Metabolic Effects of DHEA

1: J Clin Endocrinol Metab 1997 Oct;82(10):3498-505

Effect of 12-month dehydroepiandrosterone replacement therapy on bone, vagina, and endometrium in postmenopausal women.

Labrie F, Diamond P, Cusan L, Gomez JL, Belanger A, Candas B.

Clinical Endocrine Research Unit, CHUL Research Center, Quebec, Canada.

The effect of 12-month dehydroepiandrosterone (DHEA) replacement therapy has been evaluated in 14 60- to 70-yr-old women who received daily applications of a 10% DHEA cream. Vaginal epithelium maturation was stimulated by DHEA administration in 8 of 10 women who had a maturation value of zero at the onset of therapy, whereas a stimulatory effect was also seen in all three women who had an intermediate vaginal maturation index before therapy. The estrogenic effect of DHEA observed in the vagina was not observed in the endometrium, which remained atrophic in all women. Most interesting, the bone mineral density significantly increased at the hip from 0.744 +/- 0.021 to 0.759 +/- 0.025 g/cm2 after 12 months of treatment ($P < 0.05$). These changes in bone mineral density were associated with a significant 20.0% decrease ($P < 0.01$) in plasma bone alkaline phosphatase and a 28% decrease in the urinary hydroxyproline/creatinine ratio. A 2.1-fold increase over the control value ($P < 0.01$) in plasma osteocalcin was concomitantly observed. The present data describe for the first time a series of medically important beneficial effects of DHEA therapy in postmenopausal women through transformation of the precursor steroid DHEA into androgens and/or estrogens in specific peripheral intracrine tissues without significant adverse effects. The stimulatory effect on the vaginal epithelium in the absence of stimulation of the endometrium is of particular interest because it eliminates the need for progestin replacement therapy. On the other hand, the stimulatory effect on bone mineral density accompanied by an increase in serum osteocalcin, a marker of bone formation, suggests stimulation of bone formation by the androgenic action of DHEA, a finding of particular interest for both the prevention and treatment of osteoporosis.

PMID: 9329392 [PubMed - indexed for MEDLINE]

2: J Endocrinol 1996 Sep;150 Suppl:S43-50

Metabolic effects of 12-month percutaneous dehydroepiandrosterone replacement therapy in postmenopausal women.

Diamond P, Cusan L, Gomez JL, Belanger A, Labrie F.

Laboratory of Molecular Endocrinology, CHUL Research Center, Quebec, Canada.

We have evaluated the effect of dehydroepiandrosterone (DHEA) replacement therapy in 60- to 70-year-old women ($n = 15$) who received a single daily percutaneous application of a 10% DHEA cream for 12 months. While anthropometric measurements showed no change in body weight, we observed a 9.8% decrease in subcutaneous skinfold thickness at 12 months ($P < 0.05$). This was confirmed by measurements of midthigh fat and muscle areas by computed tomography where a 3.8% decrease ($P < 0.05$) in femoral fat and a 3.5% increase ($P < 0.05$) in femoral muscular areas were observed at 12 months. There was no significant change in abdominal fat measurements but the waist-to-hip ratio was only 0.83 at the onset of treatment. These changes in body fat and muscular mass were associated with a 11% decrease ($P < 0.05$) in fasting plasma glucose and a 17% decrease ($P < 0.05$) in fasting insulin levels. Treatment with DHEA had no adverse effect on the lipid or lipoprotein profile. In fact, an overall trend towards a decrease in total cholesterol and its lipoprotein fractions was observed. Plasma triglycerides were not affected. Plasma high-density lipoprotein (HDL) cholesterol decreased by 8% but the ratio HDL/cholesterol was unchanged by DHEA treatment because of a parallel decrease in total cholesterol. The index of sebum secretion showed a 73% increase ($P < 0.05$) during the 12 months of DHEA therapy followed by a return to pretreatment

values 3 months after cessation of therapy. At the same time, sex hormone-binding globulin levels decreased ($P < 0.05$) during treatment and returned to pretreatment values 3 months after the end of therapy. Serum gonadotropins were not changed by DHEA treatment. Although not significant, we observed a tendency towards an elevation in serum GH levels. Values of serum IGF-I remained unchanged while plasma IGF-binding protein-3 levels significantly decreased ($P < 0.05$) during treatment and returned to pretreatment values after cessation of DHEA therapy. The present data clearly indicate the beneficial effects of DHEA therapy in postmenopausal women through its transformation into androgens and/or estrogens in specific intracrine tissues without any significant side effects.

PMID: 8943786 [PubMed - indexed for MEDLINE]

3: J Clin Endocrinol Metab 1994 Oct;79(4):1086-90

Changes in serum concentrations of conjugated and unconjugated steroids in 40- to 80-year-old men.

Belanger A, Candas B, Dupont A, Cusan L, Diamond P, Gomez JL, Labrie F.

Laboratory of Molecular Endocrinology, CHUL Research Center, Quebec, Canada.

It is well recognized that aging in men is accompanied by a decline in the serum levels of some adrenal and testicular steroids, but little or no attention has focused on the multiple steroid metabolites that are formed by steroid-converting enzymes in target tissues. In the present study, we have examined in detail the serum concentrations of a large series of adrenal and testicular steroids and their most significant metabolites produced in intracrine peripheral tissues. The serum concentrations of 26 conjugated and unconjugated C21-, C19-, and C18-steroids were measured in 2423 men aged 40-80 yr. The serum concentrations of the major circulating adrenal C19-steroids, namely dehydroepiandrosterone (DHEA) and its sulfate (DHEA-S), androst-5-ene-3 beta, 17 beta-diol and its sulfate, and androstenedione, decreased by about 60% between the ages of 40-80 yr. The small decrease in the serum concentrations of progesterone and pregnenolone in the presence of increased levels of cortisol and markedly decreased levels of DHEA, androst-5-ene-3 beta, 17 beta-diol, and their polar metabolites suggests that adrenal 17,20-lyase is particularly affected by aging. In addition to a marked decline in the serum concentrations of adrenal C19-steroids, a smaller, but significant, decrease occurred in serum testosterone. However, serum dihydrotestosterone levels remained constant, but the glucuronidated derivatives of dihydrotestosterone metabolites (androstane-3 alpha, 17 beta-diol glucuronide, androstane-3 beta, 17 beta-diol glucuronide, and androsterone glucuronide) were reduced by 45-50%, suggesting that 5 alpha-reductase activity in peripheral tissues may show a compensatory increase during aging. Analysis of the fatty acid esters of DHEA (DHEA-FA) also revealed that these nonpolar steroids markedly decrease between 40-80 yr of age, although such a decrease in DHEA-FA levels was smaller than that in DHEA and DHEA-S, suggesting that the formation of DHEA-FA may be specifically increased during aging. In summary, the present study suggests that in contrast to the marked decline in activity of steroidogenic enzymes in the adrenals and the small decrease in the testis, the activity of the steroid-converting enzymes present in peripheral tissues does not decrease during aging. In fact, the marked decrease in DHEA formation by the adrenals leads to a decrease of about 50% in total androgens in men between the ages of 40-80 yr. Such a decrease probably affects many physiological processes during aging.

PMID: 7962278 [PubMed - indexed for MEDLINE]

4: Eur J Appl Physiol Occup Physiol 1989;58(7):699-704

Trait anxiety, submaximal physical exercise and blood androgens.

Diamond P, Brisson GR, Candas B, Peronnet F.
Department of Physiology, Faculty of Medicine, Laval University, Quebec, Canada.

This study evaluates the relationship between trait anxiety and both androgen and gonadotrophic hormone levels at rest and during severe physical exercise. Twelve volunteers were selected among 160 untrained male collegial

students and classified as anxious (N = 6) or non-anxious (N = 6) subjects according to their scores on three trait-anxiety tests (STAI, IPAT, 16 PF). Serum delta 4-androgen (testosterone and delta 4-androstenedione), delta 5-androgen (DHEA and DHEA-SO4) and gonadotrophin (LH and FSH) concentrations were measured by radioimmunoassay before, during and after 20 minutes of intensive bicycle exercise (80% of maximal heart rate). Results indicate significantly lower serum delta 4-androgens in anxious subjects before exercise. However, for each subject and irrespective of his anxiety level, all measured serum androgen concentrations increased significantly during exercise, although delta 4-androstene-dione remained lower in anxious subjects than in non-anxious ones. Serum LH concentrations (but not FSH) were significantly higher in anxious subjects throughout the observation periods. However, exercise induced in each subject a significant decrease in the serum level of both gonadotrophic hormones. The results suggest that trait anxiety level may constitute an important factor that affects both pre-exercise and exercise serum androgen concentrations in untrained subjects.

PMID: 2525467 [PubMed - indexed for MEDLINE]