SERUM DEHYDROEPIANDROSTERONE AND LIPID PEROXIDES IN HUMAN VOLUNTEERS OF DIFFERENT AGE GROUPS

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ABSTRACT

The objective of the present study was to evaluate the changes in serum dehydroepiandrosterone (DHEA) and lipid peroxide levels during ageing in human subjects. Random blood samples were collected from a total of 128 apparently normal human volunteers of both sexes, whose age ranged between 21- 70 years. The subjects were divided into groups of a decade years of age difference. Serum levels of dehydroepiandrosterone (DHEA), lipid peroxides as malondialdehyde (MDA), and insulin were analysed in all the subjects recruited in the study. In the present study there was decrease in serum DHEA levels with age (11.30 to 7.99 ng/ml). However the differences were significant only after 50 years up to 70 years. Serum MDA levels of these subjects were higher (3.91 to 4.74 ng/ml) as compared to the values reported earlier (2.64 to 3.94 ng/ml). The serum MDA levels also showed an increasing trend with age but the increase was significant only in the 40-50 years age group and values plateaued off at later ages. The MDA and DHEA levels in women in general were lower than in men and this could be due to female hormones, which are known to protect lipid against peroxidation. There was a significant negative correlation between age and DHEA ($r = -0.311$ $P < 0.05$) and positive correlation between MDA and age ($r = +0.405$ $P < 0.01$). No significant differences were seen in serum insulin, albumin and total protein levels. These preliminary findings support the possible utility of DHEA and MDA as markers for chronological ageing.

KEY WORDS

Chronological ageing, lipid peroxides, MDA, DHEA, Radioimmunoassay.

INTRODUCTION

Ageing is a multifactorial, physiological process and age related metabolic changes could be corrected or delayed (1,2). There are various theories proposed to explain the process of ageing (3) and the most popular ones are endocrine and free radical theories (4,5). The hormone dehydroepiandrosterone (DHEA) and its sulfate ester dehydroepiandrosterone sulfate (DHEAS) are the major secretory steroidal products of the adrenal gland (6,7). There are reports stating that there is a progressive decline in the endogenous production of DHEA with age in humans (8). Epidemiological data support beneficial effects of DHEA. Low serum DHEA levels are correlated with increased cardiovascular morbidity in men (9), breast cancer in women (10) and the decline of

immunocompetence during ageing (11). Data from other parts of the world indicate that, circulating levels of DHEA decrease with chronological ageing as compared to other hormones (12). It is also reported that peak circulating level of DHEA in humans is seen between 21-30 years of age (12).

Another well accepted theory of ageing has been the free radical hypothesis (4,13). Free radicals are known to cause tissue damage, and such injuries can lead to several diseases (14). During ageing, oxidative damage and free radical load increases and their scavenging activity gets decreased (4). Studies indicate that serum lipid peroxide levels tend to increase with age in humans (3). However, the literature indicates that data available so far is only from the west and there is hardly any data of this kind from India.

The characteristic differences between the Indian and western subjects of comparable age, such as body weight, nutritional deficiency status are very well known (15). It would therefore be important to validate whether serum MDA and DHEA levels are useful as markers for chronological ageing in Indian subjects. Hence, a pilot study has been conducted in healthy adult human subjects of different age groups (21-70) to validate the usefulness of the above biochemical parameters as markers for chronological ageing.

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MATERIALS AND METHODS

Subjects: Random venous blood samples were collected from 128 apparently normal human subjects (61 males and 67 females). Their age ranged between 21-70 years. The volunteers selected were the attendants accompanying the patients to the out patient wards of a local general hospital. The age was assessed in literate subjects based on the date of birth and in illiterate subjects it was done by verification of the subjects age at menarche, marriage, birth of the first child etc. Thus there could be a variation of about 2 or 3 years in such assessment of age. A questionnaire on ageing and morbidity was administered to each subject to assess his/her health status and computation of his/her BMI. Subjects who were normal and not suffering from any chronic diseases were only recruited for the study. Subjects with chronic disease and those on long-term medication were excluded from the study. Purposive samples of blood were collected to get a minimum of 20 subjects in each age group.

Serum lipid peroxide (MDA) levels were determined as per the method described by Yagi (16). Serum DHEA levels were measured using the radioimmunoassay kit purchased from Diagnostic Products Corporation, Los Angeles, USA, according to manufacture instructions. Serum insulin levels were measured by radioimmunoassay as described by Berson and Yalow (17) with slight modifications (18). Serum protein and albumin levels were measured using dye-binding methods (19,20). Comparison of serum DHEA and MDA levels among different age groups was done by analysis of variance with multiple comparison procedure and the relationship between age, MDA, DHEA and other biochemical parameters was assessed by correlation analysis using the Windows based statistical package SPSS version 10.0.

RESULTS

The age of the subjects enrolled in the study ranged from 21 to 70 years and they were divided into groups with age intervals of 10 years. Nutritional status of the subjects was assessed by anthropometry and BMI was computed from these measurements. The BMI values of the subjects ranged between 18.5 and 25.0, indicating the normal nutritional status. Increase in body weight was seen from 21 years of age, up to 50 years of age. No significant differences were seen in serum insulin, albumin and total protein levels with age.

Serum DHEA and MDA levels in subjects of different age groups are given in Fig. 1. Plasma DHEA levels decreased progressively with age but the decrease was significant only after 50 years of age. In 50-70 years age group significant ($p < 0.05$) decrease in

serum DHEA levels were observed as compared initial values (11.30 ± 0.42 to 7.99 ± 1.20 ng/ml). However, there were no significant differences between the sexes at any age group in serum DHEA levels (Fig 2). On the other hand serum MDA levels were higher in men throughout the age range of 20-60 years (Fig. 2) where as at 61-70 years of age, serum MDA levels were comparable between both sexes. Serum lipid peroxide (MDA) levels increased with age up to 50 years from 3.91 ± 0.23 at 21-30 yrs to 4.74 ± 0.17 ng/ml at 41-50 yrs and the increase was significant ($P < 0.05$) only in the 41-50 years age group. The levels remained more or less constant there after, although they were also significant compared to basal values found in younger age groups (21-30 yrs). There was a significant negative correlation between the age of subjects and serum DHEA levels ($r = -0.311$, $P < 0.05$) and a positive correlation between the age and serum MDA levels ($r = 0.405$, $P < 0.01$).

Fig. 1: Age-dependent changes in serum DHEA and MDA levels in humans of different age groups. Values are mean $\pm$ SE. * $P < 0.05$ as compared to initial values.

Fig. 2: Sex dependent changes in DHEA and MDA levels in different age groups. Values are mean $\pm$ SE

DISCUSSION

Studies from different parts of the world indicate that levels of DHEA and serum lipid peroxide (MDA) change with chronological age (12,13). However, literature on these aspects is not available from India. Keeping in view the large differences that exist between Indian subjects and those of comparable age and sex from the west, the present pilot study was conducted to assess the utility of these biochemical parameters as markers for chronological ageing in Indian subjects.

Present data indicates an age dependent increase in serum MDA levels in subjects of 40-50 years of age, which is in agreement with data published from the west (8,12). MDA levels remained more or less constant after fifty years. Further, age dependant increase in serum MDA levels was observed even after 50 years of age and the values were significant as

compared to basal values (21-30 yrs age). Interestingly, serum MDA levels observed in the present study are higher than those reported in Japanese subjects of similar age (3). This finding probably suggests greater oxidative stress in the Indian subjects of the present study, as compared to Japanese. The lower levels of serum MDA in women than men, observed in this study could be due to known protective effects of female hormones, against lipid peroxidation (21).

Circulating levels of DHEA are reported to decrease with age (8). In the present study although there was an age dependent decrease in serum DHEA levels as reported earlier (12), the differences were significant from basal values only at 51-70 years age. In subjects above 50yrs of age our findings are in partial agreement with those of sulcova et al (22) who could not find an age dependent decrease in serum DHEA levels from a screening of 160 normal subjects of 0-60 years of age. Nevertheless present data confirm the earlier observation that the serum DHEA concentrations are maximum at 21-30 years age group (12) and the DHEA concentrations observed in the present study are in good agreement with the reported normal ranges (23). There were no sex differences observed in DHEA levels. This observation is in agreement with Nafziger et al (8) where the rate of DHEA decline was directly related to age but not sex.

Hyper insulinemia is known to decrease serum DHEA concentrations (24). Hence serum insulin levels were assessed in the present study. The present data did not show any association between DHEA and serum insulin levels in subjects of different age groups. Overall, the present data indicates for the first time to the best of our knowledge an age dependent increasing trend in serum MDA and decrease in DHEA levels in adult Indian volunteers of different age group. That in the present study a significant increase in MDA levels was seen in subjects after 40 years confirms the higher oxidative stress with advancing age. Based on the significant correlation observed between age and serum DHEA or MDA, it appears these parameters may be useful as markers for chronological ageing in Indian subjects

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