Drug Monitor

Steroids in Sepsis

Is there a use for steroids in the treatment of sepsis? And if so, what's the best dosage?

The answer may depend on whether you're looking at a study published before 1989 or after 1997, according to researchers from the National Heart, Lung, and Blood Institute, Bethesda, MD and Massachusetts General Hospital, Boston, MA. They evaluated findings from 14 randomized, controlled trials of glucocorticoid treatment in adults with sepsis: nine from before 1989 and five from after 1997. In eight of the pre-1989 studies, glucocorticoids not only were nonbeneficial but actually had a consistent harmful effect on patient survival. The post-1997 studies found the opposite. Why the difference?

Before 1989, the researchers say, shorter courses of high dose glucocorticoids were administered earlier in patients' septic episodes. After 1997, by contrast, steroids were given in lower doses, to more severely ill patients, as late as 72 hours after vasopressor therapy was initiated, and for a much longer time.

The researchers say they can't identify definitively the optimal dosage or timing of steroid therapy for patients who become septic. Based on their analysis, however, they advise that patients with established vasopressor-dependent septic shock of two to 72 hours' duration may have a better chance of shock reversal and survival if they're given a five- to seven-day course of hydrocortisone 200 to 300 mg/day, followed by a tapering off period of five to seven days.

Source: *Ann Intern Med*. 2004; 141:47–56.

Diabetes Control and Weight Loss Too?

Given the prevalence of overweight and obesity in patients with type 2 diabetes, the fact that most diabetes medications tend to promote weight gain is problematic. But hope may be close at hand. Results from three phase III trials, presented at the 64th Annual Scientific Sessions of the American Diabetes Association in June, suggest that the investigational drug exenatide may help control diabetes while actually aiding in weight loss.

Exenatide is the first in a new class of drugs, called incretin mimetics, that has emerged from research into hormones involved in gastrointestinal processes, including insulin production. This particular drug is a synthetic version of exendin-4, a hormone found in the saliva of the Gila monster. This lizard eats only four times a year—the rest of the time its pancreas shuts down. Exendin-4 is secreted to reactivate the pancreas when the lizard resumes eating.

In two randomized, placebo-controlled studies (one led by an investigator from the University of Texas Health Sciences Center, San Antonio and the other by an investigator from the International Diabetes Center, Minneapolis, MN), exenatide significantly reduced glycosylated hemoglobin (HbA_{1C}) levels from baseline in patients whose type 2 diabetes hadn't responded to traditional oral therapies. In addition, the drug was associated with significant and progressive weight loss and increased beta-cell function. Most adverse effects were mild or moderate, with nausea being the most common. Some hypoglycemia also was reported, but only one episode was considered severe.

Patients from both trials were invited to participate in a 52-week, open-label extension study in which they would receive exenatide 10 µg twice daily. In this study, the 51 patients who took exenatide plus metformin had an average reduction in HbA_{1C} of 1.1% and an average weight loss of 9.9 lb. Among the 77 patients who received exenatide plus metformin and a sulfonylurea, the average HbA_{1C} reduction was 1% and the average weight loss was 7.3 lb.

The drug's developers, Amylin Pharmaceuticals (San Diego, CA) and Eli Lilly (Indianapolis, IN), are submitting these data to the FDA, which will consider its appropriateness for patients with type 2 diabetes that doesn't respond to other oral medications. ●

Sources: Heartwire News Release. June 8, 2004.

American Diabetes Association News Release. June 6, 2004.