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Mineralo-Bone Disorders in Peritoneal Dialysis Patients in Senegal (West Africa)

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Abstract

The chronic kidney disease associated with bone and mineral disorders is a cause of significant morbidity and mortality in patients with chronic renal failure. We carried on this study in the only one Peritoneal Dialysis Unit (DP) with the purpose of determining the CKD-MBD's prevalence in chronic peritoneal dialysis patients (CPD) and to analyse the clinical, biological, therapeutic and evolutionary mineral-bone disorders in these patients. This is a descriptive monocentric retrospective study from 01 January 2012 to 31 December 2016. Were included in our study all peritoneal dialysis patients' records for a minimum of 3 months' duration and having performed a phospho-calcium balance containing at least: intact parathyroid hormone (PTHi), calcemia and the phosphatemia. Thirty-two peritoneal dialysis patients' records were collected. Thirteen patients, 40.62%, had mineralo-bone disorders. The first causative nephropathy was nephroangiosclerosis (NAS) found in 43.8% of cases and 18.8% of patients had indeterminate nephropathy. The average dialysis' seniority was 24.59 ± 19.33 months. In the study, twelve patients were in continuous ambulatory peritoneal dialysis (CAPD) (96.9%) and only one in automated peritoneal dialysis (APD) (3.1%). Nine patients, 90.6% of them, benefited from 4 exchanges per day. Six patients (46.2%) had secondary hyperparathyroidism. Seven patients (53.8%) had osteomalacia. None of them had adynamic osteopathy (AO). Only one patient (6.7%) had valvular calcifications (aortic sigmoid valves). The MBD's profile changed significantly over time due to the use of new biomarkers and new therapies.

Keywords: Hyperparathyroidism; Peritoneal dialysis patients; Osteomalacia; Hemodialysis; Mineralo-Bone disorders; PTX

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Abbreviations: DP: Dialysis Unit, CDP: Chronic Peritoneal Dialysis, NAS: Nephroangiosclerosis, CAPD: Continuous Ambulatory Peritoneal Dialysis, AO: Adynamic Osteopathy, CKD: Chronic Kidney Disease, KDIGO: Kidney Disease Improving Global Outcomes, MBD: Mineral-Osseous Disorders Of Chronic Renal Disease, GNC: Chronic Glomerulonephritis; PKR: Polycystic Kidney Disease; HSF: Segmental and Focal Hyalinosis, CAPD: Continuous Ambulatory Peritoneal Dialysis.

Introduction

Metabolic disorders occur early in chronic kidney disease (CKD) and continue to worsen as it progresses. They are responsible for various types of bone and vascular lesions, leading to a significant patient's quality of life deterioration associated with an increase of cardiovascular morbidity and mortality [1]. All these disorders were rallied in 2006 by the consensus conference Kidney Disease Improving Global Outcomes (KDIGO) under the term of "mineral-osseous disorders of chronic renal disease" MBD [2]. These disorders are characterized by the phosphates' homeostasis and calcium modification and its regulatory elements, mainly PTH and 1,25 dihydroxy vitamin D, important changes in bone structure and / or bone remodelling and the occurrence of vascular calcifications. These disturbances are a long-term chronic kidney disease's complication and are almost constant in chronic dialysis patients. Many studies shown that the fractures' risk and cardiovascular complications are recurrent in this population [3,4]. At this stage the best treatment is renal transplantation. But since this kidney transplant is not available in our countries, we resort to dialysis.

In Senegal hemodialysis is the most frequently used method of substitution, 93.7% against 6.3% for peritoneal dialysis [5]. This will explain the several studies found in hemodialysis on these mineralo-bone complications while very few are made in peritoneal dialysis. The objectives of our work were to determine the prevalence of phospho-calcium metabolic disturbances in peritoneal dialysis patients and to analyze the clinical, biological, therapeutic and evolutionary aspects of mineral-bone disorders in our patients.

Patients and Methods

This is a descriptive monocentric retrospective study from January 1st, 2012 to December 31st, 2016. The study was carried on in the Peritoneal Dialysis Unit (PD) of the Nephrology Department of the Aristide Le Dantec Hospital (HALD) in Dakar, the only peritoneal dialysis unit in the whole country. Were included in our study all peritoneal dialysis patients' records for a minimum of 3 months' duration and having performed a phospho-calcium balance containing at least: intact parathyroid hormone (PTHi), calcemia and phosphatemia. The data were collected from the patient's medical records, using an exploitation sheet that aims to specify the sociodemographic, clinical, and paraclinical (biological and radiological) aspects of each patient included in the study. The data was captured by the software Le Sphinx 5.1.0.2 version and the analysis was done using SPSS software (Statistical Package for Social Science) 18 version.

We calculated simple frequencies and relative one (percentages) for qualitative variables. We calculated averages and standard deviations, and determined the minimum and maximum values.

Results

Thirty-two records of patients under peritoneal dialysis were collected. Thirteen of them, 40.62%, had mineralo-bone disorders. The average age of patients was 48.92 ± 15.5 years. There were 8 women for every 5 men, a sex ratio of 0.63. The first causative nephropathy was nephroangiosclerosis (NAS) found in 43.8% of cases, 18.8% of patients had indeterminate nephropathy (Figure 1).

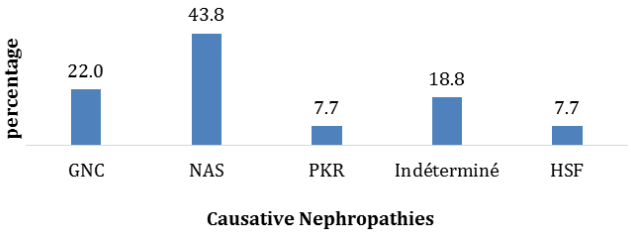

Figure 1: Distribution of PD patients with MBD according to causal nephropathy.

GNC: Chronic glomerulonephritis; NAS: Nephroangiosclerosis; PKR: Polycystic kidney disease; HSF: Segmental and focal hyalinosis; Indeterminée: undetermined

Average dialysis seniority was 24.59 ± 19.33 months, with extremes of 3 to 72 months. Four or 30.8% of patients had less than 12 months of dialysis, and 53.9% had been on dialysis for more than 2 years. Twelve patients in the study were in CAPD (96.9%) and only one in APD (3.1%).

Renal osteodystrophy

Six patients (46.2% of cases) had secondary hyperparathyroidism. Seven (53.8%) had osteomalacia. Nobody had adynamic osteopathy (AO).

Secondary hyperparathyroidism: Six patients had secondary hyperparathyroidism, including 5 women and 1 man. Among them, 4 (36.4%) had articular pain, 3 patients (27.3%) had bone pain and only 1 patient (9.1%) had a pathological fracture (Figure 2).

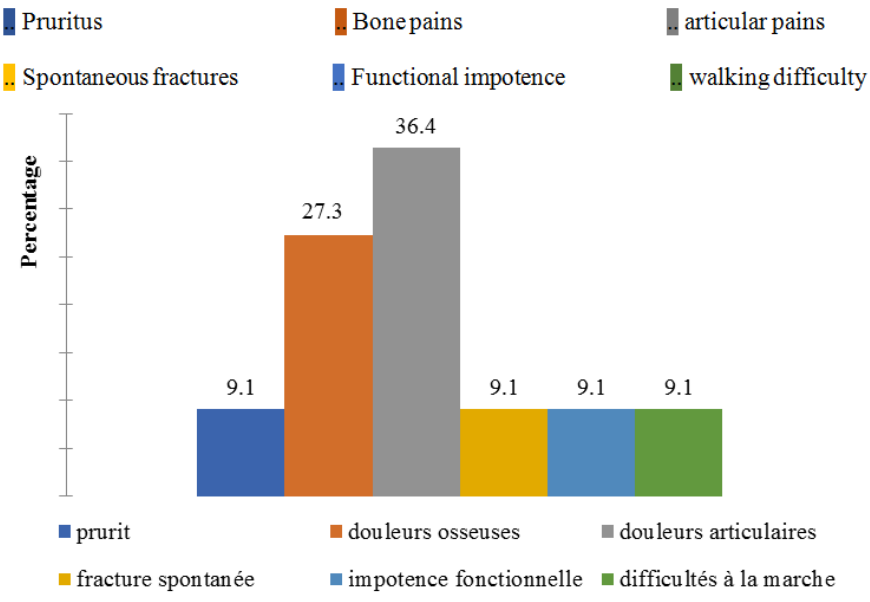

Figure 2: Distribution of DP patients with HPT II according to clinical symptomatology.

Four patients (66.6%) had a normal osteoarticular examination, in the two remaining patients the examination was abnormal (33.4%), including 2 limitations of movement and localized deformity of the foot. The average calcemia was 84.97 ± 9.54 mg / l with extremes of 61.48 mg / l and 105 mg / l. Five patients (83.3%) had hypocalcaemia, 1 or (16.7%) had normal calcemia and none of them was found with hypercalcemia. The average phosphate concentration was 56.3 ± 7.3 mg / l, with the upper limit being 112 mg. The average PTH was 659.85 ± 381.81 ng / ml, with a maximum of 1578 ng / ml or 24 times of the normal (24N). Three patients had PTH levels more than 18 times to the normal (18N). All six patients had a dosage of 25-OH vitamin D, including 1 16.7% had a 25-OH Vit D deficiency and the remaining 5 had insufficient Vit D. The average value of the 25- OH vit D was 19.24 ± 4.74 ng / ml. Bone imagery (Standard X-ray) revealed abnormalities in 4 patients: a knee x-ray (Rx) with amputation's images at the patella's articular surface, a knee Rx with osteophytes and pinch of the Interarticular line at the lateral right side, a dorsolumbar Rx with lumbar scoliosis, a patient had a fracture at the end of the right femur and a normal sacral lumbar Rx. None of them had bone densitometry. Two patients, 33.3%, benefited from cervical ultrasound, in one patient the parathyroid glands were not visualized and in the other case the parathyroid cells were free. None of them had parathyroid scintigraphy. Five patients (83.3%) with hyperparathyroidism received calcium carbonate treatment (CaCO3). Two of them (33.3%) had been treated with non-calcium phosphorus chelators (Lanthanum or Sevelamer). Three patients (50%) had received vitamin D (native and / or un-alfa) (Table I).

Treatment		Number of patients	Percentage (%)
CaCO3 (calcium carbonate)		5	83,3
Non-calcium phosphate chelators		2	33,3
Vitamin D	Alphacalcidol	1	16,6
	Native	2	33,3

Table I: Distribution of patients according to treatment received.

Under medical treatment: one patient (16.6%) had normalized his PTH, 2 patients (33.3%) had persistence of secondary hyperparathyroidism and 3 other patients (50.1%) had no biological control. No patient had been treated surgically.

Osteomalacia

Seven patients had osteomalacia, including four men and three women. All patients were symptomatic: the articular pain represented for 57.1% of symptoms, and was present in 4 patients, one with low back pain, the other with right shoulder pain and the other 2 with gonalgia. Bone pains was noted in 2 patients (28.6%). Pruritus was present in only one patient (14.3%). The average PTH was 412 ng / ml, with extremes of 247 and 620 ng/ml. the average calcemia was 84 ± 3.01 mg / l. The average phosphatemia was 44.22 ± 5.99 mg/l. The average Vit D was 21ng / ml. None of our patients had a bone biopsy.

Adynamic Osteopathy

The study did not find a case of adynamic osteopathy.

Vascular Calcifications

At the cardiac ultrasound, the 12 patients (93.3%) had a normal echocardiography. Only one patient (6.7%) had valvular calcifications (aortic sigmoid valves). One patient (3.1%) had an abdominopelvic computed tomography scan that failed to report vascular calcification. One patient had Doppler supra-aortic trunks, however, there were no objectified calcifications.

Discussion

The majority of patients in our series were in continuous ambulatory peritoneal dialysis (CAPD) (96.9%). In the literature, the phosphate associated with CAPD is better treated than automated peritoneal dialysis (APD). In DPA, we have more hyperphosphatemia. This is favoured by a small number of cycles and a shorter duration of treatment [6]. In our series 40.62% of PD patients had mineralo-bone disorders. A study in Singapore reported a mineralo-bone disorders' prevalence of 54.7% at 4-6 months when the parameters were evaluated using KDIGO targets [7]. This prevalence looks like that published in the literature [6]. Lower prevalences were reported in studies carried on in the Netherlands and Canada (5.9% and 9.4%, respectively) [8.3].

Secondary hyperparathyroidism was present in 6 patients or 46.2%. Chuang et al. found in Singapore a rate similar to 45.3%. Our result was lower than that found in Saudi Arabia by Alwakeel and al (53.3%) [6]. However, peritoneal dialysis had less risk than hemodialysis occurred from secondary hyperparathyroidism [8]. In our study, we found very high PTH's rate up to 1578 pg / ml or 24 times of the normal (24N) indicating a lack of correction and braking.

In secondary hyperparathyroidism, the average of **PTH** was 659.85 ± 381.81 pg. / ml. Two patients (36.6%) had PTH less than 2 times the upper limit of the normal, 1 patient (19.4%) had PTH between 2 and 9 times of the normal, and 3 patients (44%) had PTH superior to 9 times the upper limit of the normal. The dialysis reference values are 2 to 9 times the upper limit of the kit used (approximately 130-585 pg / ml for a 2nd generation assay). A new assay measuring so-called "bio-intact" PTH that measures only PTH 1-84 is now available [8]. The optimal concentrations of intact organic PTH associated with normal bone remodelling in diabetics are still unknown, so that this assay is still underused in Europe and not recommended by the last KDIGO consensus conference of 2009 [9]. Drug therapy for secondary hyperparathyroidism involves calcium, phosphorus chelators, calcitriol derivatives, and calcimimetics. In our series, 83.3% of patients had calcium carbonate treatment, 33.3% of them had treatment with non-calcium phosphorus chelators, 50% had received vitamin D (native and / or un-alfa) and none had calcimimetic treatment. In the Chuang's study, 84.9% of the patients were under calcium chelator phosphorous, 64.4% under calcium acetate and 35.6% under calcium carbonate. Forty-one point nine percept of the patients were also under an active vitamin D derivative: 97.2% under calcitriol and 2.8% under alfaclcidol [7]. In the Alwakeel and al's study in Saudi Arabia, twenty-one patients (77.8%) used calcitriol and 24 (85.7%) were under calcium carbonate. Five patients (18.56%) used Cinacalcet [6]. The Cinacalcet can lower serum concentrations of PTH without increasing serum calcium or phosphatemia, a major consequence of calcium and calcitriol treatments [10]. The lack of calcimimetics'use in our patients, may be explained by their cost and lack of medical insurance. In our series no patient benefited from parathyroidectomy (PTX). The prescription of calcimimetics or PTX for values above the threshold is recommended by KDIGO (PTH greater than 9 times normal). The comparison of calcimimetics versus PTX is clearly in favour of the surgery [11], which for some patients constitutes a zone of non-return of the HPTS towards the autonomised forms. Moreover, in comparison with non-operated patients, the survival of patients with PTX is better in the United States [12] as in Japan [13], and allows biological targets to be reached more frequently [14].

In our study, 7 patients or 53.8% had osteomalacia. this percentage is relatively higher than that of Eastwood [15] and Mora Palma [16] that found osteomalacia in respectively 50% and 34% of patients. Some reports are particularly contradictory regarding the prevalence of osteomalacia. Dahl and al. [17] reported that osteomalacia is extremely rare in patients before dialysis. Mora Palma and al. found a high prevalence of osteomalacia mainly in tubulointerstitial nephropathies [16].

Adynamic osteopathy has not been found in our patients. However, in the literature, there is a high prevalence of adynamic osteopathy in many PD studies, ranging up to 60% in CAPD's patients versus 36% in hemodialysis [13,18].

In our study, only one patient (6.7%) had valvular calcifications. this prevalence was less important in the results of Bezzi et al. [8] who found vascular calcification in 14% of cases. Indeed, the results of a study by Sigrist and al. showed that PD was associated with less vascular calcification compared to hemodialysis [20].

Conclusion

The profile of MBDs has changed significantly over time due to the use of new biomarkers and new therapies. However, in our developing country context, its complications are still so recurrent, with a new evolution, without doubt even before the dialysis' step often favoured by a late start up of dialysis due to lack of screening and early treatment of the MRC. In charge. Thus, patient awareness of the MBDs' severity and their complications, the regular determination of calcemia, phosphatemia, PTH and Vit D, according to KDIGO recommendations, would greatly reduce the prevalence.

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