Kidney Res Clin Pract 34 (2015) 4–12

Kidney Research and Clinical Practice

journal homepage: http://www.krcp-ksn.com
Contents lists available at ScienceDirect

Review Article

Management of chronic kidney disease–mineral and bone disorder: Korean working group recommendations

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Article history:
Received 7 February 2015
Accepted 11 February 2015
Available online 24 February 2015

Keywords:
Calcium
Dialysis
Phosphorus
Secondary hyperparathyroidism

Abstract

For Korean dialysis patients, chronic kidney disease–mineral bone disorder is a serious burden because of cardiovascular calcification and mortality. However, recent epidemiologic data have demonstrated that many patients undergoing maintenance hemodialysis are out of the target ranges of serum calcium, phosphorus, and intact parathyroid hormone. Thus, we felt the necessity for the development of practical recommendations to treat abnormal serum phosphorus, calcium, and iPTH in dialysis patients. In this paper, we briefly comment on the measurement of serum calcium, phosphorus, iPTH, dialysate calcium concentration, dietary phosphorus restriction, use of phosphate binders, and medical and surgical options to correct secondary hyperparathyroidism. In particular, for the optimal management of secondary hyperparathyroidism, we suggest a simplified medication adjustment according to certain ranges of serum phosphorus and calcium. Large-scale, well-designed clinical studies are required to support our strategies to control chronic kidney disease–mineral bone disorder in this country. Based on such data, our practice guidelines could be established and better long-term outcomes should be anticipated in our dialysis patients.

Introduction

Chronic kidney disease–mineral bone disorder (CKD-MBD) is a common complication occurring in CKD patients. In addition to hypercalcemia and hyperphosphatemia, CKD-MBD can cause vascular calcification and cardiovascular diseases (CVD), and these conditions are closely associated with an increased mortality rate. Recently, these associations have been demonstrated, even in early-stage CKD patients [1–3]. According to the end-stage renal disease registry of the Korean Society of Nephrology, there were 48,531 hemodialysis (HD) and 7,552 peritoneal dialysis (PD) patients in Korea in 2012, and CVD was the most common cause of death in dialysis patients [4].

We previously analyzed the serum levels of calcium (Ca), phosphorus (P), and intact parathyroid hormone (iPTH) from a total of 1,018 patients undergoing chronic HD in 17 centers throughout Korea [5]. The mean serum levels of Ca, P, and the Ca-P product were 9.1 mg/dL, 5.3 mg/dL and 48.0 mg^2/dL^2, respectively. When classified by the recommended range according to the Kidney Disease Outcome Quality Initiative

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http://dx.doi.org/10.1016/j.krcp.2015.02.002

(KDOQI) guidelines, about one half of the patients had uncontrolled hyperphosphatemia > 5.5 mg/dL. In addition, 270 patients (26.5%) had iPTH > 300 pg/mL whereas 435 patients (42.7%) showed iPTH < 150 pg/mL. This study demonstrated the current status of CKD-MBD in our HD patients, revealing that a relatively modest proportion of patients had values outside of the target range [5]. Those patients who were out of the target range might be associated with poor prognosis, including mortality secondary to CVD. Therefore, successful implementation of treatment guidelines is required with respect to CKD-MBD.

To improve the quality of care in CKD-MBD, global and regional guidelines were established and suggested target ranges and treatment protocols. In Korea, the KDOQI and the Kidney Disease: Improving Global Outcomes (KDIGO) guidelines are well known and commonly used [6,7]. In both global guidelines, however, the level of recommendations is low because of scarcity of randomized controlled clinical trials. On regional bases, guidelines were published from Japan (Japanese Society for Dialysis Therapy, JSDT), Australia (the Caring for Australians with Renal Impairment, CARI), Great Britain (United Kingdom Renal Association, UKRA), and Europe (European Renal Best Practice, ERBP) [8–11]. The target levels of Ca, P, and iPTH presented in the aforementioned guidelines are summarized in Table 1.

The target ranges in these guidelines are not consistent, and we may have to choose one of them because we have no well performed epidemiological data showing associations between serum mineral values and patient outcomes in our dialysis population. Furthermore, in Korea, it is practically difficult to just adapt foreign guidelines because our treatment strategies are guided by the National Health Insurance Service (NHIS) standards. With regard to this point, we reviewed the CKD-MBD guidelines from different countries and suggest that our treatment recommendations to be applied in real practices of CKD-MBD in Korea.

Measurement of serum Ca, P, and iPTH

In dialysis patients, it is important to maintain serum Ca, P, and iPTH within the appropriate ranges. For this, serum Ca and P should be measured monthly or more frequently (depending on the clinical settings). The measurement of iPTH should be conducted at least once every 3 months.

Control of hyperphosphatemia and maintenance of serum Ca, P, and iPTH levels within the target ranges in CKD patients are the mainstay of the management of CKD-MBD. Thus, biochemical tests for Ca, P, and iPTH must be performed regularly, and it is recommended to measure patients' serum Ca and P at least once per month. The measurement interval of iPTH is 3–6 months by the KDIGO guidelines, and is 3 months according to the KDOQI and JSDT guidelines. Considering these three guidelines and our NHIS, we recommend that the iPTH level should be measured once every 3 months. However, laboratory tests may be performed more frequently based on clinical decisions until the test results are optimalized. In particular, biochemical tests should be performed more frequently during active suppression of secondary hyperparathyroidism using vitamin D receptor activators (VDRAs) or calcimimetics. Even when the value of each biochemical test result falls within the target range, it is important to identify a trend of change. If the iPTH levels are increased, serum alkaline phosphatase may also be measured, as necessary. In cases of decreased serum Ca level, the serum albumin concentration should also be measured to obtain the corrected Ca because only the total, but not ionized (biologically active), serum Ca concentration may be lowered by hypoalbuminemia. The corrected Ca concentrations can be calculated by two different formulae recommended by the KDIGO and JSDT guidelines.

KDIGO method [7]:
Corrected total Ca (mg/dL) = measured Ca (mg/dL) + 0.8 × [4 – serum albumin (g/dL)].
JSDT method [9]:
Corrected total Ca (mg/dL) = measured Ca (mg/dL) + [4 – serum albumin (g/dL)].

Table 2 summarizes our recommendation on the frequency of serum mineral measurements and their target ranges. In the latter part of this article, we will describe in detail the target ranges of serum Ca, P, and iPTH.

Consideration of dialysate Ca concentration

Although dialysate Ca concentrations may be individualized for successful HD, the KDIGO [7], ERBP [11], and JSDT [9] guidelines recommend that the dialysate Ca concentration be maintained between 2.5 mEq/L and 3.0 mEq/L (1.25–1.5mM). Serum Ca levels usually change in parallel with dialysate Ca

Table 2. Recommended measurement frequency and ranges of serum calcium, phosphorus, and parathyroid hormone in chronic kidney disease stage 5D

Serum parameters	Measurement frequency	Recommended range
Calcium	Once per mo	8.4–9.6 mg/dL
Phosphorus	Once per mo	2.4–5.0 mg/dL
Parathyroid hormone	Once every 3 mo	100–300 pg/mL

Table 1. Target levels of serum phosphorus, calcium, and parathyroid hormone presented by different guidelines

	Phosphorus (mg/dL)	Calcium (mg/dL)	Intact parathyroid hormone (pg/mL)
KDIGO [7]	Towards normal range	Towards normal range	2–9 × normal range
ERBP [11]	2.4–4.5	Towards normal range	100–800
UKRA [10]	2.78–4.64	8.8–10.0	Not mentioned
CARI [8]	~4.95	8.5–10.5	100–470
KDOQI [6]	3.5–5.5	8.4–9.5	150–300
JSDT [9]	3.5–6.0	8.4–10.0	60–240

CARI, Caring for Australians with Renal Impairment; ERBP, European Renal Best Practice; JSDT, Japanese Society for Dialysis Therapy; KDIGO, Kidney Disease: Improving Global Outcomes; KDOQI, Kidney Disease Outcome Quality Initiative; UKRA, United Kingdom Renal Association.