Dehydroepiandrosterone sulfate levels in women

Relationships with body mass index, insulin and glucose levels

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ABSTRACT

Objectives: Dehydroepiandrosterone (DHEA) and DHEA-sulfate (DHEA-S) are the most abundant steroids in human plasma. Previous studies have shown that administration of DHEA-S is more effective than DHEA in reducing adipose tissue mass and cellularity in rats. Another study suggested that maintaining high levels of DHEA-S might prevent the development of obesity. Therefore, this study aims to determine the relationship of plasma dehydroepiandrosterone sulfate (DHEA-S) levels with respect to obesity, fasting insulin and glucose levels in a cohort of obese and normal weight healthy Saudi women.

Methods: This study was carried out at King Abdul-Aziz University Hospital, Jeddah, Kingdom of Saudi Arabia during the year 2001. A total of 65 healthy volunteers between 19-30 years of age with body mass index (BMI) of 15.35-38.30 kg/m^2 were grouped into 26 young obese females of BMI >27 kg/m^2 and 39 young lean females of BMI <27 kg/m^2. Weight, height, waist and hip circumference, fasting blood glucose, insulin and DHEA-S levels were measured.

Results: Dehydroepiandrosterone-S levels were found lower in the obese group than in the lean women. In all subjects, DHEA-S levels were related negatively with BMI ($p=0.02$, correlation co-efficient [r]=-0.25) and hip circumference ($p=0.03$, r=-0.27). In the obese group, DHEA-S levels showed a significant positive relationship with insulin ($p=0.03$, r=0.43). No significant relationship was found between DHEA-S and glucose levels in considering either the whole group or the obese women.

Conclusion: Hip circumference, as a corollary for peripheral obesity, was better associated with DHEA-S than the waist circumference or waist-to-hip ratio. The data indicated that BMI and hip circumference are important factors in explaining DHEA-S variability. Insulin could have an independent regulatory effect on DHEA-S secretion, but glucose metabolism is not related.

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Dehydroepiandrosterone sulfate (DHEA-S) is the most abundant circulating steroid hormone in humans.[1,2] It is generally metabolically inactive and converts to DHEA by ubiquitous tissue steroid sulfatases, and therefore, presumably serves as a reservoir for DHEA.[3,4] Dehydroepiandrosterone regulates a number of steroid hormones including the sex hormones (estrogen, testosterone) and the stress hormones (cortisol, norepinephrin).[5] It has been suggested that DHEA and DHEA-S have some

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protective effect against cardiovascular disease, obesity, hypercholesterolemia, cancer, Alzheimer's disease, insulin-dependent diabetes mellitus and other immune-modulated diseases.[6-10] Furthermore, DHEA-S has been suggested to help slow the aging process and improve memory.[11,12] Recently, Yasushi et al[13] reported that DHEA-S levels were decreased in patients with chronic heart failure (CHF) in proportion to its severity and that oxidative stress is associated with decreased levels of DHEA-S in patients with CHF.[13] Low circulating DHEA-S was also found to be associated with hypothyroidism in men.[14] The exact mechanism of action and regulation of DHEA-S is incompletely understood. It has been proposed that insulin regulates DHEA-S metabolism. Insulin appears to reduce circulating DHEA-S in men, but these effects were not observed in women.[15-20] Evidence has suggested that insulin's regulation of DHEA-S metabolism might be sex specific and germane to men only.[17,21,22] Although most of the benefits of DHEA-S with respect to insulin status have been reported in men, the actual role DHEA-S plays with respect to insulin status and obesity in each gender group is undetermined. Against this background, this study was undertaken to determine: 1. The relationship of DHEA-S concentration with indices of obesity in a group of young healthy Saudi women. 2. The correlation of DHEA-S concentration with fasting insulin and glucose levels in obese and lean individuals.

Methods. *Subject protocol.* A total of 65 healthy women were enrolled in the study. All were between the ages of 19-30 years. They were divided into 2 groups, an obese group with BMI of more than 27 kg/m^2 and a lean group with BMI of <27 kg/m^2. All subjects were judged to be in good health according to their medical history and routine laboratory tests. None of the women was taking any medication.

Assays. Blood samples were obtained after an overnight fast. Plasma was kept at -25°C until analysis. At the time of blood collection, information was recorded for all subjects including weight, height, waist and hip circumference. Plasma glucose was measured on site, using a glucose analyzer (One Touch System - Johnson and Johnson, USA). Plasma DHEA-S was determined using a commercial direct ELISA DHEA-S kit (DRG International, Germany). Insulin was determined using DRG insulin ELISA kit. All hormone measurements from an individual woman were determined in duplicate in a single assay.

Statistical analysis. The analysis was performed using statistical package for social sciences 10 for Windows. The results were expressed as the means ± standard deviation. Correlations were studied by Pearson's method to determine whether there were statistically significant differences in hormone levels between the 2 groups. Association between variables was assessed by correlation. A difference was considered to be statistically significant when $p<0.05$.

Results. **Table 1** shows the mean levels of selected variables in the study subjects. By definition, obese subjects had a higher body mass index (BMI) and waist hip ratio (WHR). All the volunteers had normal fasting glucose levels, although it was higher in the obese than in the lean group. Fasting insulin concentrations tended to be elevated in the obese group. The obese subjects had lower DHEA-S levels than the lean women. Dehydroepiandrosterone-S levels ranged between 1285.20-2047.34 ng/ml in the obese and 1846.11-2514.57 ng/ml in the lean women. To assess associations between the variables, the Pearson t-test was used. **Table 2** shows the correlations between DHEA-S, BMI, WHR, hip circumferences, insulin and glucose for the 65 subjects. The analysis showed that DHEA-S levels were related negatively with BMI ($p=0.02$, correlation co-efficient [r]=-0.25) and hip circumference ($p=0.03$, r=-0.27). **Figure 1** shows the significant inverse relationship between DHEA-S and hip circumference. The test failed to show any correlation between DHEA-S and WHR.

Although the analysis showed no correlation between DHEA-S and insulin in all subjects, a significant positive relationship between DHEA-S and insulin ($p=0.03$, r=0.43) was shown in the obese group (**Figure 2**). No significant relationship was observed between DHEA-S and glucose levels in the whole group as well as the obese subjects.

Discussion. The purpose of this work, in which Saudi women were considered, was to measure DHEA-S levels and assess their relationship to BMI, insulin and glucose. Sixty-five volunteers between 19-30 years of age with BMI 15.33-38.30 kg/m^2 were enrolled in the study. Subjects were divided into 2 groups based on BMI value. The present study documents a marked decline in DHEA-S levels with increasing BMI. The report clearly showed that DHEA-S levels were higher in lean individuals (BMI < 27 kg/m^2) than obese women (BMI >27 kg/m^2). Regarding the relationship between DHEA-S and BMI in women; little is known and there is conflicting data. In 1993, Williams et al[23] examined the association of DHEA-S level in 96 healthy females aged 28-39 years to BMI and reported no correlation. Another group evaluated serum levels of DHEA-S and BMI in 376 adult women of ages between 18-89 years and BMI between 15.7-57.8 kg/m^2. In considering the whole population, DHEA-S levels were related positively with BMI independent of age. However, this association disappeared after correction for BMI.[24] In subsequent research by the same group trying to measure DHEA-S levels in obese women with BMI ranges from 27.1-57.1 kg/m^2 and in normal females with BMI <25 kg/m^2, they conclude that DHEA-S levels positively relate with BMI.[25] Unlike the reports that showed no correlation or positive correlation between DHEA-S and BMI, the result of this study showed a negative association with BMI in the obese group. The reason for the discrepancy

Table 1 -Values (mean ± SD) of physical and fasting serum profiles of the 26 obese and 39 lean women.

Variable	Total N=65	Obese N=26	Lean N=39
Body weight (kg)	**66.51 ± 16.12**	83.30 ± 9.61	55.32 ± 7.43
Height (m)	**1.61 ± 5.69**	1.622 ± 5.31	1.60 ± 5.80
BMI (kg/m²)	**25.68 ± 5.76**	31.68 ± 3.43	21.68 ± 2.65
Hips (cm)	**104.04 ± 10.59**	115.10 ± 6.11	97.23 ± 5.95
Waist (cm)	**75.79 ± 11.69**	87.75 ± 8.97	68.42 ± 5.32
WHR	**0.73 ± 6.08**	0.76 ± 7.39	0.70 ± 3.68
DHEA-S (ng/ml)	**1971.50 ±1012.54**	1666.27 ± 943.44	2180.30 ± 1016.90
Insulin (μIU/ml)	**15.52 ± 8.57**	16.08 ± 7.16	15.13 ± 9.50
Fasting glucose (nmol/L)	**5.02 ± 0.60**	5.45 ± 0.68	4.75 ± 0.34

BMI - body mass index, WHR - waist hip ratio, DHEA-S - dehydroepiandrosterone sulphate

Table 2 - Pearson correlation between DHEA-S, BMI, WHR, hip circumference, glucose and insulin (N=65).

Variable	DHEA-S	Insulin	Glucose	Hips	WHR
BMI	-0.14	0.08	0.43†	0.91†	0.55†
WHR	-0.04	0.28*	0.34†	0.33†	
Hips	-0.27*	0.02	0.43†		
Glucose	-0.14	0.01			
Insulin obese group	0.43†				

*p<0.05, †p<0.01. BMI - body mass index, WHR - waist hip rato, DHEA-S - dehydroepiandrosterone sulphate

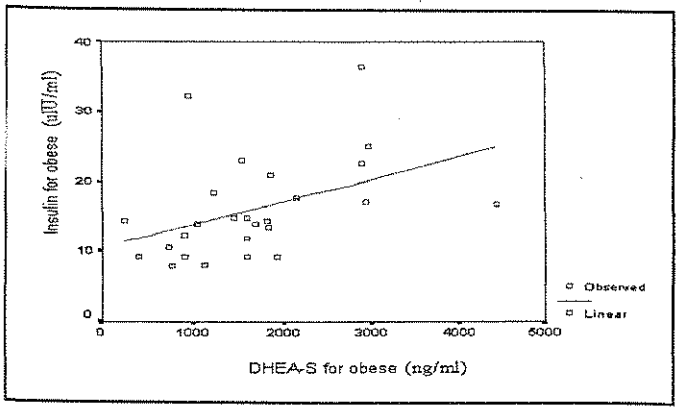

Figure 1 - The simple linear regression curve between DHEA-S and insulin levels in obese group.

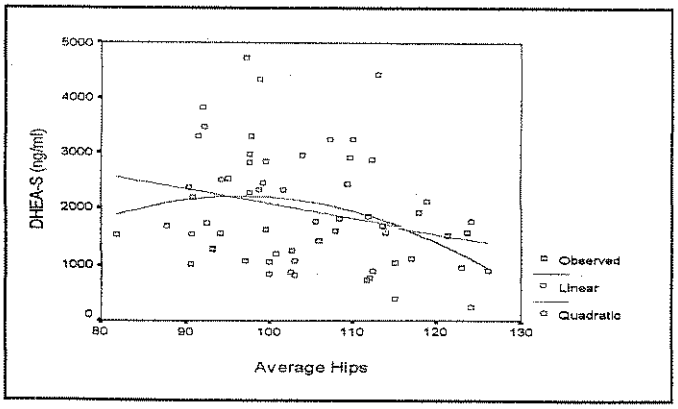

Figure 2 - The simple linear regression curve between DHEA-S and hip measurements.

is not clear, but could refer to differences in subject selection. In considering the whole group, DHEA-S levels in this study were related negatively with hip circumferences. Therefore, hip circumference appears to be a convenient and informative anthropometrics indicator. Hip measurements can be used as an indicator of DHEA-S concentrations in Saudi females. Examining the interrelations of DHEA-S and insulin, when analyzing the data of all subjects, no significant correlation was shown. Nonetheless, the significant correlation appeared only on considering the obese group. Previous studies have shown a significant effect of insulin administration on serum DHEA-S concentration and its metabolic rate, with evidence for the effect in men, but not in women.[15-17,19,20] Others suggested that insulin's regulation of DHEA-S is sex specific and germane to men only.[17,21,22] In contrast, a very recent study based on twin correlation has shown that the relationship between insulin and DHEA-S is not stronger in men than in women.[26] In view of the above observations, the result of the present study is difficult to interpret and suggests that there is an element of paradox in the correlation. Further studies on the DHEA-S insulin system are needed to better clarify the mechanism involved. Our suggestion regarding this result is that, since all the volunteers in the present study are with BMI <40 kg/m^2, the limited range of BMI could be a reason that cannot be ruled out. Future studies will address this issue. Lastly, regarding the interrelation of DHEA-S and glucose, limited information is available. A previous study showed that hyperglycemia decreases DHEA-S in Japanese men with non-insulin-dependent diabetes mellitus, but the depression of DHEA-S is independent of serum insulin level.[27] The data of the present study show no correlation between DHEA-S and glucose in young healthy individuals. However, that there was no correlation between DHEA-S and glucose levels is hard to explain. It is possible that the correlation appears only in the presence of diabetes, which influence the decreased levels of DHEA-S in the patients. Obviously, this matter needs to be taken into consideration when interpreting this type of data.

In conclusion, this study showed that obese healthy Saudi women certainly have a lower concentration of DHEA-S compared with the lean individuals due to the effect of BMI and hip circumference. The significance of these 2 factors remains to be determined in expanded studies in which the relationship of insulin may be studied and the subject age and BMI may be better controlled.

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Authors: A. B. Atkinson
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Abstract

Harvey Cushing described the disorder which perpetuates his surname at a meeting of the medico-chirurgical society of the Johns Hopkins Hospital in 1932. Due to the advent of many sophisticated tests, the disease is now frequently diagnosed in the absence of the florid classical clinical picture. The first step in diagnosis is to establish the presence of excessive cortisol production. Various procedures are available for this purpose, including measurement of urinary excretion of free cortisol, and of serum cortisol levels during low dose dexamethasone suppression. There are many causes of excessive cortisol production and proper treatment depends on their correct identification. The most useful tests are the high dose dexamethasone suppression, metyrapone, serum potassium, serum dehydroepiandrosterone and plasma ACTH levels. Added to these are methods of localization including CT scans of chest, abdomen and pituitary. The relative merits of these techniques are discussed. Appropriate treatment plans for different causes of excessive cortisol production are also outlined.