Influence of aluminium overload on the course of post-transplant parathyroid function

G. Garay1, S. Grosso1, W. Douthat1, J. L. Fernández Martín2, J. Cannata2 and P. U. Massari1

1Renal Service, Hospital Privado-Centro Médico de Córdoba, Córdoba, Argentina and 2Bone and Mineral Research Unit, Hospital General de Asturias, Oviedo, Spain

Abstract. Aluminium intoxication exerts profound effects on secondary hyperparathyroidism in chronic renal failure and could influence the evolution of post-transplant parathyroid function. We have evaluated 44 patients after successful renal transplantation, sequentially from day 0 up to day 90 from the beginning of graft function, determining serum and urinary aluminium, PTH (intact molecule) and several other parameters of mineral metabolism. Patients were grouped according to their basal serum aluminium: Group LA (n = 25) had serum aluminium less than 40 µg/l (mean 21 ± 10 µg/l), and Group HA (n = 19) had serum aluminium greater than 40 µg/l (mean 100 ± 43 µg/l). This latter group also had greater urinary aluminium excretion during the study period. Evolution of renal function was similar in both groups. Group LA had increased pre-transplant iPTH (353 ± 416 pg/ml vs 175 ± 94, P = 0.05). Seven days after regaining renal function both groups showed a marked decrease in iPTH and then a continued decline up to day 90 with mean serum values of the hormone showing no further differences between groups. The incidence of hypercalcaemia was similar in both groups but no patients in Group HA developed hypercalcaemia at post-transplant day 7 while 12% in Group LA did so. Urinary phosphate excretion and the incidence of post-transplant hypophosphataemia were similar in both groups. These findings suggest: (a) patients with more aluminium intoxication have lower values of pre-transplant iPTH and they correct parathyroid function in a different way than non-intoxicated patients in early post-transplant days; (b) they have lower and later incidence of hypercalcaemia.

Key words: aluminium; hypercalcaemia; hyperparathyroidism; renal transplant

Introduction

Aluminium intoxication may produce marked changes in the classical clinical and biochemical features of secondary hyperparathyroidism in patients on chronic haemodialysis [1,2]. A successful renal transplant usually reverses most of the biochemical markers of secondary hyperparathyroidism and its clinical manifestations [3,4]. Little is known on the effects that pre-transplant aluminium overload could produce on the evolution of parathyroid function after transplantation. Therefore, we have studied several parameters of renal function and mineral metabolism after renal transplantation and analysed them in relation to serum and urinary aluminium.

Patients and methods

We have prospectively studied 44 patients on chronic dialysis treatment who received a renal transplant at the Hospital Privado-Centro Médico de Córdoba, obtaining a satisfactory renal function during the first post-transplant month. The group comprised 14 women and 30 men with a mean age of 35 ± 15 years (range 9–65). Twenty-six received a transplant from a cadaveric donor. Only two have been on continuous ambulatory peritoneal dialysis. Chronic haemodialysis with cuprophane and/or acetate cellulose membranes was used in the rest. Mean time on dialysis was 27 ± 25 months. Patients were sent for transplantation from several dialysis units located in central and northern Argentina. Post-transplant immunosuppression consisted of a combination of steroids and azathioprine in nine patients, steroids and cyclosporine A in 16 and triple therapy in the remaining 19 patients (Table 1).

A basal blood sample was obtained at a pre-transplant

<table>
<thead>
<tr>
<th>Table 1. Demographic and clinical characteristics of the patients</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
</tr>
<tr>
<td>---</td>
</tr>
<tr>
<td>n</td>
</tr>
<tr>
<td>Age (years)</td>
</tr>
<tr>
<td>Sex (F/M)</td>
</tr>
<tr>
<td>Time on dialysis (months)</td>
</tr>
<tr>
<td>Donors (cad./live)</td>
</tr>
<tr>
<td>Immunosuppression</td>
</tr>
<tr>
<td>Steroids + azathiop.</td>
</tr>
<tr>
<td>Steroids + cyclosp.</td>
</tr>
<tr>
<td>Steroids + azathiop. + cyclosp.</td>
</tr>
</tbody>
</table>
Sequential blood and urinary samples were obtained at 7, 30, 60 and 90 days, counting as day 0 when the patients showed a diuresis of at least 1 l/day and a urinary excretion of creatinine greater than 10 mg k.d. Creatinine, phosphate and alkaline phosphatase were determined by autoanalyser (Hitachi 911®). Serum and urinary calcium were determined by atomic absorption spectrometry (Perkin Elmer 380®) and serum intact molecule PTH by double antibody immunoradiometric assay (Nichol’s Institute). Serum and urinary aluminium were determined by graphite furnace atomic absorption spectrometry with a Zeeman-3030 spectrometer, a HGA-600 graphite furnace, and AS-60 autosampler (Perkin Elmer®). The sampling as well as the separation and transfer of the serum were carried out following previously published norms, established to avoid the risk of aluminium contamination [6,7] at the laboratory of the Hospital General of Asturias.

**Statistical methods**

Results are expressed as mean±SD or otherwise stated. Student’s t-test for unpaired samples was used to evaluate the differences between groups and ANOVA was applied to the differences of sequential determinations in each group. Pearson lineal correlations treatment was applied when needed.

**Results**

Mean pre-transplant serum aluminium was 55±48 µg/l, with a range of 8–176 µg/l. For further analysis we divided patients in two groups according to whether their serum aluminium was less or more than 40 µg/l [8]. Group LA had a mean serum aluminium of 21±10 µg/l (range 8–38 µg/l) and included 25 patients (Table 2). There were 19 patients in group Group HA, having a mean serum aluminium of 100±43 µg/l (range 42–176 µg/l) (Table 2). There were no differences between these groups in regard to the evolution of renal function and serum calcium, phosphate, and alkaline phosphatase. Mean pre-transplant serum creatinine for all patients was 9.0±3.3 mg/dl and decreased to 1.5±0.5 mg/dl at day 90, showing no differences between groups (Table 2).

Serum aluminium decreased sharply in Group HA from a mean of 100±44 to 45±30 µg/l at day 30, remaining stable thereafter up to day 90. Group LA maintained stable values of serum aluminium during the entire study period (Figure 1). The urinary excretion of aluminium was very high in both groups but significantly greater in group HA when expressed as aluminium/creatinine ratio (µg/mg); this difference between groups was still present up to day 60 (Figure 2).

Pre-transplant PTH was greater in Group LA: 367±31 vs 94±32 pg/ml (P=0.05). Patients in Group LA showed a rapid decrease of PTH at day 7, and from then on there were no differences in the mean serum PTH of both groups, which followed a further continued decrease until day 90, when many patients in both groups attained almost normal values (Figure 1).
Aluminium overload and post-transplant parathyroid function

120 \leq \leq 100 \leq 80 \leq 60 \leq 40 \leq 20 \leq 0

\begin{align*}
S & \leq 67 \\
300 & \leq 400 \\
200 & \leq 100 \\
0 & \leq 0
\end{align*}

\begin{align*}
\text{p} & = 0.0001 \\
\text{p} & = 0.0001 \\
\text{p} & = 0.0001
\end{align*}

\begin{align*}
\text{Group LA} & \quad \text{Group HA}
\end{align*}

Mean serum phosphate was similar in both groups through the entire study period as well as the fraction of patients in each group showing hypophosphataemia (serum phosphate <2.8 mg/dl) at each period of time (about 50% of them).

Hypercalcaemia, defined as a total calcium greater than 10.4 mg/dl, was more frequently found in Group LA at day 7 (12% vs 0%) but was similar thereafter, reaching an incidence of 26% for Group HA and 32% for Group LA at day 90.

Discussion

Pre-transplant, renal failure-induced secondary hyperparathyroidism usually undergoes prompt resolution after successful renal transplantation. However, patients exhibit different rates of parathyroid function changes and post-transplant disorders of parathyroid function and mineral metabolism are not uncommon [3-5,9-11]. Many factors other than renal function could influence the evolution of PTH after successful grafting. Aluminium intoxication is one of the factors that is known to produce marked changes in mineral metabolism and parathyroid function during chronic dialysis treatment [1,12,13], but little is known about its influence on post-transplant PTH secretion.

In this group of patients we have found an early and rapid post-transplant diminution of PTH concomitantly with improvement in renal function. However, faster rates of early PTH changes were seen in the group of patients with low pre-transplant serum aluminium (Figure 1). Also, we found that patients with basal pre-transplant aluminium greater than 40 µg/l had smaller net changes in PTH at day 30 (Figure 3), suggesting that the magnitude of aluminium intoxication could be one of the main factors that regulate the involution of hyperparathyroidism in early post-transplant periods. Note that the net changes in PTH at day 30 (Figure 3) are quite different in both groups even when there were no differences in mean serum creatinine, calcium, or phosphate between them.

Although serum aluminium is not a good marker of aluminium intoxication and of total body aluminium burden, there is evidence that patients on chronic haemodialysis whose serum values are greater than 40 µg/l do indeed have chronic aluminium overload [8]. Moreover, if it is accepted that urinary excretion of aluminium is another index of aluminium overload [14], our patients in Group HA also met this criterion as their urinary aluminium excretion was significantly greater than in Group LA (Figure 2).

Hypercalcaemia has been reported in retrospective studies, occurring in 12–66% of post-transplant
FIG. 3. Relationship between net changes in serum PTH values and basal aluminium levels.

patients [15,16]. In our group of patients we found an overall incidence of 28% during the first 3 months after transplantation. All of these hypercalcaemic events were mild and of no clinical significance. Nevertheless, hypercalcaemia occurring during the first or second week after beginning diuresis was found exclusively in Group LA, reflecting their greater PTH concentrations.

From these observations it is concluded that pre-transplant aluminium overload is another of the factors that plays a role in the evolution of parathyroid function and mineral metabolism in early post-transplant periods. Our data show persistently elevated serum aluminium at day 90 in both groups. Consequently further evaluation and follow-up of these patients should be done in order to obtain information on long-term evolution of the parameters reported herein.

References


