

The effect of advanced aging on adrenal hormone levels on sexual dimorphism

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ABSTRACT

Ageing and adrenal function have attracted a lot of attention recently. The plasma levels of cortisol, De-hydroepiandrosterone (DHEA), DHEA-sulfate (DHEAS), and the molar ratio of cortisol/DHEAS in 50 years to 80 years old community-dwelling people are examined in this cross-sectional research. In samples collected between 7:30 hours to 11:00 hours from 857 males and 735 postmenopausal women who did not use steroid hormones, plasma hormone levels were measured. ANOVA with two factors (gender and age) was used to compare hormone levels in 10-year age groups. Overall, women had 40% lower levels of DHEA and DHEAS (collectively DHEA(S)) and 10% higher levels of cortisol than males, resulting in a 1.7-fold higher cortisol/DHEAS molar ratio for women (both, $P < 0.001$). With age, both men and women's cortisol levels gradually increased (20% overall) (both, $P < 0.01$). While both men and women saw a 60% reduction in DHEA(S) levels and a 3-fold increase in the cortisol/DHEAS ratio over the course of the 40-year age span (all $P < 0.001$), the patterns of the changes varied (all P ,

0.01 for interaction). With each passing decade, the amount of change in DHEA(S) for males decreased in a curvilinear pattern. In contrast, DHEA(S) levels in women fell 40% from the 50s to 60s, were unvarying from 60 years to 80 years of age, and declined an additional 18% in the 80s. The cortisol/DHEAS ratio increased in a linear fashion for men, but was flat during 60 years to 80 years of age range for women. Despite these differences in the effect of aging, levels of DHEA(S) remained lower and cortisol and the cortisol/DHEAS ratio higher, in women than men throughout the 50 years to 89-years age range. These results were independent of adiposity, smoking, and alcohol consumption. In conclusion, DHEA(S) levels are lower and cortisol levels are greater in women than in males among older, healthy people. Although it remains into advanced age in both men and women, the sexually dimorphic pattern of the age-related fall in adrenal androgens is present. Cortisol levels, however, exhibit a comparable, linear rise with age in both men and women. These findings may have significant ramifications for a variety of age-related processes that display gender variations, such as cardiovascular disease, bone metabolism, and brain function.

Key Words: Postmenopausal women hypoestrogenism; Dimorphic; Cortisol levels

INTRODUCTION

Endogenous adrenal hormone levels have been linked to specific gender differences in cardiovascular disease, cognitive function, mood and bone metabolism in older adults, according to epidemiological studies. This finding raises the possibility that adrenal hormones play a role in determining gender differences in disease and disability. Adrenal steroid hormone plasma levels are adversely affected by ageing. Dehydroepiandrosterone (DHEA) and DHEA-sulfate (DHEAS) [collectively DHEA(S)] concentrations in the adrenals dramatically decrease with age and without corresponding changes in baseline cortisol levels. 24 hours investigations have recently shown greater cortisol levels in elderly than younger persons, challenging the idea that glucocorticoid activity is not affected with ageing. The relevance of adrenal androgens as precursors to sex hormones in older people is known, even though their precise physiological function is still unclear. While adrenal androgen precursors generate nearly all of the active estrogens in postmenopausal women, peripheral conversion of DHEA(S) produces 50% of the androgens in older me-

n DHEA(S) may have immunostimulating, cardioprotective, antidiabetic, and antiobesity characteristics in addition to acting directly as a neurosteroid. A increasing body of research supports the idea that chronically high cortisol levels may cause hippocampus shrinkage and cognitive decline as people age. Cortisol is a key component of the Hypothalamic Pituitary Adrenal (HPA) axis response to stress. Cortisol also has a variety of metabolic effects, such as controlling lipolysis and the buildup of visceral fat. It is obvious that alterations in adrenal endocrine function with age may have profound physiological implications. According to our knowledge, no population-based studies have evaluated the endogenous levels of adrenal steroid hormones in both men and women at the same time, employing older individuals who lived in their community and controlling for important lifestyle factors. The plasma levels of cortisol, DHEA and DHEAS as well as the molar ratios of cortisol/DHEAS and DHEAS/DHEA in 1592 community-dwelling men and women were examined in this cross-sectional investigation. 50 years to 89 years old participated in a follow-up clinic visit between 1984 to 1987 among middle- to upper-middle-class Caucasian people. Standardized questionnaires were used to gather data on current

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medication usage, physical activity (three or more days of exercise per week), cigarette smoking (yes/no), and alcohol intake (number of drinks of beer, wine, or liquor converted to milliliters of alcohol per week). Examining tablets and prescriptions presented to the clinic specifically for that reason allowed for the validation of medication use. The final day of menstruation, type of menopause (natural or surgical), and, in the event of hysterectomy, the number of ovaries removed during surgery, were all questions given to the participants. Current hormone users were excluded from this investigation; past and present usage of estrogen, either alone or in conjunction with a progestin, were determined. Body mass index (BMI) (kg/m²) and Waist to Hip Ratio (WHR) were employed as indicators of obesity and fat distribution, respectively, while height, weight, and waist and hip girth were also assessed in the clinic with participants wearing light clothes and no shoes. After a requested 12 hours fast, blood samples for hormone assays were drawn through venipuncture between 7:30 hours to 11:00 hours.

Plasma was then separated and frozen at 270°C. In the endocrinology research lab of the Department of Reproductive Medicine, University of California, steroid hormone levels were assessed on first-thawed samples 6 years to 9 years later, between 1992 and 1994. (San Diego, CA). After solvent extraction and celite column chromatography, DHEA levels were evaluated by RIA; DHEAS and cortisol levels were assessed by direct RIA. The intra- and interassay coefficients of determination for cortisol were 17 mmol/L, 5.4%, and 10.5%, whereas the assay sensitivities for DHEA, DHEAS, and 0.22 mmol/L were 0.14 mmol/L, 6.1% and 7.1%, respectively.

RESULT

89% of women and 72% of males were 65 years of age or older, and the mean age for the 735 women was higher (P 0.001) than that for the 857 men. In addition to having smaller waists and WHRs than men (all P 0.003), women had a lower mean BMI. Women consumed less alcohol than males (P, 0.001) and engaged in less frequent exercise (three or more times per week) (P, 0.003) than men.