A RELATIONSHIP BETWEEN PLASMA URIC ACID CONCENTRATION AND THE APPARENT RESPONSE TO FRUSEMIDE IN NORMAL SUBJECTS

A negative correlation has been found between the apparent response to single doses of fludrocortisone plus spironolactone (as measured by the urinary $\log_{10}$ Na/K ratio) and the level of plasma uric acid prior to treatment in normal subjects (Ramsay, Hessian & Tidd, 1975). We report here the results of a preliminary study to determine whether there is a relationship between the concentration of plasma uric acid in normal

subjects and the urinary excretion of electrolytes in response to an oral dose of frusemide.

Six healthy males aged 20-25 years consented to the study and the protocol was approved by the hospital ethical committee. A single measurement of plasma uric acid concentration was taken, and 1 week later each subject received a single oral dose of frusemide (80 mg) (Lasix, Hoechst) at 18.00 h following a 6 h fast. All urine passed in the

Figure 1 Correlations between the level of plasma uric acid 1 week before treatment and the urinary potassium excretion ($r = +0.89$; $P < 0.02$) and Na/K ratio ($r = -0.94$, $P < 0.01$) from 0-5 h after oral frusemide (80 mg) in six healthy subjects.

Table 1 Correlations of plasma uric acid concentration with urine responses between 0-5 h after frusemide (80 mg) administered orally to six healthy subjects.

Subject	Plasma uric acid (mmol/l)	Volume (ml)	Sodium (mmol)	Potassium (mmol)	Na/K ratio
1	0.39	2540	188	44	4.27
2	0.42	1925	231	68	3.40
3	0.40	1960	259	45	5.76
4	0.36	2055	236	29	8.14
5	0.27	1660	179	15	11.93
6	0.35	1975	239	36	6.64
<i>r</i>	—	+0.53	+0.57	+0.89	-0.94
<i>P</i>	—	>0.1	>0.1	<0.02	<0.01

subsequent 5 h was collected under supervision. A meal containing sodium (10 mmol) and potassium (40 mmol) was taken 2 h after frusemide, and free intake of water was allowed. Plasma uric acid was measured by an automated phosphotungstate colorimetric method (Nishi, 1967) and concentrations of sodium and potassium were measured by flame photometry using lithium as the internal standard.

There was a significant positive correlation between the level of plasma uric acid 1 week before treatment and the urinary excretion of potassium following frusemide ($r = +0.89$, $P < 0.02$, Figure 1) and a negative correlation between plasma uric acid and the urinary Na/K ratio following frusemide ($r = -0.94$, $P < 0.01$, Figure 1). Correlations between plasma uric acid and the urinary volume and sodium excretion were not significant (Table 1).

It is worthy of note that the intersubject differences in potassium excretion following frusemide were large (range 15-68 mmol/5 h) and that approximately 80% of this variation could be accounted for in terms of the plasma uric acid level prior to treatment.

The observation that the level of plasma uric acid before treatment can be related to the apparent responses to both spironolactone (Ramsay *et al.*, 1975) and to frusemide suggests

that the phenomenon is unlikely to be related specifically to diuretics, but rather may reflect a relationship between electrolyte excretion and uric acid homeostasis in normal subjects. Further study is required to elucidate the mechanism of these observations and to determine whether they have any therapeutic implications.

L.E. RAMSAY & M.J. TIDD

Division of Scientific Affairs, G.D. Searle and Co. Ltd., Lane End Road, High Wycombe, Bucks HP12 4HL

R.M. AUTY, D. LEVINE & R.A. BRANCH

Department of Clinical Pharmacology, Bristol Royal Infirmary, Bristol BS2 8HW

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PUPIL RESPONSIVENESS TO TYRAMINE IN DEPRESSED PATIENTS TREATED WITH AMITRIPTYLINE

Tyramine is an effective pupil dilator. When instilled locally, tyramine (120 μ g) causes a 30% increase in the pupil diameter within 1 hour; a larger dose (500 μ g) causes a dilatation of up to 90% (Palm, Fengler, Güllner, Planz, Quiring, May, Helmstaedt, Lammer, Moon & Holler, 1971). As tyramine is an indirectly acting sympathomimetic amine (Burn & Rand, 1958), the pupil dilation is presumably due to the action of noradrenaline released by tyramine from sympathetic nerve terminals. It has been reported that tricyclic antidepressants block the uptake of tyramine into sympathetically innervated tissues (Brodie, Costa, Groppetti & Matsumoto, 1968), and thus prevent the pharmacological actions of tyramine. The abolition of the pressor response to tyramine has been used in humans as an indicator of the effect of tricyclic antidepressants on peripheral uptake mechanisms (Freyschuss, Sjöqvist & Tuck, 1970).

There have been no reports, however, how tricyclic antidepressants modify the responsiveness of the pupils to tyramine. We wish to report here some preliminary work which shows how pupil responsiveness to tyramine changes during the course of treatment with amitriptyline.

Three female patients (aged 23, 49 and 56 years, respectively) were included in this study. All three of them were diagnosed, on the basis of the psychiatric examination prior to their admission, as suffering from depressive illness. After their admission to hospital, they received no medication for the first two days. On each of these days the base-line (pretreatment) pupil response was assessed (see below), and the symptoms of depressive illness were rated using the Hamilton Rating Scale (Hamilton, 1960). On the third day, antidepressant drug treatment started (amitriptyline (Lentizol), 100 mg *nocte*). Pupil