

## Phosphate

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### GUIDELINES

**No recommendations possible based on Level I or II evidence.**

### SUGGESTIONS FOR CLINICAL CARE

(Sugestions are based on Level III and IV sources)

- **Isolated phosphate restriction is not recommended for retarding the progression of chronic renal insufficiency. (level III evidence; single small study; clinically relevant outcome; negative effect)**

### Background

Hyperphosphataemia is observed in the majority of patients with stage 4 chronic kidney disease (CKD) and has been identified as a risk factor for the progression of chronic renal failure (Klahr and Morrisey 2003). Dietary phosphorus restriction can prevent the progression of renal failure in subtotaly nephrectomized rats or in rats with nephrotoxic serum nephritis, independent of protein and caloric intake. Conversely, diets high in phosphorus content result in a more rapid deterioration of renal function (Loghman-Adham 1993). The objective of this guideline is to review the evidence that correction of hyperphosphataemia retards the progression of renal insufficiency in the clinical setting.

### Search strategy

**Databases searched:** Medline (1999 to November Week 2, 2003). MeSH terms for kidney diseases were combined with MeSH terms and text words for phosphate binders. The results were then combined with the Cochrane highly sensitive search strategy for randomised controlled trials and MeSH terms and text words for identifying meta-analyses and systematic reviews. The Cochrane Renal Group Specialised Register of Randomised Controlled Trials was also searched for relevant trials not indexed by Medline.

**Date of search:** 16 December 2003.

## **What is the evidence?**

There are no RCTs that have specifically addressed the issue of whether isolated phosphate restriction retards the progression of chronic renal insufficiency.

Many of the protein-restricted diets trialled in progressive renal insufficiency have additionally incorporated dietary phosphate restriction (Klahr 1994, Rosman 1989, Jungers et al 1987, Locatelli et al 1991, D'Amico et al 1994, Ihle et al 1989, Williams et al 1991, Bergstrom et al 1989, Hecking et al 1980, Frohling et al 1980, Maschio et al 1982, Gretz et al 1983, Oldrizzi et al 1985, Di Landro et al 1986, Schmicker et al 1986, Frohling et al 1989, Walser 1975, Mallick 1994, Burns et al 1978, Kampf et al 1980, Attman et al 1983, Frohling et al 1983, El Nahas et al 1984, Mitch et al 1984, Lucas et al 1986, Walser et al 1987, Barsotti et al 1988, Levine et al 1989, Zeller et al 1991, Alvestrand et al 1980, Barsotti et al 1981, Alvestrand et al 1983, Bennett et al 1983, Attman 1986, Hannedouche et al 1989, Klahr 1997, Simpson et al 1997, Maschio et al 1983, Barsotti et al 1983, Barsotti et al 1984, Barrientos et al 1982, Ciardella et al 1986, Gin et al 1987). However, the specific role of phosphate restriction remains uncertain due to the conflicting findings of the studies and their often poor experimental design due to small numbers, short follow-up times, variable phosphate binder usage, different degrees of renal insufficiency, concomitant protein and caloric restrictions, and the inappropriate use of plasma creatinine or creatinine clearance as a GFR measure (as these are inaccurate and influenced by diet).

Barsotti et al (1984) performed a non-randomised study of a very low phosphate, low protein diet (6.5 mg/kg/day phosphate, 0.6 g/kg/day protein) versus a conventional low-phosphate low-protein diet (12 mg/kg/day phosphate, 0.6 g/kg/day protein) in 55 patients with non-diabetic renal disease. It is not clear from the analysis whether the study was prospective or retrospective and whether the 2 groups were studied in parallel or sequentially. Both groups were followed initially on a free uncontrolled mixed diet for mean durations of 11.5 and 10.0 months, respectively. They were then switched to their special diets for average durations of 20.8 and 16.3 months, respectively. Serum phosphate significantly fell in the first group from 4.39 to 3.99 mg/dl and rose in the second group from 4.25–4.96 mg/dl. Urinary phosphate excretion differed between the 2 groups (362.3 versus 628.8 mg/day), but urinary urea excretion was comparable (7.62 versus 8.23 g/day) thereby indicating that protein intake was not significantly different. Despite comparable declines in creatinine clearance whilst on the free diet ( $-0.90 \pm 0.67$  versus  $-0.79 \pm 0.53$  mL/min/month), the patients who subsequently received a very low-phosphate diet had a slower rate of renal function deterioration compared with the other group ( $-0.07 \pm 0.38$  versus  $-0.53 \pm 0.40$  mL/min/month), although no comment was made as to whether the difference was statistically significant (the difference did not appear to be significant based on calculations from the summary data). The limitations of the study are its small size, short follow-up time, inappropriate renal function measure, lack of randomisation and inappropriate statistical analysis (t-tests in the setting of repeated measures).

## **Summary of the evidence**

There has only been 1 non-randomised study of isolated dietary phosphate restriction vs a conventional low phosphate, low protein diet in 55 patients with non-

diabetic renal disease. No significant differences were found between the 2 groups, although the study was limited by a lack of statistical power, inappropriate statistical analysis, inadequate measurement of renal function and a lack of randomisation.

### **What do the other guidelines say?**

**Kidney Disease Outcomes Quality Initiative:** No recommendation.

**UK Renal Association:** No recommendation.

**Canadian Society of Nephrology:** No recommendation.

**European Best Practice Guidelines:** No recommendation.

**International Guidelines:** No recommendation.

### **Implementation and audit**

No recommendation

### **Suggestions for future research**

No recommendation

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## **Appendices**