

## **CORRELATION BETWEEN SERUM PHOSPHATE CONCENTRATION AND RATE OF PROGRESSION OF CHRONIC RENAL FAILURE**

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### **Summary**

In 125 uraemic patients we analysed the relationship between serum phosphate and the rate of progression of chronic renal failure. The analysis was based on 1587 serum creatinine and serum phosphate values. The parameter for the rate of progression was the slope of the regression lines calculated from all reciprocal serum creatinine values between six and 10mg/dl. No correlation between serum phosphate and the rate of progression could be detected, even after stratifying for the mode of diet and the underlying renal disease.

### **Introduction**

It is well accepted that a low phosphate diet given early in the course of renal diseases prevents hyperparathyroidism and renal bone disease. In patients with chronic renal failure phosphate intake is thought to be a major factor in the progression of chronic renal disease [1,2]. This assumption is based on the fact that renal calcification has been found in end stage kidneys [3]. Furthermore Ibels et al [3] demonstrated that in rats a low phosphorus diet prevented not only renal calcification, but also deterioration of renal function. Results from experimental studies [4,5], however, rejected the hypothesis that phosphate plays a major role in the progression of chronic renal failure. In humans this hypothesis has also been questioned [6,7]. This study analyses the correlation between serum phosphorus and the rate of progression of chronic renal failure.

### **Patients and methods**

A total of 125 patients suffering from glomerulonephritis, pyelonephritis/interstitial nephritis, or polycystic kidney disease were included in the study. Of these 125 patients 38 patients (nine with glomerulonephritis, 24 with pyelonephritis/interstitial nephritis, five with polycystic kidney disease) were

on a low protein diet (30g) supplemented by keto acids (Ketoperlen, Pfrimmer, Erlangen, FRG). If necessary, patients received phosphate binders. The data on 31 patients included in this group have been reported previously [8].

Eighty seven patients (25 with glomerulonephritis, 30 with pyelonephritis/interstitial nephritis, 32 with polycystic kidney disease) were on a 'free diet' without any dietary restrictions. These patients received phosphate binders to control hyperphosphataemia. Concerning the progression of chronic renal failure the data of these patients have been reported previously [8]. For the current study the data from 20 patients had now to be omitted due to insufficient data on serum phosphorus.

Patients were accepted for analysis, if the course of their disease had been observed from a serum creatinine value below 6mg/dl to one above 10mg/dl and if within this margin five or more serum creatinine determinations and their respective serum phosphorus values were available. As the parameter for the rate of progression of the renal disease we used the slope of the regression line calculated from all reciprocal serum creatinine values of a patient between six and 10mg/dl. The analysis was restricted to this range, as including lower values results in variable slopes [9]. Furthermore data resulting from slope analyses should only be compared, if they are calculated from the same data range. The calculated slopes were plotted against the median serum phosphorus values calculated from all serum phosphorus data of a patient within the serum creatinine range: 6-10mg/dl.

Comparisons were made by using the t-test, as the variances of the variables that had to be compared were equal. For the analysis of a correlation a linear regression analysis was used.

## Results

In the 125 patients studied 1587 serum creatinine and serum phosphorus determinations were available. Thus on the average the analysis was based on 12.7 data pairs per patient.

A plot of the median serum phosphorus of all 125 patients versus the corresponding slopes of the regression lines calculated from the reciprocal serum creatinine data is given in figure 1. A regression analysis of these data resulted in:  $r=0.011$  and  $p=0.692$ ; i.e. no relationship could be detected. The mean value for serum phosphorus was  $1.73\text{mmol/L} \pm 0.3\text{SD}$ , for the slopes:  $-0.006 \pm 0.010\text{SD}$ .

When we analysed the data after subgrouping for the mode of diet (figure 1), again no correlation could be detected: 'free diet':  $r=0.136$  and  $p=0.211$ ; low protein diet:  $r=0.114$  and  $p=0.495$ . No significant difference between the median serum phosphorus values of the two groups was revealed: 'free diet':  $1.77\text{mmol/L} \pm 0.33\text{SD}$ ; low protein diet:  $1.66\text{mmol/L} \pm 0.29\text{SD}$ ;  $p=0.092$ . Interestingly also the slopes of the two groups exhibited no significant differences: 'free diet':  $-0.007 \pm 0.01\text{SD}$ ; low protein diet:  $-0.005 \pm 0.01\text{SD}$ ;  $p=0.333$ .

A striking difference in the progression rates could be detected only after further subdividing the groups according to the underlying renal disease. In

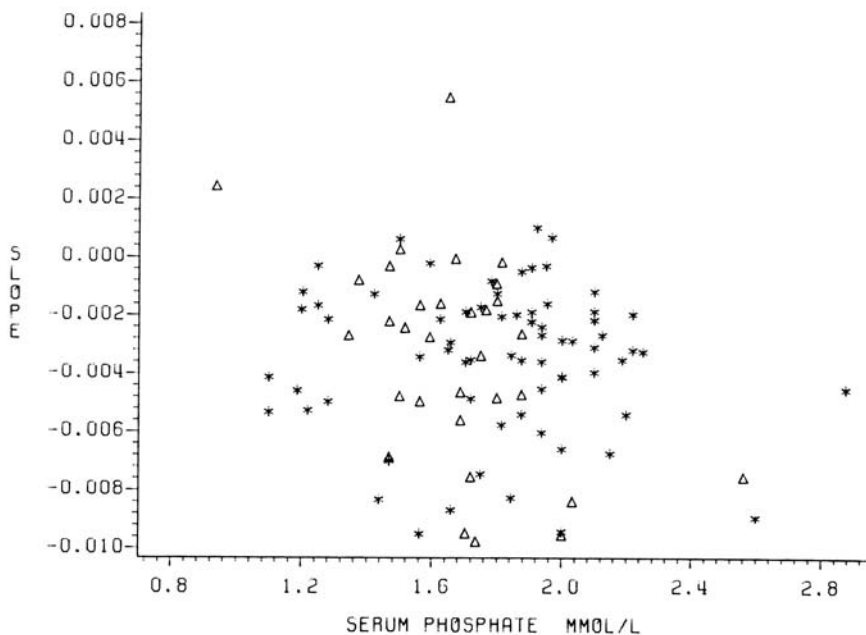


Figure 1. Plot of the median serum phosphate concentrations (mmol/L) versus the reciprocal slopes of the serum creatinine values. Stars represent patients of the 'free diet' group, triangles patients of the low protein group

that case the data did not differ from previously reported progression rates [8]. A correlation between serum phosphorus and progression rates could also not be revealed in the respective subgroups.

### Discussion

These results demonstrate that no correlation exists between serum phosphorus (range: 0.8–2.9mmol/L) and the rate of progression of chronic renal failure, irrespective of the mode of diet (low protein/'free diet') and the underlying renal disease. Furthermore this data proves that the influence of a low protein/low phosphorus diet on the rate of progression of chronic renal failure can only be assessed correctly, if the data were analysed after subgrouping for the underlying renal disease. Otherwise a high proportion of slowly progressing renal diseases in the control group might hide the effect on the rate of progression. This happened in the presented analysis. In the 'free diet' group the ratio of patients with glomerulonephritis to patients with pyelonephritis/interstitial nephritis and polycystic kidney was 1: 1.2: 1.28, whereas in the low protein group the ratio was 1: 1.28: 0.6. The slow progression rate in the low protein diet group only became obvious after subgrouping for the underlying renal disease. The differences in the progression rates of different renal diseases have been pointed out earlier [8].

Our data are in good agreement with results of Barrientos et al [6] and Mitch et al [7], but in variance with the data of Verberckmoes [10], who demonstrated that the higher the serum phosphorus concentration the faster the progression rate. Therefore he concluded that high serum phosphorus concentrations contribute to the progressive decrease of renal function in chronic renal failure.

Mitch et al [7] pointed out that in their study the average product of serum calcium and phosphorus was no lower in patients with arrested progression than in those with continued progression. This fact again points towards an insignificant influence of serum phosphorus on the rate of progression.

Barrientos et al [6] compared the progression rates of 10 patients on a low phosphorus diet and high doses of phosphate binders with that of 10 patients on a so-called 'conventional treatment'. Despite a significant difference in the serum phosphorus values: 1.18 versus 1.84 mmol/L and  $p < 0.01$ , the rate of progression was the same in the two groups. It is noteworthy that the distribution of the underlying renal diseases was exactly the same in both of their groups.

Ibels et al [3] emphasized the nephrotoxic effect of excess phosphorus intake, which is supposed to result in inflammatory and fibrotic reactions leading to renal calcification. This group also found a lower rate of progression of experimental uraemia when restricting phosphate intake. This finding was not confirmed by the data of El-Nehas et al [5] and Laouri et al [4]. These authors speculate that protection of renal function by a low phosphorus diet was due to anorexia and the consecutive reduced food intake. This seems to be possible as low serum phosphorus levels result in anorexia. Thus the more controlled studies point towards an insignificant influence of serum phosphorus on the rate of progression.

In our 125 patients we confined the analysis of our data to all serum creatinine values between six and 10mg/dl and their corresponding serum phosphorus determinations. There were several reasons for this restriction: the slopes of reciprocal serum creatinine values are continuously changing, if high serum creatinine values are included in the computation. Therefore data on slopes should be compared only, if they are based on the same data range. A further reason for this restriction was to obtain sufficient data for a regression analysis. On the average 12.7 serum creatinine and serum phosphorus determinations for each patient were available, which guarantees adequate description of the course of the disease.

### **Acknowledgment**

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