URAEMIC OXALOSIS

CHR. ALBERTS, W. DRUKKER, L. BROERSMA and C. A. WAGENVOORT
Renal Unit, Department of Medicine and Department of Pathologic Anatomy, Queen Wilhelmina University Hospital, Amsterdam, The Netherlands

Crystals of calcium oxalate have been identified in the kidneys and myocardium of patients who died of acute and chronic renal failure with uraemia (Bednar, 1961).

Many metabolic abnormalities associated with uraemia are either still unknown or poorly understood and many disturbances are apparently related to inadequate elimination of waste products and other metabolites.

Oxalate crystals in the kidney were observed in 64% of 200 patients who died of renal failure (Bednar, 1961). In 14% of the cases oxalate crystals were also identified in the myocardium and some other tissues (arteries, liver, thyroid gland). These observations have been confirmed by other investigators (Bennett, 1961; Bennington, 1964).

There may be some relation between cardiac failure and secondary myocardial oxalosis in patients with acute and chronic renal failure as has been suggested by Herles in 1964.

Fig. 1. Section of necrotic renal papilla with oxalate deposits (30 x). (Reduced 50% for reproduction.)

The first three figures are from a 52 years old male who was the first patient admitted to the Amsterdam regular dialysis treatment programme and who died from phenacetin kidneys and terminal chronic renal failure complicated by haemorrhagic pericarditis. He was dialysed for 3 months, 6 hours once weekly on a standard Twincoil artificial kidney. Figures 1 and 2 show sections of the kidney. Figure 2 was photographed in polarized light. Birefringent oxalate crystals were present in the renal tubuli and the interstitial tissue. In the third figure
identical crystals are shown in the myocardium. These crystalline deposits were composed of calcium oxalate monohydrate as was shown by chemical analysis.

These and other observations suggested that a study of serum oxalate and urinary oxalate excretion in patients with acute and chronic renal failure might be of interest.

Data in the literature on normal serum oxalate and oxalate excretion are controversial. Therefore studies of serum oxalate and oxalate excretion had to be performed in normals and the results of these studies will be presented in comparison with figures of patients with acute and chronic renal failure.

Methods

Serum oxalate was determined by the method of Köpplin (1935) and urinary oxalate by that of Archer and Dormer (1956).
Results

In 47 normal individuals a mean serum oxalate level was found of 1.5 mg\% (0.7-3.0, SD = 0.7).

No significant difference was observed between males and females and age appeared to be of no importance. In 17 normals we were able to correlate serum oxalate levels and mean 24 hours’ urinary excretion (measured over 3 days). The mean oxalate excretion was 14.7 mg/24 hours (5.6-22.0, SD = 5.0). There was no significant correlation between serum oxalate levels and 24 hours urinary output (Fig. 4).

In 4 normals urinary oxalate excretion appeared to be highly variable, even under standard conditions, as has been observed by previous investigators (Archer and Dormer, 1957) (Fig. 5).

![Fig. 4. Serum oxalate vs. urinary oxalate excretion in normals.](image)

![Fig. 5. Daily urinary oxalate excretion (normal individuals).](image)
Oxalate clearance varied between 0.4 and 1.9 ml/min. By comparing these figures with the individual values of creatinine clearance it was calculated that about 98% of glomerular filtered oxalate was reabsorbed by the tubular system.

In 31 patients with severe acute or chronic renal failure and creatinine clearances ranging from 1.0 to 10 ml/min, serum oxalate levels and urinary oxalate excretion appeared to be within normal ranges. Serum oxalate in these patients ranged from 0.4 to 2.2 mg/\% (mean 1.7, SD = 0.7), oxalate excretion from 5.2 to 24.1 mg/24 h. with a mean of 14.6 mg/24 h. (SD = 6.2).

As shown in Figure 6 no correlation was observed in patients with chronic renal failure between serum oxalate (Fig. 6a) and urinary oxalate excretion (Fig 6b) and degree of renal

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**Fig. 6.** Serum oxalate vs. creatinine clearance in chronic azotaemic patients.

**Fig. 7.** Urinary oxalate excretion during diuretic phase of acute renal failure.
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failure as measured by the creatinine clearance. However, in 2 oliguric patients with acute renal failure correlation was observed between daily urinary output and oxalate excretion (Fig. 7).

The effect of haemodialysis on serum oxalate levels was studied in a number of patients with acute renal failure. After 6 hours haemodialysis on a standard Twincoil Kolff kidney with a dialysate glucose of 1500 mg%, a mean increase of serum oxalate was observed of 1.0 mg%, (ranging from −0.5 to +1.8). With a dialysate glucose of 2000 mg%, a mean oxalate increase was noted of 1.6 mg% (ranging from +1.2 to +2.1) (Fig. 8).

![Graph showing serum oxalate changes during dialysis](image)

Fig. 8. Change in serum oxalate during 6 hrs haemodialysis.

Both changes are statistically significant.

Twincoil haemodialysis with high dialysate glucose results in high blood glucose levels as has been reported to this association previously (Drukker, Alberts and Jungerius, 1965). This may result in increased oxalate synthesis (Frutton, 1958). No interference from high blood glucose levels with serum oxalate determinations was observed.

Conclusions

In many patients dying of acute and chronic renal failure, crystals of calcium oxalate have been identified in renal and myocardial tissues.

Urinary oxalate excretion and serum oxalate levels studied in patients with acute and chronic renal failure, appeared to be within normal limits.

It is possible that endogenous oxalate production in severely azotaemic patients is increased as has been observed in primary oxalosis (Frederick, 1963).

Serum oxalate levels, however, may still remain normal notwithstanding increased production and normal excretion on account of limited solubility of calcium oxalate in body fluids. This may account for deposition of calcium oxalate in patients dying of renal failure.

Increased plasma glucose concentration (as has been observed in haemodialysis with high dialysate glucose concentration and during intravenous administration of glucose solutions) may cause an increase in oxalate production and may be harmful to patients with acute and chronic renal failure.

REFERENCES


HERLES, F. (1964): The heart in uraemic oxalosis. Cor et Vasa, 6, 203.

DISCUSSION

The Chairman: Thank you, Dr. Alberts.

This paper is now open to discussion. May I start by asking you about your first patient with this very striking oxalate deposition in the myocardium. I have never seen it so obvious except in cases of congenital oxalosis, and in these you usually find it elsewhere, including the kidneys. Did you also find it deposited in the kidney tissue?

Alberts (Amsterdam): Yes, we also found it in the kidney tissue. Oxalate depositions were not observed previously simply because we did not look for them. After this first patient we paid special attention to this and we are looking in all our patients for oxalate crystals and we have found them many times.

The Chairman: Is it easily missed in ordinary histological preparations?

Alberts (Amsterdam): Yes, you can easily miss it when you are not examining your slides with polarized light.

Cattell (London): Two points. First of all your normal serum oxalate levels. I am a little surprised that you find it so easy to measure these. Most people working in this field have had difficulty defining the normal serum oxalate level. It is usually much lower in value. I am interested therefore to know how confident you are in these figures.

Secondly I am not clear from what you said about your evidence that glucose levels affect in any way the metabolism of oxalate.

Alberts (Amsterdam): There is some confusion in the literature about the normal serum oxalate values. We did not make an attempt to determine the exact serum oxalate levels but only compared normal individuals with patients with acute or chronic renal failure; we felt that Köpplin’s method met the necessary requirements. The recovery of oxalic acid added to normal and uraemic serum was 94%.

Regarding your second question: it is generally accepted that glucose is metabolized to glycolic acid and glycine (with hydroxy-pyruvic acid as an intermediate product). There is evidence that glycine is a precursor of oxalate with glyoxyl acid as an intermediate product and it might be possible that oxalosis occurs through a deviation in glycine metabolism. Many investigators have suggested that in uraemia a metabolic error occurs involving defective conversion of glyoxyl acid to formic acid and excessive production of oxalic acid by means of an alternative oxidative pathway.

We suppose that high blood glucose levels during twincoil haemodialysis may result in an increase of oxalate production as one might deduct from Fig. 9.

Unidentified Member: We treated some patients with intestinal perfusion trying to prolong their life. The limiting feature of that particular method of management was oxalate and urate deposition in the myocardium such as has been demonstrated by you and also microscopically visible granulomatous lesions within the myocardium and extensive oxalate depositions in the arteries.

This certainly limits the efficacy of this form of treatment.

Alwall (Lund): Many uraemic patients have hypocalcaemia. Is there any relation between
the concentration of oxalic acid and hypocalcaemia? It is an old experience that cows eating vegetables with a high content of oxalic acid die from hypocalcaemic cramps. There is a problem of absorption of calcium, that is to say a high need of Vitamin D, in chronic uraemia. I wonder if the whole explanation is that a high concentration of oxalic acid binds the serum calcium.

ALBERTS (Amsterdam): There is some relationship between the limited solubility of calcium oxalate and the pH of blood and other body fluids.

ALWALL (Lund): We have found in animal experiments some ten years ago that, if we inject oxalic acid in rabbits, hypocalcaemia develops. I suppose that there was some sedimentation of calcium oxalate.

ALBERTS (Amsterdam): That might be possible.

BOSCH (Amsterdam): Have you any idea how old the deposits of oxalate are? Have you seen any tissue reactions around the crystalline deposits in the tissue?

ALBERTS (Amsterdam): In some cases there was some tissue reaction around the crystals.