

SHORT REPORT

Differences between serum and plasma for intact parathyroid hormone measurement in patients with chronic renal failure in routine clinical practice

P J Twomey, T Whitlock, D R Pledger

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Background: Parathyroid hormone (PTH) is important in the evaluation of patients with calcium metabolism disorders and/or chronic renal disease.

Aims: To assess the differences between serum and plasma PTH measurements using the Advia Centaur.

Methods: Twenty six paired serum and edetate samples from patients with chronic renal failure were analysed using the Advia Centaur.

Results: The EDTA results ranged from 2.3 to 76.1 pmol/litre and the Deming regression equation was: serum = 0.8927 EDTA – 0.447. The percentage difference plot had a mean difference of 13.8% (95% confidence interval, 2.2% to 25.4%; significant). The available time to separation and freezing ranged from 10 to 231 (median, 85) minutes. The correlation coefficient for the percentage difference against the time to separation and the percentage difference against the mean PTH concentration were –0.13 and –0.07, respectively.

Conclusions: These results go beyond the previous controlled research conditions by showing that such differences between serum and edetate plasma exist in routine clinical practice. They also show that intra-individual PTH differences as large as 25.0% can exist on the same day between serum and edetate plasma. This may partly explain some of the variability of PTH concentrations found in some patients with chronic renal failure.

forms. The time of data entry on the laboratory information system was used as a surrogate for the time of separation. Aliquots were frozen (–20°C) after centrifugation. Paired samples were analysed in singleton in the same batch by means of a two site sandwich immunoassay using direct chemiluminometric technology (Advia Centaur; Bayer, Newbury, UK). The reference interval is 0.95–5.7 pmol/litre.

RESULTS

One paired sample was deemed to be an outlier because the percentage difference between the EDTA and serum values was greater than 3 SD from the mean, and was therefore excluded from the analysis. The range of the EDTA results was from 2.3 to 76.1 pmol/litre, with the median being 21.7 pmol/litre. Twenty three samples had an edetate plasma intact-PTH concentration above the upper reference interval. The correlation coefficient (*r*) for the association between the serum and edetate plasma was 0.993 (MS EXCEL; Microsoft Corporation, Seattle, USA) and the Deming regression equation was: serum = 0.8927 EDTA – 0.447 (Analyse-it; Analyse-It Software Ltd, Leeds, UK). The 95% confidence intervals for the slope and intercept were 0.8558 to 0.9296 and –1.6361 to 0.7421, respectively. The percentage difference plot was constructed (fig 1) and the mean difference was 13.8% (SD, 5.8%; SEM, 1.16%; 95% confidence interval, 2.2% to 25.4%).

The difference between the time of data entry and the time of sampling was calculated (where possible). The time of sampling was not provided for 14 samples so that few data were available relative to time. The available time to separation and freezing ranged from 10 to 231 (median, 85) minutes (fig 2). The correlation coefficients for the percentage difference against the time to separation and the percentage difference against the mean intact-PTH concentration were –0.13 and –0.07, respectively.

DISCUSSION

We found significant differences in the intact-PTH concentration between serum and EDTA plasma in routine clinical practice using the Advia Centaur. Our results are in agreement with others.^{3–6} Data on file from Bayer Diagnostics, Newbury, UK show that there is a very slight positive bias for serum over edetate plasma when separated immediately. However, there is often a delay between sample collection and sample separation in routine clinical practice. Any difference for intact-PTH in routine clinical practice when using the Advia Centaur may be the result of the increased stability of intact-PTH when collected into EDTA. However, because our study evaluated routine clinical practice as opposed to controlled research conditions, we do not know what the intact-PTH concentrations were at the

Measurement of circulating intact parathyroid hormone (intact-PTH) is important in the evaluation of patients with disorders of calcium metabolism and/or chronic renal disease.^{1,2} One practical concern is the difference between serum and plasma for in vitro intact-PTH measurement.^{3–6} Because differences between serum and plasma may not be transferable across different assay systems, we investigated the sample type for the Advia Centaur analytical platform. Furthermore, we believe that there has been no study to date that investigated the specimen type for intact-PTH in the routine clinical setting, so that this setting was chosen, rather than the control laboratory environment.

METHOD

Blood samples from 26 patients were collected into Vacutainer™ tubes (Becton-Dickinson Ltd, Plymouth, UK) by specialist renal nurses immediately before the patients underwent haemodialysis. The tubes contained either a plastic plug and a clot enhancer (serum separator tubes) or potassium EDTA. The time of sampling (where available) was obtained from either the Vacutainer tube labels or the request

Abbreviations: PTH, parathyroid hormone

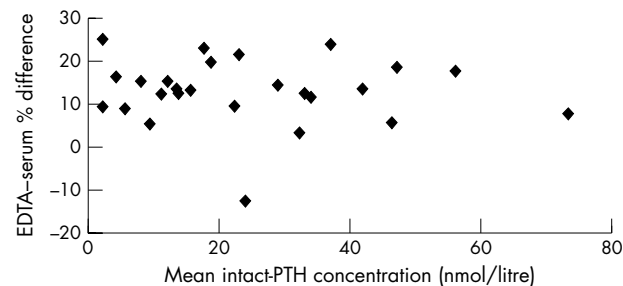


Figure 1 Parathyroid hormone (PTH) percentage difference plot. This figure shows the relation between the mean intact-PTH concentration and the percentage difference between serum and edetate for intact-PTH. After allowing for the single outlier, the 95% confidence interval for the data was 2.2% to 25.4%.

time of collection for either specimen type. Accordingly, we are unable to state categorically that differences are caused by the increased stability of intact-PTH when collected into EDTA; however, when the evidence from other analytical platforms is taken into account, the probability is that this is also the case for the Advia Centaur. Irrespective of this, our results go beyond the previous controlled research conditions by showing that such differences between serum and edetate plasma exist in routine clinical practice. The use of the percentage difference plot as opposed to the Wilcoxon matched pairs signed ranks test⁶ (which only compares the differences between the median values⁷) enabled us to examine the data from the point of view of individual samples in addition to the central tendency. Our data showed that a large inter-individual difference exists for intact-PTH when serum is used in a routine clinical setting and that this difference seems to be independent of the time to separation and the intact-PTH concentration. Accordingly, some patients may undergo large changes in intact-PTH values when serially checked using serum and EDTA collection tubes. Many hospitals use serum PTH samples for intact-PTH estimation because calcium can be measured at the same time. However, EDTA may be occasionally used because of earlier reports on the increased stability of intact-PTH.³⁻⁶ Our results show that intra-individual intact-PTH differences as large as 25.0% can exist on the same day between serum and edetate plasma. This could partly explain some of the variability of intact-PTH concentrations found in some patients with chronic renal failure.

“There is often a delay between sample collection and sample separation in routine clinical practice”

Intact-PTH is an important audit measure in chronic renal failure.^{1,2} Our routine clinical practice study shows that significant intra-individual differences may exist between edetate plasma and serum samples. Such differences may result in significant variability and/or misclassification. Laboratories using the Advia Centaur that analyse intact-PTH on both serum and edetate plasma should differentiate between the two specimen types to avoid significant sequential intra-individual variability or misclassification in routine clinical practice. Because collection into EDTA resulted in increased stability for intact-PTH compared with serum on other analytical platforms,³⁻⁶ our results probably reflect this increased stability and we recommend that EDTA alone should be used routinely for the estimation of intact-PTH when using the Advia Centaur analytical platform. We

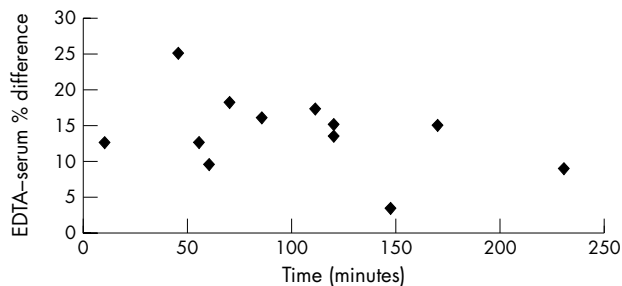


Figure 2 Intact parathyroid hormone (intact-PTH) difference over time. This figure shows the relation between time and the percentage difference between serum and edetate for intact-PTH.

Take home messages

- We found significant differences in the intact parathyroid hormone (PTH) concentration between serum and EDTA plasma in routine clinical practice using the Advia Centaur
- Intra-individual PTH differences as large as 25.0% were also found on the same day between serum and edetate plasma, which may partly explain some of the variability of PTH concentrations found in some patients with chronic renal failure
- Because EDTA samples show increased PTH stability compared with serum on other analytical platforms, we recommend that EDTA alone should be used routinely when using the Advia Centaur

acknowledge that an extra sample will be required for calcium but this should not be used as an excuse to prevent quality improvement.

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