

Support for Causal Role of Low Vitamin D in MS

Megan Brooks | September 07, 2015

A novel new study supports a causal role for low vitamin D in risk for multiple sclerosis (MS), researchers say.

"We found a very strong relationship between a lifetime of lowered vitamin D levels and an increased risk of MS," J. Brent Richards, MD, from the Departments of Medicine, Human Genetics, Epidemiology and Biostatistics, McGill University, Montreal, Quebec, Canada, told *Medscape Medical News*.

"This evidence provides rationale to further investigate whether vitamin D supplementation may reduce MS susceptibility in those most at risk," he and his colleagues say.

The study was published online August 25 in *PLOS Medicine*.

Novel Approach

"Vitamin D insufficiency is very common and has been previously associated with an increased risk of MS. However, such findings have been met with skepticism because vitamin D levels are associated with many other factors which may actually influence MS and these correlations might obscure the true relationship between vitamin D and MS," Dr Richards explained.

"To overcome such confounding, we undertook a Mendelian randomization study, which is sometimes called 'nature's randomized controlled trials' since they use natural randomization in genetics to overcome confounding," he said.

First, the researchers identified single-nucleotide polymorphisms (SNPs) associated with 25-hydroxyvitamin D [25(OH)D] levels using data from the Study of Underlying Genetic Determinants of Vitamin D and Highly Related Traits (SUNLIGHT). With more than 33,000 individuals, SUNLIGHT is the largest genome-wide association study for 25(OH)D levels published to date.

The researchers found that four SNPs located in or near genes strongly implicated in influencing 25(OH)D had genome-wide significance for 25(OH)D levels.

Next, they determined the effect of these four SNPs on 25(OH)D levels in 2347 participants from the Canadian Multicentre Osteoporosis Study. They found that each of the SNPs was strongly associated with lower 25(OH)D levels.

Finally, the researchers applied the principles of Mendelian randomization to study the association of a lifetime of genetically lowered 25(OH)D level with MS risk using data from the International Multiple Sclerosis Genetics Consortium (IMSGC), including up to 14,498 patients with MS and 24,091 healthy controls.

They found that each genetically determined 1-SD decrease in log-transformed 25(OH)D level was associated with a 2-fold increase in odds of MS, "providing strong evidence in support of a causal role of vitamin D in MS susceptibility," they say. The findings "remained robust" in multiple sensitivity analyses.

"Important Contribution"

"The most important finding of this study for clinicians is that we have provided support for the causality of low vitamin D levels in susceptibility to MS," Dr Richards told *Medscape Medical News*. "These findings suggest that

individuals at high risk for MS, such as first-degree family members, should ensure that their vitamin D levels are normal," he added.

"Whether vitamin D sufficiency can delay, or prevent, MS onset merits further investigation in long-term randomized controlled trials," the investigators point out in their paper. They note that two ongoing randomized controlled trials are assessing vitamin D supplementation for the treatment and prevention of MS, "and may therefore provide needed insights into the role of vitamin D supplementation."

Reached for comment, R. Erik Charlson, MD, assistant professor of neurology and psychiatry, NYU Langone Multiple Sclerosis Comprehensive Care Center, New York, told *Medscape Medical News* this study "makes an important contribution to the attempts to understand the links between vitamin D levels and MS."

"The study draws from a large genome-wide vitamin D database, identifying several key genetic polymorphisms implicated in vitamin D synthesis, and then demonstrates patients with genetically lowered vitamin D had a significantly increased risk of developing MS. Through its novel approach, it lends intriguing support to vitamin D homeostasis as a potentially causative risk factor for MS. Such a result is in concert with a growing body of research on vitamin D and its role in MS risk and disease activity," Dr Charlson said.

The study had no commercial funding. The authors and Dr Charlson have disclosed no relevant financial relationships.

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