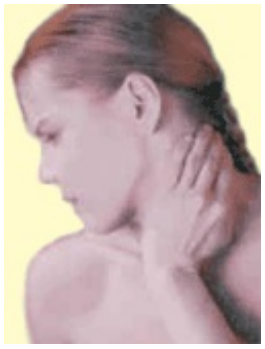
Fibromyalgia Linked to Deficient Vitamin D



Fibromyalgia syndrome (FMS) is a chronic pain condition, primarily affecting women, that manifests as widespread musculoskeletal pain, fatigue, sleep disturbance, psychological distress, and cognitive disruptions. A new clinical study suggests that having excessively low levels of vitamin D might play an important role in FMS and ameliorating such deficiencies may be beneficial. However, this was a small, uncontrolled trial and it is important to understand its limitations.

Noha T. Abokrysha, MD, from Cairo University in Egypt, enrolled 30 women with diagnosed FMS in a study to assess the prevalence of vitamin D deficiency and effects of vitamin supplementation. The women — mean age 34.56 ± 8.1 years (range 17 to 51 years) — were all attending a neurology clinic in Saudi Arabia from January to April 2011 [Abokrysha 2012].

Patients were evaluated using new clinical FMS diagnostic criteria, not relying on counting tender points but taking into account (a) pain presence in 14 major sectors of the body, (b) severity of fatigue, waking unrefreshed, and/or cognitive disruptions; and (c) the presence of 41 other symptoms, such as headache, nausea, depression, etc. This new assessment approach was discussed in an earlier *UPDATE* [here].

Women with known calcium abnormalities, hyperparathyroidism, or osteomalacia were excluded from the study. Vitamin D deficiency was defined as 25(OH)D <20 ng/mL, insufficiency as 21–29 ng/mL, and adequacy as ≥30 ng/mL. *Note:* this follows the traditional 25(OH)D levels established in past research designs, rather than the ≥20 ng/mL considered as sufficient in a 2010 Institute of Medicine report and critiqued in an *UPDATE* [here].

Results, reported in an advance online edition of *Pain Medicine*, indicated that the mean 25(OH)D level in these 30 subjects with FMS was highly deficient, 4.76 ± 1.46 ng/mL, and lower vitamin D levels were significantly correlated with greater widespread pain. Unsurprisingly, although this study was conducted in a region with ample sunshine, almost all of the women wore veils and/or other protective clothing when outside, which probably contributed to vitamin D deficiencies.

These 30 patients were treated with either high dose vitamin D3 injections (600,000 IU intramuscular single dose) or oral vitamin D3 tablets, 50,000 IU once-weekly for 8 weeks. Followup assessments were done at 1 month posttreatment with vitamin D injection or at 2 months after treatment with vitamin D tablets.

Treatment with vitamin D3 improved all FMS diagnostic criteria scores, with one exception, and differences in from baseline represented large and statistically significant positive effect sizes (P<0.001). The single exception was cognitive disruptions, which remained unchanged. Based on this evidence, Abokrysha concluded that vitamin D deficiencies are a common finding in women with FMS in the Saudi Arabian clinic population, and high-dose supplementation may facilitate resolution of most symptoms of the disorder.

COMMENTARY: Other studies have found significant relationships between low levels of 25(OH)D and widespread, nonspecific musculoskeletal pain, including fibromyalgia syndrome [see special Pain-Topics Report PDF here, and *UPDATE* here]. However, some investigations have found essentially no relationship and little benefit of vitamin D supplementation [eg, Warner and Arnspiger 2008]. Overall, research in this area has been burdened by heterogenous and inadequate trial designs, as well as incomplete reporting of methodologies and outcomes.

The present study by Abokrysha contributes some evidence for a significant relationship between FMS and vitamin D deficiency; although, this does not confirm a cause-effect association and it is still not known which condition comes first. The results also support benefits of vitamin D3 supplementation for helping to relieve many, but not all, FMS

symptoms. However, in fair balance, there are some limitations of this study to consider:

- This was a small-scale, nonrandomized, observational study without any sort of control group for comparison. With only 30 subjects, some might consider this more of a case series providing a low level of evidence. It also is possible that the vitamin D deficiencies found in the women with FMS are endemic in the Saudi Arabian population, and many other studies have found that inadequacies of 25(OH)D may commonly exist even in the most sun-drenched climes.

- Oddly, Abokrysha does not report if there were differences in outcomes between the two vitamin D supplementation regimens or, for that matter, what the posttreatment 25(OH)D levels were — other than indicating that all patients had normal calcium and vitamin D levels at followup. At least vitamin D3, rather than D2, was used; the use of D2 in many other studies may be a confounding factor skewing outcomes, as noted in a recent *UPDATE* [here]. There are still questions about whether daily administration of moderate D3 doses would be more effective than the less frequent high dosing regimen used in this study and most other research.

- Of interest, one factor in the new FMS diagnostic criteria that was unimproved was cognitive difficulties (although these were not well defined). Abokrysha proposes this might be attributed to neurobiological remodeling in the brains of persons with FMS, such as the loss of gray matter volume. This also was discussed in an *UPDATE* [here]; such neuropathology can be profound and worsen with longevity of the disease. It would be unexpected that such changes could be reversed by short-term vitamin D therapy, as this study found.

- Of further interest, a symptom often associated with FMS is depression, which Abokrysha assessed but did not report on separately, other than to comment that lower levels of vitamin D have been observed in some studies of persons with anxiety and depression. Just recently, the report of a large, multiyear study including 12,600 participants noted a significant relationship between vitamin D inadequacy and depression [Hoang et al. 2011]; again, however, it is not known which condition comes first, depression or low vitamin D, and how/if this might directly influence FMS.

- Finally, data on the concurrent use of medications or other supplements for FMS among subjects in the Abokrysha study were not collected, and this might have been an important confounding variable; however, there is no way of knowing.

Despite the shortcomings, this study suggests some promising possibilities for better care in persons with FMS, all of whom should have 25(OH)D levels assayed. As with so much of the other research on vitamin D for pain, Abokrysha pursued this study without any outside funding support, which probably accounts for many of its limitations. It is unfortunate that research on vitamin D for pain conditions of various types has not received the sort of public or private support afforded other therapies — which would allow for prospective, large-scale, controlled clinical trials providing more definitive answers to questions regarding patient selection, dosing regimen, and efficacy.

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