Dear Sir,

Despite early suggestions about aluminum (Al) absorption and toxicity in renal failure [1], Al hydroxide was widely used as a phosphate binder until a few years ago. In the late 70s, Al metabolism was more deeply investigated and its deposition in various tissues was found to be correlated with serious disorders [2]. Moreover, it was established that Al burden does not only derive from dialysate but also from gut absorption in RDT patients on Al containing phosphate binders [3].

Thus, in order to correct hyperphosphatemia while avoiding Al intoxication, calcium carbonate, that was already employed as Ca supplement, was also tested as a phosphate binder on the basis of previous observations [4], and it was confirmed as a valid therapy in correcting hyperphosphatemia in RDT patients. The risk of hypercalcemia can be prevented by adjusting dialysate Ca concentration (dCa) and administering CaCC just before meals [5-8]. In our experience a schedule including a dCa of 3.5 mEq/l and a mean CaCC dose of 9 ± 3 g given only in the interdialytic days before meals allowed in the long term a good control of divalent ions in all patients [9].

The possible use of magnesium (Mg) salts as phosphate binders, instead of CaCX¾ [10, 11], is hampered by the difficulty of associating a proper dialysate Mg concentration (dMg). In fact, the use of Mg salts, when not associated with a shade reduction of dMg, results in hypermagnesemia which can further impair bone mineralization; on the other side, when Mg salts are associated with a negligible dMg, low postdialytic serum Mg can occur with acute harmful effect [12]. Therefore, the use of Ca salts is widely accepted as first choice phosphate binders in RDT patients. However, despite a good control of divalent ions, most RDT patients developed secondary hyperparathyroidism in the long term.

Slatopolsky et al. [13] showed that intravenous boli of calcitriol (CAL) suppress elevated parathyroid hormone (PTH) concentration, probably through the saturation of parathyroid cells, CAL receptors and the consequent suppression of parathyroid activity. Since then a number of papers illustrating the beneficial effect of oral or intravenous CAL boli upon PTH secretion has been published.
As expected and pointed out by most authors, the possible side effects of such therapy are hypercalcemia and hypephosphatemia due to gut absorption of both ions stimulated by CAL [14]. This problem is far more serious in a clinical setting when CaC<sub>2</sub>O<sub>4</sub> is used as a phosphate binder. In fact, while an isolated hypercalcemia can be corrected by lowering dCa below 3 mEq/l [15], hypephosphatemia, which occurs in most patients [14], cannot be managed so easily by a substantial increase of oral CaCC<sub>3</sub> dose because this can result in a further increase of serum Ca (not fully prevented by lowering dCa) and in a possible low compliance to the therapy. In this complicated puzzle the use of Al hydroxide as phosphate binder has been rediscovered and reintroduced among the nephrologist’s tools somehow in a subdubious way, maybe forgetting the risks of Al overload, still not fully preventing hypercalcemia and hypephosphatemia. The only paper [15] that, to our knowledge, describes favorable results by combining CaCC<sub>3</sub> as the only phosphate binder, pulse CAL therapy and low dCa, could be questioned because the follow-up lasted only 6 months, whereas in our experience (unpublished observations) an altered divalent ions control occurred after a longer follow-up. It is well known that hypephosphatemia, especially when associated with hypercalcemia, results in a high Ca×Pi product (> 60-70) with a relevant risk of determining or worsening vascular calcifications. Therefore, the association of Ca salts, very low dCa and pulse CAL therapy implies a constant weekly surveillance because an adequate control of divalent ions is not guaranteed indefinitely also for the low compliance to high oral CaCC<sub>3</sub> doses. On the other hand, when CaCC<sub>3</sub> is totally or partially substituted by Al compounds, the risk of Al intoxication is additive to the risk of hypercalcemia and hypephosphatemia. In conclusion, in an overall clinical evaluation, it must be established whether the risks of a high Ca×Pi product and/or Al intoxication overwhelm those of hyperparathyroidism in end-stage renal failure. On the other hand, as largely experienced, parathyroid glands can be removed without significant surgical risks, guaranteeing a positive long-term outcome in divalent ions control and in bone structure [16].

References


114

Calabrese/Vagelli/Gonella

CAL Boli and Al\textsubscript{OH}$^+$ in Secondary Hyperparathyroidism?