Proc EDTA–ERA (1985) Vol 22

ANALGESIC NEPHROPATHY AND ALUMINIUM TOXICITY

A Schwarz, D Kraft, F Keller, W Meyer-Sabellek, *D Gawlik, G Offermann

*Klinikum Steglitz, Free University, *Hahn-Meitner-Institute for Nuclear Research, Berlin, FRG*

Summary

Haemodialysis patients with analgesic-associated nephropathy have a significantly higher mean plasma aluminium (mean±SD=2.3±1.6 versus 1.5±1.0μmol/L, p=0.002) and take significantly more aluminium-containing phosphate binders (24±13 versus 17±11g/kg BW/year, p=0.001) and antacids (1.7±2.9 versus 0.3±0.9g/kg BW/year, p=0.0003) than haemodialysis patients with other kidney diseases. This may be explained by the hyperacidity (gastritis, peptic ulcers, acidic analgesics) found more frequently in patients with analgesic associated nephropathy. Hyperacidity leads to decreased phosphate binding but increased aluminium absorption. Of 277 haemodialysis patients the four with dialysis dementia all had analgesic-associated nephropathy.

Introduction

The aluminium load of haemodialysis patients relates to the dialysate aluminium and to the intake of aluminium-containing drugs. In patients with water treated by reverse osmosis, the main source of aluminium is oral aluminium-containing compounds. As we observed a higher plasma aluminium in patients with analgesic-associated nephropathy, we investigated the sources of the aluminium load to assess the risk of aluminium toxicity in this patient group.

Methods

Plasma aluminium of 145 patients on maintenance haemodialysis was measured by graphite furnace atomic absorption spectrophotometry [1]. The patients with analgesic-associated nephropathy (n=51) were compared to the patients with other kidney diseases (n=75) who served as controls. Patients with signs of analgesic kidney damage in the presence of other kidney disease (n=19) were excluded from comparison.

The sources of the aluminium load were obtained by patient interviews and a review of the patients' records.

Bone aluminium was analysed in iliac crest specimens from eight chronic haemodialysis patients and six patients with chronic renal insufficiency by measuring neutron activity; the patients with analgesic-associated nephropathy (n=8) were compared to the patients with other kidney diseases (n=6).

Statistical evaluation was by Student's 't' test and χ^2 distribution test; correlations were tested by linear regression analysis. A p value less than 0.05 was considered to be statistically significant.

Results

Analgesic-associated nephropathy is the most frequent kidney disease (35%) causing end-stage renal failure in the patients of our haemodialysis centre (n=145). All patients, except 26 home haemodialysis patients, were treated by reverse osmosis. Plasma aluminium showed a statistically significant linear correlation to the intake of phosphate-binding agents per kilogram body weight per year (Figure 1). Patients with analgesic-associated nephropathy had significantly higher plasma aluminium, had a higher incidence of peptic ulcer and/or erosive gastritis in their history and took aluminium-containing antacids more frequently, were significantly older and more often women when compared with patients with other kidney diseases (Table I). There were no differences

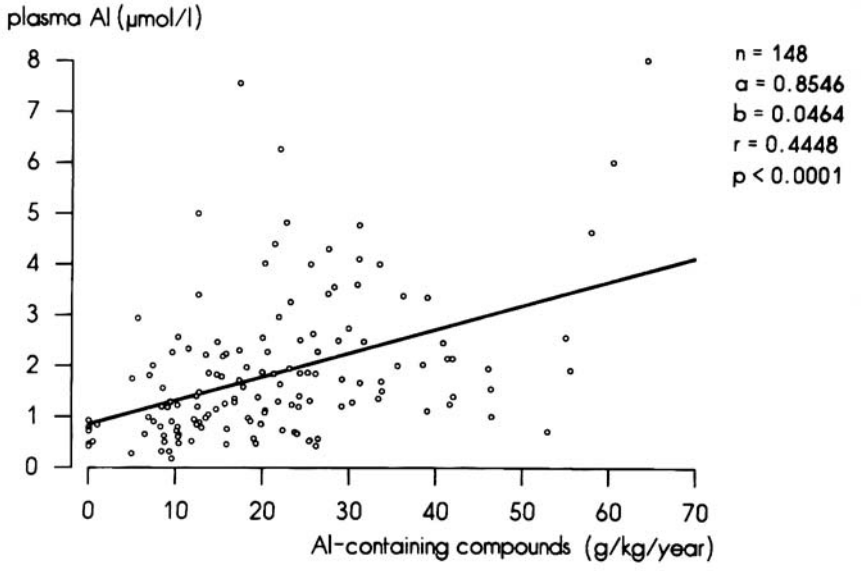

Figure 1. Correlation (y=a+bx) between the intake of aluminium-containing drugs (g per kg body weight per year) and plasma aluminium (plasma-Al) in 148 haemodialysis patients (Al=aluminium)

TABLE I. Clinical and laboratory findings in patients with analgesic-associated nephropathy (AAN) and controls

	AAN (n=51)	Controls (n=75)	Statistical significance
Age (years, means ± SD)	60±10	52±15	$p<0.001$*
Percentage of women	65%	37%	$p<0.0026$
Peptic ulcer and/or erosive gastritis	58%	25%	$p<0.001$
Plasma aluminium (μmol/L, mean ± SD)	2.29±1.62	1.51±1.04	$p=0.002$*
Intake of aluminium-containing phosphate binders (g/kg BW/year, mean ± SD)	24±13	17±11	$p=0.001$*
Intake of aluminium-containing antacids (g/kg BW/year, mean ± SD)	1.7±2.9	0.3±0.9	$p=0.0003$*
Time of haemodialysis (months, mean ± SD)	55±47	47±43	NS*
Time of taking phosphate binders (months, mean ± SD)	64±54	55±49	NS*
Home haemodialysis patients	20%	16%	NS
Calcium (mmol/L, mean ± SD)	2.5±0.2	2.5±0.2	NS*
Inorganic phosphate (mmol/L, mean ± SD)	1.8±0.4	1.8±0.5	NS*
Alkaline phosphatase (U/L, mean ± SD)	167±99	161±253	NS*
Bone aluminium (μmol/g, mean ± SD)	2.44±1.41 (n=8)	2.82±1.61 (n=6)	NS*

Statistical evaluation was done by χ^2 distribution test and Student's 't' test*

in the duration of haemodialysis, the length of time taking phosphate-binders, percentage on home haemodialysis, or the plasma calcium, phosphate and alkaline phosphatase. When the analgesic-associated nephropathy patients were matched to the others with respect to the amount of phosphate-binders plus antacids given because of stomach hyperacidity, there was no longer a statistically significant difference in plasma aluminium between patients with analgesic-associated nephropathy and the controls. All patients with stomach problems (peptic ulcer, erosive gastritis, need of regular antacid medication) were taking more phosphate-binders than other patients (26.7±13.6 versus 15.7±9.8g/kg BW/year, p=0.0001). Bone aluminium of the patients with analgesic-associated nephropathy (n=8) showed no statistically significant difference

from that of the controls (n=6) (2.44±1.41 versus 2.82±1.61μmol/g). There was no significant correlation between bone aluminium and plasma aluminium (r=0.2208, n=10).

Discussion

Haemodialysis patients with analgesic-associated nephropathy have a higher plasma aluminium than haemodialysis patients with other kidney diseases. The plasma aluminium of haemodialysis patients is significantly correlated to their intake of aluminium containing compounds (Figure 1) [2,3]. Analgesic-associated nephropathy patients have higher plasma aluminium and take more aluminium containing compounds: phosphate-binding aluminium hydroxide and antacid medications for peptic ulcer disease (Table I). This could be explained by the observation that such patients have a higher incidence of peptic ulcer and/or erosive gastritis than the controls [4,5]. Most of the usually applied antacids contain aluminium. The phosphate-binding effect of aluminium hydroxide takes place in a weakly basic milieu [6]. Therefore, patients with increased acid secretion need more aluminium hydroxide for the phosphate-binding action, since some of the aluminium hydroxide is used for buffering. Furthermore, an acidic milieu predisposes to aluminium absorption [6,7]. Thus, gastric changes caused by analgesics [5,8] play a key role in aluminium overload of patients with analgesic-associated nephropathy. The high plasma aluminium in these patients may mean a higher risk of aluminium toxicity.

One effect of an aluminium overload can be dialysis osteomalacia [9]. We did not find a difference in bone aluminium between the analgesic-associated nephropathy patients and controls, and there was no correlation between bone aluminium and plasma aluminium. Bone aluminium correlated only with the length of time of taking phosphate-binders. Thus, if the number of bone biopsied patients in our series (n=14) is not too small to allow a definite conclusion, aluminium overload of the bone might be due to a different cause.

Another effect of a high aluminium load is dialysis dementia [10]. Since 1977, we have observed four cases of dialysis dementia, all were women and all had analgesic-associated nephropathy. Three of them died between 1977 and 1980. The fourth patient, progressively developing dialysis dementia with disorientation, speech and memory disturbance, myoclonus and electroencephalographic changes, has been successfully transplanted this year, and all symptoms of dialysis dementia have disappeared. She gained 6kg of body weight and is now back working in her job as an architect. Her plasma aluminium, being 11μmol/L before transplantation, fell to a normal level (0.9μmol/L) with a functioning graft.

References

1 Gorsky JE, Dietz AA. *Clin Chem 1978; 24:* 1485
2 Fuchs C, Quellhorst E, Scheler F. *Nieren Hochdruckkr 1983; 12:* 179
3 Andreoli SP, Bergstein JM, Sherrard DJ. *N Engl J Med 1984; 310:* 1079

4 Dawborn JK, Fairley KF, Kincaid-Smith P, King WE. *Q J Med 1966; 35:* 69
5 Gsell O. *Ergebn inn Med Kinderheilk 1974; 35:* 67
6 Pogglitsch H. *Nieren Hochdruckkrankh 1981; 10:* 210
7 Kaehny WD, Hegg AP, Alfrey AC. *N Engl J Med 1977; 296:* 1389
8 Roth JLA, Valdes-Dapena A, Piese P, Buchman E. *Gastroenterol 1963; 44:* 146
9 Ward MK, Feest TG, Ellis HA et al. *Lancet 1978; i:* 841
10 Alfrey AC, Mishell JM, Burks J et al. *Trans ASAIO 1972; 18:* 257