Magnesium Prevents Chemotherapy Side Effects

By Alan R. Gaby, M.D.

Cisplatin is a platinum-based chemotherapy drug used to treat various types of cancer, including ovarian cancer, lymphoma, small-cell lung cancer, and sarcomas. It can cause a number of serious side effects, including nephrotoxicity, neurotoxicity, and hearing loss (ototoxicity). In addition, cisplatin treatment causes magnesium deficiency in up to 90% of patients who do not receive prophylactic magnesium supplementation, apparently because of renal tubular magnesium wasting. Magnesium deficiency severe enough to cause psychosis and seizures has been reported in some patients taking cisplatin.

The results of a new study indicate that prophylactic magnesium supplementation, in addition to preventing side effects that result directly from magnesium deficiency, can decrease the severity of cisplatin-induced renal damage without interfering with the anticancer effect of the drug. In fact, among cisplatin-treated cancer patients, those given magnesium had significantly slower disease progression and longer survival times, when compared with patients given a placebo.

In the new study, 40 women with epithelial ovarian cancer who were undergoing chemotherapy with cisplatin and paclitaxel every three weeks were randomly assigned to receive, in double-blind fashion, magnesium or placebo. Magnesium therapy consisted of 5 g of magnesium sulfate intravenously (with prehydration) before each cycle of chemotherapy and 500 mg of magnesium subcarbonate 3 times per day (equivalent to 370 mg/day of elemental magnesium) orally during the intervals between chemotherapy treatments. The placebo group received intravenous and oral placebos. The decrease in mean glomerular filtration rate (P < 0.01 to P = 0.03, depending on the method of assessment) and the increase in mean serum creatinine (P < 0.01) were significantly less in the magnesium group than in the placebo group. The median time to disease progression was nonsignificantly greater in the magnesium group than in the placebo group (20.9 months vs. 14.8 months; P = 0.78). The 4-year survival rate was 63% in the magnesium group and 36% in the placebo group (p < 0.3).

Some oncologists routinely administer magnesium to patients receiving cisplatin therapy, whereas others simply monitor serum levels and give magnesium only when hypomagnesemia develops. However, patients can have normal serum magnesium levels in the face of substantial intracellular magnesium depletion. Therefore, it would seem important to give magnesium to all patients who are receiving cisplatin therapy, not just those whose serum magnesium levels fall. Combining intravenous magnesium infusions on chemotherapy days with oral magnesium supplements between chemotherapy sessions is more effective than intravenous magnesium
alone for maintaining adequate magnesium status. Oral magnesium supplementation by itself does not appear to be sufficient to prevent cisplatin-induced magnesium deficiency. Although intravenous magnesium is usually administered in the form of magnesium sulfate, magnesium chloride is retained better in the body and is therefore preferable for intravenous therapy. Five grams of magnesium sulfate (the intravenous dosage used in the study cited above) is equivalent to 4 g of magnesium chloride (each provides 20 mmol of elemental magnesium).

In addition to preserving renal function and preventing adverse effects due to magnesium deficiency, maintaining adequate magnesium status might help prevent hearing loss resulting from cisplatin-induced ototoxicity. Like cisplatin, the aminoglycoside antibiotic gentamicin causes nephrotoxicity, ototoxicity, and magnesium deficiency secondary to renal magnesium wasting. In rats, a high-magnesium diet protected against the development of gentamicin-induced renal injury. Moreover, there is circumstantial evidence that magnesium deficiency plays a role in the pathogenesis of gentamicin-induced cochlear damage. A controlled trial could be done to determine whether prophylactic administration of magnesium would blunt the ototoxicity of cisplatin in humans. However, now that evidence supports vigorous magnesium supplementation for preventing cisplatin-induced renal damage, it would be unethical to devise a trial in which half the patients received less-than-vigorous magnesium supplementation.

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