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White Paper

ADVIA Centaur Vitamin D Total Assay* Accurately Measures Patients on Vitamin D Supplementation

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Introduction

The influence of supplementation on the ability of immunoassays to accurately measure and monitor vitamin D has been under recent discussion,[1,2] especially as more vitamin D automated immunoassays are available to laboratories for testing. In this study, patient samples were examined before and after supplementation in order to determine the impact of vitamin D supplementation on the ADVIA Centaur® Vitamin D Total assay*.

Background

Vitamin D is a steroid hormone involved in the intestinal absorption of calcium and the regulation of calcium homeostasis. Aiding renal absorption of calcium, vitamin D is essential for the formation and maintenance of strong, healthy bones. Vitamin D deficiency can be best diagnosed using 25(OH)vitamin D versus the other vitamin D metabolites because 25(OH)vitamin D levels in serum reflect the body's storage levels of vitamin D and correlate with the clinical symptoms of vitamin D deficiencies. Vitamin D supplementation can occur in the form of vitamin D_2 or D_3. It is important that a vitamin D assay is able to measure both 25(OH)vitamin D_2 and D_3.

Study Design

In order to determine the influence of vitamin D supplementation on a vitamin D immunoassay, 18 serial serum samples were collected from San Francisco General Hospital (SFGH), San Francisco, California, from May 2012 to February 2013. Patients considered deficient in vitamin D by in-house LC/MS/MS at SFGH were placed on vitamin D supplementation which could have occurred by D_2 or D_3 supplementation. Follow-up measurement was conducted approximately three months after the initial draw. Samples were collected, aliquotted, and stored at -20°C, and then sent to Siemens Healthcare Diagnostics (Tarrytown, NY) for vitamin D concentration determination using the ADVIA Centaur Vitamin D Total assay and in-house LC/MS/MS. The ADVIA Centaur Vitamin D Total assay* used in this study is traceable to the Ghent University ID-LC/MS/MS 25(OH)vitamin D Reference Method Procedure (RMP), which is a reference laboratory for the Vitamin D Standardization Program (VDSP).†

Results

The 18 initial samples ranged from 11.1 to 25.6 ng/mL, with a mean of 15.4 ng/mL. Post supplementation, the samples ranged from 10.1 to 71.4 ng/mL with a mean of 25.5 ng/mL (Table 1). The average bias to the Siemens internal LC/MS/MS for samples at initial draw was -4.6% and the average bias post-supplementation was -0.9%. While the bias in some of the initial patient samples varied considerably from the mean (-27% to 33%), in post-supplemented patients the bias dropped (ranging from -13% to 7%). This demonstrates there was not a significant bias observed for the ADVIA Centaur compared to LC/MS/MS due to patients being supplemented with high levels of D_2 supplementation (Figure 1).

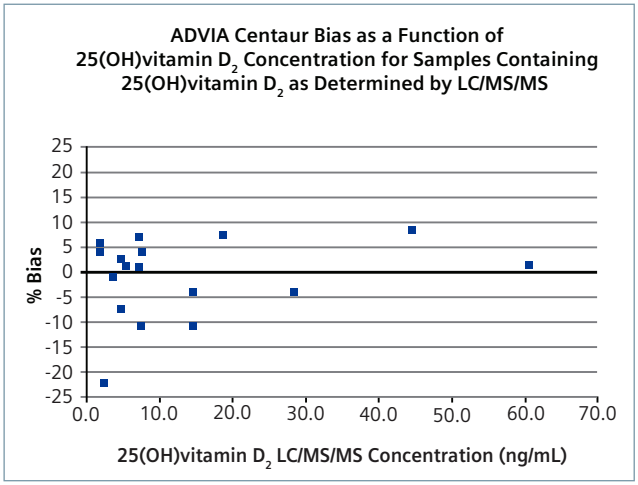

Figure 1. ADVIA Centaur bias as a function of 25(OH)vitamin D_2 concentration for samples containing 25(OH)vitamin D_2 as determined by LC/MS/MS

In this series of patients, 10 out of 18 had higher levels of vitamin D post-supplementation, whereas 8 out of 18 had no significant change in levels. This data may reflect the duration or type of supplementation, patient non-compliance, and/or gastrointestinal absorption disorders.

Table 1. ADVIA Centaur Vitamin D Total Assay Bias to LC/MS/MS in Serially Collected Samples.

Sample	D_2	D_3	Total	ADVIA Centaur	Bias
01A	<1.5	16.0	16.0	11.7	-27%
01B	46.9	8.7	55.6	59.8	8%
02A	3.5	8.2	11.7	11.5	-1%
02B	<1.5	10.4	10.4	10.5	2%
03A	<1.5	13.8	13.8	12.5	-9%
03B	<1.5	12.2	12.2	13.1	7%
04A	<1.5	14.4	14.4	15.1	5%
04B	<1.5	14.0	14.0	13.0	-7%
05A	5.9	6.5	12.4	12.8	3%
05B	2.6	6.9	9.5	10.1	6%
06A	<1.5	13.3	13.3	12.1	-9%
06B	<1.5	11.7	11.7	12.4	6%
07A	<1.5	12.4	12.4	16.4	33%
07B	17.3	8.6	25.9	27.8	7%
08A	7.9	14.8	22.7	23.6	4%
08B	8.0	14.9	22.9	20.3	-11%
09A	<1.5	17.0	17.0	13.0	-24%
09B	<1.5	15.7	15.7	13.6	-13%
10A	<1.5	18.2	18.2	17.3	-5%
10B	<1.5	29.4	29.4	26.4	-10%
11A	<1.5	14.7	14.7	13.4	-9%
11B	14.2	4.2	18.4	17.6	-4%
12A	<1.5	13.0	13.0	12.8	-1%
12B	7.7	16.0	23.7	23.9	1%
13A	<1.5	21.3	21.3	18.2	-14%
13B	28.6	12.5	41.1	39.4	-4%
14A	<1.5	11.8	11.8	11.1	-6%
14B	14.4	5.3	19.6	17.5	-11%
15A	4.1	7.9	12.0	11.2	-7%
15B	3.6	9.3	12.9	12.7	-1%
16A	6.2	9.3	15.5	15.7	1%
16B	<1.5	42.1	42.1	41.3	-2%
17A	2.6	30.3	32.9	25.6	-22%
17B	60.5	9.2	69.7	71.4	2%
18A	2.6	19.6	22.2	23.1	4%
18B	7.8	18.9	26.7	28.7	7%

Table 2 demonstrates that the ADVIA Centaur Vitamin D Total assay showed 94.5% clinical concordance (correctly identifying patients for deficiency, insufficiency, or sufficiency) with the Siemens LC/MS/MS through all 18 sample sets, and 100% clinical concordance in those samples post-supplementation. Deficiency levels are values <20 ng/mL, insufficiency levels are values between 20-30 ng/mL, and sufficiency levels are values > 30 ng/mL.

Table 2. Clinical Concordance between the ADVIA Centaur and LC/MS/MS values.

	ADVIA Centaur	LC/MS/MS
Deficient	24	23
Insufficient	8	8
Sufficient	4	5

Of particular interest in Table 3 are the seven patients where a high increase in 25(OH)vitamin D_2 levels had a corresponding decrease in 25(OH)vitamin D_3 levels. This is consistent with other findings that suggest the body adjusts for the 25(OH)vitamin D_3 levels as 25(OH)vitamin D_2 levels increase.[3,4]

Table 3. Serial Samples with Increased 25(OH)Vitamin D_2

Sample	D_2	D_3	Total	ADVIA Centaur
01A	<1.5	16.0	16.0	11.7
01B	46.9	8.7	55.6	59.8
07A	<1.5	12.4	12.4	16.4
07B	17.3	8.6	25.9	27.8
11A	<1.5	14.7	14.7	13.4
11B	14.2	4.2	18.4	17.6
13A	<1.5	21.3	21.3	18.2
13B	28.6	12.5	41.1	39.4
14A	<1.5	11.8	11.8	11.1
14B	14.4	5.3	19.6	17.5
17A	2.6	30.3	32.9	25.6
17B	60.5	9.2	69.7	71.4
18A	2.6	19.6	22.2	23.1
18B	7.8	18.9	26.7	28.7

Summary

This study demonstrates that the ADVIA Centaur Vitamin D Total assay* traceable to the 25(OH)vitamin D RMP† was shown to be as accurate as LC/MS/MS in assessing vitamin D levels for patients on vitamin D supplementation.

* The assay is standardized using the Ghent University's ID-LC/MS/MS 25(OH)vitamin D RMP. This version of the ADVIA Centaur Vitamin D Total assay is not available for sale in the US.

† Ghent University's ID-LC/MS/MS 25(OH)vitamin D RMP is traceable to the NIST SRM 2972,[5,6] and is a reference laboratory for the Vitamin D Standardization Program (VDSP).

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