Low-Dose Steroids' Safety Wrongly Disparaged

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BERLIN — Long-term low-dose glucocorticoid therapy has gotten an undeserved bad rap in terms of side effects, according to a new report by an expert panel.

Systemic corticosteroids can be likened to fine wine, Dr. Johannes W.J. Bijlsma said in summarizing the panel's findings at the annual European Congress of Rheumatology.

"We think that a little bit of glucocorticoids, like a glass of wine, may be beneficial for many people, whereas a lot of glucocorticoids, like a bottle of wine, is helpful to no one," said Dr. Bijlsma, professor of rheumatology and clinical immunology at Utrecht (the Netherlands) University Medical Center.

He was one of a dozen prominent European and American rheumatologists and endocrinologists who met recently to review the literature on the side-effect profile of systemic corticosteroids at 7.5 mg/day or less when used for years at a time in patients with rheumatic diseases. All panelists had expertise in this area, having participated in randomized controlled trials or epidemiologic studies that addressed relevant safety issues. It seemed an appropriate time to address the side effects issue in light of recent evidence that low-dose steroids have a disease-modifying effect in rheumatoid arthritis, Dr. Bijlsma explained.

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The panelists' first key finding was that despite the fact that doses of 7.5 mg/day or less are what are most commonly used in the everyday treatment of rheumatologic diseases, there are few studies looking at the associated side effects. The panel focused on five trials totaling more than 750 patients with early rheumatoid arthritis randomized to low-dose steroids or placebo for at least 1 year. Two of the studies—the West of Scotland Early Rheumatoid Arthritis Corticosteroid Trial (WOSERACT) and a German trial—aren't yet published.

The data demonstrated that the incidence of side effects associated with long-term low-dose steroid therapy was much lower than what many clinicians believe it to be, based upon rates quoted in many review articles and textbooks, sources that generally extrapolate from studies involving far higher doses.

It is often stated that long-term glucocorticoid therapy is associated with up to a 20% increased rate of new-onset hypertension.

But in the three randomized trials of long-term low-dose therapy that addressed this issue, new hypertension wasn't significantly more frequent than with placebo: 19 cases in 281 steroid-treated patients, compared with 12 cases among 276 on placebo.

Similarly, new-onset diabetes occurred in just 2 of 185 patients on long-term glucocorticoid therapy at 7.5 mg/day or less, compared with 3 of 186 on placebo, Dr. Bijlsma said.

In the five randomized trials collectively, bone mineral density after 1-4 years of low-dose steroid therapy didn't differ from placebo. Nor was there any increase in fractures with steroid therapy in four of the five studies. The outlier was the Utrecht study. It showed an increase in fractures after 3 years of steroid therapy. But this trial began in 1990, well before physicians began routinely employing preventive measures including calcium and vitamin D supplements and bisphosphonates in steroid-treated patients, as became standard practice in the more recent trials.

"Osteoporosis remains a danger, but it has become a manageable danger," he said.

Treatment-related weight gain is a major concern among patients. The data documented a modest weight gain during 2 years of low-dose steroid therapy—an average of 1.4 kg more than with placebo. "But we should also recognize there's a catabolic process in early rheumatoid arthritis—and weight gain can be one of the signs patients are improving," Dr. Bijlsma said.

Low-dose corticosteroid monotherapy wasn't associated with increased gastrointestinal side effects.

However, when used in combination with NSAIDs, the resultant increase in peptic ulcer disease was greater than with NSAIDs alone. ■