D-Facts
Vitamin D Competitive Evaluation
Abstract

101 patient samples collected across sites in Germany were used to compare the performance of the Siemens ADVIA Centaur® Vitamin D Total (VitD), Abbott ARCHITECT 25-OH Vitamin D and the Roche Elecsys Vitamin D total assays to the DiaSorin LIAISON® 25 OH Vitamin D TOTAL Assay and an LC-MS/MS reference method.

The DiaSorin assay correlates well with LC-MS/MS and demonstrates highly accurate results with a superior lower detection level when compared to other automated methods.

Both Siemens and Abbott assays demonstrated poor sensitivity and clear positive bias for doses <10ng/mL against LC-MS/MS; in this study the Siemens assay showed a negative dose bias across the measuring range when compared against LC-MS/MS.

The Roche assay exhibits poor correlation across the measuring range when compared with LC-MS/MS.

The DiaSorin assay remains the most accurate and sensitive method for the measurement of total Vitamin D.

Introduction

In 2011 several manufacturers introduced new automated methods for the detection of 25-hydroxyvitamin D in patient samples for the assessment of Vitamin D sufficiency. Despite claims of high sensitivity and accuracy of these assays by the manufacturers, variable performance has been observed in practice.

A study was designed to compare the accuracy, precision and sensitivity of the new assays of Siemens (ADVIA Centaur® Vitamin D Total (Vit D)), Abbott (ARCHITECT 25-OH Vitamin D) and Roche (Elecsys Vitamin D total) to the DiaSorin (LIAISON® 25 OH Vitamin D TOTAL Assay) assay. All immunoassay methods were also compared to an LC-MS/MS reference method.
Materials & Methods

A total of 101 patient samples were selected from various sites across Germany in order to obtain a panel which spanned the range of the immunoassays. A total of 40 samples with sufficient volume were selected for subsequent LC-MS/MS analysis and when measured by LC-MS/MS, the doses ranged from 12 to 139 ng/mL.

In addition to the samples detailed above, a further panel of samples, selected to contain low 25 OH Vitamin D concentrations, was evaluated on both the LC-MS/MS method and each of the four immunoassays in order to evaluate and compare the detection limits of the immunoassays.

Following collection, the samples were stored at -20°C until analysis on each of the automated instruments and LC-MS/MS. All four immunoassay methods were performed according to the instructions for use provided by each manufacturer.

LC-MS/MS assay results were used as an independent reference.

Analysis

In order to best analyze the data, both Linear Regression and Bland-Altman Bias plots were employed.

The Linear Regression analysis allows the direct comparison of one methodology to another; whereas the Bland-Altman bias plots highlights the accuracy of one method to the selected reference.
Summary of Results

Figure 1. Linear Regression of results from the four automated assays against LC-MS/MS.

Figure 2. Linear Regression of results from the automated assays of Siemens, Abbott and Roche against the DiaSorin assay.
Figure 3. Bland-Altman bias plots of results from the four automated immunoassays against the LC-MS/MS reference. The other immunoassays, on each respective plot, are shown with DiaSorin in order to compare the detection limits of each.
Discussion

Figure 1 indicates a clear negative bias of the Siemens assay when compared with LC-MS/MS (also Fig. 5b & f). The DiaSorin assay indicates a good correlation to LC-MS/MS with $R^2 = 0.89$; correlation to LC-MS/MS is lower for Siemens, Abbott and Roche assays – $R^2 = 0.85 / 0.87 / 0.70$ respectively. There is little scatter in the data seen with the DiaSorin assay i.e. the variation of the results across the assay range is evenly spread with the tightest $+1.96$ SD range (Fig. 5e) as compared with the other methods (Fig. 5f, 5g and 5h). Performance of the other assays indicates more variation with the Siemens (Fig. 5f) and Abbott (Fig. 5g) assays; although most variation is seen with the Roche assay (Fig. 5h). This increased level of variation could cause inaccuracies in reported patient data leading to difficulty in patient management.

Figure 2 indicates that a high level of correlation is seen between the DiaSorin and the Abbott assays (Fig. 4b). However, reduced correlation is observed with both the Siemens and Roche assays, relative to the DiaSorin assay (Fig. 4a & 4c).

There is an increased negative bias seen using the Siemens assay (Fig. 4a & 4d) with positive biases seen for both the Abbott (Fig. 4b & 4e) and Roche (Fig. 4c & 4f) assays.

Figure 3 allows a more accurate assessment of the sensitivity of the assays and accuracy at low Vitamin D levels. The DiaSorin assay shows good agreement to the LC-MS/MS values with little variation in the data. A clear positive bias, and therefore inaccurate results are observed for both the Siemens (Fig. 3a) and Abbott (Fig. 3b) assays at low Vitamin D concentrations, whereas the Roche assay (Fig. 3c) indicates more variation at higher Vitamin D levels.

What is clear from the data is that the DiaSorin assay shows a superior level of detection when compared with the assays of Siemens and Abbott. These methods did not report any values below 7ng/mL even though samples read as low as 1.2 ng/mL by LC-MS/MS.

This lower detection level achieved by the DiaSorin assay and the low variation seen at these points allows more accurate measurement of severe deficiency in patients (defined as <5ng/mL). In countries whereby Vitamin D measurement and supplementation guidelines are present, such as GRIO in France, there is a requirement for a reliable test method for detection of levels <10ng/mL. As the DiaSorin assay shows improved accuracy over the Siemens and Abbott assays at this level, it should be considered as a better candidate assay for use in such cases.
Conclusion

The DiaSorin assay shows higher accuracy, sensitivity and a better correlation with LC-MS/MS when compared with assays for Siemens, Abbott and Roche. The Siemens assay shows a clear negative bias, and the Roche assay displays considerable variation across the assay range.

Whereas similar accuracy is seen with both the Roche and DiaSorin assays at low 25 OH Vitamin D levels, Figure 3 also highlights that the DiaSorin assay accurately detects much lower levels of 25 OH Vitamin D than either the Siemens or Abbott assays.

The DiaSorin assay correlates well with LC-MS/MS and demonstrates highly accurate results with a superior lower detection level when compared with other automated methods.

Reference

Supporting Data

Figure 4. Linear Regression (a – c) and Bland-Altman bias plots (d – f) of results from three automated assays against the DiaSorin assay.
Figure 5. Linear Regression (a – d) and Bland-Altman bias plots (e – h) of results from the four automated assays against LC-MS/MS.