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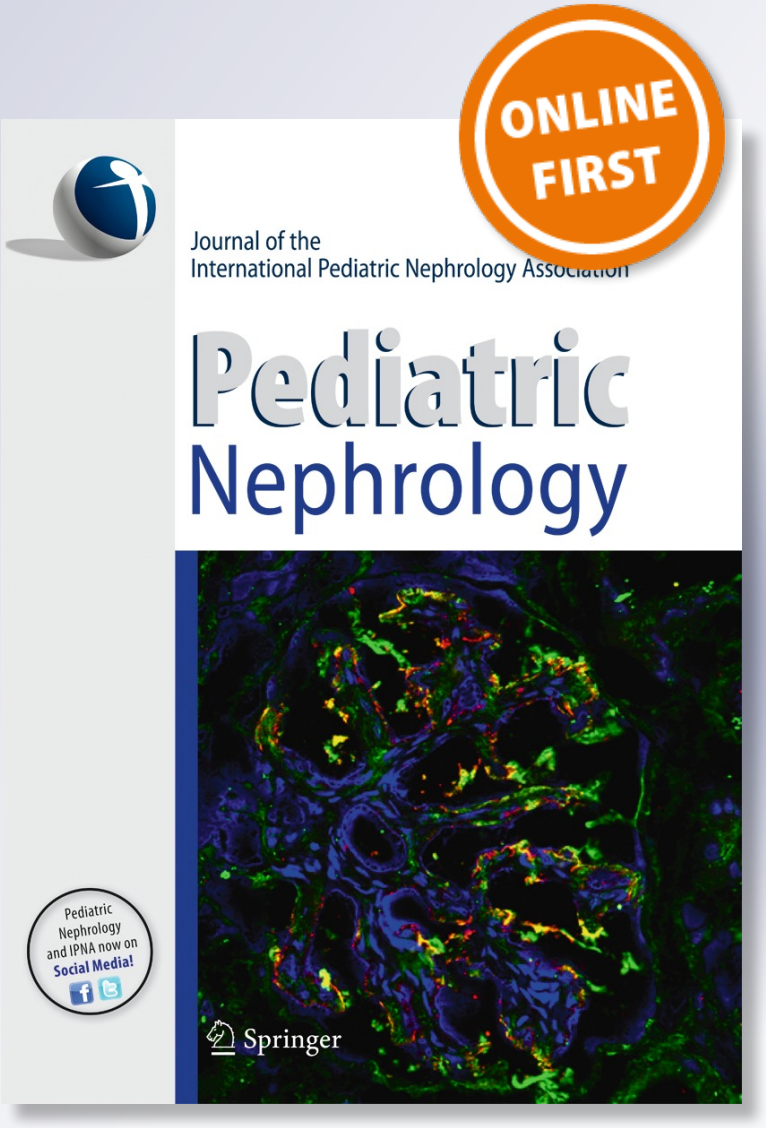

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LETTER TO THE EDITOR

The dual-tracer stable isotope method to measure calcium absorption in children on dialysis: a new use for an old technique

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Dear Editor,

In an article on phosphate binder use in chronic kidney disease (CKD), Rees and Shroff stressed the need for studies of calcium balance, in particular in children on dialysis [1]. We would like to draw attention to the potential for the new use of an old technique: the dual-tracer stable isotope method. This is an established technique that has been used to measure fractional calcium absorption in children of all ages (even premature infants) with many different medical conditions [2]. One stable isotope of calcium is given orally and a different one intravenously (IV) 2 h later. Once the absorbed and IV isotopes are equilibrated, their ratio in blood and urine is independent of differences in calcium pool size and turnover rates. The percent absorption of calcium can be calculated from the ratio of the oral tracer dose to the IV tracer dose recovered in a 24 h urine pool post-dosing. In children on dialysis, recovery from dialysate would also be required. Another approach used to estimate fractional calcium absorption is the single timed serum method, which uses a serum sample taken 4 h after the isotope given orally (and 2 h after the isotope given IV) has been given and does not need urine or dialysate collection [3]. Neither method needs complex metabolic balance studies or faecal collection. Neither has been used in CKD as yet.

Ethical committee permission was obtained from the National Research Ethics Committee, Bloomsbury, to obtain pilot data and to compare use of a single timed serum method in children on dialysis. Informed consent was taken from carers and assent from the children. Firstly, we looked at the recovery of isotopes in urine and dialysate using typical doses used previously in this age group: 3 mg of ^{44}Ca orally and 1 mg ^{42}Ca IV in an 8-year-old child on peritoneal dialysis (PD). Selection of isotopes was based on their fractional abundance (^{44}Ca at 2.083 % and ^{42}Ca at 0.647 %). Isotopic ratios were measured using magnetic sector thermal ionisation mass spectrometry. The full methodology has been previously described and validated [2].

Enrichment of the orally ingested tracer was readily analysed, but the delta percent excess of isotope was lower than anticipated, at 2.42 % and 0.63 % in the urine and 0.50 % and 0.24 % in the peritoneal dialysate for ^{42}Ca and ^{44}Ca, respectively. For the next three patients, aged 5–11 years, we studied those on haemodialysis (HD) to compare the timed serum method with the standard 24-h urine collection technique. The doses were increased to 6 mg ^{44}Ca orally and 1.5 mg ^{42}Ca IV. The mean percent calcium absorption calculated using the 24-h urine method was 15.6 ± 8.5 % (range 5.9–21.9 %) and in the 4-h serum samples 8.3 ± 7.6 % (range 3.0–17.0 %). Absorption values obtained using the ratio of oral to IV isotope in serum were all lower than the results obtained in the 24-h urine pool, on average by 10.6 % ($r = 0.73$, $p = 0.47$) between the serum and urine methods. Other studies have extended this serum collection time serum collection point to 6 h [3]. Additional studies are warranted to explore this issue, as possible alterations in peak absorption times may be evident in patients on dialysis.

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In this group of prepubertal paediatric patients, a dose of 1.5 mg ^{42}Ca IV resulted in a mean serum enrichment of 5.1 ± 2.0 % at 4 h post oral dosing (range 2.9–6.7 %), and a mean urine enrichment of 1.8 ± 0.8 % in the 24-h urine pool (range 0.9–2.5 %). Mean serum enrichment from 6 mg ^{44}Ca taken orally was 0.6 ± 0.6 % (range (0.2–1.2 %) and remained sub-optimal. Mean urine enrichment of ^{44}Ca tracer taken orally was 0.4 ± 0.3 % (range 0.2–0.7 %). With these doses, the enrichment was satisfactory for the IV dose but by calculation, a minimum dose of 8 mg of ^{44}Ca would be required to provide urine enrichment of >0.5 %, or 17 mg for >1 % as an estimate in prepubertal children aged 5–11 years.

In conclusion, this data on enrichment in serum and urine pools will assist future investigators with dosing estimations depending on the relative standard deviation of their mass spectrometer. The single serum method may remove the difficulties with complete 24-h urine collections, but the optimum timing for the sample needs further investigation. The knowledge gained from this study about the methodology of this technique in dialysis patients will help open the way to future research in children, including research into calcium absorption from calcium-containing phosphate binders, and the effect on calcium absorption of different doses of vitamin D, different phases of CKD and of age and growth.

Compliance with ethical standards

Conflict of interest The authors declare no conflict of interest.

References

1. Rees L, Shroff R (2015) The demise of calcium-based phosphate binders—is this appropriate for children? Pediatr Nephrol 30:2061–2071
2. Abrams SA (1999) Using stable isotopes to assess mineral absorption and utilization by children. Am Clin Nutr 70:955–964
3. Lee W, McCabe G, Martin B, Weaver C (2011) Simple isotopic method using oral stable or radioactive tracers for estimating fractional calcium absorption in adult women. Osteoporos Int 22:1829–1834