Effects of Profuse Sweating Induced by Exercise on Urinary Uric Acid Excretion in a Hot Environment

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Abstract

In order to determine whether exercise-induced profuse sweating could reduce urinary uric acid excretion, we simulated badminton players training and measured their uric acid in urine, sweat and blood during the training period. Thirteen male volunteers who were well-trained badminton players were recruited in this study. On the first 2 days and the last 2 days of the study period none of the subjects engaged in any intense exercise- or activity-inducing profuse sweat, but they accepted routine training 2 h per day during the middle 3 days. The results show that mean serum urate levels of thirteen volunteers rose significantly on day 4, when the concentrations increased by 18.2% over day 2 (P < 0.05). The mean ten-hour urinary uric acid excretion of seven volunteers on the 3 training days was significantly less at 178.5 µmol/day and 118.3 µmol/day than those on the preceding and subsequent days of the training days, respectively (P < 0.05). Furthermore, for six volunteers, the mean ratio of clearance of uric acid to creatinine was 6.6% on day 2, which significantly decreased to 5.4% on day 4 (P < 0.05). It is concluded profuse sweating exercise results in a decrease of urinary uric acid excretion amounts and leads to increased serum uric acid after the exercise. We suggest that persons who take vigorous exercise or are exposed to hot environments need drinking enough fluids to prevent dehydration and maintain adequate urinary output. People with profuse sweat after rigorous exercise are recommended taking sports drinks containing abundant sodium in order to decrease serum uric acid.

Key Words: profuse sweating, uric acid excretion, uric acid clearance

Introduction

Intensive physical exercise in hot climates may be accompanied by hyperuricemia (8, 18). The balance between rates of urate production and its elimination determines the concentrations of uric acid in body fluids. Exercise involving large muscle groups can be characterized on the basis of the rate of ATP turnover (14, 21), which may indicate the development of hyperuricemia because of the excessive rate of urate production.

Although it is recognized that intensive exercise in general can lead to increase serum uric acid, the potency of specific factors within the exercise-induced profuse sweating in promoting the increase remains unclear. Approximately 30% of the uric acid that is
produced daily is excreted through the biliary and gastrointestinal tract, where it is degraded by gastrointestinal bacteria in a process called uricolysis. The kidneys excrete the remaining 70% (19). It has been shown (9) that men heavily exercising in hot climates may secrete 1 to 2 liters of sweat hourly. In this situation, the urine volumes were smaller and contained higher concentrations of uric acid.

Sweat contains large amounts of electrolytes and several biochemical metabolites of clinical interest such as urea, ammonia and uric acid (15). Profuse sweating leads to losses of these materials. However, a previous study (9) revealed that the concentration of uric acid in sweat was about 24.5 µM, which was only 6.3% of that in serum, and so the amount of uric acid excreted by sweating was rather negligible. It would also be an important factor of hyperuricemia that heavy sweating results in a worked decrease or even standstill of urine production and reduces uric acid excretion.

Hyperuricemia predisposes patients to both gout and nephrolithiasis, but therapy is generally not warranted in the asymptomatic patients (20). Recognizing the risk factors of hyperuricemia, however, provides physicians with an opportunity to advise asymptomatic hyperuricemia patients that they should modify or correct the underlying acquired causes of hyperuricemia.

The purpose of this study was to simulate and determine whether exercise-induced profuse sweating could result in a decrease of uric acid excretion. Sweat, urine and serum specimens were collected during the study period. The results of our study may be applied to reducing the risk of hyperuricemia, and also be useful in prevention of gout.

Materials and Methods

The study design and experimental procedure are illustrated in Fig. 1. These details are described as follow.

Subjects

Thirteen male volunteers who were well-trained badminton players were recruited in this study. The 13 male volunteers were living in Taichung, Taiwan, and these college students who frequently played badminton. The routine training and playing sessions averaged 2 h per day in the afternoon, 5 times per week in the weekdays. The study period for each subject was consecutive seven days. The study period was consecutive 7 days.

Randomization

Thirteen male volunteers

The study period was consecutive 7 days.

Subjects were not engaged in any intense exercise on day 1, day 2, day 6 and day 7. They had routine exercise training between 3:00 to 5:00 P.M. on day 3, day 4 and day 5.

Fig. 1. The study design and experimental procedure.
but the collections of some specimens from those were diverse. Seven subjects with a mean age of 19.9 yr (range = 19 to 22), a body height of 1.73 m (range = 1.68 to 1.78), a body weight of 64.99 kg (range = 53.38 to 74.85), and body mass index of 21.6 kg/m$^2$ (range = 18.9 to 23.9) performed the experiment. In addition to specimens of serum and sweat, we collected more urine specimens on 7 consecutive days from those subjects. In addition, six subjects with a mean age of 19.7 yr (range = 18 to 21), a body height of 1.71 m (range = 1.63 to 1.77), a body weight of 66.28 kg (range = 56.94 to 74.22), and body mass index of 22.6 kg/m$^2$ (range = 19.7 to 24.7) also performed the experiment. In addition, six subjects with a mean age of 19.7 yr (range = 18 to 22), a body height of 1.71 m (range = 1.63 to 1.77), a body weight of 66.28 kg (range = 56.94 to 74.22), and body mass index of 22.6 kg/m$^2$ (range = 19.7 to 24.7) also performed the experiment. In addition, six subjects with a mean age of 19.7 yr (range = 18 to 22), a body height of 1.71 m (range = 1.63 to 1.77), a body weight of 66.28 kg (range = 56.94 to 74.22), and body mass index of 22.6 kg/m$^2$ (range = 19.7 to 24.7) also performed the experiment. In addition, six subjects with a mean age of 19.7 yr (range = 18 to 22), a body height of 1.71 m (range = 1.63 to 1.77), a body weight of 66.28 kg (range = 56.94 to 74.22), and body mass index of 22.6 kg/m$^2$ (range = 19.7 to 24.7) also performed the experiment.

**Experimental Conditions**

The study was conducted in June, 2003. The volunteers were fully informed of the objectives, procedures, and requirements for this study. They gave informed consent for this study, which had been approved by the Institutional Review Board of the Veterans General Hospital, Taipei.

The study period for each subject was consecutive seven days. Diets were prepared from common food lots, weighted, and frozen to provide a constant daily intake representative of that consumed by the average heavy demand players, according to dietary reference intakes recommended by Department of Health, Taiwan. They consumed a self-selected identical constant diet each day, providing 2850 kcal, composed of 107 g protein, 79 g fat, 428 g carbohydrate, and 350 mmol sodium. None of the subjects took diuretics, uricosurics or xanthine oxidase inhibitors in the three month period before the study.

Each subject did not engage in any intense exercise or activity inducing profuse sweat on the first 2 days (the reference days) and the last 2 days of the study period. They accepted the routine training between 3:00 P.M. and 5:00 P.M. during the middle 3 days, which were the most physically exhausting period of the program. The air temperatures during the exercise periods were between 30-35°C, and the relative humidity was 40-60%.

Measurement of body weight and sweat collection were performed in a single rest room that was adjacent to the badminton court. Windows and doors were closed, thus creating a climate chamber in which the temperatures ranged between 32-37°C. We kept wind velocity below 0.1 m/s to minimize heat exchange, and the relative humidity was 30-50% in the room.

**Sweat, Urine and Serum Samples Collection**

Sweat collections from 7 subjects were performed after the routine training on day 3 through day 5 of the study period at about 5:00 P.M. The back and chest of the players were thoroughly washed with deionized water and dried with clean towels before the collection of sweat samples. To facilitate rapid collection of newly produced sweat, we used a plastic collector with dimensions of 15 cm (length) × 9 cm (width) × 2 cm (height) and placed this collector in contact with the skin of the chest and back, letting the sweat drip into the collector. This was used instead of filter paper (12) or a macroduct (23). Five to ten ml of sweat was collected from each player within 5 min. The sweat could be obtained easily in the above-mentioned room immediately after exercise. These samples were placed in clean capped 10 ml plastic tube and kept frozen at -18°C for not more than 3 weeks before analysis.

Urine samples of the 7 volunteers were collected over the same period and commenced at 11:00 A.M. on each of the successive seven study days. The first time of urine collection was 1:00 P.M. every day. Prior to the exercise training each subject collected urine for 4 h on days 3, 4, and 5. Urine samples were collected over each 2-h period until 9:00 P.M., so a total of 10 h urine samples were collected. The purpose of collecting 10 h of urine samples was to prevent interference from the diminution of urine volume after the exercise. Each urine of samples was collected in a 250 ml plastic container, a few drops of toluene were added as a preservative, and it was then stored in a -18°C refrigerator for not more than 3 weeks before analysis. The urine volume of each urine sample was measured and recorded.

Ten ml of venous blood samples of the 7 subjects were drawn on days 2, 4, and 6 of the study period at about 5:00 P.M. The serum samples were collected by centrifuge. Each serum sample was kept frozen at -18°C in capped 10 ml plastic tube for not more than 3 weeks before analysis.

**Body Weight Measurement and Estimated Uric Acid Excretion by Sweat**

Each player’s body weight loss for the 7 subjects was determined by calculating the difference between body weight before and after each training game. The 2-h training session included pre-game training and a 1-h informal game. The players had no fluid refreshments during each training session. Since, they did not urinate during the training courses, we were able to measure weight loss strictly relative to sweating. The accuracy of the platform balance was ±20 gm. This acute weight loss represented pulmonary water vapor
loss and metabolic loss, as well as loss from sweating.

In order to calculate the uric acid excretion in sweat, we corrected the weight of sweat loss, derived from players’ weight loss after the training, by the weight loss of breathing, which we estimated to be 22 gm/h · person (11). Estimated excretion of uric acid through sweating for each training = (mean of uric acid concentrations in sweat) × (body weight loss in a training) / (specific gravity of sweat <1.002>).

Clearance of Urate and Creatinine

Simultaneous clearances of urate and creatinine of six subjects were measured on days 2, 4, and 6 of the study period. On these occasions, the studies were conducted in an air-conditioned room. All clearances were done between 5:00 to 6:00 P.M. on the 3 days. One liter to one and a half liter of water was ingested 15 min prior to clearance test to insure enough urine and make possible the collection of closely-spaced urine samples. The values for each subject were three clearances measured during consecutive collection periods of 20 min each. Blood samples were collected at each midpoint. Except when voiding, the subjects reclined during each procedure. On day 4, the values represented the 10, 30 and 50 min clearance after the training game. In the experiments, glomerular filtration rates were determined by the clearances of endogenous creatinine. Uric acid excretion is expressed as uric acid clearance in order to clarify the relation of changes in uric acid excretion to changes in renal function.

Analytic Methods

Uric acid concentrations in serum, sweat and urine were measured by the uricase-peroxidase method (6). Creatinine concentrations in serum, sweat and urine were assayed using the modified Jaffé method (1). In all instances, particular care was taken to insure adequate mixing of urine before samples were taken for analysis. All measurements were made in triplicate. A detailed description of these analytic methods has been published previously (9).

Statistical Analysis

The data of these experiments were analyzed by repeats measures ANOVA. Analysis of the significance between means was performed by using Shuffe’s procedure. Statistical significance was indicated when \( P < 0.05 \).

Results

Serum Urate Concentrations of the Subjects

<table>
<thead>
<tr>
<th>Subject</th>
<th>Day 2</th>
<th>Day 4</th>
<th>Day 6</th>
</tr>
</thead>
<tbody>
<tr>
<td>A</td>
<td>372</td>
<td>444*</td>
<td>354</td>
</tr>
<tr>
<td>B</td>
<td>324</td>
<td>360</td>
<td>402</td>
</tr>
<tr>
<td>C</td>
<td>462*</td>
<td>480*</td>
<td>420</td>
</tr>
<tr>
<td>D</td>
<td>258</td>
<td>294</td>
<td>246</td>
</tr>
<tr>
<td>E</td>
<td>324</td>
<td>420</td>
<td>276</td>
</tr>
<tr>
<td>F</td>
<td>312</td>
<td>438*</td>
<td>384</td>
</tr>
<tr>
<td>G</td>
<td>300</td>
<td>444*</td>
<td>408</td>
</tr>
<tr>
<td>H</td>
<td>276</td>
<td>342</td>
<td>390</td>
</tr>
<tr>
<td>I</td>
<td>384</td>
<td>372</td>
<td>342</td>
</tr>
<tr>
<td>J</td>
<td>354</td>
<td>414</td>
<td>306</td>
</tr>
<tr>
<td>K</td>
<td>228</td>
<td>276</td>
<td>396</td>
</tr>
<tr>
<td>L</td>
<td>282</td>
<td>294</td>
<td>318</td>
</tr>
<tr>
<td>M</td>
<td>486*</td>
<td>576*</td>
<td>492*</td>
</tr>
</tbody>
</table>

Means ± SEM 336 ± 21 396 ± 24* 364 ± 18
Range 228-486 276-576 246-492

1. The data were analyzed by repeats measures ANOVA and Shuffe’s procedure.
2. Day 2 is the reference day; day 4 is a profuse sweating day; day 6 is a day without profuse sweating.
3. *Significantly different from day 2 (\( P < 0.05 \)).
4. The normal value for serum uric acid concentration is not above 420 µM. The subjects whose serum uric acid is above 420 µM are marked as #.

The individual and the mean serum urate concentrations of the thirteen male volunteers at the same time on the three days during the study period are shown in Table 1. Except for some specimens of collection, as described earlier, the physical characteristics and experimental conditions of the thirteen male volunteers were not different. The mean serum urate concentration of the thirteen male volunteers on day 2 (the reference day) was 336 µM. Two individuals had values of 462 µM and 486 µM, clearly above normal. Mean serum urate levels rose significantly on the day 4, where the concentrations increased by 18.2% than the day 2 (\( P < 0.05 \)). Five individuals had serum urate levels above normal on day 4. The mean serum urate levels fell more on day 6 than day 4, but increased slightly by 8.5% on the day 2. Only one individual had serum urate levels above normal on day 6.

Uric Acid Excretion Amount by Sweat on the Training Days

The mean original body weight and mean body weight loss in the 7 volunteer subjects, before and
after the 3 days of training, are shown in Table 2. At the start of the 3 days training period, the mean body weight was 64.81 ± 2.71 kg; at the end of the training, the mean body weight loss was 2.53 ± 0.16 kg. The mean sweat uric acid concentration and estimated uric acid excretion by sweat on the 3 days of training are also shown in Table 2. We corrected the weight of sweat loss, derived from players’ weight loss after the training, by the weight loss of breathing. The mean sweat uric acid concentration was 19.1 ± 2.2 µM, and estimated mean uric acid excretion by sweat was 46.7 ± 5.1 µmol/day on the 3 training days.

**Table 2. Body weight loss and estimated sweat uric acid excretion of 7 volunteers after 2 h of training game**

<table>
<thead>
<tr>
<th>Study period</th>
<th>Day 3</th>
<th>Day 4</th>
<th>Day 5</th>
<th>Average</th>
</tr>
</thead>
<tbody>
<tr>
<td>Original weight (kg)</td>
<td>64.99 ± 2.74</td>
<td>64.89 ± 2.59</td>
<td>64.56 ± 2.81</td>
<td>64.81 ± 2.71</td>
</tr>
<tr>
<td>Weight loss (kg)</td>
<td>2.64 ± 0.20</td>
<td>2.61 ± 0.19</td>
<td>2.34 ± 0.18</td>
<td>2.53 ± 0.16</td>
</tr>
<tr>
<td>Sweat uric acid</td>
<td>17.9 ± 2.2</td>
<td>20.8 ± 2.5</td>
<td>18.7 ± 3.3</td>
<td>19.1 ± 2.2</td>
</tr>
<tr>
<td>Sweat uric acid excretion</td>
<td>46.6 ± 7.2</td>
<td>52.7 ± 7.2</td>
<td>41.0 ± 5.8</td>
<td>46.7 ± 5.1</td>
</tr>
</tbody>
</table>

1. Values are means ± SEM of 7 subjects.
2. The unit of sweat uric acid is µM.
3. The unit of sweat uric acid excretion is µmol, and the values are estimations. Estimated excretion of uric acid through sweating for each training = (mean of uric acid concentrations in sweat) × (body weight loss in a training) / (specific gravity of sweat <1.002>).

The mean ten hours urinary uric acid excretions of 7 volunteer subjects on the consecutive seven study days and estimated sweat uric acid excretions of the subjects on the training days are presented in Fig. 2. The mean ten hours urinary uric acid excretions on each day of the study days were significantly diverse. Ten hours urinary uric acid excretion on day 4 was less than on days 1 and 2 (P < 0.05). The mean ten hours urinary uric acid excretion on the 3 training days was less 178.5 µmol/day than that on the 2 preceding days, and was less 118.3 µmol/day than that on the 2 subsequent days. The differences were significant (P < 0.05).

We estimated that mean uric acid excretion of 7 volunteers by sweat was 46.7 µmol/day on the 3 training days. The mean uric acid excretion by profuse sweat was only 26.2% or 39.5% of decreased 178.5 µmol/day or 118.3 µmol/day uric acid excretions by ten hours urine on the 3 training days. The mean that ten hours urinary uric acid excretion amount on the 3 training days was 1309.0 µmol/day which, plus 46.7 µmol/day by sweat, was still lower than the mean ten hours urinary uric acid excretion amount on the preceding and subsequent days of the training days (P < 0.05).

The mean daily ten hours urine volumes on the preceding and subsequent days of the training days were compared similarly. The mean daily ten hours urine volume was 680.4 ± 43.3 ml/day on the preceding days of the training days and was 655.7 ± 46.1 ml/day on the subsequent days of the training days. However, the mean daily ten hours urine volume on the training days was 519.0 ± 52.7 ml/day, which was significantly lower, by 23.7% and 20.8%, than those on the preceding and subsequent days of the training days respectively (P < 0.05). Water intake was not recorded.

**The Change of the Clearance of Urate and Creatinine**

The clearance of urate and creatinine of six
volunteers are shown in Table 3. Mean uric acid clearance was 7.5 ml/min on the reference day, and 5.1 ml/min on the training day. The identical depression of filtration rate and uric acid clearance in one hour after the training game on day 4 indicated that decreased glomerular filtration rate could account for the decreased uric acid excretion. In the post-exercise on day 4, the decrease in degree of glomerular filtration rate was 16.4% of the control day. However, the decreased degree of uric acid clearance was 31.6%, which was more than the decreased degree of glomerular filtration rate.

The mean ratios of clearance of uric acid to creatinine of the 6 volunteer subjects on the three distinct days are presented in Fig. 3. The ratio of clearance of uric acid to creatinine was 6.6% on the reference day, which was a significant decrease of 5.4% from the training day ($P < 0.05$). The ratio of clearance of uric acid to creatinine was also 6.6% on day 6, which was significantly larger than the training day ($P < 0.05$). In the post-exercise on day 4, moreover, glomerular filtration rate returned to normal within 20-40 min, but uric acid clearance remained depressed for at least 40 min and was still clearly below 10.5% within 40-60 min compared to day 2.

### Discussion

The results of this study provide convincing evidence that profuse sweating exercise reduces uric acid excretion after exercise for at least one hour. Furthermore, the type of the exercise elevates the level of uric acid in serum after the exercise.

The increasing serum uric acid noted during the profuse sweating exercise can be explained at least, in part, by decreased excretion. Serum uric acid concentration is closely associated with the rate of removal of uric acid, most notably by the kidney. Uric acid excretion and clearance are increased at high rates of urine flow in normal subjects (3, 5). And an antidiuretic effect is observed during intense exercise. Changes in urine flow are dependent on the plasma antidiuretic hormone levels, which are increased by intense exercise (13). In this current, ten hours urine volume on the training days was significantly decreased 20.0% from the preceding and subsequent training days. The mean sweat uric acid concentration was 19.1 $\mu$M, and estimated mean uric acid excretion by sweat was 46.7 $\mu$mol/day in the 3 training days. A large sweat volume secreted during the training days, with a corresponding diminution of urine volume was observed. An ineffective means for elimination of uric acid by sweating caused a reduction of the ex-
cretion of uric acid because of the resulting diminution in urinary output.

Exercise induces profound changes in the renal haemodynamics. Effective renal plasma flow is reduced during exercise, which is related to the intensity of exercise and renal blood flow may fall to 25% of the resting value when strenuous work is performed (13). The reduction of renal blood flow during exercise produces a concomitant effect on the glomerular filtration rate, though the latter decreases less than the former during exertion. However, the degree of hydration has an important influence on the glomerular filtration rate. Reduction in effective renal plasma flow and glomerular filtration rate induced during exercise would be expected to reduce uric acid clearance (10). In this study, the decreased degree of glomerular filtration rate in the post-exercise was 16.4% less than the reference day. However, our study also showed that the decreased degree of uric acid clearance was 31.6%. Since uric acid clearance was depressed to a much greater degree than filtration rate, it is reasonable to assume that some of this decrease was due to other factors.

Urate excretion by the kidney has been characterized as a three-component system of filtration, reabsorption, and secretion, and also as a four-component system in which a post-secretory reabsorptive site is added to the three-component system (4). Glomerular ultrafiltration of uric acid in humans is believed to be complete, with urate concentrations in the glomerular fluid being the same as those in plasma. As in the above-mentioned, uric acid clearance was depressed to a much greater degree than was filtration rate after the exercise. This would suggest that a putative pathophysiological mechanism, which either increased reabsorption or decreased secretion of uric acid or both, would occur during and after the exercise on training days.

The normal range of Na⁺ concentrations in sweat is between 10 to 20 mM at a relatively low sweat rate, but it can reach 100 mM near the maximal sweat rate (16). The mean concentration of Na⁺ was 66.3 mM in our previous study (9), and in the current study the estimated mean Na⁺ excretion by sweat was 164.9 mmol during the exercise on the training days. Moreover, estimated Na⁺ loss from the sweat of soccer players in 1-h game was found to be 82.4 mM in another study (11). Thus the Na⁺ excretion by profuse sweat during the vigorous exercise would be meaningful. The kidneys could enhance the reabsorption of Na⁺ to maintain electrolyte homeostasis. Increased aldosterone production helps the body to maintain sodium by increasing its reabsorption from the filtered tubular fluid (13). It is biologically plausible that increased sodium reabsorption at sites of the nephron proximal to the distal tubule could also lead to more uric acid being reabsorbed, and as a consequence, cause higher serum uric acid levels (2).

Serum uric acid concentrations are also closely associated with the rate of production of uric acid. As a second consideration, hyperuricemia could be the consequence of increased uric acid production. Overproduction of uric acid in men might be related to depressed concentration of ATP within muscle cells during intense exercise. Decreased cellular concentration of ATP in the liver activates AMP-deaminase and 5-nucleotidase (24), leading to formation of inosinic acid and inosine monophosphate. These substances in turn are rapidly converted to hypoxanthine, xanthine, and uric acid. Such liberation of adenine nucleotides from skeletal muscle could well provide a substrate for increased urate production in the liver. That these mechanisms might be responsible for hyperuricemia is supported by observations that hyperuricemia is apparent immediately on completion of exercise and to such an extent that simple inhibition of urate excretion would not seem to provide a plausible explanation (17).

On the basis of these results, the form of profuse sweating induced by exercise certainly leads to increased serum uric acid, the prevention of hyperuricemia and gout in athletes requires consideration for modifications of provoking factors. Intense exercise and longer period of training should be restricted. Athletes also should restrain their exercise in hot environments. Life styles such as alcohol consumption and high-purine diets need to be controlled. Moreover, athletes need to drink enough fluids to prevent dehydration and maintain adequate urinary output. Takanishi et al. analyzed the effects of fluid ingestion and its composition on uric acid metabolism after exercise showed that the sports drinks ingestion can increase the efficiency of recovery from high serum uric acid after exercise (22). Gonzalez-Alonso et al. have confirmed that a dilute carbohydrate-electrolyte solution (per liter; 60 g carbohydrates, 20 mmol Na⁺, 3 mmol K⁺) is more effective in promoting post-exercise re-hydration than either plain water or a low-electrolyte diet cola (7). Men taking this would increase urine volume and uric acid excretion.

In summary, the form of profuse sweating exercise results in a decrease of uric acid excretion and leads to rise in serum uric acid after the exercise. The reduction in effective renal plasma flow and heavy sweat sodium loss during profuse sweating exercise could be the determining factors for the decrease of urinary uric acid excretion.

The restriction of this study is that it is a short-term study, unable to determine if regular exercise will produce a long-term alteration in urate excretion or whether a new steady-state equilibrium occurs with regular exercise. But the data of this study pro-
vides inferential evidence for the pathogeny of hyperuricemia after profuse sweating exercise.

Acknowledgments

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References