

Hyperoxaluria after resection of ileum in childhood

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Valman, H. B., Oberholzer, V. G., and Palmer, T. (1974). *Archives of Disease in Childhood*, 49, 171. **Hyperoxaluria after resection of ileum in childhood.** Hyperoxaluria was found in 4 of 10 children who had had resection of the ileum. There was no relation between hyperoxaluria and the length of the resection or period since the resection. Previous studies have shown reduced ratios of taurine-conjugated to glycine-conjugated bile salts in the small intestine after ileal resection and we have found low levels of taurine in the urine of these patients. There was no correlation between the urinary taurine level and hyperoxaluria. In view of the variable excretion of oxalate in some patients, the high incidence of renal stones in adults with secondary hyperoxaluria, and the possibility of dietary treatment, regular estimations of urinary oxalate should be performed in children who have had resection of the ileum.

Hyperoxaluria and renal stones occurring after small intestinal resection were first described by Smith *et al.* (1970). Three further reports have been published (Dowling, Rose, and Sutor, 1971; Admirand, Earnest, and Williams, 1971; Chadwick, Modha, and Dowling, 1973). The majority of the patients in these studies had regional enteritis and all were adults. We have investigated the urinary excretion of oxalate in 10 children who have had resections of ileum and have no persisting disease to show the incidence of hyperoxaluria and to determine whether it is related to the length or site of the resection and the period since the resection.

Oral taurine therapy has been reported to be of benefit in at least some patients with secondary hyperoxaluria (Admirand *et al.*, 1971; Dowling *et al.*, 1971) and it has been suggested that there is a deficiency of taurine (Admirand *et al.*, 1971). We have measured the taurine levels in plasma and urine specimens from some of our patients.

Patients and methods

The present ages of the patients and the time since their resections vary between 2 and 15 years (see Table). The percentage of small gut resected and the length of terminal ileum left is shown in the Table.

Urine oxalate was determined by the method of Giterson, Slooff, and Schouten (1970). Hockaday *et al.* (1965) and Gibbs and Watts (1969) showed that the normal range of oxalate excretion in children was similar

to the normal range in adults provided that the results in children were adjusted for surface area.

Amino acid levels in urine and in plasma after deproteinization with picric acid were determined on a Technicon amino acid analyser (21 hour) as previously described (Palmer, 1968). The standard Technicon buffer system (without methanol) was used, and the column was maintained at 35 °C for 4½ hours before raising the temperature to 60 °C.

Results

Of the 10 patients, 4 had definitely raised 24-hour urinary oxalate excretions (see Table). None of the patients has had urinary symptoms and none has radio-opaque renal stones at present. In a special study of one patient, random specimens of urine collected over a year showed the following levels: 0.15, 0.011, 0.002, 0.006, 0 mg oxalate/mg creatinine (normal range 0–0.029 mg/mg creatinine).

Every urine specimen investigated had a level of taurine near or below the lower limit of the normal range. All other urine amino acid levels were within normal limits.

One of the patients had a raised plasma cystathionine level of 0.04 mg/100 ml. Apart from this, every amino acid level in every plasma specimen investigated was within normal limits.

Discussion

In their first study, Dowling *et al.* (1971) found that 8 out of 11 adults with ileal dysfunction had

Cases	Present age (yr)	Age at resection (yr)	Percentage of small gut resected	Terminal ileum left (cm)	Time since resection (yr)
1	12	10	35	0	2
2	7	3	70	7	4
3	6	N	50	0	6
4	15	N	35*	30	15
5	8	N	70	12	8
6	6	N	40	10	6
7	7	2	35*	0	5
8	7	5	50*	2	2
9	2	N	70	26	2
10	14	N	45*	0	14
Normal					
Ages					

N, newborn.
*Estimated.

hyperoxaluria, and in a larger series (Chadwick *et al.*, 1973) there were 10 out of 18. 5 of the 18 patients with ileal resection but without nephrolithiasis described by Smith, Fromm, and Hofmann (1972) had hyperoxaluria, and the incidence in the present series is similar.

The age at resection, the percentage of gut resected, and the length of the remaining terminal ileum did not appear to be related to the oxalate excretion (see Table). This confirms the observations of Smith (1972), though there have been suggestions, without supporting details, that the oxalate excretion is related to the length of ileum resected (Stauffer and Humphreys, 1972; Chadwick *et al.*, 1973). In 2 children the amount excreted was determined on more than one occasion and was found to be variable, confirming the observation in one patient described previously (Dowling *et al.*, 1971). Similarly, random urine specimens from one child gave results both within and outside the normal range. Hence, it would be unwise to assume that children found to have a normal oxalate excretion on one occasion would never have hyperoxaluria. Dowling *et al.* (1971) found that 3 of 8 patients with hyperoxaluria had renal stones, and Smith *et al.* (1972) found stones in 7 out of 12 patients. This suggests that as the children in the present series have a long life expectancy there is a high risk of oxalate renal stones.

Ileal resection leads to a reduced reabsorption of bile salts and subsequently to increased demand for synthesis and conjugation of bile acids in the liver. A greatly increased synthesis of bile acid glycine has been shown in some patients (Smith *et al.*, 1972).

The ratio of glycine to taurine-conjugated bile salts in the small intestinal lumen is increased tenfold (McLeod and Wiggins, 1968), which may be due to a limited ability of the liver to increase the synthesis of taurine or to the inability of the jejunum to reabsorb taurine-conjugated bile salts (Hislop, Hofmann, and Schoenfield, 1967). It has been suggested that the hyperoxaluria in these patients is related to the increased ratio of glycine-conjugated bile salts (Smith *et al.*, 1970; Admirand *et al.*, 1971; Smith *et al.*, 1972) since glycine is a major precursor of oxalate (Williams and Smith, 1972). Recent studies have shown that it is more likely to result from an increased absorption of oxalate by the intestine (Chadwick *et al.*, 1973). This provides an explanation for the variability of the urinary oxalate excretion, since it would depend on the diet.

Cholestyramine has been found to reduce the urinary oxalate excretion to normal (Smith *et al.*, 1972), but in one patient the treatment had to be stopped as there was persistent diarrhoea. This drug may reduce the intestinal absorption of oxalate (Chadwick *et al.*, 1973). Oral calcium might also reduce oxalate absorption by forming insoluble calcium oxalate in the gut. However, the most effective treatment appears to be a low oxalate diet (Chadwick *et al.*, 1973), but it has been suggested that this therapy should be restricted to patients with recurrent renal stones.

Oral taurine has been found to abolish the hyperoxaluria in some patients (Dowling *et al.*, 1971; Admirand *et al.*, 1971), but has been ineffective in others (Smith *et al.*, 1972; Chadwick *et al.*, 1973). The low urinary taurine levels in our patients

chemical results

24-hour urinary oxalate (mg/1.73 m ² surface area)	Urinary taurine excretion (mg/g nitrogen)	Plasma taurine (mg/100 ml)	Reason for resection
90.3	2.1	1.25	Tuberculosis and stagnant loop syndrome
86.5, 67.0	<0.89, <0.45	1.3	Volvulus and malrotation
79.6	2.9	0.65	Volvulus and atresia
0, 52.5	4.1	1.15	Multiple atresia
42.8			Volvulus and malrotation
38.1			Septum in ileum
39.8	2.1		Long segment Hirschsprung's disease
24.8	1.3		Sickle cell crisis with infarction
0			Volvulus and malrotation
8.6	1.8, 2.9	1.0, 1.0	Atresia
0-36 mg/24 hr (range)	2.2-22 (range) (3 yr-16 yr)	0.85 ± 0.45 (mean ± SD) (3½ mth-12 yr)	

confirm that ileal resection may lead to taurine depletion but show that there is no correlation between taurine excretion and hyperoxaluria. Hyperoxaluria and low taurine excretion are two of the consequences of ileal resection but may not be directly related. Low urinary levels of taurine are found in subjects having low protein intakes (Evered *et al.*, 1969), but all our patients were having higher than normal protein intakes.

It may be surprising that plasma levels of taurine were normal while urine levels were low. A similar situation is found in normal infants, for though taurine is virtually absent from the urine of children 2 weeks to 1 year of age, plasma levels are not reduced during this period and there is a marked reduction in renal clearance (Palmer, 1973). The explanation is not known, but the possibility of a protein-bound taurine fraction in the plasma is being investigated.

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