

HIGH DOSE VITAMIN C ADMINISTRATION IS HARMFUL IN PATIENTS ON REGULAR DIALYSIS THERAPY

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Summary

In nine haemodialysis patients ascorbic acid was administered intravenously in a dose of 1g after each dialysis session for four weeks. Pretreatment plasma oxalic acid concentrations increased from $79.6 \pm 18.1 \mu\text{mol/L}$ to $191.1 \pm 29.6 \mu\text{mol/L}$ within two weeks of vitamin C treatment ($p < 0.001$). After two weeks no further statistically significant increase was noted. When ascorbic acid administration was discontinued, plasma oxalic acid fell approximately to the pretreatment values within two weeks ($p < 0.001$). Since elevated plasma oxalic acid seems to be the most important factor for calcium oxalate deposition in chronic haemodialysis patients ascorbic acid administration could aggravate these calcifications. It is concluded, that ascorbic acid should be regarded as a potentially harmful vitamin in uraemia. Vitamin C supplementation should be restricted to the minimal dose necessary to correct ascorbic acid deficiency in haemodialysis patients.

Introduction

In a high percentage of patients undergoing chronic haemodialysis vitamin C deficiency is present. Subnormal plasma ascorbic acid concentration is partly due to the avoidance of fruit and vegetables to prevent hyperkalaemia. The loss of 70–100mg ascorbic acid during each haemodialysis session contributes additionally to low values. Vitamin C supplementation is therefore commonly recommended in haemodialysis patients [1].

Oxalic acid is known to accumulate in chronic renal insufficiency resulting in secondary hyperoxalaemia [2]. Elevated plasma oxalic acid seems to be the most important factor for calcium oxalate deposition in patients on regular dialysis treatment. Arthritis, vascular and shunt disorders are clinical consequences of these deposits [3–5]. Since ascorbic acid is a metabolic precursor of oxalic acid we have investigated the influence of ascorbic acid administration on elevated plasma oxalic acid in patients undergoing chronic haemodialysis treatment.

Patients and methods

Nine patients (7 male, 2 female) on chronic haemodialysis treatment were investigated. Mean age was 41 (21–62) years: Basic renal disease was chronic glomerulonephritis in five and chronic pyelonephritis in two patients, diabetic nephropathy and polycystic disease in one case each. Mean duration of haemodialysis treatment was 31 (3–60) months. Four hours haemodialyses were performed three times a week using capillary kidneys (TECNO 1.5). The type of dialyser and the dialysis frequency remained unchanged during four weeks prior to as well as throughout the observation period. Over a period of four weeks ascorbic acid was given intravenously in a dose of 1g after each dialysis session, to a total dose of 12g for each patient. The haemodialysis patients were on a normal diet but with restriction of fruit and vegetables in order to prevent hyperkalaemia.

Arterial blood samples for determination of plasma oxalic acid, glycolic acid, creatinine, calcium and phosphate were drawn at the beginning of the haemodialysis. Oxalic acid determination was performed by a photometric method [6], glycolic acid was measured by an enzymatic method [7], calcium, phosphate and creatinine were determined by ACA-Autoanalyser (DUPONT).

Results

Mean plasma oxalic acid at the initiation of ascorbic acid supplementation was $79.5 \pm 18.1 \mu\text{mol/L}$, approximately five times the normal range ($16.8 \pm 7.2 \mu\text{mol/L}$).

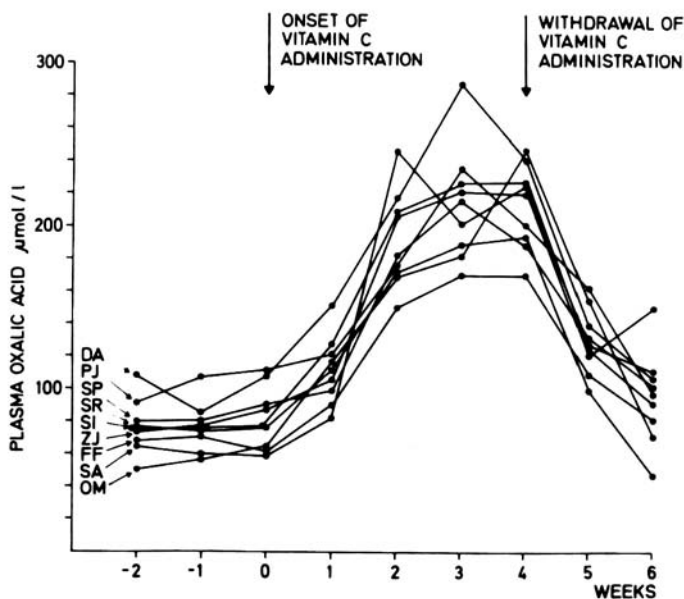


Figure 1. Changes in plasma oxalic acid concentrations in nine haemodialysis patients before, during and after ascorbic acid supplementation

When vitamin C was administered a significant increase of plasma oxalic acid was noted. After one week of ascorbic acid administration the mean plasma oxalic acid was $108.9 \pm 21.1 \mu\text{mol/L}$, after two weeks $191.1 \pm 29.6 \mu\text{mol/L}$, after three weeks $206.3 \pm 39.9 \mu\text{mol/L}$ and after four weeks $210.5 \pm 27.2 \mu\text{mol/L}$. Within two weeks of vitamin C supplementation mean plasma oxalic acid increased 240 per cent of the initial value ('t' test for paired samples: $t = 9.78$, $p < 0.001$. Figure 1).

When ascorbic acid administration was discontinued, plasma oxalic acid decreased rapidly. Mean plasma oxalic acid concentration fell to $129.0 \pm 20.9 \mu\text{mol/L}$ within one week and to $94.8 \pm 28.7 \mu\text{mol/L}$ within two weeks of the last vitamin C administration ('t' test for paired samples was: $t = 8.45$, $p < 0.001$ for the one week post-treatment period, and $t = 12.32$, $p < 0.001$ for the two week post-treatment period). To exclude major influences caused by differences in dialysis efficiency plasma oxalic acid-creatinine ratios were evaluated. The ratios were: pretreatment values 0.077 ± 0.031 , after one week 0.118 ± 0.040 , after two weeks 0.183 ± 0.057 , after three weeks 0.191 ± 0.059 , after four weeks 0.192 ± 0.050 . The increase of plasma oxalic acid creatinine ratios was highly significant ('t' test for paired samples after one week: $t = 5.98$, $p < 0.001$, after two weeks: $t = 7.35$, $p < 0.001$, Figure 2).

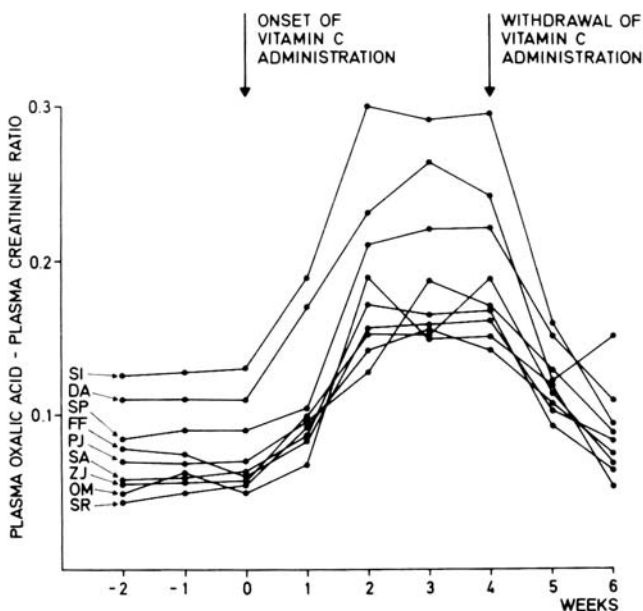


Figure 2. Changes in the plasma oxalic acid-creatinine ratios in nine haemodialysis patients before, during and after ascorbic acid supplementation

Mean plasma glycolic acid was $190.0 \pm 21.0 \mu\text{mol/L}$ before and $172.0 \pm 32.2 \mu\text{mol/L}$ after two weeks of the observation period. Pretreatment plasma calcium

and phosphate concentrations were 2.02 ± 0.12 and 2.21 ± 0.42 mmol/L respectively, after two weeks of ascorbic acid supplementation 2.24 ± 0.22 and 2.36 ± 0.31 mmol/L and remained statistically unchanged. Serial measurements of plasma oxalic acid showed that in vitro synthesis of oxalic acid was about $4 \mu\text{mol/L}$ within the determination period of two hours. This amount was neglected in our results.

Discussion

The data show, that ascorbic acid administration in patients on regular haemodialysis treatment caused a striking increase of plasma oxalic acid. Mean plasma oxalic acid concentration increased to about 240 per cent of the initial value within two weeks. After two weeks of vitamin C supplementation a plateau was reached. After withdrawal of ascorbic acid administration plasma oxalic acid fell approximately to the pretreatment values within two weeks. As the oxalic acid-creatinine ratio shows a similar behaviour, major influences caused by differences in dialysis efficiency can be excluded.

The plasma glycolic acid, another precursor of oxalic acid, remained statistically unchanged, as did plasma calcium and phosphate concentration.

The effect of ascorbic acid administration on plasma oxalic acid in our study is probably due to the augmented synthesis of oxalic acid from ascorbic acid (Figure 3). An increase of urinary oxalic acid excretion as a consequence of the augmented synthesis of oxalic acid from ascorbic acid has been found in normals only during a high dose vitamin C intake of more than 4g per day [8].

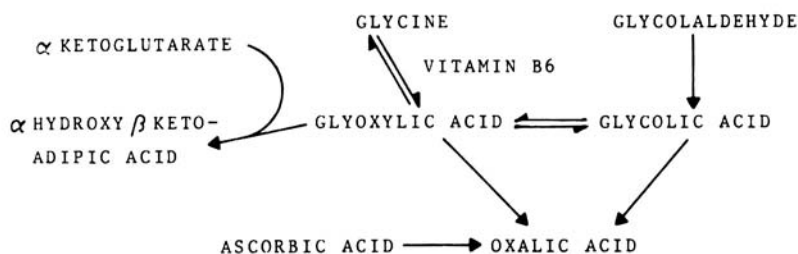


Figure 3. Pathways of oxalic acid metabolism

However, in our patients a significant rise of plasma oxalic acid was noted with a dose of only 3g weekly. The discrepancy in the doses necessary to influence oxalic acid synthesis can be explained as a consequence of accumulation of administered ascorbic acid in patients on regular dialysis treatment. Former studies showed that about 50–75 per cent of administered vitamin C are excreted in urine within 24 hours when normal kidney function is present [9]. In patients undergoing chronic haemodialysis treatment accumulation of administered ascorbic acid occurs. Pönkä and Kuhlback [10] investigated the effect of vitamin C supplementation on serum ascorbic acid concentration in patients on regular haemodialysis treatment. Under vitamin C supplementation in a dose of 0.5g

orally per day serum ascorbic acid rose from $3.9 \pm 0.6 \text{ mg/L}$ to $28.2 \pm 2.2 \text{ mg/L}$ within two weeks (normal value $4\text{--}11 \text{ mg/L}$). This concentration was higher than that found by other authors in normal volunteers with an ascorbic acid intake of 5 g per day [9].

Oxalic acid, that is normally excreted in urine in an amount of $200\text{--}500 \mu\text{mol}$ per day, accumulates in chronic renal failure resulting in elevated plasma levels [2]. Oxalic acid is derived mainly from endogenous sources, less than 10 per cent is due to intestinal absorption. Oxalic acid with a molecular weight of 90 daltons is removed during haemodialysis similar to creatinine, the decline being approximately 50 per cent [2]. Increased plasma oxalic acid seems to be the most important factor for calcium oxalate deposition in uraemic patients [3–5]. Salyer described severe calcium oxalate deposits in renal and myocardial tissues of about 70 per cent of chronic haemodialysis patients [3]. Op de Hoeck and co-workers described vascular complications caused by calcium oxalate depositions [5]. Arthritis due to calcium oxalate crystals was reported recently in patients on regular haemodialysis treatment [4]. It is remarkable that these patients were on a high ascorbic acid supplementation similar to our protocol.

Our study shows that ascorbic acid administration in chronic haemodialysis patients causes a further increase of plasma oxalic acid, probably aggravating calcium oxalate deposition in various tissues. Therefore vitamin C should be regarded as another potentially harmful vitamin in uraemia, along with vitamin A and D. We believe that vitamin C supplementation should be restricted to the minimal dose necessary to correct ascorbic acid deficiency.

References

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