RELATIONSHIPS BETWEEN CALCIUM AND OXALIC ACID INTAKE IN THE DIET AND THEIR EXCRETION IN THE URINE OF NORMAL AND RENAL-STONE-FORMING SUBJECTS

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(Received 11 February 1972)

SUMMARY

1. The short-term effects of different intakes of calcium and oxalic acid on the urinary excretion of these substances was studied in eight normal men and eight men with a history of calcium-containing renal stones.

2. The effect of dietary oxalate on urine oxalate depended partly upon the calcium intake. Thus, on a normal calcium intake an increase in oxalate intake caused an increase in oxalate excretion that corresponded to 3.6% of the additional dietary oxalate; on a low calcium diet, however, the increase corresponded to 8.1%.

3. A decrease in daily calcium intake from 1000 to 250 mg caused a fall in calcium excretion averaging 150 mg/day in the patients and 60 mg/day in the controls but this was accompanied by average rises of 10 and 7 mg/day respectively in oxalate excretion, with the result that the calcium oxalate activity products remained almost unchanged.

4. A decrease in oxalate as well as calcium intake resulted in a fall in calcium excretion that was not accompanied by a rise in oxalate excretion, and there was a statistically significant fall in the calcium oxalate activity product in both the patients and normal subjects.

Key words: urinary calcium, urinary oxalic acid, renal stones, dietary calcium, dietary oxalic acid.

Robertson, Peacock & Nordin (1968, 1971) have shown that both normal and stone-forming urines are commonly supersaturated with respect to calcium oxalate but the mean level of supersaturation is significantly higher in patients with frequently-recurring calcium stones than in normal subjects. These results support the view that calcium stone formation is due primarily to oversaturation of urine with calcium oxalate.

The higher degree of saturation of stone-forming urines is due primarily to higher concentrations of total and ionized calcium (Robertson et al., 1971; Hodgkinson, Marshall & Cochran, 1971), and this in turn can be attributed in most cases to increased calcium absorption (Peacock)

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An appreciable decrease in urine calcium concentration can be achieved by decreasing the dietary intake of calcium, but unfortunately this diet tends to raise urine oxalate (Hodgkinson, 1958; Zarembski & Hodgkinson, 1969; Nordin, Hodgkinson, Peacock & Robertson, 1971). This undesirable effect might be avoided by giving the patients a low calcium–low oxalate diet. In the present study we have examined the effects of high and low calcium and oxalate intakes on the urinary excretion of calcium and oxalic acid and on the calcium oxalate activity product.

**METHODS**

Observations were made on eight male patients with a history of calcium-containing renal stones and eight normal men of similar age and body weight (Table 1). The patients had no evidence of urinary tract infection or of a metabolic disorder such as primary hyperparathyroidism or renal tubular acidosis, although some had increased urinary calcium excretions (>275 mg/24 h for women, and >300 mg/24 h for men).

**TABLE 1. Details of subjects studied**

<table>
<thead>
<tr>
<th>Age (years)</th>
<th>Body weight (kg)</th>
<th>No. of incidents* and site</th>
<th>Composition of stones</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patients</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>V.B.</td>
<td>36</td>
<td>85</td>
<td>2 (left side), 2 (right side)</td>
</tr>
<tr>
<td>A.Mou.</td>
<td>39</td>
<td>65</td>
<td>6 (left side), 3 (right side)</td>
</tr>
<tr>
<td>K.S.</td>
<td>34</td>
<td>80</td>
<td>2 (left side), 1 (right side)</td>
</tr>
<tr>
<td>R.P.</td>
<td>57</td>
<td>85</td>
<td>1 (right side)</td>
</tr>
<tr>
<td>N.T.</td>
<td>42</td>
<td>84</td>
<td>7 (left side)</td>
</tr>
<tr>
<td>E.V.</td>
<td>43</td>
<td>68</td>
<td>Many (bilateral)</td>
</tr>
<tr>
<td>J.P.</td>
<td>32</td>
<td>70</td>
<td>Many (bilateral)</td>
</tr>
<tr>
<td>A.Mor.</td>
<td>46</td>
<td>90</td>
<td>2 (left side)</td>
</tr>
<tr>
<td>Mean</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Controls</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>B.B.</td>
<td>45</td>
<td>76</td>
<td>—</td>
</tr>
<tr>
<td>W.B.</td>
<td>57</td>
<td>97</td>
<td>—</td>
</tr>
<tr>
<td>J.H.</td>
<td>62</td>
<td>77</td>
<td>—</td>
</tr>
<tr>
<td>L.S.</td>
<td>46</td>
<td>68</td>
<td>—</td>
</tr>
<tr>
<td>R.M.</td>
<td>28</td>
<td>73</td>
<td>—</td>
</tr>
<tr>
<td>D.A.</td>
<td>25</td>
<td>100</td>
<td>—</td>
</tr>
<tr>
<td>J.B.D.</td>
<td>42</td>
<td>75</td>
<td>—</td>
</tr>
<tr>
<td>A.H.</td>
<td>48</td>
<td>70</td>
<td>—</td>
</tr>
<tr>
<td>Mean</td>
<td>44</td>
<td>79</td>
<td>—</td>
</tr>
</tbody>
</table>

* As defined by Williams (1963).
† Mixed calcium oxalate–calcium phosphate stones.

Each patient and control subject received a constant diet containing known amounts of calcium and oxalic acid for a period of 16 days, as follows:

days 1–4, low calcium–low oxalate diet (diet A, 250 mg of calcium, 50 mg of oxalate daily);
Calcium and oxalic acid in diet and urine

days 5–8, low calcium–normal oxalate diet (i.e. diet A+ 150 mg of oxalate daily);
days 9–12, normal calcium–low oxalate diet (diet B, 1000 mg of calcium, 50 mg of oxalate
daily);
days 13–16, normal calcium–normal oxalate diet (i.e. diet B+150 mg of oxalate daily).
The 150 mg of oxalate in the normal oxalate diet was taken as 10 ml of sodium oxalate (7.5 g/l)
three times daily with meals.

The 24 h urine samples were collected daily for 16 days in plastic containers to which had
been added 1 ml of 20% w/v chlorhexidine dihydrochloride (Hibitane). The volume of the
urine sample was determined and after determining the pH, 1 ml of conc. HCl was added for
each 100 ml of urine volume to dissolve any crystals of calcium salts that might be present.

Calcium and creatinine were determined by automatic colorimetry (Technicon Auto-
Analyzer Methods N-3b and N-11b respectively). Oxalic acid was determined by an improved
colorimetric method, and expressed as the anhydrous acid (Hodgkinson & Williams, 1972).

Calcium oxalate activity products were calculated for the urines collected on day 3 of each
4-day regime, using the method described by Robertson et al. (1968) and Robertson (1969).
This calculation takes into account the urine pH, ionic strength and the various soluble
complexes between the ionizable components of urine. For this purpose the following ad-
ditional urinary constituents were measured: inorganic phosphate by automatic colorimetry
(Technicon AutoAnalyzer Method N-4b), sodium and potassium by automatic flame photo-
metry (Technicon AutoAnalyzer Method N-20b), magnesium by atomic absorption spectro-
photometry (Dawson & Heaton, 1961); chloride by coulometric titration using an EEL
chloride meter (Evans Electroselectenium Ltd, Halstead, Essex, U.K.), ammonia by a colorimetric
procedure (Chaney & Marbach, 1962) and inorganic sulphate by a turbidimetric method
(Berglund & Sörbo, 1960). Citrate was determined colorimetrically by the method of Grun-
baum & Pace (1970), modified so that the extinction of the coloured product could be read in a
flow-through cell (Pye-Unicam Autocell accessory SP 625). This involved the following
changes in the procedure. To 10-ml stoppered glass test tubes were added 0.5 ml of water,
citric acid standards (10, 30 and 50 mg/100 ml) or urine samples, followed by 0.5 ml of 9 M-
H₂SO₄ and, after mixing, 0.2 ml of 1 M-KBr. After further mixing 1 ml of saturated KMnO₄
solution was added and the contents of the tube were mixed thoroughly with a Vortex mixer.
After being left for 5 min the tubes were cooled in ice water and decolorized with 6% H₂O₂.
The n-heptane (1.3 ml) was added and the stoppered tubes were placed in a mechanical
shaker for 15 min. A portion (1 ml) of the upper (heptane) layer was then transferred to a
fresh tube and 5 ml of thiourea–borax reagent (5 g of thiourea and 2 g of borax/100 ml)
was added. The tubes were mixed for a further 15 min on a mechanical shaker. The E₄₄₅ of the
yellow aqueous (lower) layer was measured in a Pye Unicam SP.600 spectrophotometer fitted
with an SP 625 Autocell accessory.

RESULTS

Urine composition in relation to diet

The urine volume, pH, creatinine, calcium and oxalic acid values for each patient and con-
trol subject are shown in Tables 2 and 3, the values for each subject being the mean of four
24 h collections. The mean values for each group on the four different regimes are also shown,
Although the patients and controls received a constant fluid intake of 1500 ml/day there were considerable variations in daily urine volumes. These variations appeared to be due in part to changes in the ambient temperature.
The urine pH of any one individual remained relatively constant on the different diets but there was some variation between individuals and the mean value on each diet was consistently higher in the patients compared with the controls. This difference was significant on
the normal calcium-normal oxalate diet ($P<0.01$) but not on the remaining three diets ($P>0.05$).

The average creatinine excretion was slightly higher in the controls compared with the patients, possibly reflecting the greater physical activity of the controls during the period of the test. Creatinine excretion was also slightly higher on the low calcium–normal oxalate diet than on the other diets and this applied to both patients and controls. However, none of these differences in body weight or creatinine excretion was statistically significant.

The variations in mean calcium and oxalic acid excretion on the different diets are shown in Fig. 1.

![Diagram of Fig. 1. Variations in mean calcium and oxalic acid excretion with diet. The values were measured in eight normal subjects (○, □, Δ, ▽) and eight patients (●, ■, △, ▼) on four diets: normal calcium–normal oxalate (○, ●); normal calcium–low oxalate (□, ■); low calcium–normal oxalate (Δ, △); low calcium–low oxalate (▽, ▼). (a) Mean daily excretion of calcium; (b) mean daily excretion of oxalic acid; (c) mean products of calcium × oxalate. The vertical lines denote ± 1 SE.](image)

**Calcium excretion**

Calcium excretion was decreased significantly by giving the patients a low calcium diet, the mean value falling from 353 to 200 mg/day on the low calcium–normal oxalate diet and to 190 mg/day on the low calcium–low oxalate diet ($P<0.001$) (Fig. 1a). A similar effect was observed in the control subjects but the average calcium excretion on the normal calcium–normal oxalate diet was significantly lower in the controls than in the patients (188 compared with 353 mg/day) ($P<0.001$) and the effect of decreasing the calcium intake was less significant ($P<0.02$). On the low calcium–low oxalate diet the mean excretion of calcium was still higher in the stone-formers than in the controls but the difference between the two was less significant ($P<0.01$) than on the normal calcium–normal oxalate diet ($P<0.001$).

**Oxalate excretion**

A decrease in the dietary intake of oxalate, with a normal calcium intake, resulted in a slight fall in oxalate excretion, but this was statistically significant only in the control subjects.
Calcium and oxalic acid in diet and urine

(P < 0.05) (Fig. 1b). A decrease in calcium intake, with a normal oxalate intake, resulted in a rise in oxalate excretion, compared with the value observed on a normal diet. Both the patients and control subjects showed a similar response and the change was statistically significant in both cases (P < 0.01). On the low calcium–low oxalate diet, however, oxalate excretion was similar to that on the normal diet and this applied to both groups. In this series there were no statistically significant differences in oxalate excretion by the controls and stone-formers on any of the four diets.

Calcium × oxalate product

The mean value of the calcium × oxalate product was significantly lower on the low calcium–low oxalate diet than on the normal calcium–normal oxalate diet and this applied to both the patients and controls (Fig. 1c). However, the decrease was more pronounced in the patients (P < 0.01) than in the controls (P < 0.02) with the result that the difference which existed between patients and controls on the normal diet (P < 0.01) was abolished on the low calcium–low oxalate diet.

Calcium oxalate activity products

In calculating the calcium oxalate activity products (Fig. 2), the urinary concentrations of calcium and oxalate were corrected to a standard urine volume of 1500 ml by the formula $(1500 \times x)/V$, where $V =$ the observed 24 h urine volume and $x =$ the concentration of calcium or oxalate (mg/100 ml). The solubility product of a given salt is defined as the product of the activities of the ions of that salt in a saturated solution at equilibrium, and the formation product of the salt as the product of activities of the ions at which precipitation spontaneously occurs in a supersaturated solution of the salt. On the normal calcium–normal oxalate–normal oxalate diet.
late diet the mean product in the stone-formers exceeded the formation product, but it was
decreased significantly on the low calcium–low oxalate diet \( P < 0.02 \) and the mean value was
now less than the formation product. A similar effect was observed in the controls but the
decrease was less pronounced \( P < 0.05 \).

On the normal diet the mean product in the stone formers was significantly higher than that
in the controls \( P < 0.02 \). This difference persisted on the normal calcium–low oxalate diet
\( P < 0.05 \) but was abolished on the two low-calcium diets.

**DISCUSSION**

Several studies of the relationship between dietary and urinary oxalate were made towards the
end of the last century (see, for example, Dunlop, 1896) but there appear to have been few
recent studies and none which included the combined effects of calcium and oxalate. Dempsey,
Forbes, Melick & Henneman (1960) observed the effect of high and low oxalate diets on urine
oxalate in one normal subject and five patients with various diseases but the oxalate content of
the diets was not reported. Archer, Dormer, Scowen & Watts (1957) studied the effect of
different oxalate intakes on the urinary excretion of oxalate in six healthy males aged 19–21
years and found that an increase in dietary oxalate caused an increase in urinary oxalate which
corresponded to less than 5% of the additional oxalate in the diet.

In a previous study on four normal subjects (Zarembski & Hodgkinson, 1969) we observed
an increase in urinary oxalate that corresponded to 2.6–4.0% \( \text{(mean} = 3.4\% \) of the additional
oxalate in the diet. A similar mean value \( 3.6\% \) was observed in the present study when the
calcium intake was normal, but a higher value \( 8.1\% \) was observed when the subjects were on
the low calcium diet. Contrary to the results in our previous study, we found no difference
between normal subjects and stone-formers in their response to changes in dietary oxalate.

The interdependence of calcium and oxalate intake in their effects on excretion was also seen
in the effect of calcium intake on oxalate excretion (Fig. 1b). Thus, a decrease in calcium intake
caused an increase in oxalate excretion, as has been observed previously, but the effect was
more marked on the normal than on the low oxalate intake.

These effects may be interpreted as follows. A decrease in calcium intake, at a constant
oxalate intake, will result in less calcium being available to form insoluble calcium oxalate in
the intestine. A proportionately greater amount of the ingested oxalic acid will therefore be
absorbed. This effect will be less pronounced, however, if the dietary intake of oxalate, and
therefore the amount of oxalate available in the intestine, is also decreased. A similar argument
may be used to explain the effects of oxalate intake on calcium excretion.

These short-term studies have shown that it is possible, by simple dietary measures, to
decrease the calcium oxalate activity product in the 24 h urines of stone-forming patients from
values which may exceed the formation product to values which are similar to those in most
normal urines. Further studies are necessary to determine the longer-term effects of these
dietary measures upon the degree of saturation of the urine.

**ACKNOWLEDGMENTS**

The authors thank Professor B. E. C. Nordin for suggesting this project, Miss E. Elliot and the
staff of the Metabolic Ward, Leeds General Infirmary, for arranging the diets and the collection
of samples and Miss L. Brown and Mr T. Thompson for skilled technical assistance.
REFERENCES


