

Evaluation of the Phosphocalcic Profile of Chronic Hemodialysis Patients in Senegal

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Abstract

Introduction: CKD-MBD are defined by the disturbances of phosphocalcic metabolism and their consequences on the skeleton (fragility by osteopenia) and on the soft tissues. Few studies have been done in Africa on this subject. Only one study limited to the city of Dakar, had been carried out in Senegal in 2014. That is why we have taken this study for all of Senegal to improve the indicators for a better care of the patients.

Methodology: It was a cross-sectional, retrospective, descriptive and analytical study that had been performed in seven hemodialysis centers in Senegal over a period of seven years (June 30, 2010 to July 1, 2017). All patients aged over 15 years and hemodialysis for at least 6 months were included in the study. Objective was to determine the epidemiological, clinical and paraclinical data of phosphocalcic disorders of chronic hemodialysis patients.

Results: The number of patients included was 315. The mean age was 50, 65 ± 13.84 years. There were 49.8% of men and 50.2% of women (sex ratio of 0.99). Mean seniority in hemodialysis patients was 47, 78 ± 32.88 months. There were 58.1% of patients who were originally from Dakar. It was noted that 91.1% dialyzed over a period of 4 hours and 84.8% received 3 sessions per week. The main causative nephropathies were vascular nephropathy (43.8%) and indeterminate nephropathies (20.3%). There were 15.2% bone pain, 10.2% joint pain and 2.86% of spontaneous fracture. The overall prevalence of phosphocalcic disorders was 27.6% for hypocalcaemia, 53.1% for hyperphosphatemia, 48.8% for hyperparathyroidism, 80.2% for vitamin D depletion and 62.2% for high total alkaline phosphatases. Regarding the percentage of patients who were in the KDIGO norms, 66.70% were found for calcemia; 40.20% for phosphatemia; 49.80% for the PTHi; 19.80% for vitamin D 25OH and 37.80% for total alkaline phosphatase. According to KDIGO standards, the average frequency of achievement of these phosphocalcic parameters was respected in 11.10% of patients for calcemia; 8.70% for phosphatemia; 8.80% for the iPTH and 15% for the total alkaline phosphatase. Standard radiography showed 62% bone demineralization and 12.1% vascular calcification. Regarding the types of bone involvement, 39.7% was indeterminate; 30.8% fibrous osteitis; 27.6% without bone involvement; 1.3% dynamic osteopathy; 0.6% osteomalacia.

Conclusion: CKD-MBD is common in chronic hemodialysis patients in Senegal. The prevalence of normality of calcemia, phosphatemia and iPTH was 11.75%. In our study, mean hyperparathyroidism was 718 pg/ml thus contributing to the high mortality with 47 deceased patients. These results encourage compliance with KDIGO recommendations.

Abbreviations: CKD-MBD: Chronic Kidney Disease Related to Mineral-Bone Disorders; KDIGO: Kidney Disease Improving Global Outcomes; iPTH: Intact Parathyroid Hormone; CKD: Chronic Kidney Disease

Keywords: CKD-MBD; Hemodialysis; Senegal

Introduction

Chronic kidney disease related to mineral-bone disorders (CKD-MBD) are almost constant complications in chronic hemodialysis patients. They cause an impairment of quality of life and an increase in cardiovascular morbidity and mortality. The prevalence of BMD in hemodialysis patients was 66.9%, with a predominance of secondary hyperparathyroidism [1]. Their overall mortality is increased because of secondary hyperparathyroidism [2,3]. Patients with CKD have a

high risk of cardiovascular disease, with cardiovascular mortality rates 10 to 20 times higher in dialysis patients than in the general population [4]. This prevalence is largely due to hyperphosphatemia and its bony consequences and to vascular calcifications, particularly coronary and valvular calcifications, whose risk is 5 times higher [2]. This work is being conducted for the second time in Senegal. The first study done in 2014 was limited to three hemodialysis centers in the city of Dakar. The second study is more exhaustive and concerns

the whole country. The goal was to refine the results and improve the statistics reported to the entire population of Senegal. The objective in this study was to determine the mineralo-osseous and phosphocalcic status and the prevalence of secondary hyperparathyroidism, to evaluate the prescribed treatment and then to make a comparison with the 2009 KDIGO recommendations.

Patients and Method

It was a cross-sectional, retrospective, descriptive and analytical study that had been performed in 7 hemodialysis centers in Senegal over a period of seven years (June 30, 2010 to July 1, 2017). All patients aged over 15 years, followed for chronic renal failure and hemodialysis for at least six months were included in the study. These public and private centers were in Dakar (Dantec, ABC, HOGGY), Saint Louis, Kaolack, Ziguinchor and Touba. For each included file, the epidemiological parameters (age, sex, profession), clinical (bone pain, joint pain, difficulty walking and functional impotence, drumstick fingers, limitation of movements and bone deformations), biological (calcemia, phosphatemia, iPTH, 25 OH Vitamin D, alkaline cell phosphatase, aluminemia, hemoglobinemia, CRP, Albuminemia), X-ray (Standard X-ray, Cervical Ultrasound of the Parathyroid Glands, Parathyroid Imaging, Cardiac and vascular ultrasound, thoraco-abdominal CT pelvic) and therapeutic (oral calcium, calcium phosphate chelators, non-calcium phosphate chelators, native and/or active vitamin D, calcimimetics, parathyroidectomy). Data were collected using an exploitation sheet and analyzed before and after therapeutic intervention.

Results

Three hundred and fifteen patient files were collected. The mean age was 50.65 ± 13.84 years [17 and 87 years]. There were 49.8% of men and 50.2% of women (sex ratio of 0.99). Vascular nephropathy was observed in 138 patients (43.8%). Indeterminate nephropathy and chronic glomerulonephritis was noted respectively in 20.3% and 15.6% of cases. Dialysis seniority was 47.78 months with extremes of 6 months to 202 months. It was noted that 84.8% (n=267) of patients had 3 dialysis sessions lasting 4 hours per week; 81% of patients performed dialysis on an arteriovenous fistula; 60 patients (19%) on catheters. Among these catheters, 46 (76.7%) were tunneled and 14 (23.3%), were temporary catheters (jugular). Eleven patients (3.5%) had a history of treated aluminum intoxication.

Clinically, 60 patients (19.04%) had functional symptomatology. On physical examination, 2.9% of patients had abnormalities. 48 patients (15.2%) had bone pain, 32 patients (10.2%) had joint pain, 16 patients (5.08%) had difficulty walking, 13 patients (4.13%) had functional impotence, 9 patients (2.86%) had spontaneous fractures and 5

patients (1.6%) had pruritus. In the biology, mean serum calcium was 88.66 mg/l [28 and 128 mg/l]. It was noted that 86 patients (66.7%) had calcemia in KDIGO standards. Its average frequency of completion was 6.10 months. In 11.1% of patients, the frequency of achievement was in the norms. Mean phosphatemia was 51.92 mg/l [7 and 304 mg/l]. There were 81 patients (40.2%) who were in the KDIGO targets. The phosphate's average frequency of completion was 6.66 months with 8.7% of patients who respected the frequency of realization of KDIGO. Twenty-nine patients (9.2%) had benefited from the determination of aluminum oxide and 52% had normal aluminum level (<20 µg/l). The other characteristics of the phosphocalcic parameters are summarized in table 1. Standard radiography performed in 34 patients (10.8%) objectified: demineralization (61.3%), fractures (32.3%), resorption of phalangeal tussles (3.2%) and geodes (3.2%). 207 patients (65.7%) had undergone echocardiography; 12.1% had valvular calcifications: aortic (48%), mitral (26%) and tricuspid (26%). Supra-aortic trunk ultrasonography and thoraco-abdominal computed tomography respectively showed carotid calcification and coronary calcification. The type of bone involvement was indeterminate in 125 patients (39.7%); the diagnosis of fibrous osteitis was retained in 97 patients (30.8%), adynamic osteopathy in 4 patients (1.3%) and osteomalacia in 2 patients (0.6%). Therapeutically, phosphocalcic disorders have been corrected over a period of one year by regular medication at the recommended dose. So, 132 patients (41.9%) had benefited from calcium supplementation (1g 2-3 times/day) because of chronic hypocalcaemia. The other characteristics of phosphocalcic treatment are summarized in table 2.

The evolution was marked by clinical improvement in one third of the patients. 47 patients had died. The causes were infectious, heart and hemorrhagic in respectively 53%, 8.5% and 8.5% of cases. The mean values of serum calcium, phosphatemia, and iPTH after treatment correction were respectively 90.5 mg/l, 38.5 mg/l and 718 µg/ml. In bivariate analysis, there was a close correlation between dialysis seniority, age, hyperparathyroidism, fibrous osteitis, bone pain, and pathological fractures with $p=0.0000$. Vascular calcifications were significantly correlated with vitamin D (<30) with p at 0.028.

Discussion

This retrospective, descriptive, analytical and multicentric study provides an overview of phosphocalcic status in 315 hemodialysis patients in Senegal. The prevalence of normality of the three main phosphocalcic parameters (calcemia, phosphatemia and iPTH) was 11.75%. This result is lower than that found by Mahamat Abderraman et al. [5] in Dakar and Benabdellah et al. in Morocco [6] with prevalence around 17.78%. The average age of the patients was young with an average of 50 years. There was a significant correlation ($p=0.000$)

Table 1: Summary of different characteristics of biological parameters according to KDIGO recommendations.

Feature	Our Study	KDIGO 2009
Calcium	Dosage (mg/l)	88.66
	Frequency of realization	88-104
Phosphate	Dosage (mg/l)	6.10 months
	Frequency of realization	1-3 months
iPTH	Dosage (pg/ml)	51.92
	Frequency of realization	6.66 months
Alkaline Phosphatase (UI/l)	Dosage	718.35 pg/ml
	Frequency of realization	21.72 months
Vitamine D	Dosage	368,86
	Frequency of realization	30-130
	Dosage (ng/l)	23.74 ng/l
		Once a year

Table 2: Summary of therapeutic characteristics.

Feature	Patient population (n)	Percentage (%)
Oral Calcium	132	41.9
Phosphate chelators	244	77.11
Calcium (1g 2-3 times/day)	224	91.8
Sevelamer (800 mg 3-6 times/day)	12	4.9
Vitamin D	129	40.96
Native (200.000 units/month)	88	68.23
Un alpha (0.5-1µg/day)	26	20.15
Cinacalcet (306180 µg/day)	12	3.8
Parathyroidectomy	18	5.8

between age, bone pain and spontaneous fractures confirming the result of Ben Salah et al. in Tunisia by [7]. Another close correlation between age and death was demonstrated in our study as reported by two studies in the United Kingdom and Italy in the DOPPS 2004 study [8]. These facts would explain the death of dialysis patients at a young age as a result of phosphocalcic disorders. The mean duration of hemodialysis in our series was 47 months, like the results of Mahamat Abderraman [5]. On the other hand, it was higher than that found by Léou S, et al. in France [9] and by Zellama, et al. in Tunisia [10], where it was respectively 24 months and 40 months. This difference could be explained by the accessibility and early use of kidney transplantation in these countries. In univariate analysis, a strong correlation ($P=0.000$) was noted between dialysis seniority and pathological fractures; this confirms the result of the DOPPSII study; the age of dialysis was a risk factor (Odds ratio: 2.92 between the first and third years of dialysis and 3.74 after the third year of dialysis); another positive correlation ($P=0.000$) with bone pain was noted. Only 3.5% of patients had a history of aluminum intoxication. Rafi, et al. [11] had objectified 15.5% of cases. Our low numbers could be explained by the improvement of water treatment rooms with double osmosis, adequate water quality control and the eviction of aluminum-based drugs. Nearly 70% of our patients had normal calcemia according to KDIGO. These results corroborate the data from the literature [12,13]. This high prevalence would be due to the fact that almost half of the patients took oral calcium in supplementation and that the dialysate calcium used in our centers was fixed at 1.5mmol/l. The average phosphatemia was 51 mg/l. More than half of our patients had hyperphosphatemia, as the results of Laradi, et al. [13] noted 50% of cases. Calcium and phosphatemia should be performed at least once every 3 months in chronic hemodialysis patients. In our study, it was greater than 6 months. The respect of the prescription of these examinations could contribute to the improvement of the clinical state of the patients and make it possible to anticipate the complications of the CKD-MBD. It is the same for hyperparathyroidism which was noted in 50% of cases. These high figures for phosphate and parathyroid hormone represent a high risk of excess mortality and cardiovascular risk with an increase in vascular calcification [13]. It was noted that 50.01% of patients had not benefited from the dosage of vitamin D certainly due to its expensive cost and low prescription by nephrologists. Its average frequency of implementation was 38.69 months against an annual dosage recommended by KDIGO. Half of the patients who had benefited from the vitamin D dosage, for the most part had low reserves. Since patients with vitamin D deficiency had a higher mortality rate [14], vitamin D supplementation would be desirable. This has been demonstrated by several studies that have reported improved survival

in hemodialysis patients who have received active vitamin D [15,16]. A significant correlation ($p=0.028$) between deficiency (and/or insufficiency) of vitamin D and vascular calcifications was noted; this is consistent with the results found by Moradi M et al. in Iran [17]. Concerning the alkaline phosphatases, few studies have been realized, to date. In our work, it was noted that 38% of patients had a rate in the standards recommended by KDIGO. In contrast, 62% of patients had a high rate. This can be explained by the high bone turnover of secondary hyperparathyroidism (48.8%). These results were difficult to interpret because only 23.49% of patients benefited from this examination. Its average frequency of completion was 112.32 months, more than 9 times the recommended duration of KDIGO [18]. This figure remains to be improved since the alkaline phosphatase values and their evolution must be considered to assess bone turnover. In our series, 6.03% of patients had bone demineralization. This result is much lower than that found by Benabdellah, et al. [6] in Morocco with 57% and in Mauritania, et al. [19] with 33%. This discrepancy is attributable to the fact that only 10.8% of patients received standard X-rays. This also explains the difference noted for fracture traits with 3.17% for our study, 7.5% for Benabdellah, et al. [6] and 6.66% in Mauritania, et al. [19]. Only 8.3% of patients had nodules on cervical ultrasound. Ultrasonography was performed in a few patients in our study. This result contrasted with that noted by Benabdellah, et al. [6] which was 16%. There were 8.57% of valvular calcifications. These results were comparable to those of Mahamat Abderraman et al. [5] in Dakar, of Benabdellah et al. in Morocco [6] who found respectively 11.1% and 9% of cases. This high rate could be explained by the average duration of hemodialysis that was 4 years and the fact that more than half of the patients had hyperphosphatemia. Thus, the interest of a good control of the phosphocalcic metabolism resides, not only in the improvement of the quantity and the bone quality of the patients and thus, in the prevention of the fracture risk; but also, in the fight against the formation of the vascular calcifications and other extra bone calcifications. It is well established that vascular calcification is partly related to mineral disorders in dialysis patients; and they are responsible for worsening cardiovascular morbidity and mortality in this already high-risk population [20]. Lindner et al. had noted in their study a very high morbidity and mortality from cardiovascular complications related to accelerated atherosclerosis [20]. In univariate analysis, there was a significant correlation between vascular calcifications with vitamin D deficiency and/or insufficiency. In bivariate analysis, the iPTH level did not influence the occurrence of vascular calcification ($p=0.066$). This was consistent with numerous studies by Bellasi, et al. [21], Sayarliogu, et al. [22] and Strozecki, et al. [23] who also found no association between biological parameters including serum calcium, phosphorus, iPTH levels and valvular calcifications.

Conclusion

CKD-MBD is common in chronic hemodialysis patients in Senegal. The prevalence of normality of the three main phosphocalcic parameters (calcemia, phosphatemia and PTHi) was 11.75%. The overall mortality of hemodialysis patients with CKD-MBD was increased by secondary hyperparathyroidism. In our study, mean hyperparathyroidism was 718 pg/ml thus contributing to the high mortality with 47 deceased patients. Our results clearly demonstrate significant hyperphosphatemia, hyperparathyroidism and a very low vitamin D level. The same is true of the frequency of these examinations, which is twice the recommended duration. This frequency of achievement is greater than 6 months for serum calcium and phosphatemia. This study, which considers all hemodialysis centers

in Senegal, gives a more precise idea of phosphocalcic parameters compared to the one we conducted in 2014 and was limited to the Dakar region alone. These results encourage compliance with KDIGO recommendations. This involves respecting the regular prescription of paraclinical examinations and the correction of phosphocalcic disorders. But its results remain perfectible because all hemodialysis patients had not benefited from the dosage of all parameters.

Conflicts of interest: The authors do not declare any conflict of interest.

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