SHORT COMMUNICATION

Plasma uric acid concentration related to the urinary excretion of aldosterone and of electrolytes in normal subjects

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Summary

1. The relations between the concentration of plasma uric acid and urinary excretion of aldosterone, sodium and potassium, were studied in ten healthy males on a diet containing 160 mmol of sodium and 90 mmol of potassium per day.

2. Plasma uric acid correlated positively with aldosterone excretion and this correlation was statistically independent of sodium and potassium excretion.

3. Plasma uric acid correlated positively with potassium excretion and negatively with the urinary sodium/potassium ratio. There was no significant simple correlation with sodium excretion but the partial correlation of plasma uric acid and sodium excretion was negative and significant when excretion of aldosterone and potassium were held constant.

Key words: aldosterone, kaliuresis, Na/K ratio, natriuresis, uric acid, urinary excretion.

Introduction

Variation in the response of normal subjects to single doses of frusemide can be related in part to differences in plasma uric acid concentration before treatment (Ramsay, Tidd, Auty, Levine & Branch, 1975b). Subjects with a higher plasma uric acid excreted more potassium and had a lower urinary Na/K ratio during the diuretic response. After a dose of ethacrynic acid the potassium excretion and the urinary Na/K ratio correlate in similar fashion with the aldosterone secretion rate measured before treatment (Espiner, Tucci, Jagger, Pauk & Lauler, 1967) and on this basis we considered that the aldosterone secretion rate and plasma uric acid might correlate positively in normal subjects. Such a correlation could explain a relationship between plasma uric acid and the Na/K ratio in urine after single doses of spironolactone (Ramsay, Hessian & Tidd, 1975a). We have therefore studied the relations between plasma uric acid, aldosterone excretion and urinary excretion of sodium and potassium in healthy subjects.

Methods

The subjects were studied during the baseline part of a study comparing the diuretics frusemide and bumetanide. Ten healthy men aged 20–25 years who had consented to the procedure were studied during two 24 h periods separated by an interval of 1 week. They were given a single dose of one of the diuretics [frusemide 121 μmol (40 mg) or bumetanide 2.74 μmol (1 mg)] immediately after the first study period. There was no trend suggesting that diuretic administration had influenced the results during the second period. During each 24 h period, the subjects consumed a diet containing 160 mmol of sodium and 90 mmol of potassium. Urine passed in the 24 h (08.00–08.00 hours) was collected and venous blood was taken at the end of the collection period (08.00 hours) for measurement of plasma uric acid. The subjects
were ambulant and took no medication other than the diuretics. Alcohol was prohibited during the period of urine collections.

Uric acid was measured by a colorimetric method (Nishi, 1967) and sodium and potassium by flame photometry with lithium as internal standard. Urinary aldosterone (total acid-labile conjugate) was measured after adjusting the sample to pH 1 with dilute hydrochloric acid, followed by hydrolysis at room temperature for 18 h.[^H]Aldosterone was added, followed by extraction twice with methylene dichloride, rapid washing with sodium carbonate (1 mol/l) and then with water. The extract was evaporated to dryness, dissolved in chloroform-methanol (1:1, v/v) and purified by paper partition chromatography with a modification of the system of Eberlein & Bongiovanni (1955). Aldosterone was measured by radioimmunoassay (Mayes, Furuyama, Kem & Nugent, 1970). Results were corrected individually for recovery, which was between 72 and 95%. Product-moment correlations were calculated with the two sets of results for each subject treated as independent observations \( (n=20) \) and also using the mean of two observations for each subject \( (n=10) \). The results were similar by either method, and those for \( n=20 \) are quoted. Partial correlations were obtained by backward stepwise multiple regression (Armitage, 1971).

### Results

There was a significant positive correlation between plasma uric acid and aldosterone excretion \( (r=+0.53, P<0.02, n=20) \). Plasma uric acid also correlated positively with the 24 h potassium excretion \( (r=+0.61, P<0.005, n=20) \) and negatively with the urine Na/K ratio \( (r=-0.57, P<0.01, n=20) \). There was no significant correlation with sodium excretion \( (r=-0.13, P>0.1, n=20) \).

In multiple regression analysis with plasma uric acid as the dependent variable, potassium excretion \( (P<0.001) \) and aldosterone excretion \( (P<0.05) \) remained significantly related to plasma uric acid as independent variables. In addition, there was a negative relationship between plasma uric acid and sodium excretion, which was significant at \( P<0.05 \). Correlations of aldosterone excretion with sodium excretion, potassium excretion and the Na/K ratio were all weak and non-significant (Table 1).

### Discussion

The urine electrolyte excretion in normal subjects after single doses of frusemide (Ramsay et al., 1975b) or spironolactone (Ramsay et al., 1975a) was related to the concentration of plasma uric acid before treatment. In each instance the urine Na/K ratio was the parameter of response which showed the highest (negative) correlation with plasma uric acid. From consideration of factors which might influence this response to two drugs with such disparate mechanisms of action, the aldosterone secretion rate seemed a probable candidate. In the present study, there was a positive correlation between aldosterone excretion and plasma uric acid concentration, and since aldosterone secretion correlates moderately well with the aldosterone secretion rate in health (Laragh, Sealey & Sommers, 1966), the results support the initial postulate.

Plasma uric acid also correlated positively with potassium excretion, negatively with the urine Na/K ratio, but not with sodium excretion. A significant negative relationship between plasma uric acid and sodium excretion emerged when potassium excretion and aldosterone excretion were 'held constant' statistically. In a separate study we have also observed a significant negative simple correlation between plasma uric acid and 24 h sodium excretion in healthy subjects.

### Table 1. Correlation coefficients between plasma uric acid, 24 h urinary excretion of aldosterone, sodium and potassium, and the Na/K ratio

Results were treated as twenty independent observations \( (n=20) \).

<table>
<thead>
<tr>
<th></th>
<th>Aldosterone excretion</th>
<th>Sodium excretion</th>
<th>Potassium excretion</th>
<th>Na/K ratio</th>
</tr>
</thead>
<tbody>
<tr>
<td>Plasma uric acid</td>
<td>+0.53 ((P&lt;0.02))</td>
<td>-0.13</td>
<td>+0.61 ((P&lt;0.005))</td>
<td>-0.57 ((P&lt;0.01))</td>
</tr>
<tr>
<td>Aldosterone excretion</td>
<td>-</td>
<td>-0.11</td>
<td>+0.21</td>
<td>-0.26</td>
</tr>
</tbody>
</table>
There may also be a more direct link between aldosterone and plasma uric acid, independent of electrolyte status, and the finding in the present study that the correlation of plasma uric acid with aldosterone excretion was statistically independent of sodium and potassium excretion is compatible with such an interpretation. Griebel et al. (1962) have suggested that mineralocorticoids may have a direct role in producing hyperuricaemia during diuretic therapy, but to our knowledge this has not been studied further.

Our findings suggest that dietary intake of sodium and potassium could have a role in determining inter-subject differences in plasma uric acid concentration in health, and that possible influences of aldosterone or angiotensin II on uric acid homeostasis should be further evaluated.

References


