France: Factors linked to low vitamin D levels in HIV-positive people

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Vitamin D helps the body absorb the minerals calcium and phosphorus, which are used to build bones. Vitamin D also plays a role in maintaining the strength of muscles. Emerging research suggests that vitamin D may also play a role in the health of many organ-systems, including the brain, kidneys, skin and immune system. A diverse range of tissues and cells have receptors that can bind to vitamin D, suggesting that many tissues interact with this vitamin.

Vitamin D and survival

Results from very large observational studies in the United States and Israel suggest that HIV-negative people who have less-than-ideal levels of vitamin D in their blood have an increased risk of dying. Even when adjustments were made for such factors as smoking, diabetes, cholesterol levels, socio-economic status, age, season and so on, Israeli scientists still found that in their study of over 180,000 people, having a vitamin D level in the blood below 50 nanomoles/litre (nmol/l) was significantly associated with an increased risk of dying from a number of different causes.

In another observational study called EuroSIDA, researchers found that vitamin D deficiency was common among HIV-positive people. Several studies in North America and even in relatively sunny Mediterranean countries such as Spain and Italy and tropical countries such as Brazil, Tanzania and Thailand have found vitamin D deficiency to be relatively common among HIV-positive people. The EuroSIDA team found that participants who had less than 12 nanograms/millilitre (ng/ml) of vitamin D in their blood (about 30 nmol/l) were at heightened risk of developing AIDS-related illnesses and dying.

France

French researchers recently completed a study with almost 3,000 HIV-positive people. It will be published in the Journal of Antimicrobial Chemotherapy. In this study, less than ideal levels of vitamin D and vitamin D deficiency were common. What made the French study interesting was that the researchers conducted analyses to find possible factors that might have lowered vitamin D concentrations. One of these possible factors may be a specific anti-HIV therapy. Previous studies have found that exposure to the anti-HIV drug efavirenz (Sustiva, Stocrin and in Atripla) is associated with low vitamin D levels. The present French study confirms this association but also attempts to assess the impact of other commonly used anti-HIV drugs on vitamin D levels.

Study details

Research teams in the following French cities collaborated for this study:

- Lille
- Nante
- Paris
- Strasbourg
- Toulouse

Researchers pooled their data collected from 2,994 participants—334 of whom were not taking potent combination anti-HIV therapy (commonly called ART or HAART). People who were being treated for osteoporosis, vitamin D deficiency or kidney failure were not enrolled.
The average profile of participants upon entering the study was as follows:

- 72% male, 28% female
- age – 45 years
- duration of HIV infection – 12 years
- CD4+ count among ART users – 570 cells
- CD4+ count among non-ART users – 500 cells
- 18% were co-infected with hepatitis B or C viruses

**Results**

Depending on their location and the manufacturer of the vitamin D assay, some researchers assess vitamin D in nanograms/ml while others use nanomoles/l.

The research team defined different vitamin D levels as follows:

- low levels of vitamin D – any value less than 75 nmol/l (30 ng/ml)
- insufficient levels of vitamin D – more than 30 nmol/l (12 ng/ml) but less than 75 nmol/l
- deficient levels of vitamin D – 25 nmol/l (10 ng/ml) or less

Based on these values, the researchers found that 87% of participants had low levels of vitamin D in their blood. This was distributed as follows:

- insufficient levels of vitamin D – 56%
- vitamin D deficiency – 31%

**Results - Factors associated with vitamin D deficiency**

Researchers found that the following factors were linked to having a vitamin D deficiency:

- smoking tobacco
- having a CD4+ count less than 350 cells
- having kidney dysfunction

**Impact of ART**

Initially researchers found that the use of ART was linked to having low vitamin D levels. However, when further analyses were done to explore this finding among the 2,660 participants who were using ART, they found that deficiency of vitamin D was linked specifically to exposure to the anti-HIV drug efavirenz. The longer a person took efavirenz, the greater the risk of developing vitamin D deficiency.

Vitamin D deficiency was not linked to the use of the following drugs:

- non-nukes – nevirapine (Viramune), etravirine (Intelence)
- nukes – tenofovir (Viread, and in Truvada, Atripla and Complera), AZT (zidovudine, Retrovir and in Combivir and Trizivir)
- protease inhibitors – including darunavir (Prezista) and ritonavir (Norvir)
- integrase inhibitors – raltegravir (Isentress)

**This and other studies**

The French study is useful because it confirms findings from other studies, namely that the use of efavirenz is associated with reduced levels of vitamin D in the blood. Also, the French study confirms that smoking tobacco is linked to reduced vitamin D levels. This finding is important because smoking among HIV-negative people has been linked to vitamin D deficiency and smoking is also a risk factor for thinner-than-normal bones (osteopenia and osteoporosis).

Another study found that replacing efavirenz with darunavir-ritonavir results in increasing levels of vitamin D.
randomized study found that participants assigned to receive rilpivirine (Edurant and in Complera) had stable levels of vitamin D while those assigned to receive efavirenz had declining levels of vitamin D.

**Why efavirenz?**

Laboratory investigation suggests that efavirenz can stimulate the activity of enzymes that degrade vitamin D$_3$ (the active form of this vitamin) and impair the activity of enzymes that convert vitamin D$_2$ to D$_3$.

**Study design**

The present French study was observational and cross-sectional in nature. It therefore only examined vitamin D levels at one point in time. Moreover, researchers were not able to take into account factors that could have biased their conclusions, such as sun exposure, skin colour and ethnicity. These limitations all mean that this study’s conclusions need to be interpreted with care. However, the findings from the French study on the impact of efavirenz on vitamin D levels were similar to those of several other studies, including randomized clinical trials. Moreover, the French study was relatively large, something that strengthens its conclusions.

This and other studies underscore the need to assess vitamin D levels in HIV-positive people. If insufficiency or deficiency is detected, there are guidelines for supplementation that have been produced by hormone specialists. Such supplementation should **always** be done under medical supervision. For more information about the vitamin D guidelines and vitamin D in general, please see TreatmentUpdate 185.

—Sean R. Hosein

**REFERENCES:**


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Decisions about particular medical treatments should always be made in consultation with a qualified medical practitioner knowledgeable about HIV- and hepatitis C-related illness and the treatments in question.

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