Effect of Sauna Bathing and Beer Ingestion on Plasma Concentrations of Purine Bases

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To determine whether sauna bathing alone or in combination with beer ingestion increases the plasma concentration of uric acid, 5 healthy subjects were tested. Urine and plasma measurements were performed before and after each took a sauna bath, ingested beer, and ingested beer just after taking a sauna bath, with a 2-week interval between each activity. Sauna bathing alone increased the plasma concentrations of uric acid and oxypurines (hypoxanthine and xanthine), and decreased the urinary and fractional excretion of uric acid, while beer ingestion alone increased the plasma concentrations and urinary excretion of uric acid and oxypurines. A combination of both increased the plasma concentration of uric acid and oxypurines, and decreased the urinary and fractional excretion of uric acid, with an increase in the urinary excretion of oxypurines. The increase in plasma concentration of uric acid with the combination protocol was not synergistic as compared to the sum of the increases by each alone. Body weight, urine volume, and the urinary excretion of sodium and chloride via dehydration were decreased following sauna bathing alone. These results suggest that sauna bathing had a relationship with enhanced purine degradation and a decrease in the urinary excretion of uric acid, leading to an increase in the plasma concentration of uric acid. Further, we concluded that extracellular volume loss may affect the common renal transport pathway of uric acid and xanthine. Therefore, it is recommended that patients with gout refrain from drinking alcoholic beverages, including beer, after taking a sauna bath, since the increase in plasma concentration of uric acid following the combination of sauna bathing and beer ingestion was additive.

EXCESSIVE PERSPIRATION may increase the plasma concentration of uric acid via dehydration, which causes hyperuricemia.[1-3] Since such an increase may induce gouty attacks in patients with gout, it is important to understand whether sweating increases the plasma concentration of uric acid via dehydration, which, to our knowledge, has not been clearly elucidated. In Japan, sauna bathing is very popular and perceived to be good for health, and many people enjoy drinking alcoholic beverages, especially beer, which increases the plasma concentration of uric acid,[4,5] after getting out of the bath. Although purine metabolism, including oxypurines and uric acid, is known to be affected by dehydration, there is no known study of the effect of sauna bathing or a combination of that and alcoholic beverage ingestion on purine metabolism. In the present study, we investigated the effects of sauna bathing and beer ingestion alone and in combination on purine metabolism, including oxypurines.

MATERIALS AND METHODS

Subjects and Study Design

The study was performed with 5 healthy males, who ranged in age from 33 to 39 years and in weight from 55 to 78 kg. Each had normal values in a routine laboratory test, which included aspartate aminotransferase (AST), alanine aminotransferase (ALT), serum creatinine, and fasting blood glucose measurements. After informed consent was obtained, the first experiment (sauna bath experiment) was performed as follows. After an overnight fast, except for water, the subjects completely voided their urine and then 1-hour urine samples were successively collected 4 times over 4 hours (first, second, third, and fourth periods, respectively). The first, second, third, and fourth blood samples were drawn with heparinized syringes at the mid-point of the respective periods.

Following collection of the first urine samples, body weight was measured and the subjects immediately entered a sauna bath, set at 90°C, twice, for 10 minutes each time with a 10-minute interval. After body weight was measured again, the second blood samples were drawn and the protocol, as described above, was continued. Two weeks later, the second experiment (beer ingestion experiment) was performed using the same protocol, except that regular beer (10 mL/kg of body weight, containing 5% ethanol) was ingested orally within 5 minutes after the second blood sample was drawn and without the sauna bath. Four weeks after the sauna bath experiment, the third experiment (combination experiment) was performed using the same protocol, with a combination of the sauna bath and beer ingestion. Purines present in beer (391 μmol/L) were determined in a previous study.[5]

Blood and Urine Sample Analyses

Plasma and urinary concentrations of hypoxanthine and xanthine were determined, as described previously,[6] using a Wakosil 5C-18 column (4.6 mm inner diameter × 250 mm; Wako Pure Chemical Industries, Osaka, Japan). Uric acid levels in plasma and urine were measured by the uricase method using an autoanalyzer, while the concentration of lactic acid in blood was measured by an enzymatic method using a Determiner LA kit (Kyowa Medix, Tokyo, Japan). The concentration of ethanol in plasma was determined as described previously.[5]

Statistics

Values are expressed as the mean ± SD. The significance of differences was assessed by analysis of variance (ANOVA) for all variables, with a P value of less than .05 considered statistically significant.

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Submitted September 6, 2003; accepted November 26, 2003.

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0026-0495/04/5306-0045$30.00/0
doi:10.1016/j.metabol.2003.11.028

RESULTS

Plasma Concentrations of Purine Bases (hypoxanthine, xanthine, and uric acid)

Sauna bathing increased the plasma concentration of uric acid from 323 ± 32 μmol/L at the first period to 338 ± 28 μmol/L ($P < .05$), 342 ± 29 μmol/L ($P < .05$), and 342 ± 28 μmol/L ($P < .05$) at the second, third, and fourth periods, respectively, while beer ingestion increased that from 320 ± 21 μmol/L at the first period and 319 ± 24 μmol/L at the second period, to 354 ± 26 μmol/L ($P < .01$) at the third period and 349 ± 29 μmol/L ($P < .05$) at the fourth period. A combination of the two increased the plasma concentration of uric acid from 320 ± 27 μmol/L at the first period, to 336 ± 238 μmol/L ($P < .05$), 384 ± 32 μmol/L ($P < .01$), and 380 ± 28 μmol/L ($P < .01$) at the second, third, and fourth periods, respectively.

Sauna bathing alone increased the plasma concentration of hypoxanthine from 1.03 ± 0.34 μmol/L at the first period to 2.76 ± 0.86 ($P < .01$), 1.56 ± 0.24 ($P < .01$), and 1.14 ± 0.15 ($P < .05$) μmol/L at the second, third, and fourth periods, respectively, while beer ingestion increased the plasma concentration of hypoxanthine from 0.92 ± 0.30 μmol/L at the first period and 0.82 ± 0.34 μmol/L at the second period, to 1.70 ± 0.66 μmol/L ($P < .05$) at the third period, although it was not significantly increased at the fourth period (1.18 ± 0.34 μmol/L) as compared to the first. A combination of the two increased the plasma concentration of hypoxanthine from 1.04 ± 0.28 μmol/L at the first period to 2.68 ± 0.94 ($P < .01$), 2.84 ± 1.06 ($P < .01$), and 1.62 ± 0.34 ($P < .01$) μmol/L at the second, third, and fourth periods, respectively.

Sauna bathing alone increased the plasma concentration of xanthine from 0.64 ± 0.12 μmol/L ($P < .01$) at the first period to1.14 ± 0.28 ($P < .01$), 0.94 ± 0.18 ($P < .01$), and 0.86 ± 0.20 ($P < .01$) μmol/L at the second, third, and fourth periods, respectively, while beer ingestion increased the plasma concentration of xanthine from 0.54 ± 0.10 μmol/L at the first period and 0.56 ± 0.12 μmol/L at the second period to 1.86 ± 0.70 μmol/L ($P < .05$) at the third period and 1.62 ± 0.56 μmol/L ($P < .05$) at the fourth period. A combination of the two increased the plasma concentration of xanthine from 0.60 ± 0.20 μmol/L at the first period to 1.22 ± 0.14 ($P < .01$), 2.24 ± 0.94 ($P < .05$), and 1.90 ± 0.86 ($P < .05$) μmol/L at the second, third period, and fourth periods, respectively. The increase in plasma concentration of uric acid in the combination experiment from the first to third period was 64 ± 10 μmol/l and from the first to fourth period was 60 ± 3 μmol/l, while the sum of increases of that in the first 2 experiments from the first to third period was 52 ± 16 μmol/l and 52 ± 19 μmol/l from the first to fourth period. The increases in plasma concentration of uric acid in the combination experiment at the third and fourth period were not significantly different from the sum of increases of uric acid at the same periods in the first 2 experiments.

Urinary Excretion of Purine Bases

Following sauna bathing, the urinary excretion of uric acid was decreased from 223 ± 50 to 150 ± 40 μmol/h ($P < .01$) at the second period and 136 ± 25 μmol/L μmol/h ($P < .01$) at the third period, whereas it did not affect the urinary excretion of uric acid at the fourth period (163 ± 41μmol/h). In contrast, beer ingestion increased the urinary excretion of uric acid from 214 ± 32 to 260 ± 33 μmol/h ($P < .05$) at the second period and 267 ± 36 μmol/h ($P < .05$) at the third period, and an increasing trend was seen at the fourth period (245 ± 30 μmol/h). The combination of sauna bathing and beer ingestion decreased the urinary excretion of uric acid from 221 ± 44 to 136 ± 20 μmol/h ($P < .01$) at the second period. However, there was no effect seen at the third (183 ± 21 μmol/h) or fourth period (239 ± 38 μmol/h).

Sauna bathing alone increased the urinary excretion of hypoxanthine from 2.40 ± 0.88 to 3.58 ± 1.02 μmol/h ($P < .05$) at the second period and to 3.15 ± 0.74 μmol/h ($P < .05$) at the third period, although the urinary excretion of hypoxanthine (2.69 ± 0.70 μmol/h) at the fourth period was not affected. Beer ingestion increased the urinary excretion of hypoxanthine from 2.47 ± 0.50 μmol/h at the first period to 3.65 ± 0.79 ($P < .05$), 5.24 ± 1.33 ($P < .05$), and 3.54 ± 0.69 ($P < .05$) μmol/h at the second, third, and fourth periods, respectively. The combination of both increased the urinary excretion of hypoxanthine from 2.61 ± 0.62 to 4.00 ± 0.85 μmol/h ($P < .01$) at the second period and to 5.80 ± 1.66 μmol/h ($P < .05$) at the third period, though it was not increased at the fourth period (3.19 ± 0.64 μmol/h).

Sauna bathing alone did not increase the urinary excretion of xanthine during any period (first period, 1.52 ± 0.48 μmol/h; second period, 1.70 ± 0.70 μmol/h; third period, 1.70 ± 0.3 μmol/h; fourth period, 1.64 ± 0.28 μmol/h). Beer ingestion increased the urinary excretion of xanthine from 1.71 ± 0.40 μmol/h at the first period to 2.56 ± 0.88 ($P < .05$), 4.17 ± 0.78 ($P < .01$), and 3.89 ± 0.67 ($P < .01$) μmol/h at the second, third, and fourth periods, respectively.

The combination of both increased the urinary excretion of xanthine from1.50 ± 0.62 μmol/h at the first period to 2.52 ± 0.52 ($P < .05$), 4.28 ± 1.39 ($P < .05$), and 3.19 ± 0.70 ($P < .05$) μmol/h at the second, third, and fourth periods, respectively.

Creatinine Clearance and Fractional Excretion of Purine Bases

Creatinine clearance did not change at any time during the experiments (Table 1). However, the fractional excretion of uric acid was decreased at the second and third periods in the sauna bath and combination experiments, as compared with the respective reference values in the first periods, whereas it was not changed at any period in the beer ingestion experiment (Table 1). Further, the fractional excretion of hypoxanthine was decreased at the second period in the sauna bath and combination experiments, suggesting that the plasma concentration of hypoxanthine peaked at the mid-point of the second period, just after taking the sauna bath (Table 1). In contrast, the fractional excretion of hypoxanthine was increased at the second period in the beer ingestion experiment because the plasma concentration of hypoxanthine was measured just prior to ingesting the beer, although it was not affected at any other period in any of the 3 experiments (Table 1). The fractional excretion of xanthine was decreased at the second, third, and fourth periods in the sauna bath experiment, and it was increased only at the

Table 1. Clearance of Creatinine and Fractional Excretion of Uric Acid, Hypoxanthine, and Xanthine in Each of the Three Experiments (N = 5)

	Period			
	1	2	3	4
Ccr (mL/min)				
Sauna bath	112 ± 9	113 ± 7	114 ± 12	111 ± 9
Beer	114 ± 4	114 ± 8	112 ± 8	111 ± 3
Combination	111 ± 9	112 ± 9	116 ± 8	111 ± 4
Fua				
Sauna bath	0.088 ± 0.045	0.057 ± 0.031*	0.049 ± 0.028*	0.060 ± 0.036*
Beer	0.083 ± 0.042	0.101 ± 0.054	0.093 ± 0.047	0.084 ± 0.042
Combination	0.088 ± 0.046	0.048 ± 0.024*	0.057 ± 0.032*	0.076 ± 0.041
Fhx				
Sauna bath	0.343 ± 0.074	0.195 ± 0.020*	0.295 ± 0.042	0.359 ± 0.117
Beer	0.427 ± 0.127	0.697 ± 0.164†	0.527 ± 0.283	0.542 ± 0.173
Combination	0.39.0 ± 0.074	0.236 ± 0.098*	0.304 ± 0.067	0.344 ± 0.099
Fx				
Sauna bath	0.361 ± 0.061	0.157 ± 0.097†	0.269 ± 0.045*	0.289 ± 0.05.5†
Beer	0.398 ± 0.033	0.733 ± 0.259*	0.418 ± 0.204	0.455 ± 0.238
Combination	0.383 ± 0.110	0.301 ± 0.074	0.310 ± 0.102	0.292 ± 0.130

NOTE. Values are means ± SD.

Abbreviations: Ccr, clearance of creatinine; Fua, fractional excretion of uric acid (uric acid clearance/Ccr); Fhx, fractional clearance of hypoxanthine (hypoxanthine clearance/Ccr); Fx, fractional clearance of xanthine (xanthine clearance/Ccr), respectively.

*$P < .05$.

†$P < .01$.

second period in the beer ingestion experiment (Table 1), indicating that the plasma concentration of xanthine was not increased just prior to beer ingestion. The fractional excretion of xanthine was not affected at any period in the combination experiment.

Plasma Total Protein Level, Body Weight, and Urine Volume

Sauna bathing increased the plasma concentration of total protein from 75 ± 4 g/L at the first period to 78 ± 3 g/L ($P < .05$) at the second period. However, a significant change was not seen at the third or fourth period (both 73 ± 2 g/L), while beer ingestion had no significant effect (77 ± 2, 77 ± 2, 78 ± 1, and 78 ± 2 g/L at the second, third, and fourth periods, respectively). The plasma concentration of total protein in the combination experiment increased from 77 ± 4 g/L at the first period to 80 ± 3 g/L at the second period ($P < .05$), although a significant change was not seen at the third or fourth period (74 ± 4 and 74 ± 3 g/L, respectively). Body weight decreased from 67.4 ± 5.9 kg just before taking a sauna bath to 66.6 ± 5.9 kg ($P > .01$) just after. In the combination experiment, body weight decreased from 66.9 ± 5.2 kg just before taking a sauna bath to 66.0 ± 5.2 kg ($P > .01$) just after. In the sauna bathing exeriment, urine volume was decreased from 131 ± 66 mL at the first period to 63 ± 36 ($P < .05$), 57 ± 12 ($P < .05$), and 55 ± 11 ($P < .05$) mL at the second, third, and fourth periods, respectively, while beer ingestion increased it from 86 ± 22 mL at the first period to 221 ± 95 mLl ($P < .05$) at the third period, and 172 ± 83 mL ($P < .05$) at the fourth period, whereas there was no significant increase at the second period. In the combination experiment, urine volume decreased from 104 ± 33 mL at the first period to 53 ± 17 mL ($P < .05$) at the second period, and then increased to 253 ± 109 mL ($P < .05$) at the third period and decreased again to 115 ± 48 mL at the fourth period.

Serum Concentrations and Urinary Excretion of Sodium and Chloride

The serum concentrations of sodium and chloride did not significantly change during any of the experiments (data not shown). In contrast, in the sauna bath experiment, the urinary excretion of sodium and chloride was decreased from 10.40 ± 5.0 and 12.1 ± 5.92 mmol/h at the first period to 4.44 ± 2.99 ($P < .05$) and 5.91 ± 3.92 ($P < .01$) mmol/h, respectively, at the second period, to 4.21 ± 2.33 ($P < .05$) and 5.06 ± 2.38 ($P < .05$) mmol/h, respectively, at the third period, and to 4.99 ± 2.49 ($P < .05$) and 6.50 ± 3.52 ($P < .05$) mmol/h, respectively, at the fourth period. In the beer ingestion experiment, which used regular beer containing negligible levels of sodium and chloride (data not shown), the urinary excretion of sodium and chloride did not change at any time (data not shown). In the combination experiment, the urinary excretion of sodium was decreased from 10.56 ± 4.77 mmol/h at the first period to 4.54 ± 2.66 mmol/h ($P < .05$) at the second period. However, it was not decreased at the third or fourth periods (data not shown), while that of chloride was decreased from 12.50 ± 3.60 mmol/h at the first period to 6.17 ± 2.38 mmol/h ($P < .01$) at the second period, 8.87 ± 4.09 mmol/h ($P < .05$) at the third period, and 9.04 ± 4.11 mmol/h ($P < .05$) at the fourth period.

Concentration of Ethanol in Plasma and Lactic Acid in Blood

The concentration of ethanol was below the limits of detection at the first and second periods, and 456 ± 23 and 321 ±

49 μg/mL at the third and fourth periods, respectively, in the beer ingestion experiment, and below the limits of detection at the first and second periods, and 455 ± 25 and 323 ± 53 μg/mL at the third and fourth periods, respectively, in the combination experiment. Further, the plasma concentration of ethanol in the beer ingestion experiment did not differ from that in the combination experiment at any period. The concentration of lactic acid in blood did not change during the sauna bath experiment (data not shown), while it was increased from 0.80 ± 0.11 mmol/L at the first period to 1.15 ± 0.18 mmol/L ($P < .05$) at the third period and 1.12 ± 0.24 mmol/L at the fourth period in the beer ingestion experiment, and from 0.76 ± 0.14 at the first period to 1.30 ± 0.28 mmol/L ($P < .05$) at the third period and 1.20 ± 0.27 mmol/L ($P < .05$) at the fourth period in the combination experiment.

DISCUSSION

In the present study, we attempted to determine whether sauna bathing alone increased the plasma concentration of uric acid, to what degree it was increased by a combination of sauna bathing and beer ingestion as compared to each alone. We found it interesting that sauna bathing alone increased the plasma concentrations of uric acid, hypoxanthine, and xanthine, as well as the urinary excretion of hypoxanthine and xanthine, although the amounts were small. These results suggest that an enhanced amount of purine degradation occurred in the subjects. In contrast, the urinary excretion of uric acid and the fractional excretion of uric acid and xanthine were decreased.

A sauna bath typically has a high temperature (~90°C) and low humidity, and is intended to cause the body to perspire heavily. Although the high temperature seems to have an effect on purine metabolism, including oxypurines and uric acid via hypermetabolism, the relationship between purine metabolism and high temperature remains undetermined. A previous study demonstrated that blood uric acid and lactic acid levels were elevated in rats in a condition of hyperthermia, suggesting that tissue hypoxemia causes purine degradation.[7] However, since the concentration of lactic acid in blood did not significantly increase in the present sauna bath experiment, tissue hypoxemia does not seem to be the main cause of the increased plasma concentration and urinary excretion of hypoxanthine, or the increased plasma concentration of xanthine. Therefore, other factor(s) associated with sauna bathing may have effects on those parameters.

Another intriguing finding was that sauna bathing decreased the fractional excretion of uric acid and xanthine (Table 1). Body weight following the sauna bath decreased by approximately 800 g from fluid loss, resulting in a transient decrease in intravascular plasma volume, as shown by the 4% increase in plasma concentration of total protein at the second period, which returned to the reference level at the third and fourth periods. In addition, urine volume and the urinary excretion of sodium were decreased in the sauna bathing experiment. These results indicated that extracellular fluid volume was decreased by sweating. Since the fractional excretion of uric acid is known to reflect extracellular fluid volume,[8,9] its decrease following the sauna bath may be ascribable to a reduced extracellular fluid volume. Several previous studies[10,11] suggested that xanthine shares a renal transport pathway with uric acid, whereas hypoxanthine does not. Therefore, since the present results demonstrated that the fractional excretion of uric acid and xanthine were decreased by sauna bathing, it is suggested that a reduced extracellular fluid volume has an effect on the common renal pathway of uric acid and xanthine.

In the beer ingestion experiment, the plasma concentrations and urinary excretion of hypoxanthine, xanthine, and uric acid were increased. These findings indicated that purines in the beer increased the production of uric acid, which resulted in increases in the plasma concentration and urinary excretion of uric acid, since a previous study has shown that beer ingestion (10 mL/kg body weight) does not increase the concentration of lactic acid in blood to a level high enough to inhibit the renal excretion of uric acid.[12] Therefore, a combination of sauna bathing and beer ingestion may have a synergistic effect on the increase in plasma concentration of uric acid, since the plasma concentration of ethanol in the combination experiment did not differ from that in the beer ingestion experiment. However, the present results demonstrated that the effect of the combination on the plasma concentration of uric acid was not synergistic, but rather additive. We considered that the ingestion of the considerable amount of fluid contained in the beer partially restored extracellular fluid volume loss.

In conclusion, the plasma concentration of uric acid was increased in an additive manner following a combination of sauna bathing and beer ingestion. Therefore, it is recommended that patients with gout refrain from drinking alcoholic beverages, including beer, after taking a sauna bath.

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