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The impact of Magnesium (Mg) on mineral metabolism in diabetic or non-diabetic patients with chronic kidney diseases (CKD)

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Abstract

Renal handling of magnesium (Mg) is adaptive mechanism, but it's affected when renal function declines. In moderate chronic kidney disease (CKD), loss of glomerular filtration is compensated by higher fractional excretion of Mg. In more advanced CKD however, (creatinine clearance <30 mL/min), overt hypermagnesemia develops frequently. Various studies show that increased serum Mg (sMg) lowers PTH, others do not prove the suggestion. Although the exact role of Mg in bone metabolism is unclear, it may have both positive and negative effects. The aim of this study is to investigate the impact of sMg on bone mineral metabolism in CKD patients with or without diabetes. 62 CKD patients (not receiving dialysis) were divided into two groups: 1st group (32 CKD diabetic patients); 2nd group (30 CKD patients without diabetes). Biochemical determinations were made, and the estimated glomerular filtration rate (GFR) was measured. Bone mineral density (BMD) was measured by dual-energy X-ray absorptiometry. sMg was inversely correlated with sCa (P<0.02) and with parathyroid hormone (sPTH) (P<0.05), with alkaline phosphatase (AP) (P<0.02), and with phosphate (P) (P<0.01) in 1st group (diabetic). The CKD diabetic patients had lower serum albumin (ALB) and a higher hypomagnesemia and osteoporosis than the nondiabetic patients. sMg inversely correlated with e-GFR in the CKD patients in both groups. sMg showed higher correlation with 25-hydroxyvitamin D in 2nd non-diabetic group (P<0.01); diabetic patients with higher sMg had a lower iPTH. The lower sMg subgroup showed a higher incidence of osteoporosis than the moderate and higher sMg subgroups did. In conclusion, low sMg may impact iPTH and enlarge osteoporosis in CKD patients, particularly with diabetes.

Introduction

Renal excretion of Mg is so adaptable, that impairment of renal function was recognized as an important reason for development of hypermagnesemia [1-3]. In moderate CKD, increase in fractional Mg excretion compensates impaired renal function, and sMg remains normal [1,3,4]. Interestingly, there seem to be differences in Mg homeostasis of diabetics and non-diabetics. When patients with and without diabetes were investigated (creatinine clearance ranging from 115 to >30 mL/min/1.73 m^2), a significant inverse correlation was found between creatinine clearance and serum magnesium in non-diabetics, but not in diabetics. As renal function further deteriorates to CKD Stages 4 and 5, the quantitative excretion of Mg tends to decrease and cannot be compensated any longer by an increased fractional excretion [5,6]. Osteoporosis is a skeletal disorder with disruption of bone architecture that leads to decreased bone mass, strength and increased fracture risk. Many factors are associated with osteoporosis: nutritional, hormonal, low calcium (Ca), Vitamin D deficiency. CKD causes abnormality of bone mineral metabolism and results in some special kinds of bone disease [5,7-9]. Mg is also a regulator of bone homeostasis, influencing PTH secretion, Vitamin D metabolism and bone structure *per se* [7,10,11].

In the present study, sMg levels, bone mineral metabolism parameters, bone mineral density, and renal function indicators were measured. The objective of this study was to evaluate the impacts of serum Mg levels on PTH and bone mineral metabolism among CKD patients with or without diabetes.

Material and methods

This study involved 62 stage 3–5 CKD patients, not receiving dialysis who were divided into two groups: 32 CKD with diabetes and 30 CKD without diabetes. Patients were residents in Sofia and Stara Zagora and were diagnosed with CKD. All patients were without a history of severe symptomatic ischemic heart disease, heart failure, liver disease, malignancy, and hypoparathyroidism.

The study protocol was approved by the Local Medical Ethic Committee and informed consent was obtained from each participant.

Blood samples were collected after an overnight fasting for the determinations of serum Mg, Ca, P, intact PTH (iPTH), alkaline phosphatase (ALP), 25-hydroxyvitamin D {25(OH)D}. (For patients with stages 3, 4, and 5 CKD, PTH should be maintained in the range

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Table 1. Characteristics of the 62 non-dialysis CKD patients with or without diabetes

Variables	Total (62)	Diabetes (32)	Non-diabetes (30)	P<
Age (y)	64.0 (63.0–75.0)	69.2 (57.0–76.6)	65.0 (52.8–76.6)	NS
GFR (mL/min)	19.5 (11.5–28.3)	14.7 (9.2–28.7)	21.4 (11.0–23.6)	0.01
CKD Stages				
Stage 3	n=16	n=9	n=6	
Stage 4	n=20	n=7	n=14	
Stage 5	n=26	n=16	n=10	
Alb (g/dL)	3.9 ± 0.5	3.6 ± 0.4	3.9 ± 0.5	0.05
sMg (mmoL/L)				
low sMg (<0.6 mmol/L)	6 (0.4 ± 0.13)	6 (0.4 ± 0.13)	-	-
Normal sMg (0.7–1.2 mmol/L)	33 (0.7-1.1)	13 (0.7-1.0)	20 (0.72-1.1)	0.02
High sMg (>1.25 mmol/L)	17 (1.1-1.45)	8 (1.1-1.37)	10 (1.14-1.45)	0.05
Osteoporosis (OP)				
With OP	n=25	n=17	n=8	
Without OP	n=37	n=17	n=20	

of 4–7 pmol/L, 7–10 pmol/L, and 15–20 pmol/L, respectively. The reference range of ALP was 50–130 (U/L) for laboratory used; vitamin D deficiency is defined as serum 25(OH)D<20 ng/mL and vitamin D insufficiency – as 25(OH)D<30 ng/mL. Bone mineral density at the both femoral necks and lumbar spine (L1–L4) was measured by dual-energy X-ray absorptiometry. Definition of CKD stages was based upon guidelines for the management of CKD.

Multiple regression was used to analyse all variables and presented in unstandardized and standardized coefficients, and at a 95% confidence interval (CI). The value P<0.05 was considered statistically significant. Statistical analysis was done using SPSS 17.0 statistical software (SPSS Inc., Chicago, IL, USA).

Results

The characteristics of the CKD patients with or without diabetes are shown in Table 1. The CKD patients with diabetes had significantly lower serum albumin (P<0.05), lower serum magnesium (P<0.02), and higher osteoporosis (0.01) than those CKD patients without diabetes. In addition, age, gender and e-GFR, were not significantly different between CKD patients with diabetes and without diabetes.

sMg was inversely correlated with serum Ca (P<0.01), serum iPTH (P<0.05) and ALP (P<0.02) in the CKD patients with diabetes. Moreover, serum Mg was inversely correlated with eGFR (P<0.01) and positively correlated with creatinine (P<0.005) and BUN (P<0.02) in the same group of patients. However, serum Mg was not significantly associated with serum P and 25(OH)D in the CKD patients with diabetes. For CKD patients without diabetes, serum Mg showed an inverse correlation with 25(OH)D (P<0.01). Moreover, serum Mg showed a positive correlation with serum creatinine (P<0.05) and an inverse correlation with eGFR (P<0.02) in the CKD patients without diabetes. There was a marginal inverse correlation between serum Mg and serum Ca in the CKD patients without diabetes. However, serum Mg had no significant correlation with serum urea nitrogen, P, iPTH, ALP in the CKD patients without diabetes. On the other hand, iPTH was inversely correlated with serum Ca (P<0.02) and 25(OH)D (P<0.02) and positively correlated with serum ALP (P<0.005) in the CKD patients with diabetes. In addition, iPTH also was not significantly correlated with renal function indicators in the CKD patients with or without diabetes. Linear regression analysis was performed to examine the impact of the serum Ca/Mg ratio on the PTH, also using sex, age, diabetes, and eGFR as adjusted variables. Our data indicated that the serum Ca/Mg ratio was inversely correlated with PTH levels in both groups (P<0.01).

Discussion and Conclusion

Mg imbalance has been neglected in disorders of bone mineral metabolism of patients with CKD [1,3,7,8]. Our study may give an additional light for improvement of medical care in CKD patients, with and without diabetes. Low serum Mg levels may cause wrong increase of PTH and may further lead to bone diseases in CKD patients, especially with diabetes. For these patients, adequate Mg intake by diet or supplement may reduce the development of low turnover bone disease [2,8,12,13]. Oppositely, the inhibitory effect of a high sMg on PTH secretion may be offset by the stimulation produced through low serum Ca in moderate-severe CKD patients, who are not receiving dialysis [5,7,9]. These patients must maintain a sCa within optimal range and avoid consuming excess Mg and, to reduce the risk of low-turnover bone diseases [7,13-15]. A routine monitoring of sMg, and balancing sCa and sMg are important in the assessment and management of bone mineral disorders in CKD patients with or without diabetes.

Disclosure statement

There is nothing to disclose.

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