A comparison of corrected serum calcium levels to ionized calcium levels in haemodialysis patients

Comparaison des valeurs corrigées du calcium sérique et des concentrations de calcium ionisé chez les patients hémodialysés

Abstract. Aberrations in calcium homeostasis are common observed in patients with chronic renal failure. Measure of total calcium does not reflect the real variation of the calcium status. The proper method to evaluate this issue in hemodialysis patients has not been completely defined. This study aimed to compare the corrected serum calcium levels to ionized calcium levels in hemodialysis patients. Thirty one patients on chronic haemodialysis admitted at the hemodialysis department were retrospectively reviewed. Calcium status was evaluated by measure of ionized levels and as a function of serum calcium levels corrected for albumin aberrations. Based on the measurement of ionized calcium and total calcium corrected, patients were classified into three categories: hypocalcemic, normocalcemic and hypercalcemic. Our result showed that the corrected serum calcium values failed to accurately classify calcium status in 41% of cases. The sensitivity and specificity of the corrected serum calcium formula to evaluate hypocalcemia were 53% and 85%, respectively. Corrected serum values underestimated the prevalence of hypocalcemia and overestimated the prevalence of normocalcemia. In total, the results obtained allow to conclude the lack of interest in the use of correction formulas. Calcium homeostasis should be evaluated by ionized calcium levels rather than as a function of serum calcium and albumin.

Key words: calcium, haemodialysis, ionized calcium, correction formulae

Résumé. Des anomalies de l’homéostasie du calcium sont couramment observées chez les patients atteints d’insuffisance rénale chronique. La mesure du calcium total ne reflète pas la variation réelle de l’état de calcium. La bonne méthode pour évaluer ce problème chez les patients hémodialysés n’a pas été totalement définie. Cette étude visait à comparer les valeurs de calcium sérique corrigé et les concentrations de calcium ionisé chez les patients hémodialysés. Trente et un patients en hémodialyse chronique admis au département d’hémodialyse ont été revus rétrospectivement. Le statut du calcium sanguin a été évalué par mesure des concentrations de calcium total ionisé. Basé sur la mesure du calcium ionisé et du calcium total corrige, les patients ont été classés en trois catégories : hypocalcémie, normocalcémie et hypercalcémie. Nos résultats montrent que les valeurs corrigées de calcium sérique ne permettent pas de classer avec précision le statut en calcium dans 41 % des cas. La sensibilité et la spécificité de la formule de la calcémie corrigée afin d’évaluer l’hypocalcémie ont été de 53 % et 85 %, respectivement. La correction des valeurs sériques a sous-estimé la prévalence de l’hypocalcémie et surestimé la prévalence de la normocalcémie. Au total, les résultats obtenus permettent de conclure au manque d’intérêt dans l’utilisation des formules de correction. L’homéostasie du calcium doit être évaluée par les concentrations du calcium ionisé, plutôt que comme par la calcémie totale, même en connaissant l’albuminémie.

Mots clés : calcium, hémodialyse, calcium ionisé, correction
Calcium plays a fundamental role in many essential for life functions. Ionized calcium represents free fraction and 50% of the total calcium in the plasma is accepted as its physiologically active form. On almost all laboratories, only total calcium is routinely measured, and ionized calcium concentration is calculated based on calcium, protein or albumin concentrations for many plasma samples or with others parameters pH [1]. Since 1935, the literature was abounded with “correction” formulae of varying degree of sophistication. Many laboratories routinely use correction formulae to either calculate an “adjusted” or “corrected” total calcium, or “ionized” fraction is calculated, but these determinations lack of accuracy or precision. Errors associated with the measurement of the other variables contribute to the difficulty in producing a useful correction formulae [4]. Many formulae to correct total calcium by albumin have been proposed but none of them has been validated in dialysis patients. However the K/DOQI guidelines recommend the use of albumin corrected total calcium for routine clinical interpretation of calcium, and the use of ionized calcium is recommended only when more exact values are required. Various studies conducted in the hemodialysis patients claim clear superiority of the direct measurement of ionized calcium versus total calcium to explore calcium status [3].

Materials and methods

This study was conducted on 51 patients on chronic hemodialysis admitted at the hemodialysis department of the Ibn Zohr hospital in Guelma, Algeria. Determinations of serum parameters were performed at the medical biochemistry laboratory during the semester review “May 2011” of chronic hemodialysis patients. Arterialized venous blood was collected for each patient’s fistula or graft. Patients were not asked to fast on the morning of the test. Total calcium was collected in sec tubes and ionized calcium in heparinized tubes. Serum was separated within 2 h and sent to the reference laboratory for analysis within 8 h. All patients had albumin, total calcium, ionized calcium level and pH determinations. Albumin was assayed by an automated bromocresol green (BCG) method using the “Dialab Autolysis”, total calcium by Arseno III, pH and ionized calcium by ion-selective electrode using the “Medica EasyLite”. The corrected calcium was calculated by the formula recommended by the guidelines of the K/DOQI (Kidney disease outcomes The Quality Initiative) : Ca (mmol/L) = CAT (mmol/L) + [0.02 × (40 - albumin (g/L)]. The ability of corrected serum levels to appropriately classify calcium status was evaluated, using ionized calcium levels as the gold standard. The reference ranges for the laboratory values are given in table 1.

All statistical analyses were performed using SPP version 2.08, and a P value < 0.05 was considered significant. All data values were expressed as mean ± standard deviation. The specificity, sensitivity and predictive values for detecting hypo-, normo and hypercalcemia were calculated for both formulae.

Results

In total, 31 patients (14 male and 17 female) were enrolled in this study. The average patient age was 45 years. Distributions of the variables are summarized in table 2. Using the normal range for albumin-corrected calcium, 2.10-2.37 mmol/L, recommended by the K/DOQI guidelines, only seven patients (22%) would have been classified as normocalcaemic. Twenty-one patients (68%) would have been classified as hypocalcaemic and three patients (9%) would have been classified as hypercalcaemic. Using ionized calcium, only two patients (6%) fell within the reference range for the laboratory. 26 patients (87%) had hypocalcaemia, and two patients (6%) had hypercalcemia. Five patients (16%) were misclassified as hypercalcemic by the albumin-corrected calcium compared to ionized calcium concentrations, and 18 patients (58%) were classified as hypocalcemic with both measurements (table 3). The sensitivity and specificity of the corrected calcium formula to evaluate hypocalcaemia were 66% and 78%, respectively. The sensitivity and specificity of the corrected serum calcium formula to evaluate hypercalcaemia were 50% and 33%, respectively. The use of albumin-corrected total calcium level seems to underestimate the prevalence of hypocalcaemia and overestimate the prevalence of normocalcaemia as compared to use of ionized calcium (table 4).

Discussion

Accurate assessment of serum calcium in haemodialysis patients is important for a number of reasons. First, both

<table>
<thead>
<tr>
<th>Parameter</th>
<th>P</th>
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<tbody>
<tr>
<td>Total calcium (mmol/L)</td>
<td>2.12 - 2.62</td>
</tr>
<tr>
<td>Ionized calcium (mmol/L)</td>
<td>1.13 - 1.31</td>
</tr>
<tr>
<td>Corrected calcium K/DOQI (mmol/L)</td>
<td>2.10 - 2.37</td>
</tr>
<tr>
<td>pH</td>
<td>7.2 - 7.4</td>
</tr>
<tr>
<td>Albumin (g/L)</td>
<td>35 - 50</td>
</tr>
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Table 1. Reference ranges for laboratory values.
hypercalcaemia and hypocalcaemia have been identified as predictors of mortality [2]. Secondly, vitamin D metabolites offer therapeutic options in the normalization of serum calcium and the prevention and treatment of hyperparathyroidism and improvements in bone histology with treatment have been observed. However, with the use of vitamin D metabolites, increases in serum calcium are common, and serial monitoring is necessary to allow detection of the increase and dose adjustment.

The results of our study clearly indicate that calcium homeostasis in the hemodialysis patients is most accurately assessed by ionized calcium levels and that corrected calcium using the formula recommended by the K/DOQI guidelines fail to detect hypocalcemia in a significant number of patients (33%).

Corrected serum calcium levels failed to accurately classify calcium status in 40% of cases. There was a striking tendency of corrected serum levels to underestimate the prevalence of hypocalcemia. Calcium levels were much more likely to be classified as hypocalcemic according to ionized values compared to corrected serum values (87% vs. 67.7%).

Use of corrected calcium levels may lead to inappropriate clinical decisions with withdrawal of vitamin D, calcium containing phosphate binders and reduction of calcium concentration in the dialysis fluid of a patient classified as hypercalcemic.

In our study corrected calcium could not substitute for ionized calcium in classifying hemodialysis patients as hypo-, normo- or hypercalcaemic. But, because of technical difficulties and the high cost of the equipment, ionized calcium dosage is not considered as a routine test today.

**Conflicts of interest:** None.

**References**


