International research adding more pieces to the vitamin D puzzle

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Many observational studies have provided evidence that low levels of vitamin D in the blood are associated with an increased risk of developing MS and are also associated with more frequent relapses in people who have MS. However, it has not been clearly demonstrated in clinical trials that vitamin D supplements can prevent MS, or reduce relapses or delay progression. The most appropriate and safe dose or blood level of vitamin D that is needed for clinical benefit also remains unclear.

To try and address these questions, two studies were recently published that looked at the effects of vitamin D supplementation on the immune system and inflammation in people with MS.

Both studies used randomised controlled clinical trial designs where participants and assessing doctors were 'blinded' as to which dose of vitamin D or placebo the participants were receiving. Both studies looked at aspects of the immune system and inflammation in MS but neither study was designed to detect whether vitamin D supplements could provide a clinical benefit.

The American study was published in *Neurology* in December. In this study, a total of 40 people with MS were randomly assigned to receive either 10,400 international units (IU) of vitamin D per day or 800 IU per day for six months. Both doses of vitamin D were well tolerated and only three individuals dropped out of the study due to the side effect of nausea (two in the high dose group and one in the low dose arm). Side effects were otherwise minimal.
The researchers found that the high dose supplement was much more effective in raising the blood level of vitamin D in the participants than the low dose. They also found that the profile of immune cell types in the blood of those in the high dose group was significantly shifted towards a less inflammatory state. In particular, there was a drop in the types of CD4 immune cells that have been implicated in MS. They also looked at the profile of inflammatory chemicals in the bloodstream of the participants but did not see any differences between the high dose and low dose groups.

The study did not have enough participants to examine the clinical effects of vitamin D supplementation, such as relapse rates and MRI lesions. However, the team conclude that high dose vitamin D supplementation appears to be safe and shows effects on the immune system that could be beneficial in MS.

A Norwegian group have also published the results of their study to examine the effect of vitamin D supplementation on eleven blood markers of inflammation in 68 people with relapsing remitting MS. In this study, which appeared in the *Journal of Neurology*, half of the participants took a high-dose oral vitamin D supplement of 20,000 IU per week for two years and half took a 'dummy' or placebo capsule. The supplement was able to more than double the average vitamin D level in the blood, but there were no significant effects on levels of inflammation-related chemicals in the blood stream when compared to the dummy drug.
The Norwegian study did not examine immune cell sub-types in the participants and therefore it is difficult to directly compare the two studies. However, the Norwegian team concluded that their results do not confirm an association between increasing vitamin D levels in the blood and reduced inflammation in relapsing-remitting MS.

Despite their apparently contradictory results, both of these studies form an important part of the much needed investigation into the role that vitamin D supplementation may play in MS. However, they also highlight the need for larger clinical trials that can look at both the effects on immune system biology, as well as the clinical impact on relapses, lesions and disability progression.

While there is much information available that appears to point towards vitamin D supplementation being an appropriate choice for people with MS, these studies emphasise that there is a great deal that we still don't know about vitamin D supplementation for MS, including safety, optimum dosage and clinical efficacy.

To this end MS Research Australia is currently funding and co-ordinating a large clinical trial of vitamin D supplementation in people at high risk of developing MS in Australia and New Zealand. The study aims to determine whether oral vitamin D supplementation can prevent or delay a second relapse in a person who has had their first attack that may be suggestive of MS. The study has been designed to investigate the effect of a range of different doses of vitamin D on the risk of experiencing a second relapse or MRI lesion. We hope that this study will provide vital information on the safety of vitamin D supplementation in people at risk of MS and the optimum blood level of vitamin D required to produce a clinical effect.

For more information on this clinical trial please visit www.msra.org.au/prevanz