

REDUCTION OF ELEVATED PLASMA OXALIC ACID BY PYRIDOXINE THERAPY IN PATIENTS ON RDT

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Summary

In eight chronic haemodialysed patients with secondary hyperoxalaemia due to renal insufficiency vitamin B₆, an important co-enzyme in oxalic acid metabolism, was administered. Mean plasma oxalic acid values decreased from 149.5 ± 67.0 mmol/L to 99.0 ± 36.4 mmol/L within two weeks and to 93.8 ± 33.1 mmol/L after four weeks of pyridoxine treatment ($p < 0.01$, $p < 0.01$). The mean reduction was 46 per cent (32.0 to 56.1). Patients with high pre-values of plasma oxalic acid had the most pronounced decrease. In order to prevent calcium oxalate deposition a reduction of plasma oxalic acid in patients on RDT seems to be an important goal in long term haemodialysis treatment.

Introduction

Elevated plasma oxalic acid concentrations due to accumulation in renal failure [1, 2] appear to be an important factor in calcium oxalate depositions in many organs of uraemic patients leading to severe complications [3, 4]. Since the activity of vitamin B₆, an important co-enzyme in oxalic acid metabolism, is frequently diminished in uraemia we studied the effect of pyridoxine administration on plasma oxalic acid concentrations in chronic haemodialysed patients.

Material

In eight chronic haemodialysed patients (mean dialysis treatment 20 (range 3–35) months) plasma oxalic acid concentrations were measured. None of the patients received drugs with a known influence on pyridoxine metabolism such as isoniazid, hydralazine or penicillamine.

Methods

Pre-dialysis plasma oxalic acid values were measured after ultrafiltration by the method of Krugers, Dagneaux and coworkers [5]. Since only a minimal amount

of oxalic acid is bound to plasma proteins ultrafiltrate concentrations do not differ from plasma values.

Results

The mean pre-treatment value of plasma oxalic acid of the eight patients under investigation was $149.5 \pm 67\text{mmol/L}$ (controls $27.0 \pm 7.4\text{mmol/L}$). Samples obtained after two weeks of pyridoxine administration revealed a mean value of $99.0 \pm 36.4\text{mmol/L}$ ($p < 0.01$) and of $93.8 \pm 33.1\text{mmol/L}$ after four weeks ($p < 0.01$). Six of the eight patients showed a striking decrease of plasma oxalic acid concentrations. The decline was 46.0 (range 32.0 to 56.1) per cent (Figure 1). The decline of oxalic acid was most pronounced in patients with high plasma values and more protracted in cases with initially lower values.

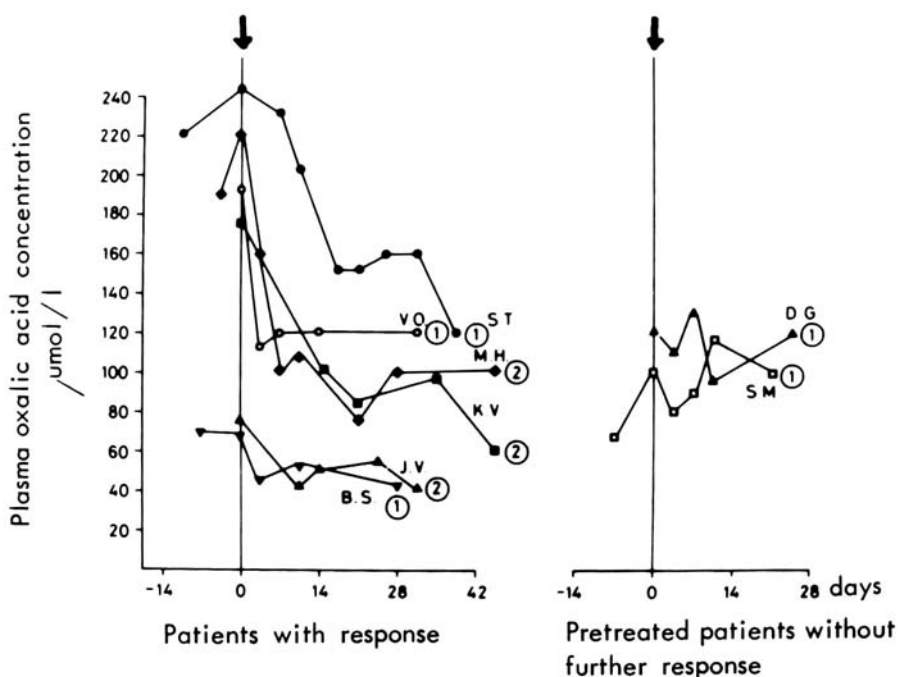


Figure 1. Changes of plasma oxalic acid concentrations before and during the trial of vitamin B6 administration. According to the therapeutic response two groups have been formed: patients with response (left) and pretreated patients without further response (right). ↓ = start of the trial of vitamin B6 administration; 1 = intravenous administration (600mg two or three times a week); 2 = oral administration (600mg daily)

The two patients having received pyridoxine prior to the study revealed low initial concentrations and showed no further decrease.

To exclude major influences caused by differences in dialysis efficiency plasma oxalic acid-creatinine ratios were evaluated. The mean plasma oxalic acid

creatinine ratio decreased from 0.1022 ± 0.051 to 0.0708 ± 0.0303 within two weeks and to 0.0712 ± 0.0350 after four weeks of pyridoxine administration ($p < 0.025$; $p < 0.0125$ respectively) Figure 2. The effect of pyridoxine was observed in patients with either oral or intravenous administration.

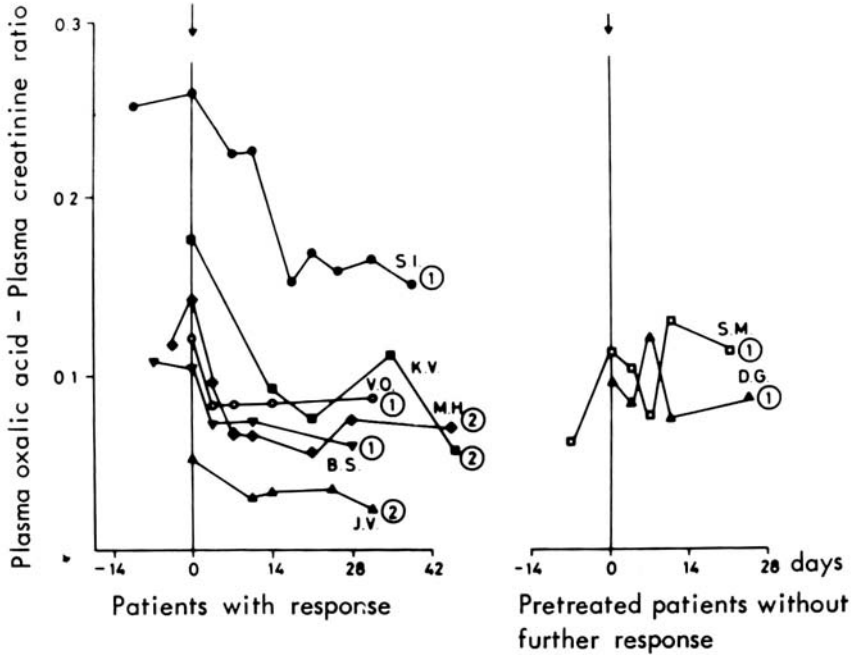


Figure 2. Changes of plasma oxalic acid-creatinine ratio before and during the trial of vitamin B6 administration. According to the therapeutic response two groups have been formed: patients with response (left) and pretreated patients without further response (right). ↓ = start of the trial of vitamin B6 administration; 1 = intravenous administration (600mg two or three times a week); 2 = oral administration (600mg daily)

Discussion

The results of our study demonstrate that administration of pyridoxine causes a decrease of plasma oxalic acid concentrations in chronic haemodialysed patients. Since high plasma oxalic acid values appear to be an important pathogenetic factor for calcium oxalate deposition, our findings indicate that long term pyridoxine treatment may be beneficial in preventing these complications. Extensive renal and myocardial calcium oxalate deposition have been reported by Salyer and Keren [3] in 57 out of 65 patients with chronic renal insufficiency at autopsy. Crystalline deposits were most pronounced in patients on RDT. In this context it is of interest that we found in a previous study higher plasma oxalic acid levels in haemodialysed patients than in patients treated conservatively

[1]. Op de Hoeck and coworkers reported shunt failure, muscle weakness and peripheral ulcers caused by an obliterative vasculitis due to oxalate deposition in the media of vessels in patients on RDT [4].

Oxalic acid is removed by haemodialysis in a similar manner to creatinine, the molecular weights of both substances differing only slightly (90 Daltons and 113 Daltons respectively). However on conventional dialysis schedules post-dialysis values do not decline to the normal range. Influences of oxalic acid intake on plasma oxalic acid concentrations seem to be negligible as only 10 per cent of the amount normally excreted in the urine is due to intestinal absorption. Furthermore protein intake has no major effect on plasma oxalic acid. Our former studies demonstrated a correlation between plasma oxalic acid concentration with creatinine but not with BUN [1].

The effect of pyridoxine treatment on plasma oxalic acid was most pronounced in patients with high pre-treatment values. In patients with low initial concentrations the reduction was protracted. Two patients who received pyridoxine prior to the study showed low pre-values, and no further decline of plasma oxalic acid concentrations could be noted during the trial of vitamin B6 administration.

A possible explanation for the efficiency of pyridoxine treatment on the behaviour on plasma oxalic acid appears to be the correction of a relative or absolute vitamin B6 deficiency. Dobbstein and coworkers found a marked pyridoxine deficiency in uraemia using the stimulation effect of pyridoxal-5-phosphate on glutamic oxalacetic transaminase activity of erythrocytes (EGOT) as a marker for pyridoxine status. Increased activation coefficients were restored to normal by oral administration of 300mg pyridoxine daily for two weeks [6].

Diminished concentrations of pyridoxal-5-phosphate, the active metabolite of vitamin B6, have been described by Stone in uraemia [7]. A deficiency of pyridoxal-5-phosphate may be due to a diminished intake, a loss during haemodialysis treatment or to an inhibition of conversion from pyridoxine by uraemic toxins. Such a metabolic inhibition also occurs with several drugs such as isoniazid, hydralazine and penicillamine.

A further explanation for the reduction of plasma oxalic acid by pyridoxine administration could be an activation of intracellular enzymes involved in oxalic acid metabolism, similar to the presumed therapeutic mechanism of vitamin B6 treatment in primary hyperoxaluria. In cases with primary hyperoxaluria the effect of pyridoxine seems mainly to be due to the increase of glyoxylate-glycine transaminase activity reducing the concentration of glyoxylic acid, the immediate precursor of oxalic acid [8].

References

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