Making sense of changes in bone density

In trial 5524s, as seen in other studies, when HIV-positive people began taking potent anti-HIV therapy, commonly called ART or HAART, their bone density fell sharply for the first six months and then generally stabilized.

Specific changes

Among people who received the nukes abacavir + 3TC (Kivexa), overall bone density decreased by about 2% and then stabilized, after which it began to increase significantly. This increase was statistically significant at weeks 144 and 192. Moreover, at those latter time points, bone density among Kivexa users was only 1% less than it was before they began to take ART.

Among people who received the nukes tenofovir + FTC (Truvada), the initial loss of bone density was steeper—falling by 4% and then gradually increasing, though by weeks 144 and 192 it was still 3% less than at the start of the study.

Even when researchers took into account traditional factors that affect bone density, differences remained between Kivexa and Truvada. This should not be surprising, as other randomized studies have also reported broadly similar findings, though trial A5224s was the longest of such studies. This trial therefore confirms that tenofovir-containing regimens have effects that “are independent of HIV infection or other antiretroviral drugs,” stated the researchers who reviewed A5224s.

There are several important questions that need to be answered, including the following:

- What causes the initial sharp decrease in bone density when ART is initiated?
- What is the medium- and long-term impact of the initial decrease in bone density?

In previous studies, researchers have noted that exposure to tenofovir has been linked to kidney dysfunction and, in rare cases, kidney damage. In particular, a part of the kidneys called the renal tubules lose their ability to reabsorb phosphorus from urine. As this mineral is used to build bones, an excessive loss of phosphorus can weaken bones over time.

Damaged renal tubules may not be able to produce sufficient vitamin D3, the active form of this vitamin, which is essential for bone health.

The decrease in bone density seen in trial A5224s is somewhat similar to that seen in women who are undergoing the first two years of menopause. The average age of people in this study was 38 years, and most were male, so it is possible that in older HIV-positive people, especially those with risk factors for thinning bones, the initial loss of bone density may have more serious consequences.

Although DEXA scans revealed decreases in bone density, they do not provide a picture of what is happening at a structural level with bones. For instance, the way that bones are formed and strengthened—their micro-architecture—is something that would require more complex and expensive scans, perhaps as well as the unpleasant procedure of bone biopsies.

The good news from trial A5224s is that there were not excessive rates of fractures among tenofovir users despite significant decreases in bone density over several years. Also, although bone density initially decreased, it then stabilized and in some cases increased. Thus, in an average otherwise-healthy HIV-positive person taking a tenofovir-containing regimen for up to four years, exposure to this drug seems to cause only minor changes to bone density.

In the everyday world outside a carefully constructed clinical trial, some HIV-positive people have other health issues...
—such as opiate use, vitamin D3 deficiency, poor kidney health, exposure to corticosteroids, hormonal issues, exposure to multiple medications and so on. In such people, changes in bone density may be more dramatic than seen in the present study.

Studies such as trial A5224s show that long-term monitoring of bone health of ART users is necessary to understand and know what these drugs are doing to bones. This will become even more important as HIV-positive people age. Furthermore, additional studies are needed to assess changes in bone health of women taking ART, particularly those who are undergoing menopause, and the role of supplementary vitamin D3.

**References:**


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