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*Review Article*

# Calcium Mass Balances in Bicarbonate Hemodialysis

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Dialysate calcium (Ca) concentration should be viewed as part of the integrated therapeutic regimen to control renal osteodystrophy and maintain normal mineral metabolism. The goals of this integrated approach are to keep the patient in a mild positive Ca mass balance (CaMB), to maintain normal serum Ca levels, to control plasma parathyroid hormone values to two to three times above normal levels, and to avoid soft-tissue calcifications. Thus, a correct net CaMB during hemodialysis (HD) is crucial in the treatment of renal osteodystrophy. Very few studies have been published which measured CaMBs in bicarbonate HD. This is mainly due to the technical difficulties in achieving an accurate measurement of CaMBs owing to the need for the collection of the total spent dialysate or of a proportional aliquot of it. Whereas no doubt exists about the fact that an inlet dialysate Ca concentration (CaD) of 1.75 mmol/L leads to a positive CaMB, more controversial is this issue, when dealing with a CaD of 1.50 mmol/L and, even more, when dealing with a CaD of 1.25 mmol/L. Another important issue is the appropriate CaD in long-hour slow-flow nocturnal HD. Finally, which CaMB should we study: ionized CaMB or total CaMB? This issue is largely discussed in the review.

Disturbances in mineral and bone metabolism are highly prevalent and are a major cause of morbidity and mortality among chronic kidney disease patients. To address this issue, current guidelines recommend a number of therapeutic strategies, such as the use of phosphate binders, vitamin D analogues, or calcimimetics [1]. However, in current practice, little attention is paid to the dialysate calcium (Ca) concentration. On the contrary, it should be viewed as part of the integrated therapeutic regimen to control renal osteodystrophy and maintain normal mineral metabolism. The goals of this integrated approach are to keep the patient in a mild positive Ca mass balance (CaMB), to maintain normal serum Ca levels, to control plasma parathyroid hormone (PTH) values from two to three times above normal levels, and to avoid soft-tissue calcifications [2]. Thus, a correct net CaMB during hemodialysis (HD) is crucial in the treatment of renal osteodystrophy.

CaMB during HD is influenced by both diffusive and convective transport. The driving force which determines the diffusive transport is given mainly by the inlet dialyzer diffusion concentration gradient between the ionized calcium (iCa) levels in the dialysate and in the plasma water. It is expressed as

$$1.12 \times \text{inlet dialyzer iCa concentration} - \text{plasma water iCa concentration}, \quad (1)$$

where 1.12 is the Gibbs-Donnan factor [3, 4].

CaMB is influenced also by the convective transport. CaMBs, which can be expressed as iCaMBs and total CaMBs, (tCaMBs) can be calculated as follows (tCaMB is taken as an example):

$$\begin{aligned}\text{tCaMB} = {} & [\text{tCa concentration in the fresh dialysate} \times \text{liters of the fresh dialysate}] \\ & - [(\text{tCa concentration in the spent dialysate} \times \text{liters of the dialysate}) \\ & + (\text{tCa concentration in the spent dialysate} \times \text{volume of ultrafiltration})]. \end{aligned} \quad (2)$$

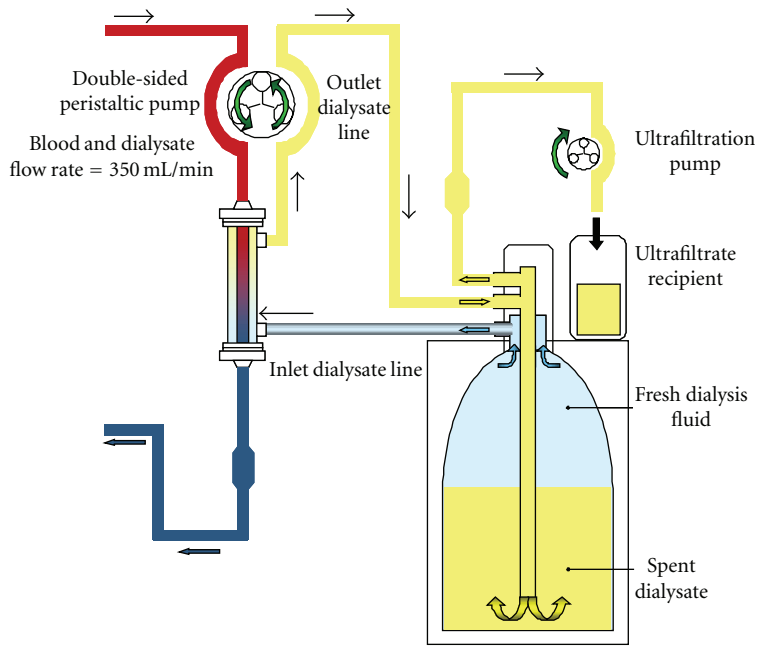


Figure 1: Flow chart of the GENIUS single-pass batch dialysis system.

Table 1: Ca mass balances in bicarbonate HD with different inlet dialysate Ca concentration (CaD).

| Authors | Hours | Number of patients | CaD (mmol/L) | Calcium mass balance (mg) |
|---|---|---|---|---|
| Malberti et al. [5] | 4 | 20 | 1.75 | +80 ± 164 |
| Hou et al. [6] | 4 | 7 | 1.75 | +876 ± 92 |
| Fabrizi et al. [7] | 3 | 6 | 1.75 | +308 ± 52 |
| Al-Heijaili et al. [8] | 4 | 13 | 1.75 | +584 ± 196 |
| Karohl et al. [9] | 4 | 23 | 1.75 | +405 ± 413 |
| Malberti et al. [5] | 4 | 20 | 1.50 | −112 ± 80 |
| Malberti et al. [10] | 4 | 11 | 1.50 | −204 ± 124 |
| Al-Heijaili et al. [8] | 4 | 13 | 1.50 | −80 ± 64 |
| Karohl et al. [9] | 4 | 23 | 1.50 | +46 ± 400 |
| Basile et al. [11] | 4 | 22 | 1.50 | +293 ± 228 |
| Basile et al. [12] | 4 | 11 | 1.50 | +285 ± 137 |
| Basile et al. [12] | 8 | 11 | 1.50 | +298 ± 132 |
| Al-Heijaili et al. [8] | 8 | 13 | 1.50 | −171 ± 287 |
| Basile et al. [11] | 4 | 22 | 1.375 | +182 ± 125 |
| Basile et al. [11] | 4 | 22 | 1.25 | +75 ± 122 |
| Hou et al. [6] | 4 | 7 | 1.25 | +216 ± 136 |
| Fabrizi et al. [7] | 3 | 6 | 1.25 | −6 ± 36 |
| Malberti and Ravani [10] | 4 | 11 | 1.25 | −324 ± 156 |
| Al-Heijaili et al. [8] | 4 | 13 | 1.25 | −328 ± 108 |
| Karohl et al. [9] | 4 | 23 | 1.25 | −468 ± 563 |
| Sigrist and McIntyre [13] | 4 | 52 | 1.25 | −188 ± 232 |
| Karohl et al. [9] | 4 | 23 | 1.00 | −578 ± 389 |

Means ± SD. Solute removal during dialysis is expressed as a negative number, whereas solute gain is expressed as a positive number.

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Total spent dialysate and ultrafiltrate can be collected in a calibrated tank. Partial dialysate collection can be performed via a time-driven sampling pump in the waste tubing. This system regularly collects a constant volume of fluid consisting of spent dialysate and ultrafiltrate [14]. Very recently, the GENIUS single-pass batch dialysis system (Fresenius Medical Care, Bad Homburg, Germany) was

utilized in studies on CaMBs [9, 11, 12]. It was chosen because it offers the opportunity of effecting mass balances of any solute in a very precise way, at variance with those obtained with the standard single-pass dialysis systems, which are always at risk of systematic errors [15]. The characteristics of the GENIUS dialysis system are shown in Figure 1 and have been described elsewhere [16].

Very few studies have been published which measured CaMBs in bicarbonate HD [5–13]. This is mainly due to the technical difficulties in achieving an accurate measurement of CaMBs owing to the need for the collection of the total spent dialysate or of a proportional aliquot of it [14].

Table 1 summarizes CaMBs obtained in the most relevant studies in bicarbonate HD [5–13]. Whereas no doubt exists about the fact that an inlet dialysate Ca concentration (CaD) of 1.75 mmol/L leads to a positive CaMB [5–9], more controversial is this issue, when dealing with a CaD of 1.50 mmol/L [5, 8–12] and, even more, when dealing with a CaD of 1.25 mmol/L [6–11, 13]. Worth noting, very recently Basile et al. showed that a CaD of 1.375 mmol/L was able to keep the patient in a mild positive tCaMB to maintain normal plasma Ca levels and not to stimulate PTH secretion [11].

Another important issue is the appropriate CaD in long-hour slow-flow nocturnal HD. This issue has been addressed in very few studies [8, 12]. Al-Hejaili et al. showed that in order to remain in positive CaMB in long-hour slow-flow HD a patient requires the CaD to be in excess of 1.50 mmol/L [8]. By contrast, Basile et al. showed that, when using a CaD of 1.50 mmol/L, both treatments (4 h and 8 h) always achieved a positive iCaMB for the patients [12].

Finally, which CaMB should we study: iCaMB or tCaMB? A very recent study by Basile et al. [11] confirmed and extended data already published by Argiles et al. [14]: mean tCaMBs were less positive than mean iCaMBs for each of the CaD studied (1.25, 1.375 and 1.50 mmol/L), even though their difference did not reach the level of statistical significance [11]. When pooling all the 66 experiments (22 patients undergoing one experimental bicarbonate HD session with the three CaD), a mean difference of 9.8 percent between tCaMBs and iCaMBs was obtained [11]. This difference was less striking (4.7 percent), but statistically significant ($P < .006$), when comparing the ratios iCa/tCa of the fresh and spent dialysate obtained in the kinetic studies [11]. The figure of 4.7 percent was close to the values obtained by Argiles et al. [14]: the mean percent differences in their study were 8.3 and 5.0 between the ratios iCa/tCa of the fresh and spent dialysate, when using, respectively, a CaD of 1.25 and 1.50 mmol/L [14]. Furthermore, Argiles et al. claimed that phosphate captured by the dialysate fluid during its passage through the dialyzer may be responsible for such a shift between Ca pools [14]. Even though this is true, complexing of iCa by phosphate is probably only part of the truth. Actually, other anions may complex iCa, such as lactate, citrate, bicarbonate, and sulphate [17]. Furthermore, kinetic studies by Basile et al. showed that the main factor leading to precipitation of Ca complexes is probably the large difference in pH existing between the inlet dialysate and the ultrafiltrate recipient (Figure 1) [11]. In fact, Moore observed a decrease in iCa of ultrafiltrates above pH 7.3–7.6; this most likely represents a solubility (kinetic) problem related to variable precipitation of certain Ca complexes [17].

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