Renal Potassium Wasting and Hypocalciuria Ameliorated with Magnesium Repletion in Gitelman's Syndrome

A woman aged 45 years was presented with hypokalemic metabolic alkalosis and hypomagnesemia associated with renal potassium and magnesium wasting. Her 24-hour urinary calcium excretion was strikingly low despite normocalcemia and normal creatinine clearance, which is one of characteristic findings of Gitelman's syndrome (GS). She was evaluated for the responses following Mg supplementation for 10 days, which showed marked increments in serum potassium and magnesium as well as improvements of the degree of renal potassium wasting and hypocalciuria. This amelioration of abnormal biochemical pictures in this patient after Mg supplementation proposes that the hypokalemia with renal potassium wasting and hypocalciuria may be caused by abnormal Mg metabolism. ***(JKMS 1997;12:157~9)***

Key Words : *Gitelman's syndrome, Treatment, Magnesium, Hypokalemia, Hypocalciuria*

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INTRODUCTION

Magnesium deficiency and hypocalciuria are, in addition to hypokalemia, the biochemical hall marks of Gitelman's syndrome (GS), a recognized variant of Bartter's syndome, sometimes referred to as a primary tubular hypomagnesemia-hypokalemia with hypocalciuria (1~3).

In previous experiments, hypomagenesemia promotes both tubular calcium reabsorption and potassium depletion (4~6). In cases of GS, it has been suggested that hypokalemia and hypocalciuria are secondary to hypomagnesemia, and both hypomagnesemia and hypocalciuria may precede potassium deficiency (2). Therefore, it can be speculated the correction of hypomagnesemia in GS corrects not only the tendency to potassium deficiency but also the decreased urinary calcium excretion, suggesting that hypomagnesemia would be one of underlying causes of hypocalciuria and renal potassium wasting in GS.

Therefore, in this study, a case of GS characterized by hypomagnesemia-hypokalemia with hypocalciuria was evaluated following Mg supplementation, and revealed the the significant correction of hypokalemia and hypomagnesemia, accompanied by the amelioration of renal potassium wasting and hypocalciuria.

CASE HISTORY

A 45 year old woman was referred for the evaluation of hypokalemia (K, 1.9~2.3 mEq/L) on the 3 repeated examinations. She was admitted to the department of plastic surgery for the reconstruction of a facial injury, which occurred in a motor vehicle accident as a driver. As a house wife with 2 children, she had no pain in joints or muscles, no polyuria or polydipsia, no sweat or weight loss and no anomalous dietary habit. She denied any significant past medical history or the intakes of medications including diuretics, laxatives, or diarrhea. Also, family history was not contributory.

Physical examination revealed a well-hydrated and nourished middle-aged woman. Vital signs were normal with BP of 110/80 mmHg. Motor and sensory functions were normal. The Chvostek's and Trousseau's signs were negative. No other gross abnormalities were found.

METHODS

Without any medications interfering K, Ca, and Mg homeostasis, she was put on 6 days of dietary adjustment with unrestricted regular well balanced diet by the close observation from a nutritional consultant of our hospital to ensure a constancy of sodium-potassium-magnesium-calcium balance. On the 7th day in hospital, baseline values of blood samples of Na, K, Ca, Mg and creatinine, and an arterial blood gas analysis were obtained with baseline plasma renin activity (PRA) and serum aldosterone levels at 7 A.M. before a breakfast on supine position after over night recumbency. Also, 24-hour urine samples for potassium, magnesium, calcium and cre-

atinine clearance were performed. For the following 10 days, she was put on the same regular diet with the additional supplementation of 2 tablets of magnesium oxide (MgO, a 600 mg tablet containing 360 mg of elemental Mg) by oral intake. Then, the same procedures for blood and urine samplings were repeated. The specific radioimmunoassays (kits from Abbott laboratory, Germany) were used to measure PRA and serum aldosterone levels. Electrolytes and creatinine were measured by an autoanalyzer (Technicon automatic analyzer, N.Y., USA).

RESULTS

The biochemical data and renin-aldosterone profiles of blood (Table 1) and the urinary biochemical data (Table 2) are summarized before and after the oral supplementation of Mg. The outstanding features in the baseline blood were hypomagnesemia (1.1 mg/dL) and hypokalemia (2.6 mEq/L) in the presence of normocalcemia (9.3 mg/dL) and normal creatinine clearance (94 ml/min). The baseline PRA and aldosterone levels were within normal range (reference values of our laboratory : PRA, 1.2~5 ng/ml/h ; aldosterone, 185~500 pg/ml). Arterial blood gas analysis showed pH 7.50, pCO_2 40 mmHg, and HCO_3 31 mEq/L, suggestive of the presence of metabolic alkalosis. The most characteristic finding in the baseline data of 24-h urine, besides the presence of hypermagnesuria (124 mg/d) and hyperkaliuria (72 mEq/d) despite hypomagnesemia and hypokalemia, was the markedly diminished urinary calcium excretion (18 mg/d) in the presence of normocalcemia.

The repeat test after of Mg supplementation for 10 days showed the increases of serum potassium from to 2.6 to 3.4 mEq/L and serum magnesium from 1.1 to 2.0 mg/dL, respectively, accompanied by the markedly diminished urinary potassium from 72 to 13 mEq/day, the mild change of the degree of urinary magnesium excretion from 124 to 143 mg/day, and, as an additional striking finding, the marked amelioration of the degree of the hypocalciuria from 18 to 102 mg/day. Repeat blood calcium, HCO_3, and renin- aldosterone profiles did not show any marked changes.

DISCUSSION

In our adult patient, the diagnosis of GS was supported by relatively asymptomatic status with the presence of hypokalemia and hypomagnesemia due to urinary wasting, and normal renin-aldosterone profiles. Furthermore, the marked hypocalciuria in the presence of normocalcemia in our case allows easy differentiation from classic Bartter's syndrome (7).

To dates, the treatments as compared to the classification and pathophysiology of GS has received little attention. In the present study, oral replacement of Mg markedly decreased renal potassium excretion and markedly increased serum potassium concentration in our patient with GS. Furthermore, the degree of hypocalciuria was ameliorated by the supplementation of Mg in this case. The mechanism by which Mg supplementation decreased potassium excretion in this syndrome is unknown. The result may be explained either by a nonspecific effect of Mg on potassium balance or by correction of an abnormal Mg metabolism.

Hypomagnesemia is a common feature in patients with disorders involving hypokalemia; this suggest a close relationship between the metabolism and that of potassium (1, 8). Adrenalectomy results in an increase of both Mg and potassium concentrations in the serum (9), and fluorohydrocortisone was reported to correct the increased concentrations of serum potassium and magnesium in a patient with Addison's disease (10). Futher-

Table 1. Blood biochemical data and renin-aldosterone profile before and 10 days after Mg supplementation

	K (mEq/L)	Ca (mg/dL)	Mg (mg/dL)	HCO_3 (mEq/L)	Cr (mg/dL)	PRA (ng/ml/h)	Aldosterone (pg/ml)
Before	2.6	9.3	1.1	31	1.0	6	560
After	3.4	9.0	2.0	29	1.2	4	515

PRA=plasma renin activity, Cr=creatinine

Table 2. Urine biochemical data before and 10 days after Mg supplementation

	Ccr (ml/min)	Urine-K (mEq/d)	Urine-Ca (mg/d)	Urine-Mg (mg/d)
Before	94	72	18	124
After	89	13	102	143

Ccr=creatinine clearance

more, Mg infusion in healthy subjects has been shown to decrease urinary potassium excretion (11). In the present study, however, baseline renin-aldosterone profile was not disturbed by the presence of hypokalemia and hypomagnesemia, and, furthermore, Mg supplementation did not affect PRA and plasma aldosterone concentration. Therefore, despite the previous view of the close relationship between aldosterone and plasma potassium (12), this finding suggests that the changes of renin-angiotensin profile would not be directly responsible for hypomagnesemia and hypokalemia in our case of GS.

A study of calcium metabolism in GS indicates that filtered Ca load is not reduced in GS whereas the ionized Ca fractional excretion is reduced markedly, suggesting the defects of tubular absorption of Ca (13). The amelioration of hypocalciuria with Mg supplementation in this study suggests that the possible cross-links of the sites and mechanisms of increased tubular reabsorption of Ca and tubular handling of Mg with hypomagnesemia in GS. However, the exact mechanisms between the metabolisms of potassium, calcium, and magnesium remains to be clarified further.

In summary, this study indicates that Mg supplementation can correct the renal potassium loss with the amelioration of hypocalciuria in patients with GS. This observation suggests that the hypokalemia with renal potassium loss and hypocalciuria would be partly related by abnormal Mg metabolism. Regardless of underlying mechanisms in GS, Mg supplementation with or without additional potassium intakes seems to be necessary for the optimal therapeutic regimen of GS.

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