Evidence for Age-Related Change in Plasma 19-Hydroxyandrostenedione

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Abstract

The steroid, 19-hydroxyandrost-4-ene-3, 17-dione (19-hydroxyandrostenedione, 19-OH-A-dione) has been known to enhance the mineralocorticoid action of aldosterone. To investigate the age-related change in the plasma 19-OH-A-dione concentration, plasma 19-OH-A-dione, androst-4-ene-3, 17-dione (A-dione), aldosterone and cortisol of 38 non-hypertensive healthy subjects (18 young men and 20 aged men) measured by specific radioimmunoassays. The basal plasma 19-OH-A-dione and A-dione concentration in aged men was significantly lower than in young men (P<0.01). Moreover, there was found to be a positive correlation between plasma 19-OH-A-dione and A-dione (P<0.01). On the other hand, plasma aldosterone and cortisol in aged men showed a tendency to decrease, but no statistical significance compared to young men was observed. This study demonstrated that there was an apparent age-related decrease not only in plasma A-dione, but also in plasma 19-OH-A-dione, an amplifier of aldosterone action.

The C19 steroid, 19-hydroxyandrost-4-ene-3, 17-dione (19-hydroxyandrostenedione, 19-OH-A-dione) possesses the amplifying effect of the action of aldosterone (Sekihara, 1983a). The administration of this steroid caused salt-retention and hypertension in rat (Sekihara, 1983a; Manabe et al., 1984). An aromatase inhibitor, delta 1-testololac-tone enhanced the hypertensinogenic action of 19-OH-A-dione by inhibiting the degradation of 19-OH-A-dione (Sekihara et al., 1987). Sekihara et al. (1985) showed that 19-OH-A-dione was present in human circulating blood. Moreover, the plasma 19-OH-A-dione concentration in pregnant women with hypertension (Martin et al., 1985) and in hypertensive patients (Sekihara, 1983b) were reported to be higher than that in non pregnant and non hypertensive subjects. It is well known that plasma A-dione

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decreases with age in man. In order to examine the age-related change in 19-OH-A-dione in human plasma, 19-OH-A-dione and other steroids were measured by radio-immunoassay (RIA) in young and aged men.

Materials and Methods

Materials
19-OH-A-dione and A-dione were obtained from Sigma (St. Louis, Mo, U.S.A.) and [6, 7-3H]-19-OH-A-dione (1.665 TBq/mmol; 45.0 Ci/mmol) and [1, 2-3H(N)]-A-dione (1.517 TBq/mmol; 41 Ci/mmol) were purchased from New England Nuclear Corp. (Boston, MA, U.S.A.).

Subjects
Eighteen young men (age: 22.4±2.1 years) and 20 aged men (age: 74.2±3.6 years) participated in this study. All subjects enjoyed healthy free living without obesity or hypertension. No salt-restricted diet was given to any subject. Blood samples were obtained between 0800 and 0900 h after an overnight fast. Plasma was separated immediately at 4°C and stored at −20°C until assayed.

Assays of Steroid Hormones
Plasma 19-OH-A-dione was assayed by RIA as described elsewhere (Higuchi et al., 1989). 19 OH-A-dione in diethyl ether treated plasma extract was separated from A-dione and dehydroepiandrosterone by LH-20 column chromatography with n-heptan-chloroform-ethyl alcohol (50:50:1, vol/vol/vol). The fraction corresponding to 19-OH-A-dione was collected and measured by RIA using the anti-serum to 19-OH-A-dione-3-oxime-BSA kindly supplied by Dr. H. Sekihara of the University of Tokyo (Sekihara et al., 1985). Intra- and interassay coefficient variation (CV) values were 15% and 18%, respectively. Plasma aldosterone and cortisol were measured with RIA kits obtained from LeCommissariat a l'Energy Atomic, France and Daiichi Radioisotope, Tokyo, respectively. Plasma A-dione was measured by a specific RIA as described previously (Nawata et al., 1985). Anti-A-dione serum was obtained from Endocrine Sciences (Tarzana, CA, U.S.A.).

Statistical Methods
All values were expressed as the mean±SD. Student's t-test was used for statistical assessments. Correlation coefficients were calculated by Pearson correlations.

Fig. 1. Basal plasma A-dione and 19-OH-A-dione values in young and aged men.
Plasma A-dione and 19-OH-A-dione were determined with specific RIAs in 18 young men and 20 aged men. Asterisks (P<0.01) indicate significant difference compared with the corresponding values for the young men. Values are mean±SD.
Results

Basal level of plasma A-dione and 19-OH-A-dione in young and aged men

Basal levels of plasma A-dione and 19-OH-A-dione in young (n=18) and aged (n=20) men are shown in Fig. 1. The plasma A-dione concentration (Fig. 1 left) in aged men (76.2±35.7 ng/dl) was significantly lower than in young men (161.8±33.7 ng/dl). Plasma 19-OH-A-dione (Fig. 1 right) in aged men (11.9±7.5 ng/dl) was also significantly lower than in young men (28.2±11.5 ng/dl). Fig. 2. shows a significant correlation between basal values for plasma 19-OH-A-dione and A-dione.

Basal plasma aldosterone and cortisol in young and aged men.

Basal plasma aldosterone and cortisol in aged men were compared with those in young men (Fig. 3). Plasma aldosterone (Fig. 3 left) and cortisol (Fig. 3 right) were 73.9±29 pg/ml, 10.4±3.8 μg/dl in aged men, and 88.1±31.6 pg/ml, 11.3±3.8 μg/dl in young men respectively. Plasma aldosterone and cortisol tended to decrease in aged men, but no significance could be demonstrated.

![Fig. 2. Relationship between basal plasma 19-OH-A-dione values and those for A-dione.](image)

![Fig. 3. Basal plasma aldosterone and cortisol values in young and aged men.](image)

Plasma aldosterone and cortisol were examined with specific RIAs in 18 young men and 20 aged men.
Discussion

We earlier demonstrated an age-related decrease in plasma A-dione as well as dehydroepiandrosterone sulfate, a major adrenal androgen in humans (Akamine et al. 1974). Recently, Sekihara et al. proposed that 19-OH-A-dione is present in human plasma irrespective of the source of synthesis, and acts as an amplifier of mineralocorticoid action of aldosterone (Sekihara 1983a). It is intriguing to search for the age-related change in the plasma 19-OH-A-dione concentration because this steroid may be a product of the adrenal zona reticularis cells, in which the steroidogenic function declined to senescence in human subjects. In the present study, we found an age-related decrease in plasma 19-OH-A-dione (Fig. 1 right). This finding suggests that the plasma concentration of 19-OH-A-dione may be another age-affected adrenocortical steroid in addition to adrenal androgens.

The organs from which plasma 19-OH-A-dione is derived are not well documented. Sekihara et al. (1985) proposed that 19-OH-A-dione may be produced by the human adrenal gland, based on the evidence that the adrenal vein were an order of magnitude higher than those in the inferior vena cava, and its release was regulated by ACTH and angiotensin II. Recently, we obtained evidence that 19-OH-A-dione was secreted directly by adrenal cells in a primary monolayer culture (Higuchi et al., 1989). Although 19-OH-A-dione is apparently produced by the adrenal glands, whether this steroid is also produced by any other organ remains to be clarified. In the present study, we found a positive correlation between plasma 19-OH-A-dione and A-dione (Fig. 2). Martin et al. (1986) also reported a significant positive correlation between plasma 19-OH-A-dione and A-dione concentrations in hypertensive pregnant women. As plasma A-dione is derived from the adrenal gland and gonads, it is possible that 19-OH-A-dione is produced by the gonads or other tissues retaining 19-hydroxylase activity (Ohigashi et al. 1989).

In this study, plasma aldosterone and cortisol tended to decrease in aged men, but no significance could be demonstrated. These findings are consistent with the previous observation that the basal concentration and response to ACTH of plasma cortisol and aldosterone in aged men are essentially the same as those in young men (Ohashi et al., 1986).

To sum up, we demonstrated an age-related decrease in basal plasma 19-OH-A-dione, and also its positive correlation with plasma A-dione.

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Reference


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