LOW-DOSE PREDNISONE THERAPY IN RHEUMATOID ARTHRITIS: EFFECT ON VITAMIN D METABOLISM

JOSEPH E. ZERWEKH, RONALD D. EMKEY, and E. D. HARRIS, JR.

It has long been recognized that treatment with glucocorticoids can produce a significant loss of bone mass (1,2). The mechanism for this steroid-induced bone loss is not fully understood, but is associated with a marked decrease in intestinal calcium absorption and an increased urinary calcium excretion that frequently accompanies administration of supraphysiologic doses of glucocorticoids (3,4).

It has been proposed that steroid-induced alterations in vitamin D metabolism are responsible for the decrease in intestinal calcium absorption produced by glucocorticoid therapy. Reports to date have suggested that 25-hydroxyvitamin D (25[OH]D) concentrations are low (5) or normal in patients treated with corticosteroids (6,7). More importantly, it has been reported that the circulating concentration of 1,25-dihydroxyvitamin D (1,25$[OH]_2$D), the physiologically active form of vitamin D, is low (8) or normal (7,9–11) in subjects receiving glucocorticoids. These contradictory results are due, in part, to the dosage and length of glucocorticoid administration used in the previous studies. All studies to date have utilized a supraphysiologic dose of glucocorticoid.

From the Section on Mineral Metabolism, Department of Internal Medicine, University of Texas Health Science Center at Dallas, Southwestern Medical School, Dallas, Texas, and the Multipurpose Arthritis Center, Dartmouth-Hitchcock Medical Center, Hanover, New Hampshire.

Supported by National Institutes of Health grant AM16061, USPHS grant P60-AM20641, and Emkey-Weisberg Arthritis Associates, Inc., Reading, Pennsylvania and Boston, Massachusetts.

Joseph E. Zerwekh, PhD; Ronald D. Emkey, MD; E. D. Harris, Jr., MD.

Address reprint requests to Dr. J. E. Zerwekh, Department of Internal Medicine, University of Texas Health Science Center at Dallas, 5323 Harry Hines Blvd., Dallas, TX 75235.

Submitted for publication January 24, 1984; accepted in revised form April 12, 1984.

In order to assess whether long-term administration of low-dose glucocorticoids affects vitamin D metabolism, we measured the circulating concentrations of the vitamin D metabolites, calcium, phosphorus, alkaline phosphatase, and immunoreactive parathyroid hormone (iPTH) in patients with rheumatoid arthritis receiving 5 mg of prednisone per day for up to 6 months (12). Since the study was conducted as a double-blind trial, an age-matched group of patients with rheumatoid arthritis who received placebo served as the control group.

Patients and methods. The details of the patient population and study protocol have been previously reported (12). Briefly, 34 patients were initiated into a double-blind trial that lasted 32 weeks. Patients were admitted who were receiving nonsteroidal antiinflammatory drugs including salicylates, or who were receiving a constant dose of gold salts or D-penicillamine for at least 12 weeks prior to beginning the study. Excluded were patients with active peptic ulcer disease or rectal bleeding, diabetes mellitus, symptomatic idiopathic osteoporosis, or active renal or hepatic disease. Patients who had received intraarticular glucocorticoid injections, vitamin D, or calcium preparations less than 6 weeks prior to entering the study were also excluded. No patient had received oral glucocorticoids. No patient received vitamin D or calcium supplements during the course of this study.

Sixteen patients (mean age 53.9) made up the placebo group and received placebo for 32 weeks. The prednisone group, 18 patients (mean age 54.9), received 5 mg of prednisone per day every morning for 24 weeks. The placebo capsule was substituted for prednisone 24 weeks into the study. The final evaluation of patients in both groups was made at 32 weeks.