International Journal of Health Sciences and Research
www.ijhsr.org ISSN: 2249-9571

Case Report

Renal Osteodystrophy in Chronic Kidney Disease with Near Normal Parathyroid Hormone Levels: A Case Report

P.V.S.S. Vijaya Babu[1], K.Lakshmi Kumari[2], K.Hari Krishna[1]

[1]Department of Biochemistry, Andhra Medical College, India
[2]Department of Anatomy, Andhra Medical College, India

Corresponding Author: P.V.S.S. Vijaya Babu

Received: 14/02/2015 *Revised: 30/03/2015* *Accepted: 04/04/2015*

ABSTRACT

Chronic Kidney Disease (CKD) results in alteration of bone and mineral metabolism. Altered bone homeostasis results in the formation of either renal osteodystrophy or adynamic bone disease. Renal osteodystrophy (ROD) is characterized biochemically by increased parathyroid hormone (PTH) and alkaline phosphatase (ALP) with decreased serum calcium. Adynamic bone disease (ABD) is a variant of ROD which shows decreased or normal PTH, normal ALP and decreased serum calcium as a part of its biochemical spectrum. As ROD is rare in patient with normal PTH values, this discrepant clinical profile prompted further investigation of the PTH assay. Same sample was sent to the reference laboratory to identify if there are any interfering factors. Results show that biotin may have an interfering role in the accurate estimation of serum intact PTH.

Keywords: Adynamic bone disease, Biotin, PTH immunoassay, PTH, Renal osteodystrophy.

INTRODUCTION

CKD occurs due to progressive decline in renal function over three or more months. CKD in young is usually due to genetically determined immune complex deposition and inflammation of the nephrons followed by progressive hypertrophy and hyper filtration of the remaining viable nephrons. [(1)] There will be a progressive decline in the glomerular filtration rate (GFR) as the disease progresses. In the initial stages of the renal failure elevated amounts of PTH will cause normal or low serum phosphate levels. [(2)] In advanced stages there will be decreased GFR results in increased phosphate retention and calcium excretion. This hyperphosphatemia there will lead to further suppression of 1α hydroxylase hampering intestinal calcium absorption and will act as a stimulus to parathyroid gland to produce more PTH. Urinary loss of calcium prompts the hyperparathyroid gland to secrete more PTH. Abnormally high levels of PTH will eventually result in ROD. [(3)] Accurate estimation of PTH is absolutely necessary to initiate the treatment and prevent the progression to hyperparathyroid bone disease. [(4)] This case report discusses the role of biotin as a significant interfering factor for PTH estimation on the Elecys platform.

CASE REPORT

A 15 year old female patient came with a chief complaint of joint pains, difficulty in walking and climbing stairs .The present complaint started 2 weeks ago and weakness is progressively increased to the present condition. General examination showed generalized skin rashes, seborrheic dermatitis. Musculoskeletal examination showed bowing of the legs and arms. Past medical history includes diabetes mellitus for the past 6 years and is currently on insulin to control her blood sugar levels .Laboratory investigations showed 7.8gm% of hemoglobin, 6.6mg/dl of serum creatinine, 136mEq/L of serum sodium and 4.7mEq/L of serum potassium, ALP is 839 IU/L, serum calcium is 7.2mg/dl, serum phosphorus is 3.8mg/dl and PTH is 40ng/L. Computed tomography (CT) scanning showed chronic renal parenchymal disease with bilateral contracted kidneys. Patient was diagnosed as end stage renal disease with osteodystrophy.

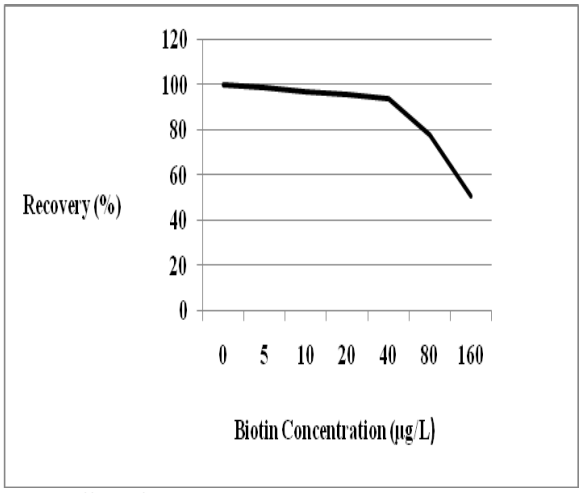

Fig 1: Effect of biotin on serum PTH. Recovery percentage is calculated by the ratio of PTH concentration after the addition of biotin to the concentration without biotin.

DISCUSSION

PTH is a single chain polypeptide with 84 amino acids with a primary function being the regulation of calcium in the body. Whenever the serum calcium reduces, the parathyroid gland releases the preformed PTH immediately. If the hypocalcemia is sustained over a couple of hours, it increases the transcription of PTH mRNA. [(5)] Increase in the cellular mass of the parathyroid gland occurs due to deficient PTH for a prolonged period of time. Maintenance of serum calcium is done by both direct action and indirect action. Direct action on the bone results in the bone resorption and decreased renal clearance of calcium whereas indirect action is through increasing intestinal absorption of 1, 25-dihydroxyvitamin D3.

Bone disorders in CKD are either due to increased bone turnover or due to decreased bone turnover. [(6)] The former involves an increase in the PTH levels resulting in osteitis fibrosa cystica while the latter is due to low or normal PTH levels resulting in adynamic bone disease (ABD) and osteomalacia. Decreased synthesis of calcitriol and hyperphosphatemia due to phosphate retention will eventually result in hypocalcemia in patients with CKD. In an effort to restore the normal calcium levels, PTH levels are increased resulting in secondary hyperparathyroidism. [(7)]

Renal osteodystrophy (ROD) is caused by secondary hyperparathyroidism with subsequent mineralization defects resulting in osteomalacia .Biochemically ROD is typically characterized by increased PTH values and increased ALP values. [(8)] Adynamic bone disease (ABD) is a variant of renal osteodystrophy seen especially in elderly and CKD patients who underwent dialysis. Biochemically ABD is characterized by decreased mineralization of the bone resulting in decreased ALP and low are normal PTH values. Repeated dialysis decreases the phosphate load and reduces the stimulus for the parathyroid to produce more PTH. [(9)] The accurate measurement of PTH is highly significant, as increased PTH levels indicate the treatment with vitamin D and calcimimetic agents while decreased

PTH levels doesn't mandate stoppage of the treatment to prevent adynamic bone disease and extra skeletal calcification.

ALP is a marker of bone turnover. Its value is substantially increased in a person with increased clinical and radiological osteomalacia changes. It's rare to have a patient with increased ALP and a near normal PTH values. This discrepant clinical profile is further investigated to figure out interfering factors in the assay of the PTH used at our institution. Assay was repeated on our Elecsys 2010 immunoassay analyzer [(10)] and another sample was also sent to the reference laboratory which used Immulite 2000 immunoassay analyzer. [(11)] Discrepant values of 40ng/L and 375ng/L were obtained respectively. Elecsys PTH assay is a stat assay which uses two step sandwich immunoassay involving streptavidin microplates and electrochemiluminescence detection. Biotin is a potential interfering affect in estimation of PTH using Elecsys platform receiving doses of biotin greater than 5mg/day, which can be negated by collecting the sample 8 hours after the administration of biotin .Further review of the patient's medical history showed that the patient is taking multivitamin tablets for nutritional deficiencies for the past 20 days. It included biotin intake of 50µg/day. Even though the sample was collected after 8 hours after last biotin dose we found that biotin has interference in the estimation of PTH.

To prove the interfering role of biotin we used two methods. In the first we used a serum of normal person whose PTH is 44ng/L which has no biotin as an interfering factor. To this serum, free biotin was added in serial mixtures at a concentration of 0, 5, 10, 20, 40, 80and160µg/L and recovery percentage was calculated. Recovery percentage is calculated by finding the ratio of PTH after the addition of biotin to that of the PTH before the addition of biotin. The recovery curve illustrated in figure below demonstrated the effect of free biotin in the measurements of PTH. It clearly shows that there is almost 50 % decrease in the PTH levels especially at high concentrations of biotin. Further confirmation of the role of biotin was done by measuring the intact PTH levels which were measured after two weeks of stoppage of biotin. The estimation was done in both Elecsys and Immulite platforms which turned out to be 160ng/L and 210ng/L.

CONCLUSION

To summarize we conclude that biotin present in the samples of patients with ROD interfered with the estimation of PTH in the Elecsys platform. This was confirmed by adding free biotin in serial mixtures and calculating the recovery percentage and also by estimating the PTH after stopping the intake of biotin by the patient. Further research in large populations need to be done in this regard to further confirm this observation.

REFERENCES

1. Vernier RL. Chronic Renal Disease in Children. AMA J Dis Child. American Medical Association; 1958 Sep 1 [cited 2015 Mar 27];96(3):306.
2. Levin A, Bakris GL, Molitch M, Smulders M, Tian J, Williams LA, et al. Prevalence of abnormal serum vitamin D, PTH, calcium, and phosphorus in patients with chronic kidney disease: results of the study to evaluate early kidney disease. Kidney Int [Internet]. 2007 Jan [cited 2015 Feb 3];71(1):31–8.
3. Brown EM, Wilson RE, Eastman RC, Pallotta J,Marynick SP. Abnormal Regulation of Parathyroid Hormone Release by Calcium in Secondary Hyperparathyroidism due to Chronic Renal Failure. J Clin Endocrinol Metab. The Endocrine Society; 1982 Jan 1 [cited 2015 Mar 30];54(1):172–9.

4. Goodman WG. Assays for Parathyroid Hormone and Their Use in Patients with End-Stage Renal Disease. Blood Purif. Karger Publishers; 2003 [cited 2015 Mar 30];21(1):118–23.
5. Moallem E. RNA-Protein Binding and Post-transcriptional Regulation of Parathyroid Hormone Gene Expression by Calcium and Phosphate. J Biol Chem. 1998 Feb 27 [cited 2015 Mar 30];273(9):5253–9.
6. Moe SM, Drüeke T, Lameire N, Eknoyan G. Chronic kidney disease-mineral-bone disorder: a new paradigm. Adv Chronic Kidney Dis. 2007 Jan [cited 2015 Mar 30];14(1):3–12.
7. Kumar R, Thompson JR. The regulation of parathyroid hormone secretion and synthesis. J Am Soc Nephrol. 2011 Feb 1 [cited 2014 Mar 27];22(2):216–24.
8. Beladi Mousavi SS, Saghafi H. Renal bone disease among patients with ESRD. Nephrourol Mon. 2013 Jul 1 [cited 2014 Apr 4];5(3):849–50.
9. Souberbielle J-C, Boutten a, Carlier M-C, Chevenne D, Coumaros G, Lawson-Body E, et al. Inter-method variability in PTH measurement: implication for the care of CKD patients. Kidney Int . 2006 Jul [cited 2014 Mar 19];70(2):345–50.
10. Roche Elecsys® Intact PTH assay package insert. 2008.V 3 English.
11. Omar H, Chamberlin A, Walker V, Wood PJ. Immulite 2000 parathyroid hormone assay: stability of parathyroid hormone in EDTA blood kept at room temperature for 48 h. Ann Clin Biochem . 2001 Sep [cited 2014 Mar 24];38(Pt 5):561–3.

How to cite this article: Vijaya Babu P.V.S.S., Kumari KL, Krishna KH. Renal osteodystrophy in chronic kidney disease with near normal parathyroid hormone levels: a case report. Int J Health Sci Res. 2015; 5(5):513-516.

****