Calcium, Magnesium and Phosphate Balance Studies in Patients under Maintenance Haemodialysis

R. VERBERCKMOES, with the technical collaboration of
A. M. HOMBROEK, L. VAN GOILLIE and
D. VANDENDAMME

Renal Unit Department of Medicine, Akademisch Ziekenhuis St. Rafael,
Leuven, Belgium

Much attention has been paid to Ca uptake or Ca loss during dialysis in patients treated by maintenance haemodialysis. Occurrence of bone lesions has been ascribed to Ca loss in the dialyzer (Curtis et al., 1968; Wing, 1968). On the other hand it has been suggested that constant phosphate depletion as well as Mg deficiency induced by dialysis may be important in the pathogenesis of bone disease in these patients (Soyannwo et al., 1968). However, the alimentary Ca, Mg and Phosphate balance has not been considered in these studies. It was generally accepted that Ca and Phosphate balances were in equilibrium or negative in patients with chronic renal failure. Recently, however, it was claimed that in advanced renal failure the Ca balance may be strongly positive (Hornum, 1968).

The aim of our study was to define the alimentary Ca, Phosphate and Mg balance in patients under maintenance dialysis. Furthermore the influence of variable doses of Vit D was studied.

METHODS

Thirteen balance studies were done in 6 patients treated with haemodialysis twice a week during 8 hours using the Twin Coil artificial kidney. Bath Ca concentration was 5.2 mg/100 ml. One of the patients (D. F.) was an adolescent (14 years); the others were adults between 22 and 42 years. In almost all cases the balance studies were done when the patients were ambulant. Duplicates of all ingested food and beverage were made by the patients or by the wife or mother. Only intelligent and cooperative patients were selected for this study. They were given explanations concerning the importance of the study and received precise instructions concerning the collection of duplicates of ingesta and of stools and urine. The material was collected in 24 hour portions in plastic containers and brought to the laboratory the morning of the next dialysis. The patients were then questioned concerning possible errors in the collections. If such errors were found the balance study was
stopped. In principle we tried to continue the balance studies during 3 weeks. In fact they varied from 9 to 23 days (mean 17 days). During the study the patients continued to take their usual foods and do their normal work. Six balance studies were done without any medical treatment other than dialysis ('standard conditions'). In 3 of them the balance study was repeated once or twice under treatment with Vit D₃ in doses varying from 2.5 to 7.5 mg/day. This treatment was started at least 10 days before the balance study was begun. In one patient a balance study was repeated after parathyroidectomy when he was treated with Vit D₃ 7.5 mg/day. In another patient a balance had been done before the start of maintenance dialysis. This study was done under hospital conditions.

Two samples of each homogenized 24 hour collection of faeces and ingesta were analyzed after acid digestion. The urine when present, was analyzed in duplicate after appropriate dilution. Ca and Mg were determined by atomic absorption spectrophotometry after addition of lanthanum chloride to the appropriate dilutions. The phosphate content was measured by the method of Fiske and Subbarow adapted to the autoanalyzer. Recovery of Ca added to the homogenized samples before acid digestion was 96%.

RESULTS
The results of the balance studies done under standard conditions are shown in Table I. In 5 of the 6 patients Ca intake was low (between 300 and 368 mg/day). The mean Mg intake was between 154 and 212 mg/day; the mean phosphate intake between 767 and 984 mg/day. In patient R.L. Ca, Mg and phosphate intake were much higher.

TABLE I. Results of 6 balance studies under 'standard conditions' (1)

<table>
<thead>
<tr>
<th>Patient</th>
<th>Ca</th>
<th>Mg</th>
<th>Phosphate</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Intake mg/day</td>
<td>Balance mg/day</td>
<td>% Excreted (2)</td>
</tr>
<tr>
<td>C.J.</td>
<td>343</td>
<td>- 5</td>
<td>101</td>
</tr>
<tr>
<td>J.A.</td>
<td>300</td>
<td>-115</td>
<td>138</td>
</tr>
<tr>
<td>D.F.</td>
<td>347</td>
<td>-113</td>
<td>132</td>
</tr>
<tr>
<td>K.M.</td>
<td>344</td>
<td>-139</td>
<td>140</td>
</tr>
<tr>
<td>V.L.</td>
<td>368</td>
<td>- 82</td>
<td>117</td>
</tr>
<tr>
<td>R.L.</td>
<td>1176</td>
<td>-141</td>
<td>112</td>
</tr>
</tbody>
</table>

(1) Patients under maintenance dialysis. No medical treatment
(2) mg Ca excreted /mg Ca ingested x 100

The Ca balance was significantly negative in 5 patients and in equilibrium in the sixth (C.J.). Calcium excretion exceeded Ca intake by 1% to 40% (mean 23%). The mean daily loss of Ca for the 6 patients was ± 100 mg.
Figure 1. Results of balance studies in patient K. M. before and during maintenance dialysis. Mean daily intake is plotted downwards from the baseline (in mg/day), output is plotted upwards from this value. A space above the baseline indicates a negative value; a space under the baseline indicates a positive value.

In contrast the Mg and phosphate balances were always positive. Of the amount ingested about 50% was retained. However, a control balance study done in patient K. M. before maintenance haemodialysis was started, showed that Mg and phosphate balances were in equilibrium. The Ca balance here was also negative (Figure 1).

Treatment with Vit D 5 mg daily in patient D. F. and with 7.5 mg daily in patient R. L. failed to result in a positive Ca balance (Figures 2 and 3).

In patient V. L. treatment with Vit D 2.5 mg/day did not significantly alter the negative Ca balance. Treatment with 7.5 mg daily, however, resulted in a positive Ca balance: 63% of the amount of Ca ingested was retained (Figure 4). Simultaneously there was an increase in the amount of phosphate retained. Under this treatment a Looser-Milkman pseudo fracture which had developed under maintenance haemodialysis, healed within 3 months.

After parathyroidectomy, treatment with Vit D 7.5 mg/day resulted in a strongly positive Ca balance in patient J. C. (Figure 5). The Ca content
Figure 2. Results of balance studies in patient D.F. under 'standard conditions' and under treatment with Vit D 5 mg/day.

Figure 3. Results of balance studies in patient R.L. under 'standard conditions' and under treatment with Vit D 7.5 mg/day.
Figure 4. Results of balance studies in patient V.L. under 'standard conditions, under treatment with Vit D 2.5 mg/day and 7.5 mg/day.

Figure 5. Results of balance studies in patient J.A. under 'standard conditions' and after parathyroidectomy under treatment with Vit D 7.5 mg/day without and with Ca supplements in the diet.
of the faeces became extremely low; when Ca gluconate was added to the diet approximately 650 mg of Ca were retained daily; simultaneously also more phosphate was retained. Radiological and histological bone lesions typical of renal osteodystrophy, present before parathyroidectomy, normalized in a few months.

DISCUSSION
Under standard conditions the alimentary Ca balance in our patients was clearly negative. Ca excretion exceeded Ca intake by a mean value of 23%. It is unlikely that this difference could be explained by systematic errors. These results are in agreement with older balance studies (Liu & Chu, 1943; Lichtwitz et al, 1958). They are at variance with the findings of strongly positive Ca balance in patients with advanced renal failure reported recently (Hornum, 1968). In presenting our results we did not take into account possible loss or gain of Ca during haemodialysis. This can roughly be estimated from the plasma flow through the dialyzer and the arteriovenous concentration difference across the dialyzer measured repeatedly during dialysis. With our usual bath Ca concentration of 5.2 mg/100 ml a clearcut Ca uptake was found only in patient V. L. who had a constant low serum Ca concentration before treatment with Vit D (5 to 6 mg/100 ml). In the other patients no important net movement of Ca was found. Increased intestinal Ca secretion as a consequence of Ca uptake during dialysis seems to be an unlikely explanation for the negative Ca balance. A negative Ca balance was also found in patient K. M. with advanced renal failure before maintenance dialysis was started. It should be mentioned here that another relatively important route of Ca loss may exist in patients regularly taking Sauna baths, sweat containing high concentrations of Ca (8-10 mg/100 ml).

In 4 patients treated with variable doses of Vit D it was found that with a dose of 7.5 mg/day a positive Ca balance was found in 2 of 3 patients. A lower dose did not result in a positive balance. When the result of the treatment with Vit D is correlated with the dose per kg body weight, we find a positive Ca balance with a dose of 0.11 mg/kg, or more, whereas with a dose of less than 0.10 mg a negative balance persists. That a negative Ca balance may be one important factor in the pathogenesis of renal osteodystrophy may be indicated by the observation that healing of bone lesions in two of our patients was preceded by strongly positive Ca balances without appearance of metastatic calcifications on radiologic examinations.

Before the start of maintenance haemodialysis in patient K. M. the Mg and phosphate balances were in equilibrium. Under maintenance haemodialysis they became positive as in all our other balance studies (Figure 1). It seems likely that Mg and phosphate are retained from the intestine in response to loss during dialysis. As in some of our patients as much as 58% of the ingested amount of Mg and 64% of the ingested amount of phosphate were retained
one may conclude that constant depletion of Mg and phosphate, postulated to be a possible cause of bone disease in patients under maintenance dialysis (Soyannwo et al, 1968), is not a well established fact (at least when no excessive amounts of aluminium hydroxide are given).

SUMMARY
Intestinal balance studies were done in 6 patients under maintenance dialysis. The Ca balance was negative in 5 and in equilibrium in the 6th patient. A mean daily loss of 100 mg Ca was found. In 4 patients treated with variable doses of Vit D it was found that at least 7.5 mg or 0.1 mg/kg/day was needed to obtain a positive Ca balance. In these patients a positive Ca balance was followed by healing of lesions of renal osteodystrophy. The Mg and phosphate balance were positive under maintenance dialysis. This is probably the consequence of Mg and phosphate loss during dialysis.

REFERENCES
Liu, S. H. and Chu, H. I. (1943) Medicine, 22, 103
Wing, A. J. (1968) British Medical Journal, 4, 145