

# Medical Update Memo

July 6, 2010

## **A phase I/II dose-escalation trial of vitamin D3 and calcium in multiple sclerosis.**

### **Summary**

Low vitamin D status has been associated with multiple sclerosis (MS) prevalence and risk, but the therapeutic potential of vitamin D in established MS has not been explored. Canadian researchers assess the tolerability of high-dose oral vitamin D and its impact on biochemical, immunologic, and clinical outcomes in patients with MS prospectively. **Burton JM, Kimball S, Vieth R, Bar-Or A, Dosch HM, Cheung R, Gagne D, D'Souza C, Ursell M, O'Connor P. *Neurology*. 2010 Jun 8;74(23):1852-9. Epub 2010 Apr 28.**

### **Details**

An open-label randomized prospective controlled 52-week trial matched patients with MS for demographic and disease characteristics, with randomization to treatment or control groups. Treatment patients received escalating vitamin D doses up to 40,000 IU/day over 28 weeks to raise serum 25-hydroxyvitamin D [25(OH)D] rapidly and assess tolerability, followed by 10,000 IU/day (12 weeks), and further down titrated to 0 IU/day. Calcium (1,200 mg/day) was given throughout the trial. Primary endpoints were mean change in

serum calcium at each vitamin D dose and a comparison of serum calcium between groups. Secondary endpoints included 25(OH)D and other biochemical measures, immunologic biomarkers, relapse events, and Expanded Disability Status Scale (EDSS) score.

Forty-nine patients (25 treatment, 24 control) were enrolled [mean age 40.5 years, EDSS 1.34, and 25(OH)D 78 nmol/L]. All calcium-related measures within and between groups were normal. Despite a mean peak 25(OH)D of 413 nmol/L, no significant adverse events occurred. Although there may have been confounding variables in clinical outcomes, treatment group patients appeared to have fewer relapse events and a persistent reduction in T-cell proliferation compared to controls.

**CONCLUSIONS:** High-dose vitamin D (approximately 10,000 IU/day) in multiple sclerosis is safe, with evidence of immunomodulatory effects.

**CLASSIFICATION OF EVIDENCE:** This trial provides Class II evidence that high-dose vitamin D use for 52 weeks in patients with multiple sclerosis does not significantly increase serum calcium levels when compared to patients not on high-dose supplementation. The trial, however, lacked statistical precision and the design requirements to adequately assess changes in clinical disease measures (relapses and Expanded Disability Status Scale scores), providing only Class level IV evidence for these outcomes.

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