

Fig. 2. Circadian profiles of core body temperature (by 20 min) of 9 healthy men studied twice: during an alcohol session (○) (consumption of 256 g of alcohol administered regularly during a 26-h period) and a control session (○). Temperature during the alcohol session was significantly higher from 0300 to 0820 ($P$ value between 0.046 and 0.007) and significantly lower in daytime, at the beginning of the trial ($P$ value between 0.047 and 0.007). At night, the mean lowest temperature value was 0.36°C higher in the alcohol session (36.48°C) than in the control session (36.12°C). Horizontal white bars, lights on; horizontal black bar, lights off.

Fig. 3. Mean value of the blood alcohol levels (g/l) in 9 subjects, corresponding to the experimental protocol.
Another explanation should be considered in light of Gallaher and Egner’s (4) report on rodents. They studied the temperature effects of ethanol injection at 0900 (during the rest period) at doses ranging from 2 to 6 g/kg. They observed a hypothermic effect but also rebound hyperthermia during the successive rest periods and persisting for several days. They hypothesized a mild abstinence syndrome or alternatively a disruption of the normal circadian temperature rhythm. Because blood alcohol levels were lower during the night than the day in our experiment, a sympathetic rebound associated with withdrawal cannot be excluded. Further experiments are needed however to confirm this hypothesis. Despite the lack of confirmation, we nonetheless find the time-dependent hypothesis more plausible, because hyperthermia in withdrawal is generally observed after long periods of alcoholism and because our subjects were not alcoholic.

**Perspectives**

Our data strongly suggest that alcohol has a hyperthermic effect at night in humans. This could have serious consequences, especially on mood and sleep. Numerous studies have reported that circadian temperature amplitude decreases in mood disorders (3) and that sleep is strongly linked to temperature rhythm (8). The dramatic decrease of the amplitude of circadian temperature rhythm that we observed may explain, at least in part, some clinical signs observed in alcoholic patients, including sleep and mood disorders. Our data suggest that alcohol consumption exacerbates the tendency toward flattening of the circadian temperature curve and consequently intensifies sleep and mood disorders. Similarly, we suggest that the pathophysiological conditions, including mood and sleep disorders, jet lag, shift work, and aging, that are known to result in alteration of temperature, are aggravated by alcohol consumption. Further data on alcoholic patients are needed to verify these hypotheses.

We thank Dr. A. Duhamel (Centre d’Etudes et de Recherche en Informatique Médicale, Lille) for statistical analysis.

This work was supported by grants from Institut National de la Santé et de la Recherche Médicale, Centre Hospitalier Régional Universitaire of Lille, and Institut de Recherches Scientifiques sur les Boissons.

**REFERENCES**