Physiologic Assessment of Magnesium Status in Humans: A combination of Load Retention and Renal Excretion

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Magnesium deficiency is defined as a reduction in total body Mg content. In humans the skeleton buffers most of the acute Mg loss but in chronic deficiency there is also some loss from muscle. Bone and muscle Mg pools are insufficient to fully compensate for long-term deficiency, and small losses from other organs may occur [1].

Bone is one of the major magnesium pools in humans, increasing during Mg excess and decreasing during its deficiency. Thus bone is the tissue of choice to be used as an indicator of total body Mg stores but it is usually unavailable during life [2].

Intravenous Mg load retention test

The intravenous Mg load retention test [Table 1] is a tissue saturation test that determines the retention percentage of a load of Mg based on body weight that is administered intravenously. When body stores are normal the kidney excretes an intravenous Mg load almost quantitatively in 48 hours and the patient shows low retention of Mg. In contrast, a deficient patient shows high retention. The Mg load retention test serves as a guide to the adequacy of the magnesium stores, but does not quantitate the deficiency. At present, it is difficult to relate the retention percentage to the total body deficit of Mg.

Cohen and Laor [3] found an indirect relationship between bone Mg concentration and the retention percent of Mg in the intravenous Mg load retention test. The lower the bone Mg concentration the higher the percent retention of Mg. This relationship suggests that the Mg retention in the intravenous Mg load retention test is retained in bone and that in normomagnesemic Mg-deficient patients a greater amount of Mg can be adsorbed to bone mineral and thus be retained in the test.

Ryzen [4] found that urinary magnesium excretion in normomagnesemic Mg-deficient patients is lower than in controls, and that they retain more of the magnesium load than normal patients and less than hypomagnesemic Mg-deficient patients. In the normomagnesemic patients and controls a significant negative correlation was found between urinary Mg excretion and the percent of Mg retained. The sensitivity of the Mg load retention test may be different between subjects with and without hypomagnesemia.

The Mg load retention test does not have the sensitivity to detect treatment effects of Mg supplementation in otherwise healthy subjects. Costello et al. [5] found that

Table1. Suggested schema for clinical use of Mg load retention test [4]

- Collect baseline urine (spot or timed) for Mg/Cr ratio
- Infuse 0.2 mEq (2.4 mg) elemental Mg/kg lean body weight in 50 ml D5W over 4 hours
- Collect urine (starting with infusion) for Mg and Cr for 24 hours
- Calculate % Mg retained using following formula:

$$\%\text{Mg retained} = 1 - \left[\frac{\textit{Post-Infusion.24h.urine.Mg} - \textit{(Pre-infusion.Mg / creatinine.x.Post-infusion.urine.creatinine)}}{\textit{Total..elemental..Mg..infused}} \right] \times 100$$

- Criteria for Mg deficiency:
  >50% retention at 24 hours = definite deficiency
  >20% retention at 24 hours = probable deficiency.

The patients are allowed a regular hospital diet during the study. An acidifying agent (hydrochloric acid or sulfamic acid) is added to the specimen container before pooling the urine specimen during the 24 hour period. An alkaline urine will lead to the precipitation of Mg salts that are difficult to solubilize. The test must not be conducted in cases of renal insufficiency, disturbances of cardiac conduction, advanced respiratory insufficiency, or pregnancy.

MG = magnesium

CR = creatinine

after 3 months of 350 mg/day magnesium supplementation, the mean retention of 37% did not change significantly. Thus, the sensitivity of the test in normal subjects is not yet validated and cannot be accepted as the primary indicator for assessing adequacy at this time.

The test is not valid when Mg deficiency is due to inability of the kidney to conserve Mg (intrinsic renal disorder or extrarenal disturbance influencing renal Mg handling). Until the Mg load retention test is validated in future studies as a primary indicator of magnesium status, attempts at correlating the results from the test to other data relating to the Mg status of the patients should be made. One such procedure is the renal excretion of Mg.

Renal excretion of Mg

It is known that diminished dietary Mg intake or intestinal malabsorption leads to appropriate renal Mg conservation in the effort to maintain Mg balance. This response is sensitive and independent of renal sodium and calcium excretion. It is clear that the fall in renal Mg excretion is not due to a drop in serum and filtered Mg, since a number of studies have reported diminished urinary Mg excretion with normal serum Mg concentration. It is believed that epithelial cells in the thick ascending limb and the distal tubule appropriately 'adapt' their transport rate according to the availability of Mg. This ability to adjust transport appears to be intrinsic to renal cells. This adaptation is rapid (detected within 5 hours), specific (without effect on sodium and calcium reabsorption), and sensitive (without detectable changes in serum Mg concentration). No extrinsic hormone controls the transport of magnesium separate from sodium and calcium handling [6].

The above findings support clinical observations that renal reabsorption is sensitively set to conserve magnesium according to the Mg status of the patient. These adjustments in renal Mg reabsorption are apparent irrespective of the cause that led to negative Mg balance – be it dietary restriction, malabsorption, or excessive renal excretion (loop diuretics).

It is important to collect a 24 hour urine specimen and calculate a 24 hour Mg clearance based on a concurrent sodium clearance. This test is of value for assessing both Mg status and Mg wasting by the kidney. If urinary clearance is low relative to dietary intake it may suggest intestinal malabsorption, whereas if urinary Mg clearance is high with a low serum Mg it may suggest a renal wasting disease [7].

In order to simplify things one can correlate the percentage of Mg retention in the Mg load retention test to the baseline urine fractional Mg excretion (Mg to creatinine ratio). In keeping with the state of Mg deficiency, one would expect a low baseline urine Mg-to-creatinine ratio to further indicate Mg retention and also to validate the test procedure, as the test procedure is considered invalid if the kidney is unable to conserve Mg.

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He had nothing to say and he said it.

Ambrose Bierce, American journalist (1842-1914), presumably about Oscar Wilde

Capsule

Cut and dried up

During inflammation, leukocytes are recruited to target areas in response to chemokines. However, cessation of this response is important for tissue healing and wound repair. McQuibban et al. propose that matrix metalloproteinases (MMPs) are key effectors of down-regulating chemokine activity. When the chemokine monocyte chemoattractant protein (MCP)-3 is cleaved by the MMP gelatinase A, it is converted from a chemokine receptor agonist to an antagonist. This conversion blocks the response of leukocytes to a variety of chemoattractants that utilize the same receptors.

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