Drug Monitor

ONLINE EDITION

Corticosteroids and Serum Glucose Levels

Inhaled corticosteroids (ICSs) are systemically absorbed, and studies have shown that their use is associated with decreased bone density, fractures, skin changes, myocardial infarctions, inflammation markers, and a decrease in glucose control. But are the drugs also associated with increased serum glucose levels?

To find out, researchers from VA Puget Sound Health Care System and University of Washington, both in Seattle, WA, identified all veterans receiving outpatient care from one of seven VA medical centers who had been prescribed an ICS, and were at least 80% adherent to their ICS dosing (determined by prescription fill dates), and had one or more glucose measurements documented during routine primary care. Of the 1,698 patients identified, 19% had self-reported diabetes.

After controlling for systemic corticosteroid use and other potential confounders (such as COPD visits and Charleston score), the researchers found no association between ICS use and serum glucose concentration in the overall cohort or in the patients without diabetes. In the patients with diabetes, however, every additional 100 µg of ICS dose was associated with an increase of 1.82 mg/dL in serum glucose concentration—a magnitude of association that might appear small but can be clinically meaningful over the range of ICS dosing, according to the researchers. They found that patients who were taking antiglycemic medications had an increase in serum glucose of 2.65 mg/dL for every additional 100 µg of ICS dose.

The researchers say that while the association between ICSs and serum glucose levels in patients with diabetes is consistent with previous findings about the biologic impacts of corticosteroids, nonbiologic explanations for the association also are possible. They note that as type 2 diabetes has been linked to reduced lung function, patients with more severe diabetes might have worse lung function and require higher doses of ICSs. (The researchers' proxy measures of symptoms and disease burden were similar among the patients with and without diabetes, however.) Another explanation for the association, they say, could be that patients who are adherent to higher doses of ICSs have worse pulmonary symptoms and, thus, are distracted from managing their diabetes appropriately.

Overall, the researchers conclude, clinicians "may want to more closely monitor serum glucose levels among patients with diabetes who were prescribed corticosteroids."

Source: *Am J Med.* 2009;122(5):472–478. doi:10.1016/j.amjmed.2008.09.048.

Predicting Responsiveness to Erythropoiesis-Stimulating Agents

Although erythropoiesis-stimulating agents (ESAs) can manage the anemia associated with chronic kidney disease successfully, some patients are hyporesponsive to the drugs. Their hyporesponsiveness can lead to very high—and, therefore, potentially ineffective or dangerous—ESA doses, and it may contribute to hemoglobin variability and have an association with increased mortality. Identifying predictors of ESA hyporesponsiveness, therefore, "may help improve anemia management and reduce hemoglobin level variability," say researchers from Harbor–University of California, Los Angeles (UCLA) Medical Center, Torrance; UCLA School of Public Health; DaVita Inc, El Segundo, CA; and Salem VA Medical Center, Salem, VA.

They set out to identify such predictors through a retrospective study of 38,328 surviving patients who underwent hemodialysis from July 1, 2001 to June 30, 2002 and received ESA continuously for at least three calendar quarters. The researchers looked for associations between the patients' degrees of ESA responsiveness and their laboratory values, comorbidities, and demographic data.

Their results indicated that responsiveness to ESA had a negative association with iron depletion, as demonstrated by the markers of serum ferritin and serum iron saturation (ISAT) ratios. Patients who were the least responsive to ESA were more likely to have serum ferritin levels less than 200 ng/mL and ISAT ratios of less than 20%, while patients who were the most responsive to ESA were more likely to have serum ferritin levels in the 500 to 1,200 ng/mL range and ISAT ratios greater than 30%. These results suggest that "achieving optimal iron status in patients with chronic kidney disease is an important endeavor," the researchers say.

In addition, significant ESA hyporesponsiveness was associated with protein-energy wasting; hyperparathyroidism; high-turnover bone disease; and such comorbidities as HIV, cancer, and heart failure. Female and African American patients were more likely to be ESA hyporesponsive.

The researchers conclude that optimizing responsiveness to ESAs among

patients with chronic kidney disease can enhance patient safety and reduce costs. They note that while intravenous iron, active vitamin D, and calcimimetics have showed short-term safety and benefit, more controlled trials are needed in these areas.

Source: *Am J Kidney Dis*. 53(5):823–834. doi:10.1053/j.ajkd.2008.12.040.