Clinical Chemistry

Effect of Vitamin D or Activated Vitamin D on Circulating 1,25-Dihydroxyvitamin D Concentrations: A Systematic Review and Metaanalysis of Randomized Controlled Trials

Article:
A. Zitterman et al.
Effect of Vitamin D or Activated Vitamin D on Circulating 1,25-Dihydroxyvitamin D Concentrations: A Systematic Review and Metaanalysis of Randomized Controlled Trials.
Clin Chem 2015;61:1484-1494
http://www.clinchem.org/content/61/12/1484.abstract

Guest:
Dr. Armin Zittermann is the head of the Study Center at the Clinic for Thoracic and Cardiovascular Surgery at the Ruhr University in Bochum, Germany.

Bob Barrett: This is a podcast from *Clinical Chemistry*, sponsored by the Department of Laboratory Medicine at Boston Children's Hospital. I am Bob Barrett.

Vitamin D deficiency is regarded as a worldwide health problem that may affect a wide range of acute and chronic diseases. Vitamin D itself is biologically inert and needs a hydroxylation at the 25 position in the liver and another hydroxylation in the kidney to be converted into its active hormonal form 1,25-dihydroxyvitamin D.

Today, the measurement of circulating concentrations of 25-hydroxy vitamin D is the laboratory standard for determining human vitamin D status. But the plasma levels of 1,25-dihydroxyvitamin D have received comparatively little attention and even the reference intervals for this form of vitamin D are not well defined.

The December 2015 issue of *Clinical Chemistry* published a systematic review and meta-analysis of randomized controlled trials on factors affecting the circulating concentrations of 1,25-dihydroxyvitamin D.

The lead author of that study is Dr. Armin Zittermann. He is head of the Study Center at the Clinic for Thoracic and Cardiovascular Surgery at the Ruhr University in Bochum, Germany. He is our guest in this podcast.

Dr. Zittermann, why should clinicians and scientists pay attention to circulating 1,25-dihydroxyvitamin D concentrations?

Dr. Armin Zittermann: Well, the 1,25-dihydroxyvitamin D is the active hormonal form of vitamin D. Usually in healthy individuals this substance is tightly regulated in circulation. However, there are some clinical

situations where this regulation does not work correctly.

We do already know that chronic kidney disease is able to suppress 1,25(OH) D into blood but it's also known to have high concentrations of the implemental remarker of C-reactive protein and also diabetes mellitus are able to suppress this 1,25(OH) D levels.

Our meta-analysis could also demonstrate that nutritional factors such as supplemental calcium are able to suppress circulatory 1,25(OH)D levels and because this 1,25(OH)D is the active hormonal form of vitamin D it's very important and that's why it's important to know the factors that may suppress this very important hormone into blood.

Bob Barrett: Doctor, do native vitamin D and activated vitamin D both increase circulating 1,25-dihydroxyvitamin D?

Dr. Armin Zittermann: Yes, our meta-analysis has demonstrated that the on-off magnitude seems to be similar for both scopes of the substances.

However, the data on activated vitamin D are based on relatively few trials only therefore future studies have to assess more detailed the dose–response relationship of vitamin D or activated vitamin D, unsaturated 25(OH)D.

However, it seems to be that both substances, the native vitamin D and also the activated vitamin D are able to increase the circulating level of 1,25(OH)D.

Bob Barrett: Are there other factors which can increase circulating 1,25-dihydroxyvitamin D?

Dr. Armin Zittermann: Yes, to my opinion it's very important that several studies demonstrating that physical activity is known to increase circulating 1,25(OH)D levels and because the 1,25(OH)D is a very important hormone in the human body it seems to be that physical activity is able to increase their hormone and therefore it may well be that physical activity is a good measure to increase circulating 25(OH)D levels.

However again future research is necessary to assess the dose–response relationship of physical activity and the increase in circulating 1,25(OH)D levels and it's also well-known that pregnancy is associated with doubling in circulating 25(OH)D levels and this is a situation you can't change. If a woman is pregnant

then the 1,25(OH)D goes up and you can't influence it very much.

Bob Barrett: Do current methods reliably assess circulating 1,25-dihydroxyvitamin D concentrations?

Dr. Armin Zittermann: Well, our meta-analysis of randomized controlled trials has demonstrated that the increase in circulating 25(OH)D levels is higher if your measurement is performed by radioimmunoassay compared with other methods.

And therefore there seems to be a need for chemical methods as standardization and to my opinion in the future it is necessary to do a chemical method standardization and it's also necessary to provide a common reference range for circulating 25(OH)D levels for all the different methods and this reference range should be based on clinical end-point studies that's important to my opinion.

Bob Barrett: Well finally doctor, do you think that in the clinical setting, the measurement of circulating 1,25-dihydroxyvitamin D will replace 25-hydroxy vitamin D measurement?

Dr. Armin Zittermann: No, I do not think that it will replace 25-hydroxy vitamin D measurement because in healthy individuals as I mentioned before 1,25(OH)D is regulated very tightly in the blood and circulating 25(OH)D is the best indicator for assessing vitamin D status in healthy individuals.

However, there is accumulating evidence that in specific clinical groups - in the specific groups of patients especially severely ill patients, the circulating 25(OH)D levels maybe the best predictor of clinical outcomes than circulating 25(OH)D.

Therefore, to my opinion it maybe that in addition to 25(OH)D, 1,25(OH)D measurements may also become useful and also become important because it's an influential risk marker for clinicians and that's because you can give – you can administer the activated hormone through activated vitamin D, you can also administer the vitamin D itself and both are able to increase the 1,25(OH)D levels and this is maybe – in future this is important for the clinicians.

Bob Barrett: Dr. Armin Zittermann is a researcher specializing in human vitamin D status and is the head of the Study Center at the Clinic for Thoracic and Cardiovascular Surgery at the Ruhr University in Bochum, Germany.

He has been our guest in this Podcast from *Clinical Chemistry* on vitamin D and its active 1,25-dihydroxy form.

I am Bob Barrett. Thanks for listening!