

Review: Vitamin D plus calcium is more effective than no therapy or calcium alone in corticosteroid-induced osteoporosis

Amin S, LaValley MP, Simms RW, Felson DT. The role of vitamin D in corticosteroid-induced osteoporosis. A meta-analytic approach. *Arthritis Rheum.* 1999 Aug;42:1740-51.

QUESTION

How effective is vitamin D compared with no therapy, calcium alone, or other osteoporosis drugs in the management of corticosteroid-induced osteoporosis?

DATA SOURCES

Studies were identified by using MEDLINE (1966 to December 1997), *Current Contents* (October 1997 to January 1998), lists of conference abstracts, and bibliographies of relevant papers and by contacting drug companies and content experts.

STUDY SELECTION

Studies were selected if they were randomized controlled trials (RCTs) on the treatment or prevention of corticosteroid-induced osteoporosis; follow-up was ≥ 6 months; they compared a formulation of vitamin D (including its active metabolites and analogues) plus calcium or vitamin D alone with no therapy, calcium alone, bisphosphonates, calcitonin, fluoride, or hormone replacement therapy; and change in lumbar spine bone mineral density (BMD) was reported.

DATA EXTRACTION

Study and patient characteristics, change in lumbar spine BMD, and rate of fracture.

MAIN RESULTS

61 RCTs were identified, and 21 studies of 23 comparison regimens met the selection criteria. Meta-analysis showed that vitamin D plus calcium decreased loss of lumbar spine BMD more than no therapy or calcium alone ($P < 0.001$, 9 studies) (Table). Similar results were shown in a sensitivity analysis comparing 2 studies of vitamin D alone and 9 studies of vitamin D plus calcium with no therapy or calcium alone ($P < 0.001$) and in subgroup analyses comparing vitamin D plus calcium with no therapy ($P < 0.001$, 4 studies), vitamin D plus calcium with calcium alone ($P = 0.009$, 5 studies), active metabolites or analogues of vitamin D with no therapy or calcium alone ($P = 0.03$, 4 studies), or vitamin D that was not in the form of an active metabolite or analogue with no therapy or calcium alone ($P < 0.001$, 5 studies). Bisphosphonates

decreased loss of lumbar spine BMD more than vitamin D ($P = 0.02$, 6 studies), as did fluoride ($P = 0.02$, 2 studies) (Table), but calcitonin did not ($P = 0.90$, 4 studies).

CONCLUSION

Vitamin D plus calcium is more effective than no therapy or calcium alone but is less effective than bisphosphonates or fluoride in decreasing loss of lumbar spine bone mineral density in corticosteroid-induced osteoporosis.

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Comparison of regimens for change in lumbar spine bone mineral density in patients receiving corticosteroids for follow-up between 6 and 24 mo

Comparisons	Standardized mean difference (95% CI)
Vitamin D plus calcium vs no therapy or calcium alone	0.60 (0.34 to 0.85)
Bisphosphonates vs vitamin D	0.57 (0.09 to 1.05)
Fluoride vs vitamin D	0.66 (0.11 to 1.22)

COMMENTARY

About 50% of patients receiving long-term glucocorticoid therapy experience bone loss and fractures (1). Vitamin D may be an effective treatment for steroid-induced osteoporosis because it stimulates calcium absorption from the gut and decreases the secretion and production of parathyroid hormone (2).

This well-conducted meta-analysis concludes that patients receiving long-term corticosteroids should, at a minimum, receive calcium and vitamin D supplementation. However, several clinically important questions, which this meta-analysis could not address because of limited data, remain unanswered. First, are all vitamin D formulations equal? Second, what is the optimum dose of vitamin D to balance efficacy and toxicity? Third, do some subgroups of patients benefit from vitamin D more than others (e.g., those with low levels of vitamin D)?

The analyses showed that vitamin D, with or without calcium supplementation, is less effective than bisphosphonate therapy. The combination of calcium, vitamin D, and bisphosphonate has been

shown to be safe and effective for the prevention and treatment of steroid-induced osteoporosis (1). However, it is unknown whether vitamin D enhances the effect.

On the basis of this meta-analysis, physicians should ensure that their patients receiving long-term glucocorticoids also receive calcium and vitamin D supplementation. A bisphosphonate should be considered for those with osteoporosis or those at high risk for developing the condition.

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References

1. Saag KG, Emkey R, Schnitzer TJ, et al. Alendronate for the prevention and treatment of glucocorticoid-induced osteoporosis. Glucocorticoid-Induced Osteoporosis Intervention Study Group. *N Engl J Med.* 1998;339:292-9.
2. Sambrook PN, Jones G. Corticosteroid osteoporosis. *Br J Rheumatol.* 1995;34:8-12.