Review Article

Get-up and Go: Adynamic Bone Disease in Chronic Kidney Disease Patient

Awad Magbri[1]*, Mariam El-Magbri[1], Pablo Abrego Hernandez[1]

[1]Marshfield Medical Center, Weston, WI, United States.

Abstract

We reported a case of adynamic bone disease (ABD) in an older woman with chronic kidney disease, stage-4 (CKD-4), with an estimate of 29ml/min glomerular filtration rate (eGFR). Similarly, the patient presented with bone pain and osteoporosis as well as intact parathyroid hormone (PTH) was suppressed (<6ng/dl) secondary to the use of vitamin D analogs for secondary hyperparathyroidism (SHPT) of CKD. Furthermore, the hypercalcemia of (11.1 mg/dl), and her dual-energy X-ray absorptiometry (DEXA) scan showed bone mineral density (BMD) of -2.6 SD. Low levels of PTH induces a state of low turnover bone disease. Numerous, factors are involved in this process in patients with ESRD on dialysis. Among these factors are the use of vitamin D analogs, the ill-effects high calcium baths, treatment of osteoporosis with bisphosphonates, etc. All these factors can singly or in combination suppress PTH and render the bone resistant to its action with the end results of a dynamic bone disease. The vitamin D analogs were stopped to allow recovery of the PTH and activation of the osteocytes and osteoblasts. Six months after stopping active vitamin D analogs, her hypercalcemia was resolved, and the PTH increased to 172 ng/dl. Her bone pain has resolved.

Keywords: Adynamic bone disease, Secondary hyperparathyroidism, Chronic kidney disease, Vitamin D analogs, Hypercalcemia, Peritoneal dialysis.

Introduction

Adynamic bone disease is a group of renal osteodystrophy (ROD) trait by decreased osteoblasts and osteoclasts activities, osteoid bone accumulation, and markedly reduced bone turnover [1-3]. It has been reported in a relatively high percentage of patients on dialysis but also has been reported in patients with CKD on conservative treatment. The clinical and histological picture of ABD is generally related to low levels of PTH relative to what is expected in patients with CKD. The low PTH levels induce a state of low turnover bone disease [4, 5]. Numerous factors are theoretically account for skeletal resistance to PTH, which can slow down bone turnover. Among these factors are the downregulation of PTH receptors in osteocytes, increased osteoprotegerin levels, decreased production of circulating levels of bone morphogenetic proteins, peripheral effects of leptin, and the effects of increased N-terminal truncated PTH molecular species. These factors have been implicated in counteracting the positive effects of the whole PTH molecule, PTH 1-84, on bone. However, the prevention and management of CKD in both men and women presented a significant breakthrough and is considered essential in society. The renal function test may decrease the burden of CKD, which accounted for 85%, 15% of agreed and disagreed.

Case History

A 74-year-old Caucasian female, nursing home resident. She has a history of chronic kidney disease stage-4 with an estimated GFR of 29ml/min, type 2 diabetes mellitus, hypertension, hyperuricemia, and atrial fibrillation on warfarin 5mg per day. Physical examinations were unremarkable except for atrial fibrillation and generalized muscle weakness (Table 1).

Table 1. Show some of the patient's biochemical data

Data	Value/unit
WBC	4.4ul
RBC	4.52ul
Hgb	11.9 g/dl
Hematocrit	37.7%
MCV	83.4fL
MCH	26.4pg
MCHC	31.6 g/dl
Platelets	207,000
PTH-Intact	<6 pg/mL
Albumin	3.6 g/dl

Address for correspondence: Awad Magbri, Marshfield Medical Center, Weston, WI, United States. elmagbri@hotmail.com

This is an open-access article distributed under the terms of the Creative Commons Attribution-Non Commercial-Share Alike 4.0 License, which allows others to remix, tweak, and build upon the work non commercially, as long as the author is credited and the new creations are licensed under the identical terms.

How to cite this article: Magbri A, El-Magbri M, Hernandez PA. Get-up and Go: Adynamic Bone Disease in Chronic Kidney Disease Patient. Arch Pharm Pract. 2023;14(x):11-5. https://doi.org/10.51847/suXosREK5t

Calcium	11.1 mg/dl
CO2	26 mmol/L
Cl	103 mmol/L
Creatinine	1.8 mg/dl
Glucose	107 mg/dl
Phosphorus	3.8 mg/dl
K	3.9 mmol/L
Na	138 mmol/L
Urea N	43 mg/dl
eGFR	29.3 mL/min
Total-Vit D	16ng/mL

WBC– white blood cell count; RBC– red blood cell count; PTH– parathyroid hormone; CO2– total carbon dioxide; Cl– chloride; K: potassium; Na – Sodium; BUN – blood urea nitrogen; eGFR – estimated glomerular filtration rate

Results and Discussion

Chronic kidney disease (CKD) is often related to disorders of mineral and bone metabolism (CKD-BMD). These disorders are collectively known as renal osteodystrophy (ROD). CKD-BMD is also associated with abnormalities of cardiovascular structure and function.

Bone is now considered an endocrine organ that plays an active role in the metabolic abnormalities in cardiovascular complications commonly encountered in CKD patients [6]. KDIGO recommended the term CKD-BMD as a broader expression of systemic disorders resulting from CKD [1, 7]. CKD-BMD may be manifested as one or more of the following:

- Abnormalities of calcium, phosphorus, parathyroid hormone (PTH), or vitamin D metabolism.
- Abnormalities of bone turnover, mineralization, linear volume growth, or strength.
- Vascular of another soft-tissue calcification.

The diagnosis of CKD-BMD rests on bone biopsy, which might show osteitis fibrosa cystica, adynamic bone disease, osteomalacia, or mixed lesion. However, a bone biopsy is rarely used in the diagnosis because of the invasive nature of the procedure.

ABD is an effective form of ROD in both peritoneal (PD) and hemodialysis (HD) patients, specifically diabetic patients [8-13]. The disease is characterized by low bone turnover and thin osteoid seams, decreased cellularity, and minimal bone marrow fibrosis. These changes occur in the absence of aluminum overload [14].

The prevalence of ABD has increased recently relative to other forms of ROD, with variation based on geographic region [9, 10, 15, 16]. In a study conducted by the KDIGO work group between 1983 and 2006, the prevalence of ABD was 18% in CKD stages 3-5, 19% in hemodialysis patients, and 50% in PD patients [7]. It is evident from this report that ABD is replacing osteomalacia and SHPT [2, 8, 11, 13, 15, 17-20]. In other studies, the prevalence of ABD in hemodialysis patients was reported to be as high as (58 to 59%), [21, 22].

The risk factors for ABD incorporate the calcium-containing phosphate binders use [13, 15], high dialysate calcium [23], and the use of active vitamin D analogs [24, 25]. Increasing age and diabetes are also contributing factors [16].

Targeting higher PTH levels and using non-calcium-containing phosphate binders and calcimimetic agents as recommended by the KGIGO group to curtail the occurrence of ABD. This may result in the resurgence of the formerly predominant bone lesions of osteitis fibrosa [26, 27].

ABD is characterized by low or absent bone formation associated with thin osteoid seams, decreased cellularity, and minimal myelofibrosis. This means that bone turnover is markedly reduced with a lack of osteoblasts and osteoclasts activities. The principal factor underlying ABD is either over-suppression of PTH release, which may be induced by high doses of vitamin D analogs, calcium-based phosphate binders, and bisphosphonate agents [14, 16, 25, 28, 29], or resistance to PTH action on the bone [30, 31].

Calcimimetics activate the calcium-sensing receptor (CaSR) on the parathyroid glands and indirectly suppresses PTH release, which may lead to reduced bone turnover. However, the use of Calcimimetics for 6-12 months in patients with SHPT decreases the bone formation rate and causes high-turnover bone disease toward normal [32, 33]. Calcimimetics may also directly affect bone since bone cells express the CaSR and may have direct anabolic action on the bone [34].

The PTH levels in patients with ABD are low but higher than the upper limit of values in a healthy population. This indicates that resistance to the bone stimulatory effects of PTH may play a more prominent role since average concentrations of PTH have been shown to be inadequate for maintaining bone turnover [30, 31].

A growing body of evidence suggests that ABD ensues in a substantial proportion of patients at the initial stages of CKD [18]. Uremic toxins such as indoxyl sulfate are blamed for inducing low bone turnover in the early stages of CKD. These uremic toxins lead to the repression of osteocyte signaling and increased Wnt antagonists to produce ABD [35-38].

ABD is primarily asymptomatic; however, some patients develop bone pain, mostly in the axial skeleton [39, 40]. Increased fracture risk due to impaired ability to repair micro-damage and hypercalcemia have also been reported [16, 28]. The incidence of hip fracture increased to 13.9/1000 patient-years [41]. Hypercalcemia may develop in ABD due to reduced bone uptake of calcium, especially if calcium carbonate is used for the treatment of SHPT [42].

Vascular calcification may be observed in imaging studies [16, 28, 43] associated with increased mortality. Aortic calcification and stiffness are well-observed features in ABD [44].

The PTH levels of <195pg/dl, a value likely to be associated with ABD, predicted fracture risk [45, 46]. The diagnosis of ABD by bone biopsy remains the gold standard. But because of the invasive nature of bone biopsy, the procedure is rarely used to diagnose CKD-MBD. However, a high degree of suspicion of the ABD diagnosis can be inferred from low PTH levels, low bone-specific alkaline phosphatase (BSAP) levels, low biomarkers of bone turnover, e.g., serum C-telopeptide crosslink (CTX), unexplained hypercalcemia, or bone imaging studies (e.g., DEXA) showing osteoporosis [47].

Persistently low levels of PTH (<100pg/ml), especially if hypercalcemia is present, or in patients with CKD who are not on dialysis with a PTH level of <65pg/ml in the setting of treatment with active vitamin D analogs are indicators to the presence of ABD.

In both dialysis and non-dialysis patients, PTH levels (100 to 500pg/ml) are more difficult to interpret, and bone biopsy is recommended to prove the presence of ABD [47]. Patients with PTH levels >500pg/ml are unlikely to have ABD [48].

In patients who have intermediate levels of PTH, symptoms of bone pain, unexplained hypercalcemia, and hyperphosphatemia, these constellations of symptoms are consistent with the diagnosis of ABD and should be treated as such [8]. In these cases, measurement of BSAP levels (>20ng/ml) virtually excluded the diagnosis of ABD, particularly if the PTH is >200pg/ml [49]. A bone biopsy is desirable if the diagnosis is still in doubt, especially for patients with low or borderline BSAP and PTH levels [27, 48-51].

The initial treatment of ABD is to allow the PTH level to rise [8]. This can be achieved by using non-calcium-based phosphate binders, decreasing or stopping the active vitamin D analogs, lowering the dialysate calcium concentration, or combining the above [13, 52, 53]. Most patients do not have biopsy-proven ABD but rather have the diagnosis suggested by laboratory findings. The principles of therapy for ABD consist of the following.

- Using non-calcium-containing phosphate binders may increase the bone formation rate [13].
- Stop the active vitamin D therapy from allowing the serum PTH concentration to increase [24, 25]. In CKD patients (creatinine clearance of 20-59 ml/min), the use of calcitriol versus placebo on bone histology showed that calcitriol decreased bone turnover, and ABD developed in 80% of calcitriol-treated patients compared to placebo [54].
- In the presence of low PTH levels, vitamin D analogs should be stopped [55].
- In dialysis patients, using low calcium dialysate (2mEq/L) if PTH remained low despite switching to non-calcium phosphate binders and stopping the vitamin D analogs administration should be considered [23].
- The use of bisphosphonate in patients with ABD should be discouraged to avoid further suppression of bone turnover. This is because bisphosphonate accumulates in bone and inhibits osteoclasts, thereby exacerbating the ABD [56, 57].
- The KDIGO guidelines state that for patients with CKD 4-5 who have biochemical abnormalities of CKD-BMD and low bone mineral density (BMD) with or without fragility fractures, a bone biopsy should be done before treatment with antiresorptive agents is initiated [27].

Monitoring of PTH levels, BSAP levels, serum calcium, phosphate, and 25-vitamin D during the treatment of ABD are recommended. Reversal of ABD is suggested by a progressive increase of PTH and BSAP levels and resolution of hypercalcemia. Reversal of ABD may take up to one year in some cases [13, 23].

The use of anabolic agents, such as teriparatide (PTH-1-34) and abaloparatide (PTH-related peptide (PTHrP) analog, may benefit patients with ABD. FDA approves both these agents for the treatment of postmenopausal osteoporosis but not for ABD. Teriparatide stimulates the osteoblasts and osteoclasts, which may result in increased bone turnover in patients with ABD [58-62]. Use of subcutaneous injection of teriparatide in ABD patients resulted in the resolution of bone pain and prevented further fractures [58, 59, 62]. However, more extensive studies are needed to demonstrate the efficacy and safety of this agent in patients with ABD.

Conclusion

ABD should be considered a skeletal disorder caused by SHPT overtreatment, rather than as a disease entity. Nevertheless, the occurrence indicates that the accumulation of uremic toxins and overuse of the vitamin analogs in SHPT impairs the ability to maintain healthy normal bone turnover. These toxins cause PTH levels to decrease beyond what is recommended by KDIGO for the level of CKD. These levels of PTH would be considered high in patients without kidney disease but not in CKD patients. Bone pain, hypercalcemia, low PTH levels, and low BSAP point to the diagnosis of ABD, especially if the patient is on vitamin D analogs.

ACKNOWLEDGMENTS: The authors would like to thank, Ms Melissa Machtan, and Mrs Sharri Rupe for their secretarial help.
CONFLICT OF INTEREST: None
FINANCIAL SUPPORT: None
ETHICS STATEMENT: The preparation of this manuscript is in accordance of the institution's policy and laws. In no time the report infringe on the patient's identity and privacy.

References

1. GUIDELINE CI. Introduction and definition of CKD-MBD and the development of the guideline statements. Kidney Int. 2009;76(113):S3-8.
2. Spasovski GB, Bervoets AR, Behets GJ, Ivanovski N, Sikole A, Dams G, et al. Spectrum of renal bone disease in end-stage renal failure

patients not yet on dialysis. Nephrol Dial Transplant. 2003;18(6):1159-66.
3. Moe SM, Drüeke TB. A bridge to improving healthcare outcomes and quality of life. Am J Kidney Dis. 2004;43(3):552-7.
4. Cunningham J, Sprague SM, Cannata-Andia J, Coco M, Cohen-Solal M, Fitzpatrick L, et al. Osteoporosis in chronic kidney disease. Am J Kidney Dis. 2004;43(3):566-71.
5. Rocha LA, Higa A, Barreto FC, dos Reis LM, Jorgetti V, Draibe SA, et al. Variant of adynamic bone disease in hemodialysis patients: fact or fiction? Am J Kidney Dis. 2006;48(3):430-6.
6. Vervloet MG, Massy ZA, Brandenburg VM, Mazzaferro S, Cozzolino M, Ureña-Torres P, et al. Bone: a new endocrine organ at the heart of chronic kidney disease and mineral and bone disorders. Lancet Diabetes Endocrinol. 2014;2(5):427-36.
7. Moe S, Drüeke T, Cunningham J, Goodman W, Martin K, Olgaard K, et al. Definition, evaluation, and classification of renal osteodystrophy: a position statement from Kidney Disease: Improving Global Outcomes (KDIGO). Kidney Int. 2006;69(11):1945-53.
8. National Kidney Foundation. K/DOQI clinical practice guidelines for bone metabolism and disease in chronic kidney disease. Am J Kidney Dis. 2003;42(4 Suppl 3):S1-201.
9. Martin KJ, Olgaard K, Coburn JW, Coen GM, Fukagawa M, Langman C, et al. Diagnosis, assessment, and treatment of bone turnover abnormalities in renal osteodystrophy. Am J Kidney Dis. 2004;43(3):558-65.
10. Changsirikulchai S, Domrongkitchaiporn S, Sirikulchayanonta V, Ongphiphadhanakul B, Kunkitti N, Stitchantrakul W, et al. Renal osteodystrophy in Ramathibodi Hospital: histomorphometry and clinical correlation. J Med Assoc Thai. 2000;83(10):1223-32.
11. Brandenburg VM, Floege J. Adynamic bone disease-bone and beyond. NDT Plus. 2008;1(3):135-47.
12. Morrow B, Qunibi W. Specific bone and mineral disorders in patients with chronic kidney disease. Clin Rev Bone Miner Metab. 2012;10(3):184-208.
13. Ferreira A, Frazão JM, Monier-Faugere MC, Gil C, Galvao J, Oliveira C, et al. Effects of sevelamer hydrochloride and calcium carbonate on renal osteodystrophy in hemodialysis patients. J Am Soc Nephrol. 2008;19(2):405-12.
14. Hercz G, Pei Y, Greenwood C, Manuel A, Saiphoo C, Goodman WG, et al. Aplastic osteodystrophy without aluminum: the role of "suppressed" parathyroid function. Kidney Int. 1993;44(4):860-6.
15. D'Haese PC, Spasovski GB, Sikole A, Hutchison A, Freemont TJ, Sulkova S, et al. A multicenter study on the effects of lanthanum carbonate (Fosrenol) and calcium carbonate on renal bone disease in dialysis patients. Kidney Int Suppl. 2003;(85):S73-8.
16. Sherrard DJ, Hercz G, Pei Y, Maloney NA, Greenwood C, Manuel A, et al. The spectrum of bone disease in end-stage renal failure--an evolving disorder. Kidney Int. 1993;43(2):436-42.
17. de Oliveira RA, Barreto FC, Mendes M, dos Reis LM, Castro JH, Britto ZM, et al. Peritoneal dialysis per se is a risk factor for sclerostin-associated adynamic bone disease. Kidney Int. 2015;87(5):1039-45.
18. Barreto FC, Barreto DV, Canziani ME, Tomiyama C, Higa A, Mozar A, et al. Association between indoxyl sulfate and bone histomorphometry in pre-dialysis chronic kidney disease patients. J Bras Nefrol. 2014;36(3):289-96.
19. Coen G, Mazzaferro S, Ballanti P, Sardella D, Chicca S, Manni M, et al. Renal bone disease in 76 patients with varying degrees of predialysis chronic renal failure: a cross-sectional study. Nephrol Dial Transplant. 1996;11(5):813-9.
20. Coen G, Ballanti P, Bonucci E, Calabria S, Costantini S, Ferrannini M, et al. Renal osteodystrophy in predialysis and hemodialysis patients: comparison of histologic patterns and diagnostic predictivity of intact PTH. Nephron. 2002;91(1):103-11.
21. Sprague SM, Bellorin-Font E, Jorgetti V, Carvalho AB, Malluche HH, Ferreira A, et al. Diagnostic Accuracy of Bone Turnover Markers and Bone Histology in Patients With CKD Treated by Dialysis. Am J Kidney Dis. 2016;67(4):559-66.
22. Malluche HH, Mawad HW, Monier-Faugere MC. Renal osteodystrophy in the first decade of the new millennium: analysis of 630 bone biopsies in black and white patients. J Bone Miner Res. 2011;26(6):1368-76.
23. Haris A, Sherrard DJ, Hercz G. Reversal of adynamic bone disease by lowering of dialysate calcium. Kidney Int. 2006;70(5):931-7.
24. Kuizon BD, Goodman WG, Jüppner H, Boechat I, Nelson P, Gales B, et al. Diminished linear growth during intermittent calcitriol therapy in children undergoing CCPD. Kidney Int. 1998;53(1):205-11.
25. Goodman WG, Ramirez JA, Belin TR, Chon Y, Gales B, Segre GV, et al. Development of adynamic bone in patients with secondary hyperparathyroidism after intermittent calcitriol therapy. Kidney Int. 1994;46(4):1160-6.
26. National Kidney Foundation. K/DOQI clinical practice guidelines for chronic kidney disease: evaluation, classification, and stratification. Am J Kidney Dis. 2002;39(2 Suppl 1):S1-266.
27. Kidney Disease: Improving Global Outcomes (KDIGO) CKD-MBD Work Group. KDIGO clinical practice guideline for the diagnosis, evaluation, prevention, and treatment of Chronic Kidney Disease-Mineral and Bone Disorder (CKD-MBD). Kidney Int Suppl. 2009;(113):S1-130.
28. Malluche HH, Monier-Faugere MC. Risk of adynamic bone disease in dialyzed patients. Kidney Int Suppl. 1992;38:S62-7.
29. Bover J, Ureña P, Brandenburg V, Goldsmith D, Ruiz C, DaSilva I, et al. Adynamic bone disease: from bone to vessels in chronic kidney disease. Semin Nephrol. 2014;34(6):626-40.
30. Quarles LD, Lobaugh B, Murphy G. Intact parathyroid hormone overestimates the presence and severity of parathyroid-mediated osseous abnormalities in uremia. J Clin Endocrinol Metab. 1992;75(1):145-50.
31. Hernandez D, Concepcion MT, Lorenzo V, Martinez ME, Rodriguez A, De Bonis E, et al. Adynamic bone disease with negative aluminium staining in predialysis patients: prevalence and evolution after maintenance dialysis. Nephrol Dial Transplant. 1994;9(5):517-23.
32. Malluche HH, Monier-Faugere MC, Wang G, Frazã O JM, Charytan C, Coburn JW, et al. An assessment of cinacalcet HCl effects on bone histology in dialysis patients with secondary hyperparathyroidism. Clin Nephrol. 2008;69(4):269-78.
33. Behets GJ, Spasovski G, Sterling LR, Goodman WG, Spiegel DM, De Broe ME, et al. Bone histomorphometry before and after long-term treatment with cinacalcet in dialysis patients with secondary hyperparathyroidism. Kidney Int. 2015;87(4):846-56.
34. Díaz-Tocados JM, Rodríguez-Ortiz ME, Almadén Y, Pineda C, Martínez-Moreno JM, Herencia C, et al. Calcimimetics maintain bone turnover in uremic rats despite the concomitant decrease in parathyroid hormone concentration. Kidney Int. 2019;95(5):1064-78.
35. Fang Y, Ginsberg C, Seifert M, Agapova O, Sugatani T, Register TC, et al. CKD-induced wingless/integration1 inhibitors and phosphorus cause the CKD-mineral and bone disorder. J Am Soc Nephrol. 2014;25(8):1760-73.
36. Drüeke TB, Massy ZA. Changing bone patterns with progression of chronic kidney disease. Kidney Int. 2016;89(2):289-302.
37. Evenepoel P, D'Haese P, Brandenburg V. Sclerostin and DKK1: new players in renal bone and vascular disease. Kidney Int. 2015;88(2):235-40.
38. Graciolli FG, Neves KR, Barreto F, Barreto DV, Dos Reis LM, Canziani ME, et al. The complexity of chronic kidney disease-mineral and bone disorder across stages of chronic kidney disease. Kidney Int. 2017;91(6):1436-46.
39. Piraino B, Chen T, Cooperstein L, Segre G, Puschett J. Fractures and vertebral bone mineral density in patients with renal osteodystrophy. Clin Nephrol. 1988;30(2):57-62.
40. Drüeke TB. The pathogenesis of parathyroid gland hyperplasia in chronic renal failure. Kidney Int. 1995;48(1):259-72.
41. Coco M, Rush H. Increased incidence of hip fractures in dialysis patients with low serum parathyroid hormone. Am J Kidney Dis. 2000;36(6):1115-21.
42. Kurz P, Monier-Faugere MC, Bognar B, Werner E, Roth P, Vlachojannis J, et al. Evidence for abnormal calcium homeostasis in patients with adynamic bone disease. Kidney Int. 1994;46(3):855-61.
43. London GM, Marty C, Marchais SJ, Guerin AP, Metivier F, de Vernejoul MC. Arterial calcifications and bone histomorphometry in end-stage renal disease. J Am Soc Nephrol. 2004;15(7):1943-51.
44. London GM, Marchais SJ, Guérin AP, Boutouyrie P, Métivier F, de Vernejoul MC. Association of bone activity, calcium load, aortic

stiffness, and calcifications in ESRD. J Am Soc Nephrol. 2008;19(9):1827-35.
45. Danese MD, Kim J, Doan QV, Dylan M, Griffiths R, Chertow GM. PTH and the risks for hip, vertebral, and pelvic fractures among patients on dialysis. Am J Kidney Dis. 2006;47(1):149-56.
46. Atsumi K, Kushida K, Yamazaki K, Shimizu S, Ohmura A, Inoue T. Risk factors for vertebral fractures in renal osteodystrophy. Am J Kidney Dis. 1999;33(2):287-93.
47. Ketteler M, Block GA, Evenepoel P, Fukagawa M, Herzog CA, McCann L, et al. Executive summary of the 2017 KDIGO Chronic Kidney Disease-Mineral and Bone Disorder (CKD-MBD) Guideline Update: what's changed and why it matters. Kidney Int. 2017;92(1):26-36.
48. Barreto FC, Barreto DV, Moysés RM, Neves KR, Canziani ME, Draibe SA, et al. K/DOQI-recommended intact PTH levels do not prevent low-turnover bone disease in hemodialysis patients. Kidney Int. 2008;73(6):771-7.
49. Ureña P, Hruby M, Ferreira A, Ang KS, de Vernejoul MC. Plasma total versus bone alkaline phosphatase as markers of bone turnover in hemodialysis patients. J Am Soc Nephrol. 1996;7(3):506-12.
50. Couttenye MM, D'Haese PC, Van Hoof VO, Lemoniatou E, Goodman W, Verpooten GA, et al. Low serum levels of alkaline phosphatase of bone origin: a good marker of adynamic bone disease in haemodialysis patients. Nephrol Dial Transplant. 1996;11(6):1065-72.
51. Ureña P, De Vernejoul MC. Circulating biochemical markers of bone remodeling in uremic patients. Kidney Int. 1999;55(6):2141-56.
52. Mathew S, Lund RJ, Strebeck F, Tustison KS, Geurs T, Hruska KA. Reversal of the adynamic bone disorder and decreased vascular calcification in chronic kidney disease by sevelamer carbonate therapy. J Am Soc Nephrol. 2007;18(1):122-30.
53. Ok E, Asci G, Duman S, Ozkahya M, Ceylan M, Toz H, et al. Reduction of calcium exposure slows down progression of vascular calcification and improves adynamic bone disease. Clin J Am Soc Nephrol. 2008;3:RB01-4.
54. Baker LR, Abrams L, Roe CJ, Faugere MC, Fanti P, Subayti Y, et al. 1,25(OH)2D3 administration in moderate renal failure: a prospective double-blind trial. Kidney Int. 1989;35(2):661-9.
55. Teng M, Wolf M, Ofsthun MN, Lazarus JM, Hernán MA, Camargo CA Jr, et al. Activated injectable vitamin D and hemodialysis survival: a historical cohort study. J Am Soc Nephrol. 2005;16(4):1115-25.
56. Amerling R, Harbord NB, Pullman J, Feinfeld DA. Bisphosphonate use in chronic kidney disease: association with adynamic bone disease in a bone histology series. Blood Purif. 2010;29(3):293-9.
57. Ott SM. Bisphosphonate safety and efficacy in chronic kidney disease. Kidney Int. 2012;82(8):833-5.
58. Lehmann G, Ott U, Maiwald J, Wolf G. Bone histomorphometry after treatment with teriparatide (PTH 1-34) in a patient with adynamic bone disease subsequent to parathyroidectomy. NDT Plus. 2009;2(1):49-51.
59. Palcu P, Dion N, Ste-Marie LG, Goltzman D, Radziunas I, Miller PD, et al. Teriparatide and bone turnover and formation in a hemodialysis patient with low-turnover bone disease: a case report. Am J Kidney Dis. 2015;65(6):933-6.
60. Cejka D, Kodras K, Bader T, Haas M. Treatment of Hemodialysis-Associated Adynamic Bone Disease with Teriparatide (PTH1-34): A Pilot Study. Kidney Blood Press Res. 2010;33(3):221-6.
61. Mitsopoulos E, Ginikopoulou E, Economidou D, Zanos S, Pateinakis P, Minasidis E, et al. Impact of long-term cinacalcet, ibandronate or teriparatide therapy on bone mineral density of hemodialysis patients: a pilot study. Am J Nephrol. 2012;36(3):238-44.
62. Giamalis P, Economidou D, Dimitriadis C, Memmos D, Papagianni A, Efstratiadis G. Treatment of adynamic bone disease in a haemodialysis patient with teriparatide. Clin Kidney J. 2015;8(2):188-90.