ENDOCRINOLOGY

The Relationships of Dehydroepiandrosterone Sulfate, Erectile Function and General Psychological Health

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ABSTRACT

Introduction: Dehydroepiandrosterone sulfate (DHEAS) has been reported to be associated with sexual function and general psychological health respectively, however, no one has ever examined their mutual relationships in a single study.

Aim: The aim of the present study was to find out whether DHEAS, general psychological health, and erectile function were all associated with each other.

Methods: A cross-sectional study was conducted on 34 patients with erectile dysfunction (ED) and 32 healthy controls (HC). The levels of serum DHEAS were assessed by chemiluminescence method. Erectile function and general psychological health were measured by International Index for Erectile Function-5 (IIEF-5) and General Health Questionnaire 20(GHQ-20) respectively.

Main Outcome measure: The primary outcome measure of this study was the mutual correlations of serum DHEAS levels, general psychological health and erectile function.

Results: Compared to HC, patients with ED had a significant lower serum levels of DHEAS (6.43 ± 2.70 μmol/L vs 9.48 ± 2.82 μmol/L, $P < .001$) and higher scores on GHQ-20 (35.06 ± 8.56 vs 24.97 ± 2.55, $P < .001$). Multivariate binary logistic regression showed that both serum levels of DHEAS (OR = 0.667, 95% CI = 0.512−0.869, $P = .003$) and psychological distress (scores of GHQ-20 > 28) (OR = 6.921, 95% CI = 1.821−26.305, $P = .005$) were significantly associated with ED. However, no significant association between psychological distress and serum levels of DHEAS was found (OR = 0.798, 95% CI = 0.623−1.021, $P = .072$) after controlling for ED. Partial correlation analysis revealed that both scores of GHQ-20 ($r = -0.595$, $P < .001$) and DHEAS ($r = 0.450$, $P < .001$) were significantly correlated with scores of IIEF-5, while no significant relationship was found between scores of GHQ-20 and DHEAS ($r = 0.116$, $P = .363$) after controlling for scores of IIEF-5 and age.

Conclusion: Both serum levels of DHEAS and general psychological health are significantly associated with erectile dysfunction in sexually active adult men but the relationship between general psychological health and erectile function seems to be independent of DHEAS. **Li K, Liang S, Shi Y, et al. The Relationships of Dehydroepiandrosterone Sulfate, Erectile Function and General Psychological Health. Sex Med 2021;9:100386.**

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Key Words: Dehydroepiandrosterone Sulfate; Erectile Function; General Psychological Health; General Health Questionnaire 20

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INTRODUCTION

Erectile dysfunction (ED) is a common disease in adult men with a high prevalence and incidence worldwide, accompanied by a young trend in recent years. According to the Massachusetts men's aging study (MMAS), 52% of men aged 40−70 years have ED in varying degrees.[1] A variety of endocrine hormones may be involved in the regulation of penile erection. However, among the 17 hormones investigated in MMAS subjects, dehydroepiandrosterone sulfate (DHEAS) is the only one significantly related to the occurrence of ED.[1]

DHEAS is the most abundant steroid hormone in humans, mainly synthesized from dehydroepiandrosterone (DHEA) in the adrenal zona reticularis by hydroxysteroid sulfotransferase,[2] both of which are regarded as representative of adrenal androgen. The serum DHEAS levels is about 250 times higher than serum DHEA levels, serving as the main form of DHEA/DHEAS.[3] For adult men, the concentration of DHEA/DHEAS peaks between the ages of 20 and 30, and then decreases by 10% on average every 10 years.[4] In addition, DHEAS is also abundant in brain where it can be synthesized de novo, contributing to regulate the activity of neurons.[5]

DHEAS plays an important role in the regulation of sexual function. Previous studies showed that reduced serum levels of DHEAS increased the risk of ED in adult men,[6] especially for elderly men.[7] Serum levels of DHEAS were also found to be significantly lower in patients with ED than in age-matched healthy men.[8] Moreover, DHEA treatment was found to improve erectile function in patients with ED.[9]

However, the mechanism about how DHEAS participates in the regulation of sexual function is not very clear. On one hand, DHEAS is the precursor of many other sex hormones, which are involved in the regulation of sex function. On the other hand, DHEAS can directly influence the function of vascular endothelial cells.[10] Furthermore, DHEAS might impact on the mental health, which is regarded as an important factor associated with ED.[11,12] As a proxy for overall health, perceived general health can buffer against the increased age-related risk of ED.[13] Clinical studies have demonstrated that low DHEA levels are significantly associated with psychological disorders and depressive symptoms,[14] which could be ameliorated by DHEA supplementation.[15,16] However, the DHEA's efficacy on mental health is yet to be confirmed. For example, a double blind crossover study found that healthy men with a physiological decline of DHEA production did not benefit from 4 months of DHEA supplementation.[17]

To the best of our knowledge, no one has ever examined DHEAS, general psychological health and erectile function in a single study. What are the exact mutual relationships of them? Whether general psychological health is involved in the association between DHEAS and erectile function? To answer the questions, we are going to simultaneously assess serum levels of DHEAS, general psychological health and erectile function and then explore their mutual relationships among a sexually active male population.

MATERIALS AND METHODS

Participants

This is a cross-sectional study. All the cases in this study came from the inpatients that sought medical help because of erectile dysfunction in the VIP ward of the Third Affiliated Hospital of Sun Yat-sen University between August 1, 2017 and November 31, 2018. Patients were admitted to hospital to perform a thorough medical examination to exclude organic erectile dysfunction and receive a comprehensive treatment, which was hard to be completed in an outpatient visit. All the healthy controls (HC) came from the visitors who sought medical examination at the same period. All subjects were married or had a regular sexual partner, aged from 20 to 50 years, and were willing to submit written informed consent. For the case group, participants had to have a history of ED for more than 3 months and scored lower than 22 on IIEF-5 at the baseline. For the HC group, IIEF-5 score must be higher than 22 with the absence of history of ED. Participants who were currently suffering from any other DSM-Ⅳ-TR axisⅠmental disorders or any active organic disease would be excluded. In addition, hormone, antidepressants, antipsychotics, antiandrogens, antihistamines, and addictive drugs were not allowed to be taken in the last 6 months before entry into this study.

All procedures used in the present study were reviewed and approved by the Clinical Research Ethics Committee of the Third Affiliated Hospital of Sun Yat-Sen University. (approval number: [2017]02-233-01).

Measurement

Laboratory testing. All the biochemical and hormonal measurements for an individual subject were performed by the same blood sample. Serum concentrations of total cholesterol (TC), triglycerides (TG), LDL-cholesterol (LDL-c), HDL-cholesterol (HDL-c), fasting plasma glucose were measured via automated enzymatic assay by 7600-020 autonomic analyzer (Hitachi, Japan). Plasma hormones were assessed via chemiluminescence method as follows. The assay for the measurement of DHEAS, androstenedione, and adrenocorticotropic hormone (ACTH) were by IMI2000 (Siemens, Germany), for thyroid stimulating hormone (TSH), free thyroxine (FT4), free triiodothyronine (FT3), Luteinizing hormone (LH), follicle stimulating hormone (FSH), total testosterone (TT), estradiol and prolactin were by I2000 (Abbott, USA), and for plasma cortisol were by Ceutaur XP (Siemens, Germany). The intra-assay and inter-assay coefficients of above variations were all lower than 10%, respectively. The reference levels of DHEAS for the male population in the assay were (2.17 ± 15.20) μmol/L.

Erectile function assessment. All subjects were assessed by the Chinese version of International Index for Erectile Function-5 (IIEF-5).[18] IIEF-5 is a self-administered questionnaire, consisting of 5 items. Each item was rated on a scale of 1 (almost never or never) to 5 (almost always or always). A score of 0 indicated no attempt at sexual intercourse, and a score of lower than 22 were considered to have erectile dysfunction.[19]

Psychological health assessment. Psychological health was measured with the Chinese version of General Health Questionnaire-20 items (GHQ-20).[20] The questionnaire consisted of 20 items with responses over a 4-point scale (0−3), which ranged from "less than usual" to "much more than usual."[21]This scale included both positively phrased items implying psychological health and negatively phrased items implying psychological distress. A cut-off point of total score 28 was utilized as psychological distress.[22]

Statistical analysis

Subjects were categorized into ED group and HC group according to the inclusion criteria. For normally distributed data, independent-sample t-test was used to test the difference between groups, while for non-normally distributed variables, comparison between groups were analyzed with Wilcoxon rank sum test. Differences in categorical parameters between groups were tested using Chi-square test. Multivariate binary logistic regression model was established to assess the relationships between ED, distress and DHEAS. Partial correlation analysis was used to test the relationships between IIEF-5, GHQ-20, and DHEAS. Odds ratios and 95% confidence intervals were used to quantify the strength of associations. The results were considered significant at $P < .05$. All data were analyzed using commercial statistical package SPSS 24.0 (SPSS, Inc., Chicago, IL).

RESULTS

Clinical and biochemical characteristics of the participants

Totally, 34 ED patients and 32 healthy controls were involved in this study. Their clinical and biochemical characteristics were listed in Table 1. As the table demonstrated, the age of ED patients seemed to be smaller than that of HC, but only marginally reached significance ($P = .093$). No statistical differences was found in marital status, level of education, prevalence of smoking and drinking between ED group and HC group (all $P > .05$). All the subjects' BMI, blood pressure, fasting blood glucose, plasma levels of lipid (TC, LDL, HDL, TG) and hormones including LH, FSH, TT, estradiol, prolactin, TSH, FT4, FT3, ACTH, and cortisol were in normal range, and did not statistically significantly differ between 2 groups.

Table 1. Clinical and laboratory characteristics of all the subjects

	Erectile dysfunction (n = 34)	Healthy controls (n = 32)	*P* Value
Age (years)	36.47 ± 8.14	39.94 ± 8.39	.093
Married [n (%)]	30 (88.2)	29 (90.6)	.535
Education			
Primary school or lower	5 (14.7)	3 (9.4)	.775
Middle or high school	17 (50.0)	21 (65.6)	.199
College or higher	12 (35.3)	8 (25.0)	.363
Alcohol drink [n (%)]	4 (11.8)	5 (15.6)	.460
Smoking [n (%)]	7 (20.6)	7 (21.9)	.568
SBP (mmHg)	130.12 ± 6.92	127.81 ± 6.69	.174
DBP (mmHg)	76.32 ± 6.09	77.50 ± 6.19	.439
BMI (kg/m^2)	24.64 ± 2.83	23.67 ± 2.55	.151
TC (mmol/L)	4.81 ± 0.82	4.87 ± 0.82	.749
LDL-C (mmol/L)	3.09 ± 0.88	3.11 ± 0.85	.946
HDL-C (mmol/L)	1.18 ± 0.32	1.22 ± 0.26	.575
TG (mmol/L)	1.21 (1.16,1.95)	1.10 (1.02,1.44)	.156
FBG (mmol/L)	5.12 ± 0.90	5.02 ± 0.51	.555
Cortisol (nmol/L)	425.95 ± 98.59	399.21 ± 85.32	.244
ACTH (pmol/L)	4.28 ± 1.19	3.86 ± 1.39	.187
FT3 (pmol/L)	4.55 ± 0.93	4.66 ± 0.96	.648
FT4 (pmol/L)	16.75 ± 3.53	17.58 ± 3.04	.315
TSH (uIU/ml)	2.14 ± 0.95	2.24 ± 1.07	.683

ACTH = adrenocorticotropic hormone; BMI = body mass index; DBP = diastolic blood pressure; FBG = fasting blood glucose; FT3 = free triiodothyronine; FT4 = free thyroxine; HDL-C = high-density lipoprotein cholesterol; LDL-C = low-density lipoprotein cholesterol; SBP = systolic blood pressure; TC = total cholesterol; TG = triglyceride; TSH = thyroid stimulating hormone.

Comparisons of sexual hormones and level of erectile function, general psychological health between ED patients and healthy controls

As shown in Table 2, serum levels of DHEAS and IIEF-5 were significantly lower in ED patients than in HC group, while the scores of GHQ-20 were significantly higher in ED patients than in HC ($P < .001$). In terms of prevalence of distress, the prevalence of distress was also significantly higher in ED patients than in HC ($P < .001$).

Models of relationship between ED, distress and DHEAS

Multivariate binary logistic regression equation was built respectively with ED (ED = 1, HC = 0) and psychological

Table 2. Comparisons of sex hormones and level of erectile function, general psychological health between ED and non-ED groups

	Erectile dysfunction (n = 34)	Healthy controls (n = 32)	*P* Value
DHEAS (μmol/L)	6.43 ± 2.70	9.48 ± 2.82	<.001
Androstenedione (nmol/L)	6.28 ± 3.08	6.83 ± 3.08	.474
Testosterone (nmol/L)	13.18 ± 5.52	14.23 ± 5.70	.450
PRL (uIU/ml)	249.20 ± 98.36	242.03 ± 97.19	.767
LH (mIU/ml)	3.46 ± 1.32	3.73 ± 1.41	.426
Estradiol (pmol/L)	138.95 ± 38.11	137.89 ± 33.13	.904
IIEF-5	11.29 ± 4.27	23.50 ± 1.08	<.001
GHQ-20	35.06 ± 8.56	24.97 ± 2.55	<.001
Psychological distress [n (%)]	25 (73.5)	6 (18.8)	<.001

DHEAS = dehydroepiandrosterone sulfate; GHQ-20 = General Health Questionnaire 20; LH = luteinizing hormone; PRL = prolactin.

Table 3. Models of relationship between ED, psychological distress and DHEAS by multivariate logistic regression analyses

	Exp (B)	95% CI	*P* value*
Model 1†			
Psychological Distress	6.921	1.821–26.305	.005
DHEAS	0.667	0.512–0.869	.003
Model 2‡			
DHEAS	0.798	0.623–1.021	.072
ED	6.683	1.788–24.984	.005

Note
*Adjusting for age.
†Multivariates binary logistic regression with ED as dependent variable.
‡Multivariates binary logistic regression with distress as dependent variable.
DHEAS = dehydroepiandrosterone sulfate; ED = erectile dysfunction.

distress (distress = 1, non-distress = 0) as dependent variable, the other 2 variables as independent variables, and age as covariate. The results were displayed in Table 3. As seen in Table 3, model 1 showed that both serum levels of DHEAS (OR = 0.667, 95% CI = 0.512−0.869, *P* = .005) and distress (OR = 6.921, 95% CI = 1.821−26.305, *P* = .003) exerted impact on ED. According to model 2, serum levels of DHEAS imposed negative impact on distress but did not reach significance (OR = 0.798, 95% CI = 0.623−1.021, *P* = .072), while ED significantly influenced on distress (OR = 6.683, 95% CI = 1.788−24.982, *P* = .005).

Correlation between IIEF-5, GHQ-20, and DHEAS

Partial correlation analysis was conducted between IIEF-5, GHQ-20, and DHEAS with age as a covariate. The results were demonstrated in Table 4. According to Table 4, both scores of GHQ-20 (r = −0.595, *P* < .001) and DHEAS (r = 0.450, *P* < .001) were significantly correlated with scores of IIEF-5, while no significant relationship was found between scores of GHQ-20 and DHEAS (r = 0.116, *P* = .363) after controlling for scores of IIEF-5 and age.

DISCUSSION

In line with most of previous studies,[1,6,8] our study duplicates the finding that serum levels of DHEAS are significantly lower in patients with erectile dysfunction than age-matched healthy control. In addition, our study finds that erectile dysfunction is significantly associated with general psychological health, which is consistent with previous findings that perceived general health can decrease age-related risk of ED.[13,23] DHEAS is considered as a weak androgen and pre-hormone that can convert to other androgen such as androstenedione and testosterone, which may be convenient for penile erectile. As inferred, DHEAS may exert its effect on erectile function through a G-protein dependent activation and induction of endothelial nitric oxide (NO) synthase independent of androgen receptors.[24] The latter effect was

Table 4. Correlations between IIEF-5, GHQ-20, and DHEAS

r (*P*)	IIEF-5	GHQ-20	DHEAS
IIEF-5	-	−0.595 (<0.001)*	0.450 (<0.001)†
GHQ-20	−0.595 (<0.001)*	-	−0.116 (0.363)‡
DHEAS	0.450 (<0.001)†	−0.116 (0.363)‡	-

Note
*Controlling DHEAS and age.
†Controlling GHQ-20 and age.
‡Controlling IIEF-5 and age.DHEAS = dehydroepiandrosterone sulfate; GHQ-20 = General Health Questionnaire 20; IIEF-5 = International Index for Erectile Function-5.

proved by the phenomenon in which DHEA increased NO production from intact endothelial cells in vitro.[25]

However, in contrast to our expectation, the association between erectile function and general psychological health is found to be independent of DHEAS. That is to say, the impact of general psychological health on erectile function seems not to be mediated by DHEAS. As far as we know, this has not been examined before. As a neurosteroid, DHEAS was found to have positive allosteric modulation on GABAA receptors at low, nanomolar concentrations.[26] In animals, low dose of DHEAS was found to have anxiolytic effect.[27] In human, serum level of DHEAS was proved to be a prediction of affective disorder.[28] In addition, DHEAS level was also found to be negatively correlated with severity of depression[14] in patient with major depression. However, the association between DHEAS and depressive symptoms could not be verified in the general population after controlling for potential confounding factors.[29] Even in study with positive findings,[30] the relationship between serum levels of DHEAS and general psychological health was only found in women, not in men. Moreover, no study has ever examined the relationships between sexual dysfunction, DHEAS and general psychological health simultaneously. Taking the Michael's study[14] as an example, it is hard to tell whether the association between DHEAS level and severity of depression would still exist after adjusting for erectile dysfunction, since sexual function was not assessed. The above-mentioned inconsistence between studies regarding the association between general psychological health and DHEAS reflects the effect of DHEAS on humans' physical and mental well-being might be more complicated than we expected.

Caution should be exercised when interpreting this study's results. First, the cross-sectional design of this study limits causal conclusions regarding the relationship between erectile dysfunction and general psychological health or DHEAS. Second, the sample size of this study is relatively small. However, the match in age, education, marital status, blood pressure, BMI, blood glucose, serum lipid, thyroid function and other neuroendocrinal hormones between case and control group helps improve the power of test. Third, only male subjects were recruited, so whether the conclusion about the relationship between general psychological health and DHEAS can be generalized to female is yet to be confirmed. Finally, patients with erectile dysfunction in this study were recruited only when they were admitted to our hospital for medical help, therefore, potential selection bias could not be excluded.

CONCLUSION

In conclusion, our study finds that both serum levels of DHEAS and general psychological health are significantly associated with erectile dysfunction in sexually active adult men but the relationship between general psychological health and erectile function seems to be independent of DHEAS.

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STATEMENT OF AUTHORSHIP

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