

## Minerals in pre-dialysis patients

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### GUIDELINES

Agents containing aluminium should be used with caution in predialysis patients. (Level II evidence)

### SUGGESTIONS FOR CLINICAL CARE

(Suggestions are based on Level III and IV evidence)

- The recommended daily allowances for the general population should be used as a basis for the chronic kidney disease (CKD) population subgroup. Aluminium, copper, zinc and selenium are special cases. (Opinion)

#### Copper:

Deficiency does not appear to occur in renal failure. Copper may accumulate in CKD but it rarely increases to levels that are problematic. Apart from the situation of symptoms or signs suggestive of copper overload, and laboratory test confirmation in a particular patient, there is inadequate evidence to recommend routine measurement of copper in CKD patients.

#### Zinc:

Zinc is one of the most important trace elements and is a component of many metabolic metalloenzymes. Zinc levels fall in CKD (Gilmour et al 1998); the cause of the low levels has not been clarified. Dietary protein is a major source of zinc and limited protein intake due to low-protein diets or the anorexia of CKD may contribute to a low zinc level. Apart from the situation of symptoms or signs suggestive of zinc deficiency, and laboratory test confirmation in a particular patient, there is inadequate evidence to recommend routine measurement or dietary supplementation with zinc in those with CKD.

The regular monitoring of serum zinc levels in patients with CKD who are following a protein-restricted diet is recommended.

#### Selenium:

Similar to zinc, proteins are a rich source of selenium. Diets can be deficient in selenium in areas where the natural supply (in soils) of selenium is poor (e.g. New Zealand). Deficiency in selenium may be associated with cardiovascular disease, skeletal muscle myopathy, anaemia and problems with immune function (Dworkin et al 1987). Selenium is renally excreted, but it is unknown how much selenium accumulates in CKD.

**Selenium has a small therapeutic window. Selenium toxicity occurs when the soils are rich in selenium (e.g. some parts of the US), when excess oral intake from naturopathy therapies has occurred, or from hyperalimentation.**

**Apart from the situation of symptoms or signs suggestive of selenium deficiency, and laboratory test confirmation in a particular patient, there is inadequate evidence to recommend routine measurement or dietary supplementation with selenium in CKD.**

**Regular monitoring of serum selenium levels in patients with CKD who are following a protein-restricted diet, especially in New Zealand, is recommended.**

**Aluminium:**

**Aluminium clearance is reduced in renal failure. Aluminium absorption from the gastrointestinal tract can be enhanced in the presence of citrate, and so citrate-containing agents (e.g. sodium citrate) should be avoided in patients concurrently being administered aluminium-containing phosphate binders. Apart from the situation of symptoms or signs suggestive of aluminium overload and laboratory test confirmation in a particular patient, or patients on aluminium phosphate binders, there is inadequate evidence to recommend routine measurement of aluminium in patients with CKD.**

**Other trace elements/minerals:**

**Elevated serum levels of chromium, lead, silicon, strontium, tin and vanadium, and reduced serum levels of nickel and rubidium have been observed in CKD patients (Gilmour et al 1998). The clinical significance of this is not known.**

## **Background**

Minerals are essential to life. They are water soluble, and their handling by the body in CKD is expected to be affected. Generally, there are carrier proteins or intracellular stores of minerals, and their plasma levels do not reflect their intracellular metabolism.

There is little research on minerals in both the general population with normal renal function, and in the CKD population. Apart from those minerals specified below, there is no evidence to recommend any different daily allowance of minerals for the CKD patient from the daily allowances recommended for the general population (Gilmour et al 1998).

This guideline aims to summarise the recommended daily intake of minerals: iodine, copper, zinc, selenium, aluminium, magnesium, chromium, lead, nickel, rubidium, strontium, tin, vanadium and silicon. It will assess whether there is an association between morbidity, mortality and abnormalities measured in these minerals. This includes blood test/plasma, serum levels and dietary intakes.

## **Search strategy**

**Databases searched:** MeSH terms and text words for kidney disease were combined with MeSH terms and text words for minerals then combined with the Cochrane highly sensitive search strategy for randomised controlled trials and search filters for identifying prognosis and aetiology studies. The search was carried out in Medline (1996 – November Week 2, 2003). The Cochrane Renal Group Trials Register was also searched for trials not indexed in Medline.

**Date of searches:** 27 November 2003.

## **What is the evidence?**

One randomised controlled trial enrolled 70 CKD patients and performed a 3-month aluminium loading test to evaluate potential toxic side effects on iron metabolism (Lin & Leu 1996). The treatment group received one tablet of  $\text{Al}(\text{OH})_3$  (approx. 320 mg aluminium/day) three times daily for 3 months. The control group did not take any aluminium-containing agents. They showed that a greater increment of aluminium absorption was associated with a greater depletion of iron stores in CKD patients. Long-term, low-dose aluminium exposure can decrease iron stores in pre-dialysis patients.

## **Summary of the evidence**

Refer to the Tables in the Appendices.

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

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

**British Renal Association:**  
No recommendation.

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

**European Dialysis & Transplant Nurses Association/ European Renal Care Association:**

The dietician/nutrition advisor will ensure that the dietary intake of minerals in the pre-dialysis patient is adequate and advise on supplements as required.

## **Implementation and audit**

1. A blood test for the levels of selenium and zinc if dietary levels are low (e.g. low soil content or on protein-restricted diet) should be performed at least once prior to

dialysis. If levels are found to be low, correction of the deficiency with diet or pharmaceutical supplementation should occur. Regular monitoring thereafter is recommended.

2. If there is a clinical suspicion of copper overload disease, then serum copper levels should be checked. There is otherwise no recommendation for routine copper measurement in renal failure.

3. Serum aluminium levels should be checked at least 3-monthly if the patient is on regular dosing of oral aluminium-containing medications – as either a phosphate binder or antacid medication.

### **Suggestions for future research**

No recommendation.

## **References**

Gilmour ER, Hartley GH, Goodship TH. Trace elements and vitamins in renal disease. In: Mitch WE, Klahr S, editors. Handbook of nutrition and the kidney. 3<sup>rd</sup> ed. Philadelphia: Lippincott-Raven; 1998. p. 107–22.

Lin JL, Leu ML. Aluminium-containing agents may be toxic in predialysis chronic renal insufficiency patients. J Intern Med 1996; 240: 243–48.

Dworkin B, Weseley S, Rosenthal WS et al. Diminished blood selenium levels in renal failure patients on dialysis: correlations with nutritional status. Am J Med Sci 1987; 293: 6–12.

## Appendices

**Table 1 Recommended daily allowances of four key minerals**

Element	Males	Females*
Iodine	150 µg	120 µg
Selenium	85 µg	70 µg
Magnesium	320 mg	270 mg
Zinc	12 mg	12 mg

\* Additional supplementation is recommended for pregnant and lactating women.

**Table 2 Characteristics of included studies**

Study ID (author, year)	N	Study Design	Setting	Participants	Intervention (experimental group)	Intervention (control group)	Follow up (months)	Comments
Lin and Leu 1996	70	Randomised controlled trial	Hospital, Taiwan	77 chronic renal insufficiency patients	Low dose Al(OH) <sub>3</sub> 3 x daily	No intervention	3	

**Table 3 Quality of randomised trials**

Study ID (author, year)	Method of allocation concealment	Blinding			Intention-to-treat analysis	Loss to follow up (%)
		(participants)	(investigators)	(outcome assessors)		
Lin and Leu 1996	Not specified	No	No	No	Unclear	0.0

**Table 4 Results for continuous outcomes**

Study ID (author, year)	Outcomes	Intervention group (mean [SD])	Control group (mean [SD])	Difference in means [95% CI]
Lin and Leu 1996	Creatinine clearance (mL/min <sup>-1</sup> ) post- loading	35.3 (18.3)	29.8 (22.1)	5.50 (-5.86, 16.86)
	Serum iron (µg dl <sup>-1</sup> ) post-loading	87.3 (38.0)	81.3 (24.7)	6.00 (-9.10, 21.10)
	Transferring saturation (%) post-loading	27.9 (9.8)	29.1 (7.7)	-1.20 (-5.53, 3.13)
	Serum ferritin (µg L <sup>-1</sup> ) post-loading	188.6 (90.04)	237.2 (168.2)	-48.60 (-126.43, 29.23)
	Serum Al (mg L <sup>-1</sup> ) post-loading	13.2 (9.9)	6.0 (5.5)	7.20 (3.55, 10.85)