RED BLOOD CELLS INDICES AND ALUMINIUM TOXICITY IN HAEMODIALYSIS PATIENTS

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Summary

Microcytic, hypochromic anaemia is a feature of aluminium toxicity. To detect the possible influence of aluminium on erythropoiesis in a general haemodialysis population we studied the evolution of red blood cell parameters and aluminium status in 30 patients (27 without aluminium toxicity symptoms). Aluminium status was assessed by serum aluminium measurements before (BAI) and after (PAI) a desferrioxamine infusion. The evolution with time (\(\Delta\)) of PAI and DAI (= PAI − BAI) during the prospective study inversely correlated with \(\Delta\) mean corpuscular volume (2.\(\Delta\)<0.01) and \(\Delta\) mean corpuscular haemoglobin (2.\(\Delta\)<0.001).

Patients with DAI ≥ 180µg/L had lower mean corpuscular haemoglobin values (\(p<0.05\)). These findings suggest that aluminium inhibits haemoglobin synthesis even in haemodialysis patients free of aluminium toxicity symptoms.

Introduction

Aluminium toxicity has become one of the most preoccupying problems in the long-term management of haemodialysis patients. Besides the neurological manifestations [1] and vitamin D-resistant osteomalacia [2], severe aluminium intoxication can be responsible for a microcytic hypochromic anaemia [3–5].

The present prospective study was conducted to detect a possible influence of exposure to aluminium on erythropoiesis in a general haemodialysis population.

Patients and methods

We prospectively studied 30 haemodialysis patients (18 men, 12 women) whose mean age was 49.8 years (range: 23–85). They had been on regular haemodialysis for a mean period of 63.1 months (range: 5–132). They were dialysed nine to 12 hours weekly, with hollow fibre cuprophan dialysers. Dialysate was prepared from softened water; its aluminium content had been randomly assessed during
the last three years and never exceeded 25μg/L. Aluminium containing phosphate binders had been prescribed to each patient at doses varying with time of 0 to 4g/day.

Diet, dialysis schedules, vitamin and drugs regimens remained unchanged throughout the study as did our transfusion policy: one unit packed red blood cell was transfused when the weekly-measured haematocrit fell below 25 per cent. The individual transfusion rate ranged from 0 to 3 units per month.

Patients who developed systemic infection, hepatitis, overt bleeding, who had iron, vitamins or nutritional deficiencies or underwent surgery during the study period or the six preceding months were excluded. Among the 30 patients retained for the study, three had been previously identified with aluminium-induced bone disease [2] and were treated with desferrioxamine [6] during the study (2g at the end of each dialysis). The 27 others remained free of any symptoms of aluminium toxicity.

Each patient was evaluated at the start of the study (time 0) and six to 12 months later (time 1) for erythropoiesis and aluminium status. The latter was assessed by a ‘desferrioxamine test’ [7]: serum aluminium was measured by flameless atomic absorption spectro-photometry [8] before (basal aluminium, BAI) and 48 hours after (peak aluminium, PAI) a single 50mg/kg desferrioxamine infusion, and the difference (DAI) was calculated. Several red blood cell parameters (assessed by an automatic counting procedure) were determined at times 0 and 1 by calculating the mean of the values available during the two months preceding the ‘desferrioxamine test’: haematocrit, haemoglobin, number of red blood cells and their indices (mean corpuscular volume, mean corpuscular haemoglobin and mean corpuscular haemoglobin concentration). The evolution with time (△) of serum aluminium and red blood cell indices was expressed by the difference of their values at the start (time 0) and the end (time 1) of the prospective study.

Results were expressed as means ± SEM. Statistical analysis was performed using Student’s ‘t’ test for unpaired data and correlation test.

Results

Some prominent characteristics of the studied population at the start of the study are shown in Table I. Among the studied patients, only one disclosed microcytosis (mean corpuscular volume < 80fl) and six had hypochromia (mean corpuscular haemoglobin < 27μg). Twenty-five had a DAI over 180μg/L. Aluminium (BAI, PAI, and DAI) were not correlated with haematocrit, haemoglobin, mean corpuscular volume, mean corpuscular haemoglobin or mean corpuscular haemoglobin concentration. On the contrary, △PAI and △DAI during the prospective study were negatively correlated with △mean corpuscular volume (r = -0.505, 2α<0.01 and r = -0.521, 2α<0.01, respectively) and △mean corpuscular haemoglobin (r = -0.629, 2α<0.001 and r = -0.633, 2α<0.001, respectively). △mean corpuscular volume and △mean corpuscular haemoglobin were also correlated together (r = 0.88, 2α<0.001). △mean corpuscular haemoglobin concentration was not correlated with △mean corpuscular volume, △mean corpuscular haemoglobin, or △aluminium. Moreover, patients
with DAI over 180µg/L also had a significantly lower mean corpuscular haemoglobin (28.2 ± 0.5 vs 30.4 ± 0.6, p<0.05); mean corpuscular volume was also lower in that subpopulation but the difference failed to reach significance (87.4 ± 2.3 vs 91.9 ± 1.5, NS).

**TABLE I. Characteristics of the studied patients at time 0**

<table>
<thead>
<tr>
<th></th>
<th>mean</th>
<th>± SEM</th>
<th>range</th>
</tr>
</thead>
<tbody>
<tr>
<td>BAl (µg/L)</td>
<td>78.7</td>
<td>11.7</td>
<td>7.2–275.1</td>
</tr>
<tr>
<td>PAI (µg/L)</td>
<td>407.4</td>
<td>46.8</td>
<td>90.1–1037.0</td>
</tr>
<tr>
<td>DAI (µg/L)</td>
<td>328.8</td>
<td>41.5</td>
<td>77.8–1002.8</td>
</tr>
<tr>
<td>Hct (%)</td>
<td>27.2</td>
<td>0.5</td>
<td>23.6–32.4</td>
</tr>
<tr>
<td>Hb (g/dl)</td>
<td>8.7</td>
<td>0.1</td>
<td>6.8–10.2</td>
</tr>
<tr>
<td>MCV (fl)</td>
<td>88.8</td>
<td>1.0</td>
<td>78.0–96.8</td>
</tr>
<tr>
<td>MCH (pg)</td>
<td>29.0</td>
<td>0.4</td>
<td>25.2–32.6</td>
</tr>
<tr>
<td>MCHC (%)</td>
<td>32.1</td>
<td>0.2</td>
<td>28.6–33.6</td>
</tr>
<tr>
<td>Tx*</td>
<td>-</td>
<td>-</td>
<td>0–3</td>
</tr>
</tbody>
</table>

*number of packed red blood cell units transfused monthly to maintain Hct at 25 per cent
Hct = haematocrit; Hb = haemoglobin; MCV = mean corpuscular volume; MCH = mean corpuscular haemoglobin; MCHC = mean corpuscular haemoglobin concentration

**Discussion**

Severe aluminium intoxication has been demonstrated to cause a non-iron deficient microcytic hypochromic anaemia in haemodialysis patients [3–5]. That conclusion was also supported by more recent experimental data in aluminium-loaded uraemic rats [9].

The haemodialysis population presented in this work was free of manifestations of aluminium toxicity and the mean corpuscular volume and mean corpuscular haemoglobin remained within normal limits. However, it seems evident that most patients were aluminium-overloaded on the basis of the ‘desferrioxamine test’. Indeed, in a study by Milliner et al [7] a DAI over 180µg/L was always associated with increased aluminium tissue stores, as demonstrated by specific staining of bone tissue specimens.

In one aluminium-intoxicated patient, Touam et al [9] were able to demonstrate an inverse correlation between mean corpuscular volume and aluminium. In our population we did not observe any correlation between serum aluminium and red blood cell indices. However, this fact is not surprising since the determination of red blood cell indices such as mean corpuscular volume and mean corpuscular haemoglobin must be multifactorial (role of genetic factors, nutritional and iron status, mixing with transfused red blood cells, possible influence of aluminium exposure and so on). Thus, in looking for a possible influence of aluminium on those parameters it seemed more appropriate to study their
evolution with time in a given population. This allowed us to demonstrate a high inverse correlation between the changes in PAI and DAI (which are good indicators of total body aluminium [7] and those in mean corpuscular volume and mean corpuscular haemoglobin. Moreover in patients with significant aluminium overload (defined by DAI>180μg/L) mean corpuscular haemoglobin was significantly lower, while remaining within normal limits.

In conclusion, although microcytosis and hypochromia seem to be hallmarks of severe aluminium intoxication, the present findings suggest that milder degrees of aluminium exposure could inhibit haemoglobin synthesis and aggravate anaemia in haemodialysis patients, even in the absence of overt aluminium toxicity symptoms, microcytosis or hypochromia. Also, in the absence of iron deficiency a fall in mean corpuscular volume and mean corpuscular haemoglobin with time in a given patient must raise the possibility of aluminium overload.

Acknowledgments

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References

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