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Original Research Article

Comparison of two parathyroid hormone (pth) assay methods in the monitoring of black african hemodialysis patients in the ivory coast (Maglumi® vs Vidas Biomerieux® Kits)

Yao Epse Yapo Carine Mireille[1]*, Yayo Sagou Eric[1], Kouacou Kadio Morel[1], Konan Konan Jean-Louis[1], Kone Dakouri Benedicte[2]

[1] *Dept of Biochemistry, Félix Houphouet Boigny University and Samu Laboratory, Abidjan, Côte d'Ivoire*
[2] *Felix Houphouet Boigny University, Abidjan, Côte d'Ivoire*

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ABSTRACT

Background: Parathyroid hormone (PTH) testing is recommended once or twice a year to prevent bone complications resulting from chronic kidney disease. However, its interpretation is subject to many factors, including the generation of the PTH test used. For this reason, it is recommended that each laboratory establish its own PTH Upper Limit of Normality (ULN). In order to guarantee optimal management of hemodialysis patients in the public sector in Côte d'Ivoire (West Africa), it proved important to compare the diagnosis of hyperparathyroidism made using two platforms used in the laboratory in charge of monitoring these patients: PTH VIDAS® (3rd Generation) and PTH MAGLUMI® (2nd Generation).
Materials and Methods: This was a cross-sectional study of 65 haemodialysis patients in Abidjan. PTH determinations were performed simultaneously on VIDAS® and MAGLUMI® platforms. The results obtained were interpreted on the basis of PTH threshold values pre-established in the laboratory.
Results: 86.15% of patients had concordant diagnoses on both platforms, compared with 13.85% with discordant diagnoses. Statistical analysis of these results showed a non-statistically significant difference.
Discussion: The limitation posed by differences in PTH concentration given by different platforms can be circumvented by using PTH ULN stablished for each platform for a given population. Conclusion: The diagnoses made by the two platforms are thus superimposable using their respective PTH ULN.

1. Introduction

Chronic kidney disease (CKD) is a real public health problem, affecting 5 to 10% of the world's population.[1] In Côte d'Ivoire, its prevalence is 7.5%[2] at the stage of end-stage chronic renal failure (ESRD). This condition poses a real threat in many countries, due to a steady rise in its incidence and prevalence, and its medical, social and economic consequences.[3]

The progression of chronic kidney disease (CKD) is marked by a number of complications, notably affecting phosphocalcium homeostasis, and leading to bone alterations and cardiovascular morbidity and mortality.[4,5]

The management of end-stage renal disease therefore includes biological monitoring to adapt treatments and reduce the deleterious effects of these complications. Biological monitoring includes measurement of parathyroid hormone (PTH), the main hormone regulating phosphocalcic metabolism. The accepted values in hemodialysis patients should be between 2 and 9 times the upper limit of normal (ULN) according to the KDIGO.[6]

* *Corresponding author*.
E-mail address: camireille@yahoo.fr (Y. E. Y. C. Mireille).

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Appropriate interpretation of PTH must therefore take into account the nature of the test used. Indeed, PTH assay methods have undergone several evolutions since the 1960's. After the 1st generation methods, now abandoned, the 2nd and 3rd generation methods developed later have improved test specificity.

These last two generations of tests are still in use today, and are available in the laboratory for biological monitoring of patients with chronic renal failure undergoing dialysis in the public sector in Côte d'Ivoire. This raises the problem of concordance between the diagnosis made on these two platforms in the follow-up of these dialysis patients. In other words, is the diagnosis of PTH elevated beyond acceptable target values the same regardless of the platform used? The aim of this study is therefore to compare the diagnosis produced by the two generations of tests.

2. Material and methods

2.1. Ethical considerations

This study was approved by the Comité National d'Ethique et de la Recherche (CNER) of the Ministry of Health and Public Hygiene of the Republic of Côte d'Ivoire under number 072 /MSHP/C NER- Kp. A free and informed consent form was obtained from all participants.

2.2. Participants

This was a cross-sectional analytical study involving. Adult black African dialysis patients of both sexes, followed at the Centre national de prévention et de traitement de l'insuffisance rénale (CNPTIR) for two four-hour sessions per week, who came to the laboratory for their annual follow-up check-up - and who had given their consent to participate in this study approved by the national ethics committee. Pregnant women and minors were not recruited.

Our sample size was set at 65 to meet the requirements of method comparison standards ($n \geq 40$)[7] and to satisfy the size of a large sample from a statistical point of view ($n \geq 60$).

Sampling was carried out by successive recruitment of dialysis patients until the expected number of patients was reached.

Epidemiological data, i.e. sex, age, length of dialysis in months, were collected by questioning hemodialysis patients and also from records available in the hemodialysis departments.

2.3. Method

2.3.1. Pre-analytical phase

Each patient in the study had his or her blood drawn in the morning on an empty stomach, at the bend of the elbow within the laboratory. Whole blood was collected in a dry, anticoagulant-free tube with separating gel (yellow cap) and centrifuged at 3500 rpm for 5 minutes.

The serum collected was divided into aliquots. These were stored at -20°C for subsequent PTH determination two weeks later.

2.3.2. PTH determination

The two kits compared for PTH determination were MAGLUMI® (2nd generation) and BioMérieux VIDAS® (3rd generation).

PTH (parathyroid hormone) was assayed on both sets of equipment in accordance with their respective principles and operating procedures, i.e. a mini VIDAS® from BIO MERIEUX laboratories using a standardized 3rd-generation assay technique, and a MAGLUMI SNIBE® using a non-standardized 2nd-generation technique.

The reagents used for patient PTH determinations are ready-to-use reagents adapted to each device (BIO MERIEUX VIDAS ® PTH Kit REF 422010 and SNIBE MAGLUMI ® PTH Kit REF 130211004M). The assay results obtained were interpreted on the basis of PTH normal range pre-established within the laboratory from a population of presumably healthy blood donors (normal blood count, negative serology for HIV and Hepatitis B and C, normal blood calcium, phosphorus and 25 OH vitamin D concentrations). The standard used to define PTH targets was that of the latest KDIGO recommendations, i.e. PTH should be maintained within a range of two to nine times the upper limit of normality.

The pre-established normal ranges within the said laboratory according to KDIGO rules were respectively 280.4-1261.8 pg/ml for the MAGLUMI platform and 83.8-377.1 pg/ml for the VIDAS BIOMERIEUX platform.

2.4. Statistical analysis of data

Results were analyzed using SPSS version 20 software. Qualitative data are presented as patient numbers and percentages, while quantitative data are presented as means, standard deviation, median, range (minimum, maximum). The concordance of the diagnosis of the two methods was made using the Cohen's Kappa statistical test at the 5% level of significance. A p-value (P) < 5% was considered significant.[7] (Table 1).

The table 1 summarizes the analysis criteria for PTH results.

3. Results

The mean age of the haemodialysis patients recruited was 46 years, with extremes ranging from 20 to 75 years. With the exception of the 40 to 60 age group, the male/female distribution was relatively homogeneous in the population.

Most patients had been on dialysis for more than 64 months, i.e. just over 5 years, with extremes ranging from 5 months to 264 months (around 22 years). The characteristics of the study population are presented in Table 2.

As for PTH values, within the study population, 33.85% of dialysis patients had a PTH value above the threshold value on the Maglumi® kit, compared with 41.54% on the Vidas® kit (Table 3).

The contingency table based on the threshold values of the two assay platforms showed that 86% of patients were in diagnostic agreement (Table 4).

The Cohen Kappa test revealed good diagnosis agreement between the two platforms (Table 4).

Table 1: Interpretation of Kappa values [8]

Kappa values	Interprétation (agreement)
< 0	Very poor
0 - 0,20	Poor
0,21 - 0,40	Fair
0,41 - 0,60	Mean
0,61 - 0,80	Good
0,81 - 1	Very good

Table 2: Patients characteristics

Characteristics	Mean +/- Standard deviation	Median (min, max)
Mean Age (years)	46 +/- 12	46 (20-75)
Male n (%)	24 (36,9%)	
Lenght of time on dialysis (months)	63 + /-49	67 (5 – 264)

Table 3: Distribution of patients according to PTH by platform

PTH value	Numbers (perrcentage)	
	Normal	High
MAGLUMI (threshold) = 1261,8 pg/ml)	43 (66,15%)	22 (33,85%)
VIDAS (threshold) = 377,1 pg/ml)	38 (58,46%)	27 (41,54%)

Table 4: Comparison of high PTH diagnoses on the two platforms (MAGLUMI®vs VIDAS®)

	Numbers	Perrcentage (%)	KAPPA
Concordant diagnoses	56	86,15	K= 0,7071
Discordant diagnoses	9	13,85	
Total	65	100	

4. Discussion

In our study, we noted a male predominance with a sex ratio of 1.7. This observation has also been made by several authors including Samaké et al.[8] in Mali (Sex-ratio 1.13), Ramilitiana et al.[9] in a Madagascar (Sex-ratio 1.46, Asseradji et al.[4] in Morocco (Sex-ratio 1.78), Diallo et al.[10] in Côte d'ivoire (Sex-ratio 1.61).

This could be explained by the relative financial stability and literacy rate in favor of the male sex, which would give men an advantage over women in access to healthcare in our countries. In addition, some authors have described a greater frequency of renal disease in men than in women, and a more rapid progression to chronic renal failure.[11]

The predominant age group in our series is [40-50[years with a frequency of 40% with a mean age of 47 years and extremes from 20 to 75 years. These results are similar to those also observed in Côte d'Ivoire in 2016 by Kropka A. et al.[12] with a mean age of 45 years and extremes of 18 to 74 years, in Togo with a mean age of 42.62 years and extremes of 20 and 82 years in the study conducted by Dosseh et al.[13] in patients also with chronic renal failure at the dialysis stage. This value was slightly higher in Morocco in 2012, with an average age of 49.3 years in the study by Hasni et al.,[14] and even higher in France, where the average age of dialysis patients reached 65 years in the study by Masse et al.[15] This finding could be explained by better access to healthcare for populations in Maghreb and developed countries, compared with populations in sub-Saharan francophone Africa.[16,17]

Around 41% of patients in the study had been on haemodialysis for 12 to 60 months. This group also represented the majority of patients by Abe in 2016[18] and Kropka in 2018[12] in their series of hemodialysis patients still at the Abidjan SAMU. The average length of service in our series was 63 months, compared with 48 months in that of Taleb et al.,[19] in Algeria in 2016.

This finding seems paradoxical in view of the better dialysis conditions in this country (11 hours per week versus 8 hours per week in Côte d'Ivoire). However, the explanation could lie in the greater access to kidney transplantation in North African countries, which would not oblige these patients to remain on dialysis for long periods.

The main objective of our study was to compare the VIDAS® BIO MERIEUX and SNIBE MAGLUMI PTH platforms in the monitoring of hemodialysis patients at the SAMU, based on previously established threshold values. After PTH measurement on both platforms, the values obtained for the same patients were very different. The values obtained on the MAGLUMI platform were much higher than those obtained on the VIDAS platform. This may be explained by the fact that, unlike the VIDAS platform, the MAGLUMI platform (2nd generation) assays various circulating forms of PTH other than the active 1-84 form, such as C-terminal and N-terminal fragments.[20]

However, the use of threshold values for each platform, obtained from healthy subjects, enabled us to classify patients into different categories according to their PTH concentration. On the one hand, we had patients whose

PTH value fell within the target range established on the basis of KDIGO guidelines: 280.4-1261.8 pg/ml on the MAGLUMI platform and 83.8-377.1 pg/ml on the VIDAS platform. On the other hand, we had patients whose PTH value was above the threshold value; 1261.8 pg/ml on MAGLUMI and 377.1 pg/ml on VIDAS. Thus, 86.15% of patients had concordant diagnoses on both assay platforms, whereas 13.85% of patients had discordant diagnoses from one platform to the other. Statistical analysis of these results using the Kappa test showed that this observed difference was not statistically significant. The diagnosis made by the two platforms are therefore superimposable using their respective target values. Several studies corroborate this observation. In 2012, Cavalier et al.[21] compared several 2nd generation platforms, including Beckmann Access, Abbott Architect and Diasorin N-tact IRMA. The PTH concentrations given by this equipment for the same hemodialysis patients averaged 460, 330 and 197 pg/ml respectively for each assay platform. This shows a wide dispersion of results between 2nd generation assay platforms and the need to determine reference values for better harmonization of diagnoses. Similarly, J. Douglas et al.[22] compared the MAGLUMI platform with seven other 2nd and 3rd generation automated systems, including the Beckman Access and Diasorin 1-84 PTH, after determining the upper limits of the normal value of the kit used, but this time in the context of primary hyperparathyroidism. This study showed that the 2nd and 3rd generation platforms gave the same clinical diagnoses in primary hyperparathyroidism when interpreted with the normal values established for each equipment. In 2018, to evaluate the performance of the VIDAS kit, a study conducted by BIO MERIEUX SA compared the results obtained with VIDAS and another commercially available PTH immunoassay (1-84) scored (X) in 21 patients recruited at 3 different time points. According to the new KDIGO guidelines, agreement between these two tests was 88.89% after statistical analysis. These studies are in line with our own. Furthermore, in 2012 Almond et al.[23] carried out a pilot study in 21 haemodialysis patients on PTH measurement by five 2nd and 3rd generation immunoassay platforms namely; Beckman Access Dxl, Diasorin liaison, Roche modular E170, Siemens ADVIA centaur and Siemens Immulite 2000. The differences between the lowest and highest immunoassays ranged from 1.4 to 4.2 times, although the manufacturer's reference ranges for the lowest and highest immunoassays were similar (1- 6.5 and 1.2 -7.6 pmol/L, respectively).

The pilot study confirmed significant differences between dosages that are not reflected in the relevant reference intervals and could affect treatment decisions. In an in-depth study of 98 patients, the same authors showed that patients were classified differently according to immunoassays when manufacturers' reference interval data were used. They therefore recommended the use of normal values specific to each laboratory and platform for the interpretation of PTH concentrations.

Similarly, Cavalier et al. in 2018[24] and Laradi et al.[25] in 2014 also noted the importance of each laboratory establishing its reference values in order to optimize the accuracy of the diagnosis made. Thus, the limitation constituted by differences in PTH concentration given by different platforms can be circumvented by using normal values established for each platform for a given population.

Our study has therefore shown that, by establishing our threshold values at laboratory level, we can use either a second- or third-generation platform and obtain identical diagnosis.

5. Conclusion

The management of dialysis patients requires proper monitoring of biological parameters, including PTH levels. The interpretation of PTH values is an important aspect in the management of dialysis patients and the improvement of their quality of life. In our study, we compared two second- and third-generation assay platforms in the biological monitoring of dialysis patients at the SAMU (Abidjan), using threshold values previously established by the laboratory. Statistical analysis of the diagnoses provided by the two platforms showed no significant difference.

The PTH values given by these two platforms, which were extremely different, could be reconciled using the threshold values established by the laboratory. In other words, from a biological point of view, the results provided by the MAGLUMI platform (2nd generation) and those provided by the VIDAS platform (3rd generation) are superimposable. The EMS laboratory can therefore use either platform to monitor dialysis patients.

This study therefore confirms the need for each laboratory to establish its own PTH normal range, to ensure better monitoring of mineral-bone disorders linked to chronic kidney disease by clinicians.

6. Limitations of this Study

A larger sample would have been desirable to attest to this concordance of diagnosis between the two platforms.

7. Source of Funding

None.

8. Conflict of Interest

None.

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Author biography

Yao Epse Yapo Carine Mireille, -

Yayo Sagou Eric, Professor

Kouacou Kadio Morel, -

Konan Konan Jean-Louis, -

Kone Dakouri Benedicte, -

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