DREAM: Dual-Release Hydrocortisone Improves NK Cell Levels in AI

Written by Emma Hitt Nichols, PhD

A once-daily, dual-release oral formulation of hydrocortisone (HC) led to significant improvement in natural killer (NK) cell levels, body weight, and systolic blood pressure in patients with adrenal insufficiency (AI) compared with patients who received conventional therapy with either cortisone acetate or oral HC. Andrea M. Isidori, MD, PhD, Sapienza University of Rome, Rome, Italy, presented data from the DREAM trial [NCT02277587].

Treatment of AI with conventional glucocorticoid therapies is associated with early mortality compared with the general population, as a result of cardiovascular disease, infection, and malignancies. A potential mechanism for this is that conventional glucocorticoid therapies do not adequately mimic circadian cortisol release, resulting in inappropriate exposure time. The purpose of the DREAM trial was to determine if a once-daily, dual-release HC tablet (DR-HC) would more closely mimic natural circadian cortisol release compared with conventional therapies.

In the single-blind, parallel, phase 4 DREAM study, 80 patients were randomly assigned to continue their conventional therapy or receive DR-HC for 6 months; interim analysis was conducted on 58 patients. Primary AI was present in 21 patients, 22 patients had secondary AI, and 15 patients served as healthy controls. All patients with AI were treated with cortisone acetate or HC upon enrollment.

At baseline, patients with AI had significantly lower levels of NK cells compared with the healthy controls (5.5%±5.7% vs 10.9%±4.2%; $P<.01$) and a trend of greater classical monocyte levels (28.9%±17.0% vs 21.5%±3.5%; $P=.08$); T-cell and granulocyte levels were similar among both groups. All patients underwent biochemical, hematologic, and metabolic assessments at 0, 3, and 6 months.

At the 3-month analysis, patients with AI who received DR-HC experienced a significant increase in NK cells (+5.2±7.4; $P<.01$) compared with patients who received conventional therapy (cortisone acetate or HC; +0.8±5.9) or healthy controls (+1.0±3.4). The improvement occurred regardless of primary vs secondary AI or type of glucocorticoid treatment at enrollment. In addition, patients who received DR-HC experienced significant improvement in body weight ($P<.01$) and systolic blood pressure ($P<.05$), as well as a trend toward decreased HbA_{1c} levels ($P=.07$), compared with patients who received conventional therapy.

Prof Isidori stated that the difference in monocyte levels between the DR-HC and conventional therapy arms may be immune suppression as a result of a difference in bioavailability of the agents; however, the significant increase in NK cell levels in patients treated with DR-HC refuted this mechanism, suggesting that a chronobiological effect was the most likely explanation. In addition, Prof Isidori suggested that improvement in NK cell levels in patients with AI is an important finding because NK cells play a critical role in fighting infections and malignant cells.

VIDOS: Vitamin D Supplementation Does Not Improve the Incidence of Falls

Written by Emma Hitt Nichols, PhD

Elderly women who received 1600 to 3200 IU QD of vitamin D supplementation experienced a lower incidence of falls compared with women who received lower or higher doses of vitamin D or placebo, but overall differences were not significant. Shervin Yousefian, MD, Creighton University, Omaha, Nebraska, USA, presented data from the VIDOS study [NCT00472823].

Results regarding the effect of vitamin D supplementation on falls and physical performance in elderly patients have been inconsistent. The purpose of VIDOS was to evaluate the effect of vitamin D supplementation on falls and physical performance in vitamin D–deficient postmenopausal women living in the community.

In this interventional study, 163 postmenopausal white women were randomly assigned to receive vitamin D supplementation with 400, 800, 1600, 2400, 3200, 4000, or 4800 IU QD or placebo for one year. Women were required to be vitamin D deficient, with a serum 25-hydroxyvitamin D (25[OH]D) level of ≤20 ng/mL. The mean age of the 147 women who completed the study was 66.2 years and the mean body mass index was 30.3 kg/m^2. Patients were excluded if they had active nephrolithiasis, chronic kidney or liver disease, persistent hypercalcemia, or a medical condition prohibiting physical activity or if they had a disease or were receiving medication that affected calcium or bone metabolism. Accounting for data from 7-day food diaries, calcium supplementation was administered to achieve a daily calcium intake of 1200 mg.

In the placebo arm, patients who did not experience falls had greater serum levels of 1,25 dihydroxyvitamin D ($1,25[OH]_2D$) than patients who did experience falls. Patients who received vitamin D supplementation