**Excessive immune activation and vitamin D - lessons from multiple sclerosis**

HIV infection causes prolonged and excessive activation of the immune system. As cells of the immune system interact with many organ systems, prolonged activation of the immune system causes many cells in the body to release chemical messengers that incite inflammation. Although the use of potent combination anti-HIV therapy—commonly called ART or HAART—greatly reduces HIV-related inflammation, this problem of immune activation persists. Some researchers think that prolonged inflammation seen in HIV infection likely plays a role in the apparent accelerated aging of the brain, bone, cardiovascular, kidney and other organ-systems.

Researchers have been testing different compounds for their ability to reduce HIV-related inflammation. Most recently, such compounds have included the cholesterol-lowering medications called statins and concentrated fish oil. Clinical trials with one statin—atorvastatin (Lipitor)—have found only modest reductions in immune activation in HIV-positive people. A clinical trial with low-dose fish oil has found minimal changes in immune activation in HIV-positive people. So researchers are considering other compounds, such as high-dose vitamin D$_3$.

**A lesson from MS**

With multiple sclerosis (MS), inflammation in the central nervous system—the brain and spinal cord—occurs. Also, the layer of insulation that sheaths nerve fibres is attacked by T-cells. These attacks cause the electrical signals to leak, rendering nerve impulses weaker. This helps weaken control of muscles, affects balance and causes other problems.

Laboratory experiments with cells and animals suggest that vitamin D$_3$ may be able to partially suppress the activity of T-cells. These and other cells of the immune system, such as macrophages, have receptors for vitamin D. Also, these cells can convert vitamin D$_2$ into vitamin D$_3$. Other cells of the immune system, such as dendritic cells, whose function is to help amplify the immune response, can also have some of their functions weakened by vitamin D.

In addition to having the insulation that covers nerves attacked, people with MS have other abnormalities—for instance, their immune system may respond abnormally to common proteins in the body and environment. Lab experiments have found that vitamin D$_3$ can reduce these abnormalities in cells taken from patients with MS.

A recent Canadian clinical trial has found that very high doses of vitamin D$_3$ decreased symptoms of MS and reduced excessive T-cell activation. This finding may be of interest to researchers who study the long-term effects of HIV on the immune system.

**Study details**

Researchers in Montreal and Toronto recruited 49 volunteers who had signs and symptoms of MS and randomly assigned them to be in one of the following groups:

- vitamin D$_3$ (25 participants)
- control (they did not receive vitamin D)

Vitamin D$_3$ was given in a complex regimen of increasing doses between 4,000 IU and 40,000 IU per day over the course of one year. On average, participants in the vitamin D group received 14,000 IU of vitamin D$_3$ daily over the course of the study. Additionally, participants in the vitamin D group received 1,200 mg of calcium per day.

Participants assigned to the control group were not provided with vitamin D$_3$ by the research team but were allowed
to take up to 4,000 IU of vitamin D₃ if they wished.

**Results**

At the start of the study, all participants had about 78 nmol/litre of vitamin D in their blood, and this level was not different between the two study groups.

A year later, vitamin D levels in the control group were 83 nmol/litre and 179 nmol/litre among people who took high doses of this vitamin.

Cells of the immune system of people with MS tend to react abnormally to a range of proteins in lab tests. Specifically, the immune cells of patients with MS unnecessarily attack proteins that they should not. At the start of the study, such abnormalities were similar in both study groups. However, by the end of the study, participants who received high-dose vitamin D₃ had a more normal level of immunological responses to proteins associated with MS. These proteins represented about 38% of all test proteins used to assess immunologic responses during the study. So the results suggest that excessive immune activation was normalized in people who received high-dose vitamin D₃. This change was statistically significant, not only within the vitamin D₃ group but also in comparison to the control group.

Researchers also found that as vitamin D levels in the blood increased there was a measurable decrease in immunologic reactivity to certain proteins from milk and brain tissue.

Levels of a molecule in the blood called hsCRP (high-sensitivity C-reactive protein) rise during periods of inflammation and fall when inflammation decreases. There were no changes to CRP levels in this study. The researchers speculated that perhaps the lack of change was due to the already high levels of vitamin D in participants.

There were no significant changes in levels of proteins in the blood associated with the building up or tearing down of bone. This should not be surprising because previous studies have found that when the concentration of vitamin D in the blood is at 75 nmol/litre or greater, markers or proteins associated with bone metabolism do not generally change when additional vitamin D is taken.

A previous study found that high-dose vitamin D₃ (20,000 IU per day) for 12 consecutive weeks can cause CD4+ cells to increase their production of anti-inflammatory chemicals. However, no significant changes were found in levels of such chemicals in the present study.

No toxicity due to high-dose vitamin D₃ was reported.

The present study in MS patients showed that high doses of vitamin D₃ are safe. Moreover, such doses of vitamin D₃ have the ability to reduce the immune system’s attacks on the body—such attacks are called autoimmunity. The findings from the present study support large, randomized placebo-controlled clinical trials of high-dose vitamin D₃ in other health conditions where excess immune activation and autoimmunity are present, such as HIV infection.

—Sean R. Hosein

**REFERENCES:**


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