

Cochrane Nursing Care Field: Intervention for bone disease in children with chronic kidney disease

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Review question

To investigate the benefits and harms of interventions for preventing and treating bone disease in children with chronic kidney disease (CKD).

Relevance for clinical practice

Estimates of the incidence of bone disorders in children with CKD stages 2–5D (glomerular filtration rate $<90\text{mL}/\text{min}/1.73\text{m}^2$) can be anywhere from 28% to 81%. Disabling deformities and fractures can occur. Treatments for bone disease include vitamin D preparations, phosphate binders, surgical interventions as well as the manipulation of dietary intake; however, there remains uncertainty about the efficiency of these treatments in children.

Characteristics of the evidence

The review included 15 randomised controlled trials (RCTs) and quasi-RCTs, a total of 369 children (not exceeding the age of 21 years old) with CKD stages 2–5. Different interventions (for example, dietary, pharmacological, surgical, herbal or alternative treatments and changes in dialysis prescription) used to prevent or treat bone disease were considered and compared with placebo, no treatment or other agents. Frequency and mode of administration and dose and duration of treatment were also considered

The outcome measures for this review were: patient-centred outcomes (for example, growth, fractures, deformities), surrogate outcomes (for example, change in bone histology, serum parathyroid hormone [PTH] levels) and adverse events.

The included studies measured

- Intraperitoneal (IP) calcitriol compared with oral calcitriol (two studies).
- Intermittent oral administration of calcitriol compared with daily oral administration (three studies).
- Different vitamin D preparations given orally or intravenously (IV) compared with placebo or no specific treatment (four studies).
- Different vitamin D preparations (two studies).
- Calcium carbonate versus aluminium hydroxide (two studies).
- Sevelamer versus calcium-containing phosphate binders (two studies).

Studies ranged from eight weeks to 1.2 years duration and were undertaken between 1983 and 2007.

Concerns about the risk of bias were raised. One study was deemed at high risk due to inadequate allocation concealment while it was unclear in

Keywords

Renal bone disease; children; chronic kidney disease; prevention; treatment.

another six studies. Five studies were at high risk of bias due to a lack of blinding. Fourteen of the studies were unclear as to whether selective reporting occurred. Meta-analysis was undertaken where possible.

Results

One study ($n=7$) showed no significant difference in PTH levels, the number of children with hypercalcaemia and the number of peritonitis episodes between the use of intraperitoneal versus oral calcitriol.

Another study ($n=33$) also compared IP with oral calcitriol demonstrating significantly lower mean PTH levels in IP calcitriol compared with oral calcitriol. There was no significant difference in the number of children with abnormal bone histology.

Three parallel studies ($n=104$) compared intermittent oral versus daily oral calcitriol and found no significant differences in growth, PTH, serum calcium or phosphorus.

Four parallel studies compared vitamin D preparations versus

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placebo or no specific treatment. Two (n=28) compared 1 α hydroxyl Vitamin D with no specific treatment with one demonstrating PTH levels were significantly lower in the treated children compared with the control. The other two studies (n=57) compared IV calcitriol or IV paricalcitol given three times/week with a placebo. The IV vitamin D preparations significantly reduced the number of children failing to achieve a 30% fall in PTH levels on at least two occasions; however, the changes in mean PTH levels during treatment were not significantly different compared with the placebo.

Two studies (n=97) compared calcitriol with other vitamin D preparations of dihydrotachysterol or ergocalciferol and both found no significant differences in growth between preparations.

Two studies (n=29) compared calcium carbonate with aluminium hydroxide as phosphate binder. One study reported no significant difference in mean final height yet did report the number of abnormal bone biopsies at the end of the treatment was significantly lower in children treated with calcium carbonate compared with aluminium hydroxide. In the other study the results were not reported separately for each group. Plasma aluminium levels were significantly higher at the end of the aluminium treatment compared to the calcium carbonate treatment.

Two studies compared the non calcium-containing phosphate binder sevelamer with calcium carbonate or calcium acetate. In one study (n=29) there were no significant differences in the reported outcomes yet serum calcium levels were significantly lower in the sevelamer treated children. In the other study (n=unknown) there were no significant

differences between groups. Both studies did, however, report more hypercalcaemic episodes in calcium carbonate-treated children.

Implications for clinical practice

This review demonstrated that there is no consistent difference between routes of administration, frequencies of dosing or vitamin D preparations in regard to interventions for preventing and treating bone disease in children with CKD. Caution should be considered in interpreting the results as RCTs were small with few data available on patient-centred outcomes.

Implications for research

Only 15 RCTs were identified over 23 years and they provide limited data on the efficacy of interventions for the prevention and treatment of renal bone disease in children.

As newer vitamin D sterols, calcimimetic agents and phosphate binders are developed, more robust comparisons with standard therapies will be required in well-designed, adequately powered paediatric RCTs using standardised outcome measures including those of direct clinical relevance to children and their families such as growth, fractures, bone deformities and measures of bone health as well as surrogate biochemical markers.

Reference

- Geary DE, Hodson EM & Craig JC (2010). Interventions for bone disease in children with chronic kidney disease. *Cochrane Database of Systematic Reviews*, Issue 1, Art No.: CD008327, DOI: 10.1002/14651858.

