Inter-method variability in bone alkaline phosphatase measurement: clinical impact on the management of dialysis patients

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OBJECTIVES

Bone-specific alkaline phosphatase (BAP) is now recommended to assess bone turnover in hemodialysis (HD) patients. A cut-off ≥ 20µg/L is generally proposed to differentiate high bone-turnover from normal-low. However, little is known about potential variability between methods available to measure BAP.

METHODS

We measured BAP in 76 HD patients with six different assays (Beckman-Coulter Ostase IRMA, IDS iSYS Ostase, IDS Ostase enzyme immunoassay, DiaSorin Liaison Ostase and Quidel MicroVue BAP).

Summary of the methods used in the study.

Method	Measures	Has been calibrated against	Origin of the antibodies	Origin of the antigen	CV
Beckman-Coulter Ostase IRMA	Mass of the enzyme. Provides results in µg/L	Hybritech Tandem-R Ostase	Beckman-Coulter	Beckman-Coulter	<13.6%
Beckman-Coulter Ostase Access	Activity of the enzyme. Provides results in mass (µg/L) after calibration	Hybritech Tandem-R Ostase	Beckman-Coulter	Beckman-Coulter	<6.5%
IDS iSYS Ostase	Activity of the enzyme. Provides results in mass (µg/L) after calibration	Beckman-Coulter Ostase Access	Beckman-Coulter	Beckman-Coulter	<9%
IDS Ostase BAP EIA	Activity of the enzyme. Provides results in mass (µg/L) after calibration	Beckman-Coulter Ostase Access	Beckman-Coulter	Beckman-Coulter	<6.4%
DiaSorin Liaison Ostase	Mass of the enzyme (µg/L)	Beckman-Coulter Ostase Access	Beckman-Coulter Ostase Access for the capture antibody, DiaSorin for the second, isoluminol bound, antibody	DiaSorin	<8.1%
Quidel MicroVue	Activity of the enzyme (U/L)[a]	1 unit of BAP is defined as 1 µmol of p-nitrophenylphosphate hydrolyzed per minute at 25 °C	Quidel (Metra)	Quidel (Metra)	<7.6%

[a] U/L values were divided by 0.488 to yield µg/L.

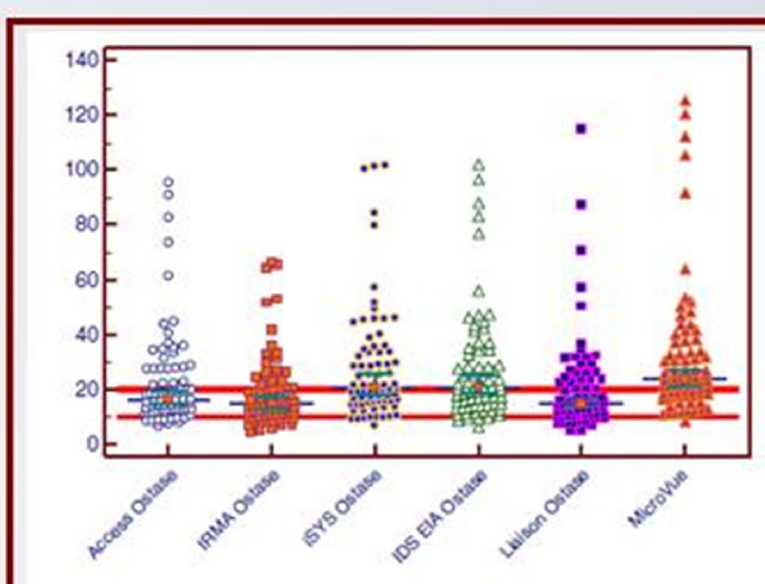

Fig. 1. Distribution of BAP levels observed in 76 hemodialyzed patients according to the different methods used in the study. The solid reference lines at 10 and 20 µg/L represent the different cut-offs proposed to define low and high bone-turnover in hemodialyzed patients, obtained with the former Hybritech Tandem Ostase assay.

Concordance of the different methods to classify identically the patients when they present BAP values ≤10, between 10 and 20 and ≥20 µg/L with the Beckman-Coulter Access Ostase assay.

Assay	Concordance with Access: BAP ≤10 µg/L	Concordance with Access: BAP comprised between 10 and 20 µg/L	Concordance with Access: BAP ≥20 µg/L
Beckman-Coulter IRMA Ostase	100%	79.5%	79.2%
IDS iSYS Ostase	70%	66.7%	100%
IDS Ostase BAP EIA	50%	61.5%	100%
DiaSorin Liaison Ostase	90%	80.5%	88.9%
Quidel MicroVue	10%	38.4%	100%

Equivalent concentrations obtained with each BAP assay, when the value measured with the Beckman-Coulter Access is 10 or 20 µg/L.

Assay	BALP (µg/L)	BALP (µg/L)	Mean bias (%)
Beckman-Coulter Access Ostase	10	20	0
Beckman-Coulter IRMA Ostase	9.6	16.9	−9.8
IDS iSYS Ostase	13.2	24.7	27.8
IDS Ostase EIA	13.2	24.2	26.5
DiaSorin Liaison Ostase	7.7	17.4	−18
Quidel MicroVue	14.4	27.9	41.8

These values were calculated according to the equations presented in Table 2. The mean bias value, expressed in %, is, for a given method, the mean bias observed when the "X" of the Deming equation is replaced by 10 and 20 µg/L.

RESULTS

We observed a high correlation between all the assays ranging from 0.9948 (IDS iSYS vs. IDS EIA) to 0.9215 (DiaSorin Liaison vs. Quidel Microvue).

However, using the regression equations, the equivalent concentration of a Beckman-Coulter Access value of 10 µg/L can range to 7.7 – 14.4 µg/L and of 20 µg/L can range to 16.9 – 27.9 µg/L with other assays.

According to Beckman-Coulter Access, 13%, 50% and 37% of the patients presented BAP values ≤10, between 10 and 20 and ≥20 µg/L, respectively. Discrepancies are observed when other assays are used (concordance from 10 to 100%).

CONCLUSIONS

Analytical problems leading to inter-method variation should be overcome to improve the usefulness of this marker in clinical practice.

According to correlation results, recalibration of BAP assays is necessary but should not be a major issue.

Nephrologists should be aware that, just like PTH, b-AP results are not transposable from one laboratory to the other. More then ever, dialogue between laboratories and nephrologists remain essential.

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