A systematic review of randomized, double-blind, placebo-controlled trials examining the clinical efficacy of vitamin D in multiple sclerosis


CRD summary
The authors' cautious conclusion that there was a lack of evidence to support vitamin D as a treatment for multiple sclerosis, can be considered to be reliable.

Authors' objectives
To review the evidence for vitamin D in the treatment of multiple sclerosis.

Searching
PubMed and Cochrane Central Register of Controlled Trials (CENTRAL) were searched to August 2012. Keywords were reported. Personal files, reference lists, and reviews of vitamin D supplementation were searched. No language restrictions were applied.

Study selection
Randomised controlled trials (RCTs), comparing placebo with vitamin D supplementation, for patients diagnosed with multiple sclerosis, were eligible for inclusion. The outcomes of interest were clinical efficacy and toxicity.

In most of the included trials, the participants were diagnosed with relapsing-remitting multiple sclerosis. In the other trials, they were diagnosed with multiple sclerosis, but the eligibility criteria varied. Vitamin D was given as D3 or D2, taken daily, weekly or monthly, depending on the trial; the dosage varied. All trials reported Expanded Disability Status Scale (EDSS) results, and most reported at least one other outcome, such as disease progression, relapse rate, cognitive functioning, health-related quality of life, or neuroimaging results. Treatment lasted between six months and two years.

Two reviewers independently screened records for inclusion, and any disagreements were resolved by discussion.

Assessment of study quality
The Jadad scale was used to assess the quality of randomisation, blinding, and description of withdrawals and drop-outs. The maximum score was 5. It was unclear how many reviewers assessed the quality.

Data extraction
It was unclear how many reviewers extracted the data.

Methods of synthesis
No statistical synthesis was performed, due to variation in the vitamin D treatment and outcomes reported. A brief narrative summary was presented.

Results of the review
Five RCTs were included (265 participants; range 23 to 68). Four trials used vitamin D3 on a weekly or monthly basis, and the other trial compared high versus low doses of vitamin D2, on a daily basis. Four trials were high quality on the Jadad (5), and the other trial scored 2, with a lack of information on randomisation, blinding, and withdrawals and drop-outs.

Four RCTs found no significant beneficial effects from vitamin D, for the multiple sclerosis outcomes. One RCT reported statistically significant reductions in the number of T1 (magnetic resonance imaging, spin-lattice relaxation time)-enhancing lesions, and some trends in burden-of-disease scores. All five trials were small, and at least three were unlikely to be powered to detect differences in the clinical outcomes.

Three trials reported mild gastrointestinal adverse effects.

Two ongoing larger high-quality trials of high dosages of vitamin D3 were identified.
Authors' conclusions
The evidence for vitamin D in the treatment of multiple sclerosis was inconclusive, and larger trials were needed.

CRD commentary
The review addressed a clear question, with appropriate inclusion criteria. The search was limited in scope, and may have missed potentially eligible trials. The review processes were only partly described making it difficult to rule out reviewer error and bias in assessing trial quality and data extraction.

The trials were assessed for quality, but a summary score can obscure the quality details. The authors discussed the problems of small underpowered trials and identified their flaws. A brief narrative summary was provided, and this seems to have been appropriate given the variation in dose, duration and type of supplement.

The authors’ cautious conclusions recognised the potential for publication bias, the ongoing trials, and the lack of evidence to support vitamin D as a treatment for multiple sclerosis.

Implications of the review for practice and research
Practice: There was a lack of evidence to support vitamin D as a treatment for multiple sclerosis, and there were no guidelines on dosage or duration.

Research: Large high-quality trials, with follow-up of more than one year, were needed to explore the optimal dosage and duration of treatment. They should examine the impact of treatment on health-related quality of life. Two large ongoing trials were identified.

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