

to also have HPT with Parathyroid Adenoma (PA) and Vitamin D Deficiency.

A 64-year-old female presented to the emergency room for social needs. She had not received medical care for the past 10 years and had known history of SC, previously treated with prednisone and methotrexate. She also noted a long-standing history of elevated calcium (Ca) up to 11 mg/dL. She was fasting for the past 1 month for spiritual reasons and was not taking any medications or supplements. Initial labs were significant for Ca of 13.2 mg/dL, Albumin 4.4 g/dL, ionized Ca 1.43 mmol/L. Creatinine was 1.1. EKG revealed T-wave inversions in V1, 2, 3. She received IV fluids and Ca improved to 11 mg/dL. HC was attributed to known history of SC. However further evaluation revealed parathyroid hormone (PTH) level high at 156 pg/mL, 25-OH Vit D level low at 8.5 ng/mL with normal 1,25 hydroxy Vit D levels at 46 pg/mL. Parathyroid sestamibi scan revealed a left parathyroid adenoma. Surgery was deferred because patient was asymptomatic and did not meet criteria for parathyroidectomy. On discharge, Ca levels remained stable and she was started on Ergocalciferol 50,000 units weekly.

HC can be either parathyroid mediated, non-parathyroid mediated, or due to medications. In primary HPT, the elevated PTH levels cause increased bone resorption through activated osteoclasts and increased intestinal Ca absorption. Malignancies involving solid tumors and leukemias can lead to HC through osteolysis and osteoclasts or PTH-related peptide. Thiazide diuretics increase renal Ca absorption that lead to mild HC which can be reversed when the medication is discontinued. Other endocrine disorders that can lead to HC include thyrotoxicosis-induced bone resorption, adrenal insufficiency and pheochromocytoma.

Management of hypercalcemia depends upon the level of Ca. Mild HC (Ca < 12mg/dL) is usually asymptomatic and improves with hydration. Asymptomatic or mildly symptomatic patients with chronic moderate HC (Ca 12-14 mg/dL) may not require immediate treatment. Severe HC (Ca >14mg/dL) is treated with IV hydration with normal saline (NS), calcitonin and zoledronic acid. Administration of calcitonin and NS results in substantial reduction in Ca within 12-48 hours.

Although, HC was initially attributed to SC, primary HPT and low 25-OH Vit D levels also contributed to HC in this patient. Thus, it is important to evaluate patients with known HC from sarcoid for other etiologies.

Reproductive Endocrinology

CLINICAL STUDIES IN FEMALE REPRODUCTION

I

Segesterone Acetate (SA) Serum Levels with a Statistical Model of Continued Use of the SA/Ethinyl Estradiol (EE) Contraceptive Vaginal System

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The novel, ring-shaped, contraceptive vaginal system (CVS; Annovera™), contains 103 mg of SA and 17.4 mg of EE, and delivers a mean dose of SA 0.15/EE 0.013 mg/day. The CVS was designed to last thirteen cycles in a 21 day-in/7 day-out regimen. Objectives of these analyses were to determine the amount of SA/EE remaining in the CVS after 13 cycles of use and to estimate the SA level in serum after 1 year of continuous use.

Residual SA/EE levels from CVS used by women (n=18) for 13 cycles of 21/7 regimen in a phase 3 clinical trial were further analyzed in vitro. Hypothetical SA level in serum after 1 year of continuous use was estimated using data from 39 women who participated in a 13-cycle pharmacokinetic study of the 21/7 CVS regimen. The serum data were used to construct a statistical model for the change in serum SA concentrations from cycle 1 to cycle 13. The data from each individual subject was modeled to estimate the serum SA level based on days of use. Each subject's model was then used to estimate the serum SA level after 364 days of continuous CVS use. The average of all 364-day values from valid models was then calculated.

After 13 cycles of a 21/7 regimen, the amount of SA/EE remaining in the CVS was 61.7 mg/14.0 mg (60%/80% of the original SA/EE load), which established the release of 0.15 mg SA and 0.013 mg EE per day for a total of 273 days. The model predicted that the mean serum SA level after 364 days of continuous use was 71 pmol/L with a lower limit of the 90% CI of 52 pmol/L.

A high percentage of SA/EE remained in the CVS after 13 cycles of use. Serum SA levels predicted by the model following 1 year of continuous use were similar to those previously observed (mean 73 pmol/L) at 1 year in a SA silicone implant trial in which there were no reported pregnancies at 1 year (Sivin et al, *Contraception*. 2004;69:137-144). No pregnancy or PK data with continuous use of the CVS is available at this time. Further study on the continuous use of the CVS is warranted.

Adipose Tissue, Appetite, and Obesity

NEURAL MECHANISMS OF OBESITY

The Role of the Focal Adhesion Kinase Family in Leptin Receptor Signaling

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Overweight and obesity are global concerns affecting nearly one third of the world population. These conditions are characterized by increased adiposity and are accompanied by a proportional increase in circulating leptin, an anorexigenic adipokine. Leptin is responsible for signaling peripheral energy status to the central nervous system to modulate food intake and energy expenditure. As such, neurons within the hypothalamus expressing the long isoform of leptin receptor (LepRb), a type I cytokine receptor, are primarily responsible for mediating the effects of leptin, which signal predominantly through