Effects of Uric Acid on Exercise-induced Oxidative Stress

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Abstract

We studied effects of uric acid on exercise-induced oxidative stress in humans based on a hypothesis that uric acid acts as an antioxidant to prevent from exercise-induced oxidative stress. Relation between uric acid level in plasma and increase of thiobarbituric acid reactive substance (TBARS) after the cycle ergometer exercise was examined. Thiobarbituric acid reactive substance in plasma increased after the ergometer exercise. High uric acid in plasma did not result in low increase of TBARS. We did not obtain the evidence that uric acid prevents from exercise-induced oxidative stress.

Key words Uric acid, Antioxidant, Exercise, Malonaldehyde, Thiobarbituric acid reactive substance

Introduction

Oxygen free radical theory postulates that oxygen free radicals are produced in the course of normal energy metabolism. Oxygen free radicals can elicit widespread damage to cell constituents such as membrane lipids, mitochondrial enzymes, and DNA. During evolution living organisms have developed antioxidant systems to cope with the deleterious effects of oxygen free radicals. The antioxidant systems include chemical compounds capable of scavenging reactive oxygens, e.g., vitamins E and C, \( \beta \)-carotene, and
glutathione, as well as a series of enzymes catalyzing reactive oxygens.

Exercise influences oxidative metabolism and increases the generation of oxygen free radicals and lipid peroxidation (Alessio 1993; Davies et al. 1982; Jenkins 1988; Lovlin et al. 1987; Sjodin et al. 1990). The magnitude of oxidative damage occurring after exercise is dependent on the dynamic balance of antioxidants (Gohil et al. 1986; Kanter et al. 1993; Machlin and Bendich 1987; Meydani et al. 1993; Packer 1984; Quintanilha 1984; Sumida et al. 1989; Tappel and Dillard 1981). The supplementation of vitamin E reduced the oxidative stress and lipid peroxidation induced by exercise (Dillard et al. 1978; Meydani et al. 1993; Simon-Schnass and Pabst 1988; Sumida et al. 1989; Tappel and Dillard 1981). Vitamin E deficiency was associated with increased lipid peroxidation during exercise (Packer 1984; Quintanilha 1984).

Ames et al. (1981) and Proctor (1970) proposed that uric acid may be an important antioxidant in humans. This hypothesis is supported by the ability of uric acid to scavenge hydroxyl radicals (Howell and Wyngaarden 1960), singlet oxygen (Kellogg and Fridovich 1977), and oxo-heme oxidants (Howell and Wyngaarden 1960). Uric acid protected erythrocyte membranes from peroxidation by t-butyl hydroperoxide (Smith and Lawing 1983). The antioxidative activity of uric acid was suggested also in vivo (Ames 1989). However, antioxidative properties of uric acid have not been discussed enough in a physiological context in humans. Plasma uric acid concentration is known to increase after exercise and be kept at considerably high level as shown following three reports. First, plasma uric acid level rose from a pre-run value of 267 mmol/l to peak value of 431 mmol/l at 45 min following the 800 m-run. The uric acid concentration had not returned to normal at 10 h following the run (Westing et al. 1989). Secondly, a progressive increase of 40% was observed on day 1 in plasma uric acid
concentration for the subjects who cycled the exercise at 120% VO₂max for 1 min followed by 4 min recovery until fatigue or until 24 repetitions. On day 2, pre-exercise values remained elevated over day 1 and showed a further 23% increase with exercise (Green et al. 1988). Thirdly, plasma uric acid concentration reached to a peak at 2 h and still remained 9.9% highre level over a pre-exercise value at 24 h after the exhaustive test with cycle ergometer exercise (Ito et al. 1984).

The increase of uric acid after exercise may be a protective response to the exercise-induced oxidative stress (Duthie et al. 1991; Green and Fraser 1988; Westing et al. 1989; Maxwell et al. 1993). Indeed, antioxidative vitamins C and E were reported to rise after exercise (Duthie et al. 1991; Gleeson et al. 1987; Maxwell et al. 1993).

We study here antioxidative properties of uric acid in humans. If uric acid acts as an antioxidant in humans, uric acid could reduce exercise-induced lipid peroxidation. We measured thiobarbituric acid reactive substance (TBARS) in plasma as an indicator of lipid peroxidation and discussed the correlation between plasma uric acid level and the increase of TBARS after the cycle ergometer exercise.

**Materials and Methods**

Sixteen healthy male students aged 15-17 years were recruited into the study. They were divided two groups of athlete and non-athlete. Athlete group was composed of road cyclists, who maintained their physical activities. Non-athlete group was composed of ordinary students, who took no physical training. All the subjects gave their consent to participate the program after being informed of the nature and risks involved in the test procedures. They all were non-smokers without unusual dietary habits. None of the subjects routinely took vitamin supplements. Physical
characteristics of the subjects are shown in Table 1.

Table 1 Characteristics of subjects

<table>
<thead>
<tr>
<th></th>
<th>Athlete (n=8)</th>
<th>Non-athlete (n=8)</th>
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</thead>
<tbody>
<tr>
<td>Age (yr)</td>
<td>16.4 ± 0.3</td>
<td>16.8 ± 0.4</td>
</tr>
<tr>
<td>Height (cm)</td>
<td>169.2 ± 1.8</td>
<td>168.3 ± 1.8</td>
</tr>
<tr>
<td>Weight (kg)</td>
<td>64.4 ± 1.5</td>
<td>57.6 ± 1.9*</td>
</tr>
<tr>
<td>Body fat (%)</td>
<td>14.9 ± 0.9</td>
<td>11.3 ± 1.2*</td>
</tr>
<tr>
<td>( \dot{V}O_2 \text{max} ) (ml/kg/min)</td>
<td>57.8 ± 2.2</td>
<td>48.1 ± 1.6***</td>
</tr>
</tbody>
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Values are mean ± SE,  *: P<0.05,  ***: P<0.001,  \( \dot{V}O_2 \text{max} \): maximum oxygen consumption

The exercise was performed as a maximum oxygen consumption (\( \dot{V}O_2 \text{max} \)) test on a cycle ergometer. Heparinized blood samples 10ml each were collected from an arm vein before and after the exercise. Plasma was separated from blood sample by centrifugation and aliquots were stored under -80°C. Uric acid in plasma was measured by an automated method based on the uricase-peroxidase system. Thiobarbituric acid reactive substance (TBARS) was assayed according to the method of Uchiyama et al. (1987) with a slight modification. The concentration of TBARS was calculated as malonaldehyde (MDA) equivalent using the MDA molar extinction coefficient of 153,000 at 535 nm (Esterbauer et al. 1984 ). All parameters after the exercise were corrected for changes in plasma volume due to shifts of body water. Haemoglobin concentrations were used for estimation of changes in plasma volume.

**Results and Discussion**

Athlete group showed significantly higher level of plasma uric acid
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than non-athlete group (Fig. 1). This result was accordant with other reports (Duthie et al. 1991; Nishioka et al. 1977). After the exercise uric acid level did not change for athlete group but decreased for non-athlete group (Fig. 1). It was reported that plasma uric acid level increased after

![Uric Acid Level Graph](image)

**Fig. 1** Uric acid level in plasma before and after the ergometer exercise. Values are means ± SE. ns: not significant, **: P<0.01, ***: P<0.001.

1-2 hours of exhaustive exercise on a cycle ergometer though the increase was little at 3 min after the exercise (Ito and Ikawa 1974; Ito et al. 1984). In the present study uric acid was measured immediately after the exercise. Then the increase of uric acid level was not significant for athlete group. However, it is not clear why uric acid level decreased after the exercise for non-athlete group.

Concentration of TBARS in plasma increased significantly after the exercise for both groups (Fig. 2) as a result of increased lipid peroxidation. The increases were 28 % for athlete group and 15 % for non-athlete group.
The magnitude of the increase of TBARS approximates the values appeared in the literature cited (Braun et al. 1991; Kanter et al. 1993; Kanter et al. 1988; Lovlin et al. 1987). The increase of TBARS is considered to be due to oxidative stress during the exercise. There was no significant difference in the increase of TBARS between two groups (Fig. 2), though the increase of athlete group was slightly higher. The increase of TBARS was divided by oxygen consumption per body weight during the exercise. The increases of TBARS per oxygen consumption per body weight were almost the same for two groups (Fig. 3). Athlete group demonstrated higher level of plasma uric acid but did not have lower increase of TBARS after the ergometer exercise.

Uric acid is a putative antioxidant in vivo (Ames et al. 1981; Dillard et al. 1978; Howell and Wyngaarden 1960; Proctor 1970; Simon-Schnass and
In our study the subjects with higher uric acid level did not show lower increase of TBARS after the ergometer exercise. This result suggests that uric acid is not a main protective factor against exercise-induced oxidative stress.

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References


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