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# Balancing Bone Health in Pediatric CKD: A Time-Series Trial of Calcium-Based vs. Calcium-Free Phosphate Binders

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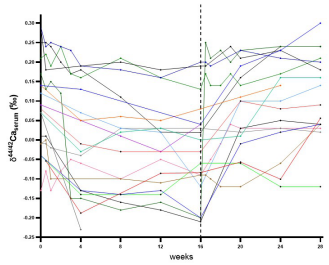
Children with chronic kidney disease (CKD) experience dysregulated calcium (Ca) and phosphate (P) homeostasis, leading to reduced bone mineral density, increased fracture risk, and vascular calcification. The use of phosphate binders, which can be Ca-based or Ca-free, is a standard treatment in CKD. However, their impact on bone calcium balance (BCaB) remains unclear. This study evaluates changes in BCaB in children receiving a Ca-free phosphate binder (sevelamer carbonate) compared to a Ca-based binder (calcium carbonate), using a novel non-invasive method based on stable Ca isotope ratios in serum and urine. This single-center, open-label, time-series trial included children aged 5–17 years with CKD stages 3b–5 or on dialysis. Participants initially received a Ca-based phosphate binder, which was switched to sevelamer carbonate for 16 weeks, followed by a return to the Ca-based binder for an additional 12 weeks. BCaB was assessed through Ca isotope ratios in serum (**CIM_serum**) and urine (**CIM_urine**), alongside standard biomarkers of bone turnover and mineral metabolism. A significant and immediate decline in **CIM_serum** values (by 0.1‰, $p < 0.002$) was observed within the first four weeks after switching to sevelamer, indicating increased bone resorption. **CIM_serum** values subsequently rose after reintroducing usual Ca supplementation, suggesting bone mineralization recovery. **CIM_urine** values remained stable, likely due to compensatory Ca reabsorption via parathyroid hormone (PTH) regulation. Standard serum biomarkers of bone metabolism showed no significant changes, while bone formation markers (BAP, P1NP) decreased and bone resorption markers (TRAP-5b) increased during the sevelamer phase.

**$\delta^{44/42}Ca_{serum}$ in all patients**




**Bone turnover markers**