PARATHORMONE AND BONE DISORDERS IN BLACK ADULT HEMODIALYSIS PATIENTS IN THE PUBLIC SECTOR IN ABIDJAN

Abstract :

Introduction
The progression of chronic kidney disease (CKD) is characterized by several complications, including disorders of phosphocalcium metabolism characterized by secondary hyperparathyroidism. For this reason, major international recommendations call for at least annual parathyroid hormone (PTH) determinations in patients suffering from CKD, particularly in the terminal phase.
This study aims to explore parathyroid hormone status and bone disorders in adult hemodialysis patients in the public sector of Abidjan, West Africa.

Material and methods
This was a cross-sectional study of 100 end-stage chronic renal failure patients treated by hemodialysis. Parathyroid hormone (PTH) was determined by ELFA enzyme-linked immunosorbent assay on the VIDAS® platform.PTH values were interpreted in relation to the range of 2 to 9 times the upper normal limit in healthy subjects, in line with current KDIGO recommendations, and compared with clinical bone complications.

Results
Median PTH level was 315.95 (123.37-725.22) pg/mL. 48% of patients had PTH levels above the recommended threshold. Of these, almost half had no bone complications.

Conclusion
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Keywords: parathyroid hormone – black – hemodialized – bone disorders

1. INTRODUCTION

Chronic kidney disease (CKD) is a widespread pathology worldwide, with an estimated prevalence of 10% in 2020(1). In Africa, and particularly in Côte d'Ivoire, prevalence remains poorly known due to a lack of data in the general population. In the terminal phase, the disease requires suppletive treatment, dominated by hemodialysis in developing countries. (2)
The evolution of CKD is characterized by the progressive destruction of nephrons, which impairs kidney function(3). Alteration of these functions induces various disturbances, including disorders of phosphocalcic metabolism characterized by secondary hyperparathyroidism(4). Parathyroid hormone (PTH) is secreted by the parathyroid glands

and regulates phosphocalcium homeostasis. An increase in parathyroid hormone leads to complications such as fractures, bone deformities and calcifications, known as renal osteodystrophy (5).
In order to prevent these complications, the KDIGO (Kidney Disease Improving Global Outcomes) expert committee recommends biannual or annual PTH measurement in chronic hemodialysis (HD) patients, with internationally accepted targets of between 2 and 9 times the upper normal limit (6,7). Failure to perform this check-up exposes patients to the development of undiagnosed hyperparathyroidism, potentiating the risk of bone complications without adequate management. The aim of this study was to explore parathyroid hormone status and bone disorders in adult haemodialysis patients in the Abidjan public sector.

2. METHODS

2.1 - Study design and patients

This is a cross-sectional analytical study conducted by the Biochemistry Laboratory of the UFR Sciences Pharmaceutiques et Biologiques, Université Félix Houphouët-Boigny, Abidjan, Côte d'Ivoire. It included 100 HD patients, followed for more than 3 months at the national center for the prevention and treatment of renal failure (CNPTIR) in Abidjan, Côte d'Ivoire. These patients were receiving HD replacement therapy for 4 h, twice a week.

2.2 - Method

Socio-demographic and clinical data, i.e. sex, age, length of time on dialysis, bone complications observed, were collected from medical records available in the hemodialysis departments and by questioning hemodialysis patients.
Fasting venous blood sampling at the elbow, on an anticoagulant-free vacuum tube containing a separating gel, was performed in all HD patients. Samples were centrifuged within one hour of collection. The serum collected after centrifugation was used to measure the various parameters on the same day. Calcemia and phosphoremia were determined on a HITACHI 704® automated system using colorimetric methods, Arsénazo III and ammonium molybdate respectively, with end-point measurements. PTH (1-84) was measured using a two-step sandwich enzyme-linked immunosorbent assay with final fluorescence detection on the VIDAS® platform. The standard used to define PTH targets was that of the KDIGO recommendations, i.e. PTH should be maintained within a range of two to nine times the upper limit of the kit used.
Threshold values were calculated on the basis of previously available data from healthy subjects, multiplied by 2 and 9(7). The normality interval pre-established within the said laboratory was 83.8-377.1 pg/ml for the VIDAS BIOMERIEUX platform.

2.3 - Statistical analysis

Quantitative variables were described using the mean, standard deviation, extremes, median and interquartile range (25th percentile (P25)-75th percentile (P75)). Each of the qualitative variable modalities was described in terms of numbers and percentages. Comparative analysis of the different parameters was performed using the Chi2 test. Values < 0.05 are considered significant.

3 - RESULTS

A total of 66 men and 34 women, all HD, participated in the study. These patients had a mean age of 45.34 ± 12.26 years. They had been on hemodialysis for an average of 64 months(

justover 5 years). Table 1 summarizes the demographic and clinical characteristics of the entire hemodialysis population. Bone pain was the most frequent complication (92.31%) in the 39 patients with bone disorders (Figure 1).

Table 1 : Socio-demographic and clinicalcharacteristics of hemodialysis patients in Ivory Coast

Characteristics	Values
Patients (n H)	100 (66)
Age (years)	
Average ±sd	45,34 ± 12,26
Median (P25; P75)	45 (37;54,25)
Min - Max	
Sex-ratio (men/women)	1,9
Age of hemodialysis (years)	
Average ± sd	64 ± 34
Median (P25; P75)	48,05 (36;84)
Min - Max	
Bone complications n (%)	39 (39 %)

n: staff, sd: standard deviation; H: men; F: women; P25: 25th percentiles; P75: 75th percentiles); Min: minimum; Max: Maximum

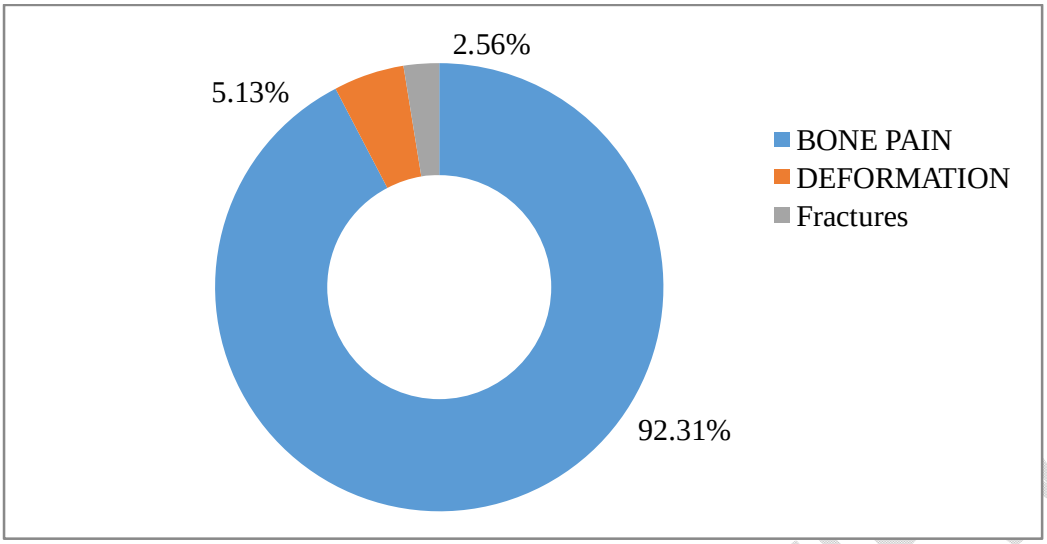

Figure 1: Types of bone complications seen in HD patients

Biological markers of phosphocalcic metabolism in HD patients are shown in Table 2. Serum calcium and phosphorus levels ranged from 70 to 110 mg/l and from 13.80 to 92 mg/l respectively, with mean values of 97.85 ± 9.05 mg/l and 46.89 ± 13.40 mg/l. The median PTH level was 315.95 (123.37-725.22) pg/mL, with extremes of 9.60 and 1500 pg/mL. Hypocalcemia and hyperphosphatemia were present in 16% and 35% of HD patients respectively, while 48% had PTH levels above the threshold of 377 pg/mL.

Table 2: Biological Markers of Phosphocalcium Metabolism in HD Patients

Parameters	Values			
	Average±sd	**Median (P25;P75)**	**limit**	**(n%)**
Total calcium (mg/L)	97,85 ± 9,05	100 (92-105)	< 90	16 (16%)
Phosphatemia (mg/L)	46,89 ± 13,40	46 (37,07-54)	≥ 50	35 (35%)
Serum THP (pg/ml)	499,77 ± 468,20	315,95 (123,37-725,22)	≥ 377,1	48 (48%)

sd: standard deviation; P25: 25th percentiles; P75: 75th percentiles

No significant relationship was found between PTH status and bone complications in our study population (Table 3).

Table 3: PTH Status by Bone Complications

		PTH (ng/ml)		pvalue (Khi 2)
		NORMAL	HYPERSECRETION (≥ 377,1)	
Bone complications	YES	16	23	0,079
	NO	36	25	

4 –DISCUSSION

Social-demographic and clinical characteristics

The mean age of HD patients was 45 years, with extremes of 18 and 75 years. There were 66 men (36%) and 34 women (34%), with a sex ratio of 1.9 (Table 1). Age distribution showed that over 2/3 (68%) of the study population were under 50 years of age, highlighting the relative youthfulness of hemodialysis patients in our study. The young age of renal failure patients was also found by Yao et al. (8) in Côte d'Ivoire and Gerard et al. (9) in Burkina Faso, with mean ages of 39 and 45 respectively. This finding is different in Caucasian countries, notably in the United Kingdom, where the mean age of CKD patients is over 60 (10), and in France, where the median age of dialysis patients reached 70 according to the 2016 report of the Société Francophone de NéphrologieDialyse et Transplantation (11). This age difference between African countries and the West could be explained by better management of cardiovascular risk factors and accessibility to healthcare in the West, thus delaying the progression of CKD to the terminal stage(12).

Generally speaking, the male predominance of HD patients found in our study (sex ratio = 1.9) is corroborated by numerous authors and could be explained by a higher frequency of kidney disease in men and a more rapid deterioration in renal health compared with women (12).

HD patients had been receiving hemodialysis replacement therapy for an average of 64 months, or just over 5 years, with extremes of 6 months and 20 years (Table 2). These results are in line with those of Yao et al (13) (63 months) in the same treatment center some five years earlier. However, this average length of dialysis remains lower than in Morocco, where the length of dialysis is much higher, reaching ten years according to Mhammedi et al. (14).This difference in our context could be explained by the costs associated with dialysis, delays in diagnosis leading to late initiation of dialysis, as well as the drop in dialysis frequency caused by the growing number of patients and the inadequacy of dialysis machines.

Biochemical markers and bone disorders

The phosphocalcemic disorders observed in our series are represented by hypocalcemia (16% of patients) and hyperphosphatemia (35%) (Table 2). Hypocalcemia is the consequence of a lack of synthesis of an active vitamin D metabolite in the kidneys. Calcium and/or vitamin D supplementation adopted in follow-up treatment protocols for CKD patients in the public sector in Côte d'Ivoire could explain the relatively low frequency of these disorders in our study(15,16).

In our study, the median PTH concentration was 315.95 (123.37-725.22) ng/mL. Almost half (48%) (Table 2) of haemodialysis patients had a PTH value above the threshold (377.1 pg/mL) accepted for haemodialysis patients, indicating hyperparathyroidism. Similar studies on the same black African population of patients with chronic kidney failure, notably those by Mondé et al. (17) and Cavalier et al. (18), also revealed severe hyperparathyroidism in 47.14% and 30% of haemodialysis patients respectively.

This secondary hyperparathyroidism, generally found in chronic hemodialysis patients, represents one of the most common disturbances in the progression of chronic kidney disease, and could be explained by the release of intact PTH into the bloodstream under hypocalcemic conditions. Indeed, during renal failure, hypocalcemia will directly stimulate the synthesis of PTH mRNA, leading to hypersecretion by the parathyroid glands (19). In contrast, Coulibaly et al (20) in Burkina Faso reported serum PTH concentrations of 934 ± 887.4 pg/ml. This difference may be explained by the different method used to measure serum PTH in the two studies: 2nd generation in Coulibaly et al. versus 3rd generation in ours.

Bone complications were observed in 16 patients with normal PTH concentrations. This observation may be justified by the multifactorial nature of bone disorders involving various biological markers of bone remodeling, notably PTH, total alkaline phosphatases, bone-derived alkaline phosphatases (PALO) and cross-lapses (CTX) (21).

However, the bone complications observed in these patients were mainly minor pain complications (with no fractures or deformities) (figure 1). Analysis of PTH concentrations in relation to the presence of bone complications in our cohort revealed no statistically significant relationship between these 2 parameters (p=0.079) (Table 3). Paradoxically, the majority of patients with high PTH had no bone complications. This observation may be explained by a loss of bone sensitivity or differential reactivity to high PTH, depending on the population (22). Thus, the thresholds set by European and American recommendations of 2 and 9 times the upper limit of normal PTH (KDIGO, 2017) may not be applicable to our black African populations.

This is all the more true as in other population groups, notably in Asia, narrower PTH concentration targets have been accepted - the Japanese Society of Dialysis Therapy recommends a PTH target of 1 to 4 times the upper normal limit (23). Thus, assuming that thresholds may vary between population groups, in relation to differential desensitization of bone to the action of PTH, thresholds higher than 9 times the upper normal limit could help explain the paradox observed in our cohort between PTH concentrations and bone complications.

5- CONCLUSION

The metabolic disturbances observed in the present study lead us to propose the systematic dosage of parathyroid hormone as part of the biological follow-up work-up, and the need to promote appropriate therapies for each HD patient.

For African populations, this study suggests a possible inadequacy of international PTH targets in Europe and America. A more extensive study involving a larger population, combined with the establishment of reference values for PTH and specific markers of bone remodelling, should help to elucidate this assertion.

ETHICAL CONSIDERATIONS

The study was approved by the local ethical committee of the Ministry of Health: theComité 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 138-22 /MSHP/CNESVS-km. A free and informed consent form was obtained from all participants.

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