Dietary risk factors for hyperoxaluria in calcium oxalate stone formers

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Dietary risk factors for hyperoxaluria in calcium oxalate stone formers.

Background. Hyperoxaluria is a major predisposing factor in calcium oxalate urolithiasis. The aim of the present study was to clarify the role of dietary oxalate in urinary oxalate excretion and to assess dietary risk factors for hyperoxaluria in calcium oxalate stone patients.

Methods. Dietary intakes of 186 calcium oxalate stone formers, 93 with hyperoxaluria (≥0.5 mmol/day) and 93 with normal oxalate excretion (<0.4 mmol/day), were assessed by a 24-hour weighed dietary record. Each subject collected 24-hour urine during the completion of the food record. Oxalate content of foods was measured by a recently developed analytical method.

Results. The mean daily intakes of energy, total protein, fat and carbohydrates were similar in both groups. The diets of the patients with hyperoxaluria were estimated to contain 130 mg/day oxalate and 812 mg/day calcium as compared to 101 mg/day oxalate and 845 mg/day calcium among patients without hyperoxaluria. These differences were not significant. The mean daily intakes of water (in food and beverages), magnesium, potassium, dietary fiber, and ascorbic acid were greater in patients with hyperoxaluria than in stone formers with normal oxalate excretion. Multiple logistic regression analysis revealed that urinary oxalate excretion was significantly associated with dietary ascorbate and fluid intake, and inversely related to calcium intake. Differences of estimated diet composition of both groups corresponded to differences in urinary parameters.

Conclusions. These findings suggest that hyperoxaluria predominantly results from increased endogenous production and from intestinal hyperabsorption of oxalate, partly caused by an insufficient supply or low availability of calcium for complexation with oxalate in the intestinal lumen.

Calcium oxalate is the major component of about 75% of all urinary stones [1]. Hyperoxaluria is a primary risk factor in calcium oxalate stone formation. An elevated oxalate excretion can result from an increased dietary intake, an increased intestinal absorption of oxalate from the diet, or an increased endogenous production of oxalate from ingested or metabolically-generated precursors.

Studies suggest that between 10 and 50% of the urinary oxalate is derived from the diet [2, 3]. Some food-stuffs, particularly vegetables and cereals, contain high amounts of oxalic acid and can result in a significant increase in urinary oxalate excretion [4]. Moreover, a number of nutrients may influence the excretion of oxalate, for example, an increased consumption of ascorbic acid or a decreased intake of calcium and magnesium. Intestinal hyperabsorption of oxalate can make a considerable contribution to urinary oxalate, even in the absence of gastrointestinal disorders. A recent study using [13C2]oxalate revealed an increased absorption of oxalate in 34% of patients with calcium oxalate stone disease [5]. A deficiency of oxalate degradation by Oxalobacter formigenes in the intestine may contribute additionally to an increased absorption and urinary excretion of oxalate [6].

There is no established therapy for the reduction of urinary oxalate excretion in calcium oxalate stone patients with idiopathic hyperoxaluria. The avoidance of oxalate-rich foods can reduce this component, although the dietary contribution of oxalate to its urinary excretion in stone formers is still unknown. Interpretation of studies on the impact of dietary oxalate on hyperoxaluria has been limited by inaccurate or lacking data on the oxalate content of foods. To address this issue, we have developed a selective and sensitive method for the determination of oxalate in foods using a high-pressure liquid chromatography (HPLC)-enzyme-reactor [7]. This method combines enzymatic conversion and chromatographic separation with amperometrical detection of oxalate. The aim of the present study was to clarify the role of dietary oxalate in urinary oxalate excretion and to assess dietary risk factors for hyperoxaluria in calcium oxalate stone patients.

Key words: dietary oxalate intake, urinary oxalate excretion, calcium oxalate stone formation, renal stones.

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CLINICAL NEPHROLOGY – EPIDEMIOLOGY – CLINICAL TRIALS
METHODS

Patients

We conducted a case control study of recurrent calcium oxalate stone patients enrolled in the “Bonn Urolithiasis Follow-up Study.” Individuals were included in the study without knowledge of their prior oxalate excretion. The case group was limited to patients with a diagnosis of hyperoxaluria. Hyperoxaluria was defined as the urinary oxalate excretion of greater than 0.500 mmol/day in both sexes. Of the 142 calcium oxalate stone patients with hyperoxaluria (18%) enrolled in the study, 93 patients met the inclusion criteria. These 93 cases comprised 73 male and 20 female patients.

The controls were 93 age- and sex-matched calcium oxalate stone formers without hyperoxaluria who were chosen at random from the same cohort. Controls were excluded if they had a urinary oxalate excretion above 0.400 mmol/day, defined as mild hyperoxaluria.

Patients with definite causes of hyperoxaluria or hypercalcuria, such as renal tubular acidosis, hyperparathyroidism, sarcoidosis, primary hyperoxaluria or inflammatory bowel disease, were excluded. The same exclusion criteria were applied to controls as were applied to cases. Subjects were instructed to avoid taking medications that might influence calcium or oxalate metabolism, such as phosphorus binding antacids or vitamin supplements. Patient characteristics are shown in Table 1. The number of stone episodes indicated the number of stones removed through spontaneous passage of the calculus, extracorporeal shock wave lithotripsy, percutaneous nephrolithotomy or other interventional procedures.

Study design

Each patient completed a 24-hour weighed dietary record and collected their urine over the same period of time. The patients provided a detailed description of types and weighed amounts of all food items consumed. The nutrient content of foods was calculated by a nutritionist using the computer program PRODI 4.4 (Nutri-Science GmbH, Freiburg, Germany). Oxalate values of foods that had been measured at our laboratory [7] were entered into the software database.

Urine collection bottles contained thymol dissolved in isopropanol as the preservative to prevent bacterial growth and were kept under refrigeration. To prevent an incomplete dissolution of calcium oxalate crystals and degradation of ascorbate to oxalate, urine samples were acidified with 25% hydrochloric acid (resulting urinary pH <1).

Analytical procedures

For the determination of total oxalate content in foods, oxalate was extracted with 2 N hydrochloric acid from homogenized samples. Analysis of filtrates was performed by the HPLC-enzyme-reactor method [7]: Oxalate was separated from matrix substances by an anion exchange column. A mobile phase of 2 g ethylenediaminetetraacetic acid (EDTA)/L distilled water was adjusted to pH 5.0 by adding 15 μL 0.3% NaOH. The enzyme reactor contained 5 units of immobilized oxalate oxidase that oxidized the oxalate to hydrogen peroxide and carbon dioxide. The resulting hydrogen peroxide was detected amperometrically (Pt: 0.5V). Relative coefficient of variation for oxalate was 3.87%.

Analysis of oxalate concentration in urine was performed by suppressed ion chromatography [8]. Urine volume, pH value (potentiometry) and the concentrations of creatinine (Jaffe reaction), calcium and magnesium (atomic absorption spectrophotometry), chloride (coulomb metric titration), sodium and potassium (flame emission spectrophotometry), sulfate (nephelometry), phosphate (phosphate molybdate reaction), ammonium (ion selective electrode), citrate (enzymatically, citrate lyase), and uric acid (enzymatically, uricase) were measured by standard methods.

The risk of calcium oxalate stone formation, computed as relative supersaturation of each urine (RS CaOx), was obtained by iterative approximation of the ion-activity product of calcium oxalate using the component-based computer program EQUIL2 [9].

Statistical analysis

Results are expressed as means ± SD. The differences between the groups were assessed by the two-tailed Student unpaired t test. Categorical variables were compared with Fisher’s exact test and Cochran-Armitage trend test where appropriate. The number of stone episodes was compared between stone formers with and without hyperoxaluria using the nonparametric Wilcoxon rank-sum test because of the skewness of the data. Multiple logistic regression analysis was used to examine the relative risk, estimated by the odds ratio, of selected nutrients and nutritional status (body mass index, BMI) on hyperoxaluria. For each relative risk the two-sided significance level and 95% confidence interval were computed. Based on the results of the multiple logistic regression analysis, the odds ratios (ORs) and confidence intervals (CIs) were additionally calculated for different amounts of calcium, ascorbic acid and fluid intake to elucidate the risk of clinically relevant quantities. Statistical analysis was performed using the Statistical Package for the Social Sciences (SPSS Inc., Chicago, IL, USA) and SAS (Statistical Analysis System Institute, Cary, NC, USA) computer software. All reported P values are two-sided.

RESULTS

Patient profile

Age, body weight, height, and BMI were similar in patients with and without hyperoxaluria. The total number
A family history of stones was reported with a similar frequency both in patients with and without hyperoxaluria (44.0% vs. 36.3%). In 34.1% of patients with hyperoxaluria and in 27.5% of stone formers with normal oxalate excretion parents were involved. Stones were less frequent in siblings and other relatives.

No differences in frequency of anatomic anomalies of the urinary tract were found between groups. Anomalies were present in 18.9% of calcium oxalate stone formers with normal oxalate excretion and in 13.0% of patients with hyperoxaluria. The most common anomalies of the urinary tract were renal cysts, duplication, ureteral and calyx stenosis.

### Nutrient intakes

The mean daily intakes of energy and the three main nutrients (protein, carbohydrates, fat) did not differ in both groups. The diets of the patients with hyperoxaluria were estimated to contain 130 mg/day oxalate and 812 mg/day calcium as compared to 101 mg/day oxalate and 845 mg/day calcium among patients without hyperoxaluria. The differences in calcium and oxalate intake between both groups were not significant (Table 2). The number of patients ingesting large amounts of oxalate (that is, >250 mg/day) was small in both groups (Table 3). Although the number of patients with an oxalate intake above 150 mg/day was higher in the hyperoxaluric group (14.0%) compared with controls (6.5%), the distribution of patients with a low, medium or high oxalate intake did not significantly differ between both groups ($P = 0.099$).

The mean daily intakes of water (in food and beverages), magnesium, potassium, dietary fiber, thiamine, pyridoxine, and ascorbic acid were greater in patients with hyperoxaluria than in stone formers with normal oxalate excretion (Table 2).

### Table 1. Characteristics of calcium oxalate stone formers ($N = 186$)

<table>
<thead>
<tr>
<th></th>
<th>Oxalate excretion</th>
<th>$&lt;0.4$ mmol/24 h</th>
<th>$\geqslant0.5$ mmol/24 h</th>
<th>$P$</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number</td>
<td>93</td>
<td>93</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Age* years</td>
<td>48.4 ± 11.5 (46.1; 50.8)</td>
<td>48.2 ± 11.8 (45.8; 50.6)</td>
<td>0.900</td>
<td></td>
</tr>
<tr>
<td>Height† cm</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male ($N = 73$)</td>
<td>174.0 ± 5.8 (172.6; 175.3)</td>
<td>175.6 ± 7.7 (173.8; 177.4)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Female ($N = 20$)</td>
<td>163.5 ± 6.4 (160.5; 166.4)</td>
<td>165.9 ± 5.0 (163.6; 168.2)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Weight† kg</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male ($N = 73$)</td>
<td>77.0 ± 10.2 (74.6; 79.3)</td>
<td>80.0 ± 11.2 (77.4; 82.6)</td>
<td>0.379</td>
<td></td>
</tr>
<tr>
<td>Female ($N = 20$)</td>
<td>67.6 ± 12.8 (61.6; 73.6)</td>
<td>70.7 ± 14.0 (64.1; 77.2)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>BMI† kg/m²</td>
<td>25.4 ± 3.5 (24.7; 26.1)</td>
<td>25.8 ± 3.3 (25.2; 26.5)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Stone episodes per year‡ $N$</td>
<td>1.0 (0; 2)</td>
<td>1.0 (0; 3)</td>
<td>0.566</td>
<td></td>
</tr>
<tr>
<td>Total stone episodes‡ $N$</td>
<td>5.0 (2; 10)</td>
<td>5.5 (3; 20)</td>
<td>0.049</td>
<td></td>
</tr>
</tbody>
</table>

*Mean ± standard deviation (95% confidence interval), t test
†Median (lower quartile; upper quartile), U-test
‡Median (lower quartile; upper quartile), U-test

### Table 2. Dietary intake in calcium oxalate stone patients with ($N = 93$) and without hyperoxaluria ($N = 93$)

<table>
<thead>
<tr>
<th>Nutrient intakes</th>
<th>Oxalate excretion</th>
<th>$&lt;0.4$ mmol/24 h</th>
<th>$\geqslant0.5$ mmol/24 h</th>
<th>$P$</th>
</tr>
</thead>
<tbody>
<tr>
<td>Energy kcal/day</td>
<td>2409 ± 662</td>
<td>2374 ± 692</td>
<td>0.721</td>
<td></td>
</tr>
<tr>
<td>Carbohydrates g/day</td>
<td>242 ± 81</td>
<td>255 ± 83</td>
<td>0.289</td>
<td></td>
</tr>
<tr>
<td>Protein g/day</td>
<td>95 ± 27</td>
<td>92 ± 32</td>
<td>0.418</td>
<td></td>
</tr>
<tr>
<td>Animal protein</td>
<td>67 ± 26</td>
<td>60 ± 28</td>
<td>0.076</td>
<td></td>
</tr>
<tr>
<td>Vegetable protein</td>
<td>28 ± 12</td>
<td>31 ± 11</td>
<td>0.111</td>
<td></td>
</tr>
<tr>
<td>Fat g/day</td>
<td>102 ± 41</td>
<td>96 ± 40</td>
<td>0.392</td>
<td></td>
</tr>
<tr>
<td>Cholesterol mg/day</td>
<td>430 ± 219</td>
<td>387 ± 219</td>
<td>0.186</td>
<td></td>
</tr>
<tr>
<td>Dietary fiber g/day</td>
<td>21.7 ± 9.5</td>
<td>26.9 ± 11.7</td>
<td>0.001</td>
<td></td>
</tr>
<tr>
<td>Potassium mg/day</td>
<td>3144 ± 781</td>
<td>3637 ± 1233</td>
<td>0.001</td>
<td></td>
</tr>
<tr>
<td>Magnesium mg/day</td>
<td>400 ± 111</td>
<td>439 ± 132</td>
<td>0.027</td>
<td></td>
</tr>
<tr>
<td>Calcium mg/day</td>
<td>845 ± 409</td>
<td>812 ± 320</td>
<td>0.546</td>
<td></td>
</tr>
<tr>
<td>Oxalate mg/day</td>
<td>101 ± 145</td>
<td>130 ± 181</td>
<td>0.229</td>
<td></td>
</tr>
<tr>
<td>Purines mg/day</td>
<td>614 ± 204</td>
<td>661 ± 233</td>
<td>0.139</td>
<td></td>
</tr>
<tr>
<td>Phosphate mg/day</td>
<td>1431 ± 351</td>
<td>1452 ± 432</td>
<td>0.726</td>
<td></td>
</tr>
<tr>
<td>Ascorbic acid mg/day</td>
<td>103 ± 71</td>
<td>178 ± 186</td>
<td>&lt;0.001</td>
<td></td>
</tr>
<tr>
<td>Thiamine mg/day</td>
<td>1.48 ± 0.67</td>
<td>1.74 ± 0.87</td>
<td>0.025</td>
<td></td>
</tr>
<tr>
<td>Pyridoxine mg/day</td>
<td>1.88 ± 0.57</td>
<td>2.30 ± 0.87</td>
<td>&lt;0.001</td>
<td></td>
</tr>
<tr>
<td>Fluid mL/day</td>
<td>2751 ± 785</td>
<td>3060 ± 883</td>
<td>0.013</td>
<td></td>
</tr>
</tbody>
</table>

Data are mean ± SD.

### Table 3. Oxalate intake in calcium oxalate stone patients with ($N = 93$) and without hyperoxaluria ($N = 93$)

<table>
<thead>
<tr>
<th>Oxalate intake</th>
<th>Oxalate excretion</th>
<th>$&lt;0.4$ mmol/24 h</th>
<th>$\geqslant0.5$ mmol/24 h</th>
<th>$P$</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;50 mg/day</td>
<td>16 (17.2%)</td>
<td>10 (10.8%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>50–100 mg/day</td>
<td>44 (47.3%)</td>
<td>44 (47.3%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>100–150 mg/day</td>
<td>27 (29.0%)</td>
<td>26 (28.0%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>150–200 mg/day</td>
<td>4 (4.3%)</td>
<td>7 (7.5%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>200–250 mg/day</td>
<td>1 (1.1%)</td>
<td>2 (2.2%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>&gt;250 mg/day</td>
<td>1 (1.1%)</td>
<td>4 (4.3%)</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Data are number of patients (%).
Multiple logistic regression analysis of the main nutritional risk factors showed a significantly positive association with the risk of hyperoxaluria for ascorbic acid and fluid intakes and a negative association (that is, a protective effect) for calcium intake. Body mass index and the intake of dietary fiber and oxalate were not associated with the risk of hyperoxaluria (Table 4).

**Urinary composition**

Differences of estimated diet composition between both groups corresponded to differences in urinary parameters. Urinary volume, potassium, and magnesium were higher in patients with hyperoxaluria than in stone formers with normal oxalate excretion, whereas no differences in urinary calcium and citrate excretion were found between both groups. Moreover, the urinary pH value and phosphate excretion levels were higher among patients with hyperoxaluria than among controls (Table 5).

Due to the greater urinary oxalate excretion, relative supersaturation with calcium oxalate (EQUIL 2) was higher in stone formers with hyperoxaluria than in those with normal oxalate excretion ($P < 0.001$). According to these findings, a significantly higher number of total stone episodes was assessed in calcium oxalate stone patients with hyperoxaluria.

**Serum parameters**

No difference in serum calcium and uric acid concentration was found between both groups, whereas the serum creatinine concentration was higher in calcium oxalate stone formers with hyperoxaluria (Table 6).

**DISCUSSION**

Among the environmental factors, diet is suggested to play the major role in idiopathic hyperoxaluria. To determine dietary risk factors, nutrient intake, nutritional status and urinary excretion of inhibitory and lithogenic substances were compared in patients with hyperoxaluria and with normal oxalate excretion.

The essential finding of this study is a significantly positive association with the risk of hyperoxaluria for ascorbic acid and fluid intakes and a negative association (that is, a protective effect) for calcium intake. Body mass index and the intake of dietary fiber and oxalate were not associated with the risk of hyperoxaluria (Table 4).

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organism [2]. Previous studies have shown a significant relationship between dietary ascorbic acid intake and urinary oxalate excretion in stone formers [10, 11, 12] or a higher ascorbate intake in patients compared to healthy controls [13, 14]. The present data confirmed a higher intake of ascorbate by hyperoxaluric stone formers and a higher OR for the intake of ascorbate. It needs to be stressed that the dietary intake of vitamin C in the hyperoxaluric group exceeded the current recommendation by 80% [15].

Substantial controversy remains about whether the increased urinary oxalate is attributable to increased intestinal absorption of oxalate, converted non-enzymatically from unabsorbed ascorbic acid in the alkaline environment of the small intestine [16] or to endogenous metabolism of absorbed ascorbate, or whether a high ascorbate intake is a marker for a high consumption of oxalate-rich fruits and vegetables. Urinary ascorbate, if present at high concentration in association with alkaline pH, also may be locally degraded to oxalate, potentially leading to calcium oxalate crystal deposition in the urinary tract [17].

There is no evidence for the oxidation of ascorbic acid during collection and handling of the specimens, producing artifactual oxalic acid, since our own investigations failed to demonstrate an erroneously high analytical oxalate level in the presence of thymol/isopropanol as a urine preservative compared to hydrochloric acid [18].

The data provide evidence that the quantity of the ingested oxalate is not a major risk factor for hyperoxaluria. Although dietary oxalate intake was higher by 30% in calcium oxalate stone formers with hyperoxaluria (130 mg/day) than in patients with normal oxalate excretion (101 mg/day), neither univariate nor multivariate analysis revealed an association between dietary intake and urinary excretion of oxalate. Moreover, the number of patients ingesting large amounts of oxalate (that is, >250 mg/day) was small in both groups.

The results suggest that hyperoxaluria is more likely due to an intestinal hyperabsorption of dietary oxalate. The effect of intestinal oxalate hyperabsorption on urinary oxalate excretion has been evaluated by a recent study in normal subjects and recurrent calcium oxalate stone formers after application of $[^{13}C_2]$oxalic acid under standardized conditions [5]. Oxalate hyperabsorption was defined as an absorption exceeding 10%. According to this definition, 34% of the patients exhibited hyperabsorption of oxalate. Of the 24 hyperabsorbers, 18 (75%) absorbed between 10 and 15%, 3 (12.5%) between 15 and 20% and 3 (12.5%) even more than 20%.

An insufficient supply of calcium was shown to be a significant risk factor for calcium oxalate stone disease [19, 20]. In the past many calcium oxalate stone formers were advised to decrease dietary calcium intake by restricting milk and dairy products. In the present study, the mean intake of calcium in both groups of patients was below national and international recommendations (1000 to 1200 mg/day) [15, 21]. Holmes, Goodman and Assimos investigated the importance of the dietary calcium content to the oxalate absorption from the diet in healthy subjects [3]. By decreasing the calcium content of the diet containing 250 mg oxalate/2500 kcal from 1002 mg to 391 mg, urinary oxalate excretion increased by 24.3% ($P = 0.007$). In a recent randomized trial in 120 men with recurrent calcium oxalate stones, Borghi et al were able to achieve a significant reduction in oxalate excretion and incidence of recurrent stones for patients on a normal calcium (1200 mg/day), low animal protein, low salt diet compared to a low calcium diet (400 mg/day) [22]. The present study confirmed an inverse association between dietary calcium intake and the risk of hyperoxaluria. These findings support the evidence for a protective effect of dietary calcium mainly through the ability of calcium to complex oxalate and to limit its availability for absorption.

Magnesium has been suggested to be nearly as effective as calcium in decreasing oxalate absorption and urinary excretion. Dietary magnesium may reduce the risk of stone formation by forming complexes with intestinal oxalate, thereby decreasing absorption [23]. Comparison of dietary magnesium of our patients revealed a significantly higher magnesium intake of patients with hyperoxaluria compared to stone formers with normal oxalate excretion. Since urinary magnesium excretion corresponded to the intake levels, it can be concluded that the influence of dietary magnesium on urinary oxalate excretion appears to be minor.

Moreover, urine flow has been reported to modify oxalate excretion. Previous studies revealed a significant positive correlation between urinary oxalate and total volume, which is consistent with a passive tubular re-absorption of oxalate in the kidney [12, 24, 25]. The present data demonstrated that a higher urine flow consequent to a higher fluid intake may have accounted for a higher oxalate excretion, since patients with greater urine volumes were apparently at higher risk of hyperoxaluria.

Obesity has been shown to be associated with an increased oxalate excretion [26]. The results of a recent prospective epidemiological study demonstrated that the prevalence and incidence of stone disease increased with increasing body mass index in two large cohorts of men and women [27]. In the present study, the link between nutritional status, as reflected by BMI, and hyperoxaluria was not confirmed by univariate or multivariate analysis. Moreover, the total energy intake did not differ between normo- and hyperoxaluric patients.

Although a high animal protein intake has been reported to be correlated with an increased urinary oxalate excretion [28], no association between dietary protein
Dietary fiber and phytic acid have been suggested to increase the risk of stone formation by increasing hyperoxaluria through binding of intestinal calcium, resulting in an increased absorption and urinary excretion of oxalate [29, 30]. Additionally, the oxalate content of many foods high in fiber is also high. Although in the present study a higher dietary fiber ingestion was found in calcium oxalate stone formers with hyperoxaluria as compared to patients with a normal oxalate excretion, the intake was not associated with the risk of hyperoxaluria.

Pyridoxine is an essential cofactor in the conversion of glyoxylate to glycine and its deficiency can lead to glyoxylate accumulation, resulting in hyperoxaluria. Another metabolic pathway in the formation of oxalate, the degradation of glyoxylate to α-hydroxy-B-ketoadipate, requires thiamine pyrophosphate, whereby a low activity probably results in an increased formation of oxalate. The present data indicate a sufficient supply with vitamin B₁ and vitamin B₆, since the mean daily intakes of thiamine and pyridoxine exceeded recommendations for men and women [15].

The results demonstrate that hyperoxaluria contributes substantially to the risk of stone formation by increasing the urinary supersaturation of calcium oxalate (RS CaOx). Moreover, the higher number of stone episodes in patients with hyperoxaluria resulted in a slightly impaired renal function as indicated by an increased serum creatinine level.

In conclusion, these findings indicate that hyperoxaluria predominantly results from increased endogenous production and from intestinal hyperabsorption of oxalate, partly caused by an insufficient supply or low availability of calcium for complexation with oxalate in the intestinal lumen. The higher intake of dietary fiber, magnesium, potassium and ascorbic acid suggest that hyperoxaluria is related to a higher consumption of plant foods such as fruits, vegetables and cereals in exchange for meat and dairy products. A low calcium intake or complexing intestinal calcium by the phytic acid in cereals may facilitate the increased absorption of oxalate and accentuate hyperoxaluria. A sufficient dietary calcium intake, therefore, is required to compensate for the higher oxalate content and the lower availability of calcium from vegetable foods. Since the mean calcium intake was below the recommended levels, an increased consumption of lean dairy products may be considered to meet the current dietary recommendations for calcium (1000 to 1200 mg/day). Controlled feeding studies are inevitable to clarify the effect of variations in calcium intake on calcium and oxalate excretion. Although dietary oxalate intake was not identified as a risk factor for hyperoxaluria in patients with an increased intake of oxalate as well as in patients with enteric hyperoxaluria, restriction of foodstuffs rich in oxalate might be essential.

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