IONISED CALCIUM DURING HAEMODIALYSIS

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Summary

In spite of the popularity of high calcium dialysate internationally, most centres in the United Kingdom continue to use a dialysate calcium of 1.5 to 1.6 mmol/L. In eleven patients studied throughout dialysis against such dialysate we conclude that it is sufficient to raise ionised calcium. Patients so treated have little elevation of PTH pre-dialysis and it is further suppressed during dialysis.

Introduction

In the last forty years it has been an enormous challenge to develop a precise, reliable and easy method of measuring ionised calcium. So far, no method has received universal acceptance. Recent work in the Orion Biomedical Research Laboratories for the National Aeronautics and Space Administration, USA, has resulted in a new and improved calcium ion-selective electrode, the 'Orion Model SS-20 Ionised Calcium System'\(^1,2\).

We have studied serum ionised calcium in 65 normal volunteers. Table I shows that our mean value, normal range and SD are extremely similar to the results obtained by Jackson using the same instrument SS-20, at University

<table>
<thead>
<tr>
<th>TABLE I. Ionised Calcium in Normal People. A Comparative Study in Two Different Populations</th>
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</thead>
<tbody>
<tr>
<td>Newcastle Serum</td>
</tr>
<tr>
<td>No.</td>
</tr>
<tr>
<td>Mean</td>
</tr>
<tr>
<td>S.D.</td>
</tr>
<tr>
<td>Range</td>
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College Hospital, London 3.

The present study was undertaken to evaluate the changes in ionised calcium, total calcium, phosphate, total protein, albumin and PTH during dialysis against a dialysate calcium of 1.6 mmol/L.

Patients and Methods

Our investigations were carried out in 11 patients randomly selected from our dialysis population. They were comparable to the whole dialysis population, there being no significant difference from the whole population in age, sex ratio, diagnosis or duration of uraemia before the start of dialysis. The composition of

<table>
<thead>
<tr>
<th>TABLE II. Dialysate Composition</th>
<th>mEq/l</th>
<th>mmol/l</th>
<th>mg%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sodium chloride</td>
<td>90.0</td>
<td>130</td>
<td>—</td>
</tr>
<tr>
<td>Sodium acetate</td>
<td>40.0</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>Potassium chloride</td>
<td>1.57</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>Calcium chloride</td>
<td>3.20</td>
<td>1.6</td>
<td>6.4</td>
</tr>
<tr>
<td>Magnesium chloride</td>
<td>1.69</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>Dextrose</td>
<td>200.0 mg/100ml</td>
<td>—</td>
<td>—</td>
</tr>
</tbody>
</table>

the dialysate is shown in Table II and all of the patients used the same concentrate. Six were treated in our home training unit where dialysate is made from softened water, five in our hospital dialysis unit where deionised water is used. However, the results in these two subgroups were indistinguishable so they have been considered together.

The patients were aged 23 to 55, average age 38. There were 8 men and 3 women. They were dialysed thrice a week for 5 to 6 hr periods with Meltec multi-point 1m² dialysers and a single-patient Lucas MK 2 proportionating unit. Blood and dialysate flow rates averaged about 180–200 mL/min and 530 mL/min respectively. Dialysate was maintained at 38°C and was not recirculated. The mean transmembrane pressure was 80 mmHg.

The patients received initially 5,000 IU of heparin and another 12,000 IU during the course of dialysis by infusion. Only one of our patients was taking phosphate-binding agents. Specimens of arterial blood, dialysate (inlet) and dialysate (outlet) were taken before dialysis and then hourly during dialysis. Ionised calcium was measured by the method already cited. Total calcium, phosphate, total protein, and albumin were estimated by Technicon Auto-Analyzer. Plasma total calcium was corrected for total protein assuming a constant value of 72 mmol/L. PTH was determined by radioimmunoassay method, using antiserum MRC 211/32 prepared against bovine PTH. The normal range is from undetectable to 1.3 U/L, values being measurable in 90% of fifty normal subjects studied.
Results

Figure 1 shows the significant changes occurring in plasma ionised calcium, the constancy of the dialysate inlet free calcium concentration and a significant drop in the [Ca$$^{++}$$] at the second hour in the dialysate outlet.

Figure 1. Mean values (± SE) of plasma, dialysate inlet and dialysate outlet ionised calcium during dialysis

Figure 2 illustrates the pre-dialysis values and the variations obtained in the following 5 hours of dialysis for total calcium, ionised calcium, PTH and phosphate. Ionised calcium rose from 1.01 to 1.13 mmol/L and total calcium from 2.43 to 2.53 mmol/L. However, the real increment occurred during the second hour of dialysis. Plasma PTH fell progressively from 1.74 at the start to 0.88 U/L after the second hour of dialysis showing a striking negative correlation with the ionised calcium levels. In the third hour of dialysis PTH levels rose slightly and then remained unchanged. Plasma phosphate fell steadily from its pre-dialysis levels of 2.27 to 1.42 mmol/L in the third hour of dialysis and then increased to 1.56 mmol/L at the end of dialysis.

Figure 3 shows the mean percentage changes with respective ‘p’ values of [Ca$$^{++}$$], total calcium, PTH and PO$_4$$_3$ occurring during dialysis when compared to its respective pre-dialysis values. No PTH was detected in effluent dialysate.

Figure 4 illustrates the correlation coefficient between plasma ionised calcium and plasma PTH levels. In 6 of the 11 patients it was significant (p < 0.05).

Discussion

Several groups4,5,6,7,8 have always advocated a dialysis calcium concentration of 7 to 8 mg/100 ml having shown that the risk of uncontrolled hyperparathy-
Figure 2. Mean values (± SE) of plasma total calcium, ionised calcium, PTH and PO₄ occurring throughout dialysis.

Figure 3. Changes of plasma ionised calcium, total calcium, PTH and PO₄ during haemodialysis expressed as a mean percentage change in relation to pre-dialysis values (paired T-Test).

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Figure 4. Relationship between plasma ionised calcium and PTH. Each regression line represents the correlation coefficient of (Ca\textsuperscript{++} x PTH) for individual patients.

(---------- Significant  -------- NS)

roidism is reduced, provided plasma phosphate concentrations are maintained within the normal range.

In spite of this popularity, most centres in the United Kingdom continue to use a dialysate calcium of 1.5 to 1.6 mmol/L.

The net transfer of calcium during dialysis is a linear function of the concentration gradient between plasma calcium and the dialysate calcium concentration. None of our patients had a negative calcium balance during dialysis. The net gain of calcium per dialysis ranged from 2.4 to 15 mmoles (equivalent to 9.6 to 60 mg).

Our findings in eleven patients selected in a random manner suggest that a dialysate calcium of 1.6 mmol/L is sufficient to raise plasma ionised calcium significantly during dialysis. This increase, however, maintained plasma ionised calcium in the normal range, avoiding post-dialysis hypercalcaemia but suppressing PTH secretion in six of our patients.

The incidence of secondary hyperparathyroidism in our patient population has not been an insurmountable problem. On the other hand metastatic calcification in our population has been nearly non-existent.

Acknowledgments

We acknowledge the help of numerous colleagues engaged in the care of these patients, notably Dr RW Elliott, Dr T Feest and Dr R Wilkinson.

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References

1 Instruction Manual – Model SS-20 Ionised Calcium Analyser, Orion Biomedical, USA (1976)
3 Jackson, M (1977) Personal communication, University College Hospital, Ward 1/1, London

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Open Discussion

MASSRY (Los Angeles) Was the level of ionised calcium to begin with lower than normal in some of your dialysis patients?

CONCEICAO Yes, we had just two patients with pre-dialysis hypocalcaemia.

MASSRY So nine of them were normal?

CONCEICAO Yes.

MASSRY The highest levels of ionised calcium were at the end of dialysis. Why did the parathyroid hormone level continue to rise despite the rise of ionised calcium?

CONCEICAO We have plotted the mean percentage changes during dialysis (Figure 3). Considering the pre-dialysis values as zero and then first, second, third, fourth and fifth hours, PTH levels even at the end of dialysis are still significantly lower when compared with pre-dialysis. I cannot tell you exactly why, but if you look at the p values, we have a trend during dialysis of nearly the same significance as the big drop at the second hour. Finally I think that the difference between the real values was about 3.2 units/L which means that it could just be a standard error of the method.

MASSRY You stated that dialysis with 1.6 mmol calcium is very helpful in overcoming secondary hyperparathyroidism. Do you have any data as to what happens to ionised calcium and PTH levels towards the next dialysis? Surely you are suppressing it slightly during dialysis, but the patient has another three days till the next dialysis, and if the ionised calcium goes down, PTH goes up. So what you are showing is only temporary suppression. There are data using even higher dialysis calcium from the Mayo Clinic and other places. They again show that PTH goes down with dialysis, but if you follow them for a month, the levels of PTH in the pre-dialysis state is either the same or continues to rise.

CONCEICAO In the last ten years in Newcastle-upon-Tyne the calcium dialysate concentration has been 1.6 mmol/L. Newcastle is well known for osteomalacia and dialysis bone disease. We have just the same incidence of hyperparathyroidism as the others have. I cannot tell you what happens in the period between dialyses because I have not measured that.

MASSRY If you survey most dialysis units, they have very high levels of parathyroid hormone in the blood of their patients. So I am not sure that changing
dialysis calcium is of great significance in suppressing the activity of the parathyroid glands.

KLINKMANN (Rostock) You are drawing certain conclusions without telling us anything about the pH or the serum protein levels. If you do not consider the whole as a complex it is pretty hard to accept your conclusions. Can you give us any figures about your pH values and your actual protein levels?

CONCEICAO We have not studied pH or magnesium. With proteins, we got hyper-concentration during dialysis — about 7% rise on average.

BAKER (London) I know in Newcastle sometimes you dialyse with phosphate in the dialysate. Have you done these experiments under these circumstances? If so how did PTH levels behave if plasma phosphate did not change?

CONCEICAO We have not.

PARSONS (Leeds) May I challenge your statement concerning the inflow calcium levels and the outflow calcium levels indicating a positive balance of calcium in the patient. I do not think you can draw this conclusion unless you include the amount of calcium that is ultrafiltered, which I suspect is greater than the difference between inflow and ourflow levels.

CONCEICAO Yes, we did not measure ultrafiltrate. We are now starting to study calcium in the ultrafiltrate.