

HYPERCHROMIUMAEMIA IN CHRONIC DIALYSIS PATIENTS

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Summary

A nearly twenty-fold rise in serum chromium concentration in haemodialysis and continuous ambulatory peritoneal dialysis patients was found compared to patients with chronic renal failure and normal controls. Dialysate contamination leads to systemic absorption of chromium during dialysis.

Introduction

Uraemic patients on maintenance haemodialysis and continuous ambulatory peritoneal dialysis (CAPD) are subjected to disturbance in trace metal metabolism secondary to uraemia per se, dietary restriction and the dialysis procedure. We studied chromium metabolism in uraemic and chronic dialysis patients.

Patients and methods

1. Serum chromium concentration were measured in 25 patients each with chronic renal failure not yet on dialysis (creatinine clearance <10ml per min), on haemodialysis, CAPD and compared with 20 normal controls.
2. Chromium transfer studies were performed on eight haemodialysis patients during a four hour haemodialysis. Serial samples of blood and dialysate going into and out of the dialyser were collected and analysed for chromium concentration. Dialysis transmembrane pressure was set at zero and serial haematocrit monitored to minimise the effect on serum chromium concentration caused by haemoconcentration.
3. Serial serum chromium concentrations were measured in six patients each before and after they were commenced on haemodialysis or CAPD.
4. The chromium concentration in 10 different batches of CAPD dialysate, haemodialysis dialysate concentrate and water were measured.

Methods

Chromium was measured by electrothermal atomic absorption spectrometry using matrix-matched standards. The method has a detection limit of 2nmol/L which is close to normal values but allows satisfactory determination of higher serum chromium concentrations as found in the uraemic and chronic dialysis patients in this study. To prevent contamination, all samples were withdrawn through a plastic cannula and stored in nitric acid washed tubes.

Results

1. Our normal serum chromium concentration was 4 ± 3 nmol/L (range <2 to 12 nmol/L). There was a greater than twenty-fold increase in the serum chromium concentration in both haemodialysis and CAPD patients. (Figure 1).

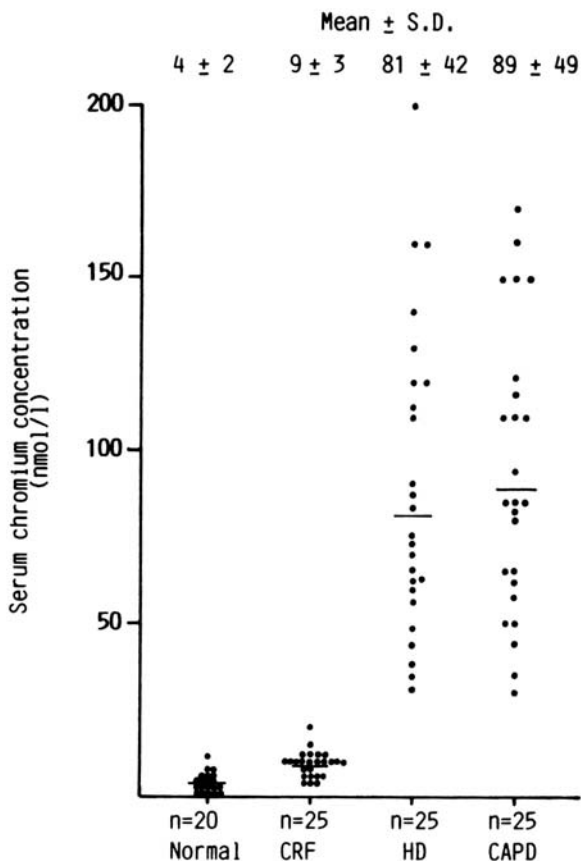


Figure 1. Distribution of serum chromium concentration. Conversion from SI to Traditional Unit $100 \text{ nmol/L} = 5.2 \mu\text{g/L}$

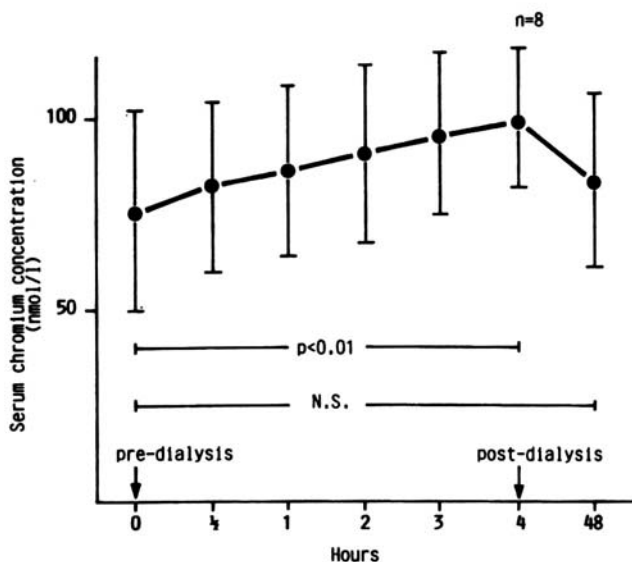


Figure 2. Chromium transfer studies in haemodialysis

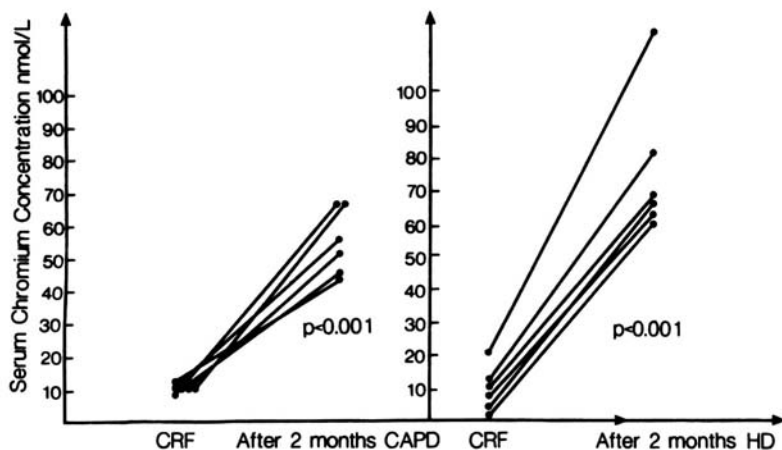


Figure 3. Longitudinal study: Showing marked rise in serum chromium after commencement of chronic dialysis. CRF = Chronic renal failure CAPD = Continuous ambulatory peritoneal dialysis -HD = Haemodialysis

2. Haemodialysis transfer study: A net transfer of chromium from dialysate to the systemic circulation was evident as an increase in serum and decrease in dialysate chromium concentration. There was a trend for the serum chromium concentration to rise during haemodialysis and the mean serum chromium concentration at the end of four hours was significantly higher than pre-dialysis ($p < 0.01$) (Figure 2).

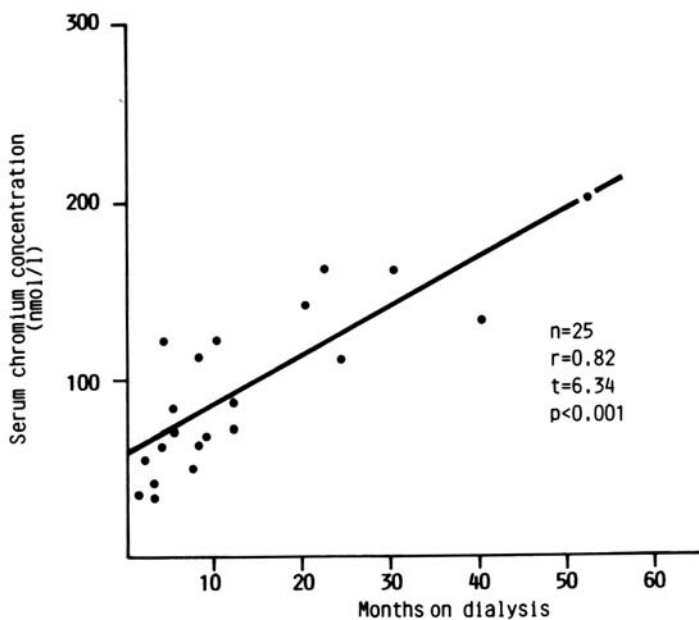


Figure 4. Haemodialysis: correlation between serum chromium concentration and duration of dialysis

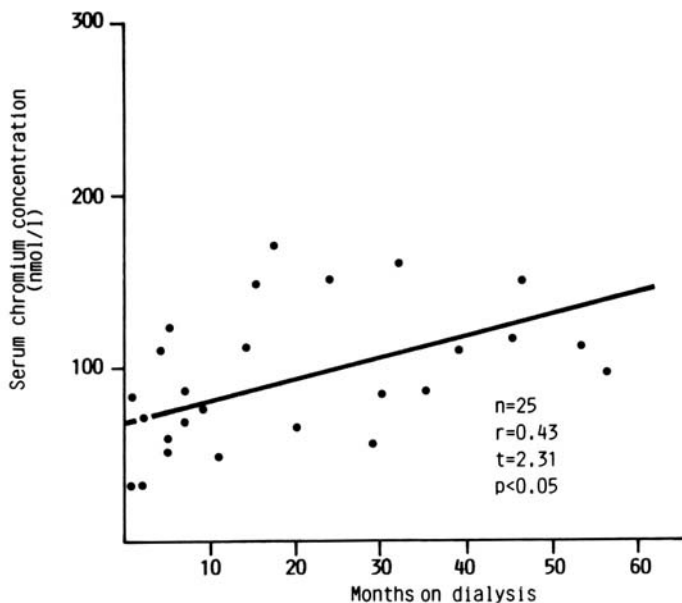


Figure 5. CAPD: correlation between serum chromium concentration and duration of dialysis

3. Longitudinal follow-up study: A striking rise in serum chromium was found in both the six haemodialysis and CAPD patients (Figure 3).
4. The mean chromium concentration of 10 different batches of:

CAPD dialysate	= 43 ± 12 nmol/L
Haemodialysis dialysate concentrate	= 454 ± 349 nmol/L
Water (no reverse osmosis)	= $3 + 1$ nmol/L
Haemodialysis dialysate (1 part concentrate mixed with 37 parts water)	= 18 ± 8 nmol/L
5. A positive correlation was found between serum chromium concentration and duration of dialysis (Figures 4 and 5).

Discussion

Several trace metals such as aluminium, cobalt and nickel have been reported to have either acute or chronic toxic effects in uraemic and dialysis patients [1–3]. Chromium is another potentially toxic trace element especially its possible carcinogenic effect [4]. Previous studies on chromium metabolism in normal and uraemic patients have yielded very conflicting results because of the problem of contamination in sample collection and analysis [5]. To obtain accurate results, blood samples must be collected avoiding the use of stainless steel needles and transported in acid-washed containers. The serum chromium concentration in our normal controls is in close agreement with the published acceptable values [5,6] although in our method the closeness to the detection limit does not allow the range to be defined as precisely as in other studies.

The increase in serum chromium in haemodialysis and CAPD have previously been reported by Cornelis et al and our group [7,8]. Thomson et al, measuring whole blood chromium has also found a significant rise of chromium in haemodialysis and CAPD patients.

The magnitude of the increase in serum concentrations in haemodialysis and CAPD is alarming. The moderate rise in serum chromium in chronic renal failure patients can be explained by reduced renal function since chromium is mainly excreted by the kidneys. In the haemodialysis and CAPD patients, however, the dialysis procedures are clearly the main cause of chromium accumulation as evident by:

1. Both the CAPD and haemodialysis dialysate contain much higher chromium concentrations than normal serum. In haemodialysis, the dialysate concentrate rather than the water is contaminated.
2. The results of longitudinal studies showing an increase in serum chromium from chronic renal failure to CAPD or haemodialysis.
3. The net chromium transfer during haemodialysis.

Chromium is widely used in many metal alloys and it is likely that contamination by this metal has occurred during the manufacturing process of dialysis fluid.

Chromium, especially in the hexavalent state, has potentially carcinogenic effect in animals [4]. Wear particles from prostheses made in cobalt chromium alloy has also been shown to possess carcinogenic effects [9].

The exact biochemical form and protein binding status of chromium in humans is not fully known but it seems likely that trivalent chromium which is protein bound and penetrates cells poorly is the major form present in serum [10]. The result of our haemodialysis transfer study also suggests a high degree of protein binding of chromium in serum.

Whether this marked rise in serum chromium concentration in dialysis patients reflects increase in total body and tissue burden is not absolutely certain but seems likely. The clinical significance of this gross biochemical disturbance in chromium metabolism in dialysis patients needs urgent investigation.

Acknowledgment

We thank Dr JW Dobbie, Dr MEM Allinson and Dr JM Boulton Jones for permission to study their patients and Mrs Freda McKenna for her excellent technical assistance.

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