Controversy in vitamin D dosing

As interest in vitamin D has greatly increased over the past decade given the many studies on this vitamin, doctors and patients seek credible sources of information to guide daily dosing. In November 2010, the Institute of Medicine (IOM), a non-profit group affiliated with the prestigious US National Academy of Sciences, issued a report that took an extremely conservative view on vitamin D. In essence, the report stated that the high blood levels of vitamin D advocated by many physicians and researchers were not necessary. Moreover, it generally suggested that most adults should be satisfied with a daily dosage between 400 and 600 IU of vitamin D.

In June 2011, the American Endocrine Society—an association of 14,000 researchers, physicians and other health and scientific professionals—issued comprehensive evidence-based guidelines that specifically focused on the use of vitamin D not just by healthy people, but also those people with chronic health conditions. Its analysis and recommendations are extensively covered in this issue of Treatment Update. We have focused on the Endocrine Society’s guidelines in part because the Society has been regularly reviewing the literature on vitamin D research and also because it addresses the specific health needs of people living with HIV. Also, HIV-positive people appear to be at increased risk for thinner-than-normal bones and the Endocrine Society’s guidelines partially address that issue. Moreover, the Endocrine Society’s recommendations about dosing are similar to what scientists conducting clinical trials with HIV-positive people have found: Generally, larger-than-normal doses are required to raise vitamin D to levels associated with health, particularly skeletal health. Indeed, researchers at Toronto’s Hospital for Sick Children, commenting on their experience with a randomized trial of vitamin D supplementation in children with HIV, suggested that higher doses than those recommended by the IOM may be necessary in children and adults with HIV infection and perhaps other chronic medical conditions.

Usually the IOM’s reports are taken very seriously and set the agenda for a particular issue in North America and elsewhere. However, instead of addressing some of the confusion about vitamin D, the IOM’s report has triggered unease and in some cases outright unrest—unusual reactions to an IOM report.

Researcher and endocrinologist Michael Holick, based at Boston University’s School of Medicine, said: “The IOM was too definitive in its recommendations.” A proponent of evidence-based medicine, Canadian researcher and professor Gordon Guyatt from McMaster University said, “Basically, the [IOM’s] vitamin D recommendations are based on low-quality evidence.” He adds, “I think that admitting that would have made some of the angst disappear.”

In the past decade, because vitamin D has become associated with many health conditions, the “medical and scientific communities have become preoccupied with how it might prevent chronic disease,” reported the scientific journal Nature. The publication also noted that some physicians “recommend doses of up to 6,000 IU/day to make up for the time that people spend indoors. This is less than the amount a fair-skinned person without sunblock might make in half an hour of exposure to the midday summer sun.”

Not for everyone

According to Nature, the IOM’s mandate was to “set the levels [of vitamin D] that protect most people, but not all.” Furthermore, according to bone researchers in Germany and Switzerland and bio-statisticians in California, the IOM made a mathematical mistake in its calculations of the ideal level of vitamin D in the blood that is associated with strong bones. The IOM choose a level of 50 nmol/litre. However, an examination of the evidence suggests that setting the level of vitamin D at 75 nmol/litre (as done by the American Endocrine Society) would likely protect more people.

Members of the IOM’s panel stand by their calculations, saying that their methodology is “standard procedure for dietary recommendations.”
Tension about toxicity

One criticism of the IOM report is that it cited a clinical trial in which elderly women given 500,000 IU of vitamin D annually in a single dose experienced more falls and fractures than women of similar age who were given placebo. According to *Nature*, many researchers found that study “ridiculous.” Edward Giovannucci, a nutritional epidemiologist at the Harvard University School of Public Health, said, “No one absorbs 500,000 IU a day from the sun, so why would you give that as a supplemental dose?” But another Harvard University epidemiologist, JoAnn Manson, says that the mega-dose clinical trial should be factored into concerns about toxicity. She notes, “Within the first three weeks of this trial, when serum levels were at or above 100 nmol/litre, there was an increased risk of falls and fractures.”

Clinical trials to the rescue

Many clinical trials testing different doses and schedules of vitamin D are underway (some are mentioned later in this issue of *TreatmentUpdate*). Harvard’s JoAnn Manson is one of the scientists leading a five-year, 20,000-person study designed to assess the impact of vitamin D supplementation on cancer and cardiovascular disease.

Not all researchers are patient with the current pace of clinical trials of vitamin D. Reinhold Vieth, PhD, a world-renowned vitamin D scientist at the University of Toronto, calls the demand for huge clinical trials a “cop-out.” He says that there is good evidence that higher doses of vitamin D would reduce rates of multiple sclerosis, but a clinical trial to test this would require thousands of people and 30 years.”

Experts vs. data

*Nature* has suggested that the IOM panel members “underestimated the passion present in the vitamin D field.” Dr. Clifford Rosen, a member of the IOM panel and a respected member of the bone-research community, summarized the ongoing controversy about the IOM report as follows:

“This is the beginning of a whole new phase.... In the old days of medicine we believed experts, and now we say, show us the data.”

—Sean R. Hosein

REFERENCES:

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