JAMA Diagnostic Test Interpretation

Urinary Magnesium in the Evaluation of Hypomagnesemia

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A 63-year-old woman with a medical history of type 2 diabetes, atrial fibrillation, hypothyroidism, and hypertension was referred for refractory hypomagnesemia. Her blood pressure was 148/68 mm Hg, heart rate 96/min, and weight 106.4 kg. Medications included liraglutide, metformin, apixaban, sotalol, metoprolol, levothyroxine, venlafaxine, lisinopril, ranitidine, and magnesium oxide (400 mg, 2 times/d). Her prior serum magnesium levels ranged from 1.4 mg/dL to 1.6 mg/dL and a recent hemoglobin A_{1c} level was 10.8%. Following baseline blood testing (**Table**), the patient collected a 24-hour urine sample after discontinuing magnesium supplements for 24 hours.

Table. Laboratory Assessment at Time of Consultation

	Patient's values	Reference range
Blood		
Sodium, mmol/L	135	135-146
Potassium, mmol/L	4.4	3.5-5.3
Chloride, mmol/L	100	98-110
Bicarbonate, mmol/L	26	23-30
Glucose, mg/dL	361	70-99
Creatinine, mg/dL	0.88	0.5-1.5
Calcium, mg/dL	9.6	8.5-10.5
Albumin, g/dL	42	3.5-5
Phosphorus, mg/dL	3.6	2.5-4.5
Magnesium, mg/dL	1.4	1.8-2.4
24-Hour urine		
Volume, L/d	5.094	0.5-3.0
Urine creatinine, mg/d	1528	Varies
Albumin, mg/d	1355	<30
Calcium, mg/d	188	Varies
Sodium, mmol/d	357	Varies
Potassium, mmol/d	126	Varies
Phosphorus, mg/d	1528	Varies
Glucose, g/d	>152.82	0
Urea, mg	10 494	Varies
Magnesium, mg/d	117	Varies
Chloride, mmol/d	377	Varies
Osmolality, mOsm/kg	561	Varies

WHAT WOULD YOU DO NEXT?

A. Evaluate for alcoholism as the cause of hypomagnesemia.

B. Improve glycemic control due to urinary magnesium loss from polyuria.

C. Start insulin to promote magnesium reabsorption at the proximal convoluted tubule.

D. Stop ranitidine due to concern for reduced gastrointestinal magnesium absorption.

Quiz at jamacmelookup.com

Answer

B. Improve glycemic control due to urinary magnesium loss from polyuria.

Test Characteristics

While more than 60% of the body's magnesium stores reside in bone, nearly 70% of the serum magnesium circulates freely, not bound to plasma proteins. This unbound magnesium is freely filtered at the glomerulus and enters the tubules where more than 95% of filtered magnesium is reabsorbed by the kidney.[1] Magnesium is reabsorbed primarily at the ascending loop of Henle and the last site of regulation is the distal convoluted tubule, where a positive lumen potential is required for reabsorption paracellularly.[1]

When evaluating hypomagnesemia, the first step is to differentiate renal vs nonrenal losses using urine magnesium testing. A 24-hour urine magnesium sample is recommended over a spot (1-time) sample because magnesium excretion varies with dietary intake, diurnally with circadian rhythm, and because the 24-hour measure allows for an assessment of daily urine volume.[2] Medications that influence urinary magnesium excretion, such as diuretics or magnesium supplements, should be stopped prior to the urine collection.[3] If only a spot urine assessment is possible, urinary magnesium must be adjusted for urinary creatinine (fractional excretion; FE_{Mg}) to account for variations in urine volume.

$$FE_{Mg} = \text{Serum Creatinine} \times \text{Urine Magnesium}/0.7 \times \text{Serum Magnesium} \times \text{Urine Creatinine}$$

In the formula for fractional excretion of magnesium, the serum magnesium is multiplied by 0.7 in the denominator to account

Box. Common Causes of Renal and Nonrenal Magnesium Wasting Disorders

Nonrenal Hypomagnesemia (Decreased Fractional Excretion of Magnesium)
- Redistributive (eg, refeeding, insulin therapy)
- Reduced magnesium intake
- Reduced gastrointestinal absorption (proton pump inhibitors)
- Alcohol use
- Diabetes

Renal-Wasting Hypomagnesemia (Increased Fractional Excretion of Magnesium)
- Diuretics
- Antimicrobials (amphotericin B, aminoglycosides)
- Calcineurin inhibitors (cyclosporine, tacrolimus)
- Epidermal growth factor receptor inhibitors (cetuximab)
- Cytotoxic drugs (cisplatin, carboplatin)
- Hypercalcemia
- Hyperthyroidism, hyperparathyroidism
- Alcohol use
- Diabetes

for the nonalbumin–bound fraction. Renal magnesium wasting is defined as a fractional excretion of magnesium greater than 4% or a daily urinary magnesium excretion of more than 1 mmol per day (24.31 mg/d). Medicare reimbursements for laboratory evaluation are $6.70 for urinary magnesium and $5.18 for urinary creatinine.[4]

Application of Test Result to This Patient

The 24-hour urine creatinine test helps evaluate the completeness of the 24-hour sample (estimated to be 15 mg/kg/d in females; 20 mg/kg/d in males). This patient's level was 1528 mg (1590 mg expected), indicating a valid urine sample. In this patient, 117 mg per day of magnesium excretion in the setting of hypomagnesemia confirms magnesium wasting in the kidney. The **Box** lists the disorders and medications implicated in renal magnesium wasting.

The 24-hour urine volume helps assess for polyuria (urine output >3 L/d), a common cause of renal magnesium wasting. Polyuria increases urinary transit time, reducing the contact time of electrolytes with tubular epithelial cells, thereby attenuating the ability to establish a transepithelial voltage gradient and reducing the tubular reabsorption of magnesium.[5] This patient had a urine volume of more than 5 L. When polyuria is present, a urine osmolality greater than 300 mOsm/kg is indicative of a solute/osmotic diuresis.[6] In this case, the urine osmolality is 561 mOsm/kg, consistent with an osmotic diuresis and making the total daily solute excretion

$$561\ \text{mOsm/kg} \times 5.094\ \text{L} = 2857\ \text{mOsm/d}.$$

A person on a typical western diet is expected to excrete 600 to 800 mOsm per day. In this case, glucose is the main contributor to the excess solute load, and therefore, a glucose-mediated osmotic diuresis is the likely explanation of this patient's hypomagnesemia. While alcoholism is a common cause of hypomagnesemia, the absence of alcohol use in the patient's history and lack of associated laboratory abnormalities, such as hypokalemia, hypophosphatemia, and hypocalcemia, make alcoholism less likely, thus choice (A) is incorrect.[7] Choice (C) is incorrect because the proximal tubule is not a major site of magnesium homeostasis. Choice (D) is incorrect because proton pump inhibitors, but not H2 blockers, are associated with reduced gastrointestinal magnesium absorption.[8]

Alternative Diagnostic Testing Approaches

A fractional excretion of urinary magnesium may also aid in the diagnosis, but based on the variability of the urinary magnesium, the 24-hour urine sample remains the standard.

Patient Outcome

Glycemic control improved with lifestyle modifications, hemoglobin A_{1c} improved to 6.5% and serum glucose improved to an average of 144 mg/dL, which is below the threshold (180 mg/dL) for glycosuria. At 3-month follow-up, magnesium was normal without supplementation. At 1-year follow-up, hypomagnesemia recurred due to poor glycemic control.

Clinical Bottom Line

- A urinary magnesium test differentiates between renal and nonrenal causes of magnesium wasting.
- In the evaluation of hypomagnesemia, a 24-hour urine is preferred because the volume of urine is also obtained.
- Improved glycemic control is the treatment of hypomagnesemia secondary to glycosuria-induced polyuria.

ARTICLE INFORMATION

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