Journal of
Stem Cell Research & Therapy

Liu et al., J Stem Cell Res Ther 2015, 5:7
DOI: 10.4172/2157-7633.1000291

Research Article Open Access

The Metabolic Change of Serum Dehydroepiandrosterone Sulfate, Free Fatty Acids and Desaturase Activity in Isolated Post-Challenge Hyperglycemia

Liyan Liu, Ying Li and Changhao Sun*

Department of Nutrition and Food Hygiene, Public Health College, Harbin Medical University, Harbin, China

Abstract

The aim of this study is to investigate the association between endogenous dehydroepiandrosterone sulfate (DHEA-S) and fatty acid, desaturase in isolated post-challenge hyperglycemia (IPH) subjects. 241 IPH subjects aged 35 to 70 years participated. Serum DHEA-S concentration was measured using the enzyme-linked immunosorbent assays. Fatty acid profiles were detected by gas chromatography-mass spectrometry, and desaturase activities were expressed by fatty acid product-to-precursor ratios. Relationships were assessed using multiple regression. The results suggested that DHEA-S concentration was negatively associated with palmitic acid ($P < 0.001$), and positively with γ-linolenic acid and eicosatetraenoic acid in men ($P = 0.002$ and $P = 0.001$, respectively), and negatively with palmitic acid ($P = 0.037$) and positively with docosapentaenoic acid, docosahexaenoic acid ($P = 0.018$ and $P < 0.001$, respectively) in women. In addition, a positive association was observed between DHEA-S and delta-9-desaturase (D9D-18, $P = 0.031$) in men, and also delta-6-desaturase (D6D, $P = 0.034$) in women. In Conclusions, there is different DHEA-S, fatty acid profile and the desaturase activities in both genders with the IPH subjects.

Keywords: Isolated post-challenge hyperglycemia; Dehydroepiandrosterone sulfate; Free fatty acids; Desaturase activity

Introduction

Isolated post-challenge hyperglycemia (IPH), characterized by 2-h postprandial plasma glucose (2h-PG) ≥ 11.1 mmol/L and fasting plasma glucose (FPG) < 6.0 mmol/L, is a subtype of type 2 diabetes (T2D). The prevalence of IPH is variable, but it has been reported to account for as much as 70% of all undiagnosed diabetes in elderly women [1] and is also common among the non-obese [2]. In the Third National Health and Nutrition Examination Survey, 41% of undiagnosed diabetes was IPH [3]. In an urban Iranian population, the prevalence of IPH was 3.1%, being 40% of total new cases of T2D, a prevalence that increases with age [4]. Although there was not the data of the prevalence of IPH in China, our previous studies found out that IPH was about 40% of the newly diagnosed T2D in Harbin of province of Heilong Jiang [5,6]. Therefore, it is important to study the metabolic change of IPH subjects. Although many studies have illustrated fatty acid and steroid metabolic disorders in type 2 diabetes, these metabolic change in IPH have not been systematically investigated. In this study, we detected the change of dehydroepiandrosterone sulfate (DHEA-S), free fatty acids (FFAs) and desaturase activity in different gender of IPH subjects.

Materials and Methods

Subjects

All subjects in this study were from the Harbin People's Health Study which characteristics of subjects has been published previously [7]. The study was approved by the Ethics Committee of Harbin Medical University and conducted in accordance with the Declaration of Helsinki. Informed consent was obtained from each participant. A total of 241 subjects with newly diagnosed IPH were included and subjects enrolled were not on any medication. IPH subjects were diagnosed according to the 1997 American Diabetes Association (ADA) criteria (Report of the expert committee on the diagnosis and classification of diabetes mellitus 1997). The cutoff value for FPG of IPD patients was 6.0 mmol/L and for 2h-PG was 11.1 mmol/L. All blood samples were collected in the morning before breakfast and fasting blood samples were immediately centrifuged at 3,000 *g* for 10 min at room temperature and then stored at −80°C until analysis.

Clinical chemistry measurements

Blood glucose was measured using Kyoto blood sugar test meter and test strip (Arkray, Inc. Kyoto, Japan). Serum total cholesterol (TC) and triglyceride (TG) were assayed using standard enzymatic colorimetric techniques and commercial kits (Biosino Biotechnology Ltd, Beijing, China) with an auto-analyzer (AUTOLAB PM 4000, AMS Corporation, Rome, Italy). Serum insulin was measured using commercial kits (Tosoh Corporation, Tokyo, Japan) with an auto-immunoassay analyzer (AIA-2000 ST, Tosoh Corporation, Tokyo, Japan). Serum DHEA-S concentration was measured by a commercial kit (IBL Corporation, Hamburg, Germany) of enzyme-linked immunosorbent assays (ELISA). The homeostasis model assessment of insulin resistance (HOMA-IR) index was calculated from the fasting plasma glucose (FPG, mmol/L) and insulin values (FINS, mU/L) as HOMA-IR = FPG×FINS/22.5.

Free fatty acid measurement and estimation of desaturase activity

Samples were randomly selected for the extraction of FFAs and Gas Chromatography/Mass Spectrometer (GC/MS) acquisition. The fatty acid methyl esters were prepared as described previously [5]. GC/MS

***Corresponding author:** Changhao Sun, Department of Nutrition and Food Hygiene, Public Health College, Harbin Medical University, Nangang District, Harbin, China, Tel: +86 0451 87502801; Fax: +86 0451 87502885; E-mail: changhaosun2002@163.com

Received May 29, 2015; **Accepted** July 13, 2015; **Published** July 15, 2015

Citation: Liu L, Li Y, Sun C (2015) The Metabolic Change of Serum Dehydroepiandrosterone Sulfate, Free Fatty Acids and Desaturase Activity in Isolated Post-Challenge Hyperglycemia. J Stem Cell Res Ther 5: 291. doi:10.4172/2157-7633.1000291

analysis was performed using gas chromatography coupled to an ion-trap mass spectrometer (TRACE GC/PolarisQ MS, Thermo Finnigan, USA). Separation was performed on a J&W DB-WAX capillary column (30 m × 0.25 mm I.D, 0.25 μm film thickness). This methylated FA was used to determine the percentage composition.

The product-to-precursor ratios of individual free fatty acids in serum were used to estimate desaturase activities as follows: Delta-9-desaturase (D9D) = 16:1 n-7/16:0 and 18:1 n-9/18:0; Delta-6-desaturase (D6D) = 18:3 n-6/18:2 n-6 and Delta-5-desaturase (D5D) = 20:4 n-6/20:3 n-6.

Statistical analysis

All analyses were done for men and women with IPH separately. Student's t test and the chi-square test were used to assess differences in clinical characteristics and DHEA-S between men and women for continuous variables and categorical variables, respectively. Analysis of variance (ANCOVA) was used to compare serum free fatty acid levels and desaturase activities between men and women, adjusting for potential covariates (alcohol consumption, 2h-PG, fasting insulin and DHEA-S). The Spearman correlation coefficient was used for testing the relationships between DHEA-S, and clinical characteristics and the different fatty acid fractions. Multiple linear regression between serum DHEA-S, free fatty acids and desaturase activities was also performed to control for potential confounding variables including age, BMI, TG, TC, 2h-PG and insulin. All *P* values were two-sided, and values less than 0.05 were considered statistically significant. Statistical analyses were carried out with SPSS 13.0 (SPSS, Chicago, IL).

Results

Baseline characteristics of the subjects

241 subjects with IPH were divided into two subgroups according to the gender (Table 1). The mean age of subjects was 52.2 for men and 52.4 for women. There were no differences in smoking, dietary intake, BMI, diastolic blood pressure (DBP), systemic blood pressure (SBP), FPG, TG, TC, glycosylated hemoglobin (HbA1c), HOMA-IR and insulin between men and women (Table 1). Moreover, women had a higher 2h-PG and fasting insulin than men. DHEA-S level and alcohol consumption were significantly lower in women than men (DHEA-S, 1274.48 ± 329.14 vs. 1407.54 ± 314.97 ng/mL; $P < 0.05$).

Parameter	Men (n =122)	Women (n = 119)
Smoker/non-smoker	35/86	26/93
Alcohol consumption	54.76%	23.45%*
Age (years)	52.2 ± 8.4	52.4 ± 8.8
BMI (kg/m²)	26.4 ± 4.3	26.4 ± 3.7
DBP (mmHg)	86.5±11.7	86.2±13.7
SBP (mmHg)	140.4 ± 23.4	145.7 ± 25.9
FPG (mmol/l)	5.1 ± 0.6	5.2 ± 0.6
2h-PG (mmol/l)	16.6 ± 5.2	17.1 ± 4.8**
TG (mmol/l)	2.3 ± 1.1	2.4 ± 0.9
TC (mmol/l)	5.1 ± 1.0	5.2 ± 1.2
Fasting insulin (mU/l)	8.68 ± 3.58	9.64 ± 4.44*
HOMA-IR	2.84 ± 0.94	2.98 ± 0.97
HbA1c%	6.21±0.42	6.17±0.37
Total energy (kJ/d)	9681 ± 2615	9221 ± 2054
Protein (en%)	12.3 ± 2.2	13.0 ± 2. 6
Carbohydrate (en%)	57.8 ± 5.2	58.4 ± 6.7
Fat (en%)	29.2 ± 4.3	28.4 ± 4.9
DHEA-S (ng/mL)	1407.54 ± 314.97	1274.48 ± 329.14*

(* P < 0.05; BMI: Body mass index; SBP: Systolic blood pressure; DBP: Diastolic blood pressure; TG: Triglycerides; TC: Total cholesterol. FPG: Fasting plasma glucose; 2h-PG: 2 h Postprandial plasma glucose).

Table 1: Clinical characteristics of 241 subjects (mean ± SD).

FFA (%)	Men (n =122)	Women (n = 119)
Total SFA	28.02 (3.68)	28.67 (3.38)
C14:0	0.18 (0.03)	0.17 (0.02)
C16:0	21.94 (2.72)	22.57 (2.74)
C18:0	5.90 (2.05)	5.94 (1.62)
Total MUFA	22.56 (2.98)	21.72 (3.125)
C16:1	2.43 (0.66)	2.21 (0.42)*
C18:1	20.14 (2.85)	19.51 (3.00)
Total PUFA	49.46 (4.28)	49.66 (5.52)
Total n-3	4.30(0.98)	4.33(1.09)
C18:3	0.68 (0.30)	0.66 (0.28)
C20:5	0.20 (0.13)	0.26 (0.16)*
C22:5	0.88 (0.64)	0.96 (0.70)
C22:6	2.53 (0.64)	2.45 (0.53)
Total n-6	45.17 (4.17)	45.32 (5.10)
C18:2	35.64 (3.88)	35.61 (4.31)
γ-C-18:3	0.54 (0.11)	0.53 (0.09)
C20:3	0.67 (0.20)	0.61(0.26)
C20:4	8.31 (1.85)	8.59 (1.92)
D9D-16(16:1n-7/16:0)	0.11 (0.03)	0.10 (0.02)*
D9D-18(18:1n-9/18:0)	3.88 (1.63)	3.48 (0.88)
D6D(18:3n-6/18:2 n-6)	0.015 (0.003)	0.015 (0.003)
D5D(20:4n-6/20:3 n-6)	13.20 (3.65)	15.35 (4.59)*

Abbreviations: SFA, saturated fatty acids; MUFA, monounsaturated fatty acids; PUFA, polyunsaturated fatty acids; Delta-9-desaturase (D9D); Delta-6-desaturase (D6D); Delta-5-desaturase (D5D). (ANCOVA analysis by adjusting for alcohol consumption, 2h-PG, fasting insulin and DHEA-S; * p < 0.05.)

Table 2: Free fatty acids composition and desaturase activities in serum (mean ± SD).

Serum FFAs composition and desaturase activities of the study subjects

The palmitoleic acid (C16:1) was significantly higher in men than in women (2.43 ± 0.66 vs. 2.21 ± 0.42, $P < 0.05$), whereas there was lower eicosapentaenoic acid (C20:5) in men than women (0.20 ± 0.13 vs. 0.26 ± 0.16, $P < 0.05$). The percentage of saturated fatty acids (SFA), monounsaturated fatty acids (MUFA) and polyunsaturated fatty acids (PUFA) were not significantly different in men and women with IPH subjects. The same findings were observed in n-3 and n-6 fatty acids. With regard to desaturase activities, D5D were significantly higher in women than in men (Table 2).

Correlations between serum DHEA-S levels and various metabolic parameters

Serum DHEA-S level was significantly decreased when age increased in both men and women ($P < 0.05$ and $P < 0.001$, respectively) and BMI decreased in women ($P < 0.05$). Furthermore, higher levels of fasting insulin, 2h-PG, TC and TG were associated with lower DHEA-S level in men, and the same results were obtained in women except for that there was not statistically significant between TC and DHEA-S level ($P = 0.12$). Moreover, other variables including DBP, SBP and FPG did not show a measurable association with DHEA-S level (Table 3).

Relation among DHEA-S level, FFAs composition and desaturase activities

DHEA-S level was significantly decreased with an increasing

Parameters	Men (n =122)		Women (n = 119)	
	r	p	r	p
Smoker/non-smoker	-	-	-	-
Alcohol consumption	-	-	-	-
Total energy (kJ/d)	-	-	-	-
Protein (en%)	-	-	-	-
Carbohydrate (en%)	-	-	-	-
Fat (en%)	-	-	-	-
Age (years)	-0.31*	0.04	-0.52**	0.001
BMI (kg/m^2)	0.34*	0.01	0.39**	0.002
DBP (mmHg)	-	-	-	-
SBP (mmHg)	-	-	-	-
FPG (mmol/l)	-	-	-	-
2h-PG (mmol/l)	-0.42**	0.004	-0.26*	0.04
Parameters	Men (n =122)		Women (n = 119)	
	r (β)	p	r (β)	p
TG (mmol/l)	-0.35* (-0.31*)	0.02(0.03)	-0.48**(-0.39**)	0.001(0.005)
TC (mmol/l)	-0.38* (-0.32*)	0.01(0.02)	-0.20*(-0.19*)	0.02(0.04)
Fating insulin (mU/l)	-0.48**(-0.41**)	0.004(0.008)	-0.48**(-0.35**)	< 0.001(< 0.001)

Table 3: Metabolic parameters correlated with the serum DHEA-S levels by Spearman correlation analysis.
(- : no correlation. * p< 0.05; ** p < 0.01; r: Spearman correlation coefficient. β: Multiple linear regression coefficient.
A multiple linear regression analysis between DHEA-S levels and insulin, and lipid levels have been performed by adjusting for age, BMI and 2h-PG).

FFA (%)	Men (n =122)				Women (n = 119)			
	Model 1		**Model 2**		**Model 1**		**Model 2**	
	r	p	β	p	r	p	β	p
Total SFA	-0.717**	< 0.001	-0.581**	< 0.001	-0.489**	< 0.001	-0.284**	0.009
C14:0	-0.240	0.117	-0.101	0.453	-0.003	0.979	0.130	0.184
C16:0	-0.646**	< 0.001	-0.450**	< 0.001	-0.350**	0.006	-0.215*	0.037
C18:0	-0.393**	0.008	-0.358*	0.005	-0.376**	0.003	-0.127	0.232
Total MUFA	0.292	0.054	0.021	0.883	0.132	0.309	0.131	0.171
C16:1	-0.180	0.242	-0.089	0.451	-0.164	0.206	-0.116	0.223
C18:1	0.394**	0.008	0.144	0.310	0.089	0.494	0.133	0.170
Total PUFA	0.464**	0.002	0.378*	0.001	0.336**	0.008	0.211*	0.035
Total n-3	0.202	0.188	0.081	0.520	0.584**	< 0.001	0.392**	< 0.001
C18:3	0.326*	0.031	0.192	0.139	0.165	0.205	0.170	0.078
C20:5	0.045	0.773	0.121	0.370	0.066	0.612	0.042*	0.737
C22:5	0.311*	0.040	0.099	0.438	0.410**	0.001	0.237*	0.018
C22:6	0.110	0.477	0.033	0.795	0.562**	< 0.001	0.341**	< 0.001
Total n-6	0.425*	0.004	0.374**	0.001	0.217	0.093	0.142	0.158
C18:2	0.178	0.249	0.225	0.055	0.260*	0.043	0.148	0.154
γ-C-18:3	0.507**	< 0.001	0.422**	0.002	0.286*	0.025	0.163	0.093
C20:3	-0.005	0.974	-0.029	0.813	-0.104	0.426	-0. 026	0.802
C20:4	0.383*	0.010	0.397**	0.001	0.003	0.980	0.071	0.461
D9D-16(16:1n-7/16:0)	0.181	0.240	0.279	0.061	0.050	0.699	0.026	0.793
D9D-18(18:1n-9/18:0)	0.484**	0.001	0.373**	0.006	0.275*	0.032	0.012	0.907
D6D(18:3n-6/18:2 n-6)	0.407**	0.006	0.191	0.168	0.367**	0.004	0.216*	0.034
D5D(20:4n-6/20:3 n-6)	0.006	0.968	0.046	0.728	0.047	0.719	0.049	0.630

Table 4: FFAs compositions and desaturase activities correlated with the serum DHEA-S levels by Spearman. correlation analysis and Multiple linear regression analysis (* p < 0.05; ** p < 0.01; Model 1: Spearman correlation coefficient. Model 2: Regression coefficient adjusted for age, BMI, TG, TC 2h-PG and fasting insulin).

proportion of total SFA, palmitic acid and stearic acid in men and women (Table 4). And there was no significant correlation between DHEA-S and stearic acid when adjusted age, BMI, TG, TC, 2h-PG and insulin in women. Moreover, DHEA-S level was positively associated with total PUFA, total n-6 fatty acids, docosapentaenoic acid, γ-linolenic acid and eicosatetraenoic acid in men. The correlation of DHEA-S with docosapentaenoic acid disappeared (P = 0.438) after controlling variable in men. In women, there were significant correlation between DHEA-S with total PUFA, total n-3 fatty acids, docosapentaenoic acid, docosahexaenoic acid, linoleic acid and γ-linolenic acid. After we performed a multiple linear regression analysis in women, the results indicated that there were no significant correlation between DHEA-S with linoleic acid and γ-linolenic acid (P = 0.154 and P = 0.093, respectively).

When evaluating the relationship between desaturase activities and DHEA-S, DHEA-S correlated positively with D9D-18 and D6D in men and women (Table 4). After adjusting age, BMI, TG, TC, 2h-PG and insulin, a positive association between DHEA-S and D9D-18 ($r = 0.31$, $P = 0.031$) is shown in men and D6D was positively associated with DHEA-S in women ($r = 0.261$, $P = 0.034$).

Discussion

In this study, we demonstrated that DHEA-S level is lower in women than in men with IPH subjects. DHEA-S is the most abundant steroid produced by the adrenal gland. DHEA-S seems regulated by insulin which is able to inhibit DHEA-S synthesis in the adrenals [8] and acutely decrease circulating DHEA-S levels [9]. Our results showed that there was higher level of insulin in women than men, which maybe imply that the low DHEA-S in women was affected by the insulin. Furthermore, our results suggested that the insulin was negatively associated with the DHEA-S, which was supported by Shriock's study that a negative association between insulin and DHEA-S level in normal humans [10]. Thus, insulin hypersecretion in IPH subjects would decrease DHEA-S level. Moreover, DHEA-S was positively correlated with BMI and negatively related with age in both sexes. Several cross-sectional studies have examined the relationship between overweight or obesity and plasma level of DHEA-S. Consistent with our results, several studies [11,12] reported a positive correlation between DHEA-S and BMI. However, two studies found that DHEA-S was negatively associated with measures of obesity [13,14]. The reason for these discrepancies is that the age may have been a significant confounding factor in this association. The association between DHEA-S and BMI in two studies [13,14] was not statistically adjusted for age. Further, our study and some studies [15] indicated DHEA-S was related to age. Thus, differences in the age of subjects may have represented an important confounding factor in the study of the relationship between obesity and DHEA-S.

Serum DHEA-S level is closely associated with lipid metabolism. Epidemiological studies have shown that DHEA-S level was significant negative related with TG and TC levels [16,17]. Consistent with these studies, our result suggested a significant negative relationship between DHEA-S and these variables. A possible mechanism of the relationship between DHEA-S and lipid might involve an indirect effect of this hormone on the peroxisomal β-oxidation pathway in animal experiment [18,19].

Of note was that DHEA-S was associated with the fatty acid profiles. Our results showed that the DHEA-S level was significantly decreased with an increase of total SFA in both sexes, which suggested that endogenous DHEA-S was negatively related with total SFA. The relationship between total SFA and DHEA-S was mainly attributed to a concomitant increase of palmitic acid (16:0). The negative correlation between palmitic acid and DHEA-S may explain some of the beneficial properties of DHEA-S which may contribute to improve insulin sensitivity [20]. Palmitic acid seems to impair insulin sensitivity by its conversion into ceramides, which interference with the insulin signaling pathway [21]. Furthermore, DHEA-S level was positively associated with total n-6 fatty acids, γ-linolenic acid and eicosatetraenoic acid in men, and total n-3 fatty acids, docosapentaenoic acid, and docosahexaenoic acid in women. However, there is still a disagreement about the role of n-6 fatty acids in the development of metabolic alterations. Several authors have attributed a deleterious role to n-6 fatty acids [22] and the other study also recognized a protective role of n-6 fatty acids against obesity related alterations [23]. Further studies are necessary to confirm if the relation of plasma n-6 fatty acids and DHEA-S observed in the study is beneficial or not. Nevertheless, with regard to n-3 fatty acids, it has been widely reported that n-3 fatty acids are inversely associated with metabolic syndrome and may improve insulin sensitivity. Therefore, the beneficial effect of DHEA-S on the insulin sensitivity may be contributed to the association between DHEA-S and n-3 fatty acids.

Earlier studies have reported that DHEA-S is able to modulate fatty acids metabolism by changes in the activity of several hepatic enzymes involved in FA biosynthesis and oxidation [24]. In this study, the correlation of DHEA-S and several desaturases was estimated and our results suggested that DHEA-S level correlated positively with D9D-18 (stearoyl-CoA desaturase) in men and D6D in women (Table 4). Desaturase is important enzymes of fatty acids biosynthesis and mainly included D9D-18, D6D, D5D, and so on. D9D-18 converts stearic acid (C18:0) to oleinic acid (C18:1) by introducing a double bond in the delta 9-position and D6D is a desaturase which is responsible for the conversation of polyunsaturated fatty acids by introducing a double bond in the delta 6-position. These desaturase activities are determined primarily by transcription of the genes and regulation of mRNA levels [25]. It has been demonstrated that DHEA-S either bind or activate several families of transcription factors like peroxisome proliferator-activated receptor (PPAR) and other receptors that can modulate desaturase mRNA levels [26]. Further, high correlations were observed between DHEA-S and desaturase activities in rats and obesity women [27]. In short, the correlations between DHEA-S and desaturase suggested that DHEA-S has an effect on the fatty acid metabolism.

Several limitations of our study deserve comment. First, our hypothesis that serum fatty acids were correlated with DHEA-S was based on findings in the literature. However, these studies mainly involved in the effect of exogenous DHEA-S on fatty acids and none of them was the relationship between endogenous DHEA-S and fatty acids in human. Therefore, our results need to further validate in the large population. Second, we did not measure desaturase activity directly, but rather estimated it from the ratio of the specific substrate to the corresponding product of the respective enzyme. Third, although we adjusted for factors known to influence fatty acid metabolism and DHEA-S, the possibility of residual confounding cannot be excluded. Finally, our study subjects did not represent a random sample of the Chinese population, and thus caution is required in generalizing the present results to the entire Chinese population. In conclusion, there is different DHEA-S, fatty acid profile and the desaturase activities in both genders with the IPH subjects and the association between DHEA-S and fatty acids, desaturase activities is dependent on some factors including age, BMI, TC, TG, 2h-PG and insulin.

Acknowledgment

This work was funded by Natural Science Foundation of China (No. 81202186), Natural Science Foundation of China Key Project (NO. 81130049), National High Technology Research and the National 12th Five-Year Scientific and Technical Support Program of China (2012BAI02B02).

The novelty statement

At present, less attention has been paid to the metabolic change of the IPH subjects. In this study, the association of DHEA-S and FFA, desaturase were investigated in isolated post-challenge hyperglycemia (IPH) subjects. The results suggested DHEA-S was partly correlated with FFA composition and desaturase in IPH subjects. These findings partly explain the beneficial role of exogenous DHEA-S in lowering the risk of type 2 diabetes.

References

1. Barrett-Connor E, Ferrarra A (1998) Isolated postchallenge hyperglycemia and the risk of fatal cardiovascular disease in older women and men. Diabetes Care 21: 1236-1239. [Pubmed]

2. DECODE Study Group (1998) Will new diagnostic criteria for diabetes mellitus change phenotype of patients with diabetes? Reanalysis of European epidemiological data. Brit Med J 317: 371-375. [Pubmed]

3. Resnick HE, Harris MI, Brock DB, Harris TB (2000) American diabetes association diabetes diagnostic criteria,advancing age, and cardiovascular disease risk profiles: results from the Third National Health and Nutrition Examination Survey. Diabetes Care 23:176–180. [Pubmed]

4. Hosseinpanah F, Rambod M, Azizi F (2008) Likelihood of having isolated postchallenge hyperglycemia in an Iranian urban population. Diabetes Res Clin Pract 79: 490–496. [Pubmed]

5. Liu LY, Li Y, Guan CM, Li K, Wang C, et al. (2010) Free fatty acid metabolic profile and biomarkers of isolated post-challenge diabetes and type 2 diabetes mellitus based on GC–MS and multivariate statistical analysis. J Chromatogr B 878:2817–2825. [Pubmed]

6. Liu LY, Wang MQ, Yang X, Bin MX, Na LX, et al. (2013) Fasting serum lipid and dehydroepiandrosterone sulfate as important metabolites for detecting isolated postchallenge diabetes: serum metabolomics via ultra-high-performance liquid chromatography/mass spectrometry. Clin Chem In press.

7. Huang L, Xue J, He Y, Wang J, Sun C, et al. (2011) Dietary calcium but not elemental calcium from supplements is associated with body composition and obesity in Chinese women. PLos One. 6: e27703. [Pubmed]

8. Nestler JE, McClanahan MA, Clore JN, Blackard WG (1992) Insulin inhibits adrenal 17, 20-lyase activity in man. J Clin Endocrinol Metab **74:** 362–367. [Pubmed]

9. Nestler JE, Usiskin KS, Barlascini CO, Welty DF, Clore JN,et al. (1989) Suppression of serum dehydroepiandrosterone sulfate levels by insulin: an evaluation of a possible mechanism. J Clin Endocrinol Metab 69**:** 1040–1046. [Pubmed]

10. Shriock ED, Buffington CK, Hubert GD, Kurtz BR, Kitabchi AE, et al. (1988) Divergent correlation of circulating dehydroepiandrosterone sulfate and testosterone with insulin levels and insulin receptor binding. J Clin Endocrinol Metab 66: 1329–1331. [Pubmed]

11. Tchernof A, Despre´s JP, Be´langer A, Dupont A, Prud'homme D, et al. (1995) Reduced testosterone and adrenal C19 steroid levels in obese men. Metabolism 44: 513–519. [Pubmed]

12. Ravaglia G, Forti P, Maioli F, Boschi F, Bernardi M, et al. (1996) The relationship of dehydroepiandrosterone sulfate [DHEAS] to endocrine-metabolic parameters and functional status in the oldest-old. Results from an Italian study on healthy free-living over-ninety-year-olds. J Clin Endocrinol Metab 81: 1173–1178. [Pubmed]

13. Couillard C, Gagnon J, Bergeron J, Leon AS, Rao DC, et al. (2000) Contribution of body fatness and adipose tissue distribution to the age variation in plasma steroid hormone concentrations in men: the HERITAGE family study. J Clin Endocrinol Metab 85: 1026–1031. [Pubmed]

14. Abbassi A, Duthie EH Jr, Sheldahl L, Wilson C, Sasse E, et al. (1998) Association of dehydroepiandrosterone sulfate, body composition, and physical fitness in independent community-dwelling older men and women. J Am Geriatr Soc 46: 263–273. [Pubmed]

15. Maccario M, Mazza E, Ramunni J, Oleandri SE, P Savio, et al. (1999) Relationships between dehydroepiandrosteronesulphate and anthropometric, metabolic and hormonal variables in a large cohort of obese women. Clin Endocrinol 50: 595–600. [Pubmed]

16. Haffner SM, Mykka¨nen L, Valdez RA, Katz MS (1993) Relationship of sex hormones to lipids and lipoproteins in nondiabetic men. J Clin Endocrinol Metab 77: 1610–1615. [Pubmed]

17. Bendlová B, Vrbíková J, Hill M, Vanková M, Lukásová P, et al. (2008) Dehydroepiandrosterone in relation to adiposity, glucose tolerance and lipid spectra in Czech non-diabetic population. Physiol Res 57: S67-S76. [Pubmed]

18. Suga T, Tamura H, Watanabe T, Yamada J (1996) Induction of peroxisomal enzymes by dehydroepiandrosterone metabolic activation by sulfate conjugation. N Y Acad Sci 1996; 804:284–296. [Pubmed]

19. Waxman DJ (1996) Role of metabolism in the activation of dehydroepiandrosterone as a peroxisome proliferator. J Endocrinol150: 129–147. [Pubmed]

20. Sanchez J, Perez-Heredia F, Priego T, Portillo MP, Zamora S, et al. (2008) Dehydroepiandrosterone prevents age-associated alterations increasing, insulin sensitivity. J Nutr Biochem 19:809–818. [Pubmed]

21. Straczkowski M, Kowalska I, Nikolajuk A, Dzienis-Straczkowska S, Kinalska I, et al. (2004) Relationship between insulin sensitivity and sphingomyelin signalling pathway in human skeletal muscle. Diabetes 53: 1215–1221. [Pubmed]

22. Bousserouel S, Brouillet A, Bereziat G, Raymondjean M, Andreani M (2003) Different effects of n-6 and n-3 polyinsaturated fatty acids on the activation of rat smooth muscle cells by interleukin-1 beta. J Lipid Res 44: 601–611. [Pubmed]

23. Poudel-Tandukar K, Nanri A, Matsushita Y, Sasaki S, Ohta M, et al. (2009) Dietary intakes of alpha- linolenic and linoleic acids are inversely associated with serum C-reactive protein levels among Japanese men. Nutr Res 29: 363–370. [Pubmed]

24. Imai K, Kudo N, Koyama M, Kawashima Y (2003) Effects of dehydroepiandrosterone on oleic acid accumulation in rat liver. Biochem Pharmacol 65:1583–1591. [Pubmed]

25. Sjögren P, Sierra-Johnson J, Gertow K, Rosell M, Vessby B, et al. (2008) Fatty acid desaturases in human adipose tissue: relationships between gene expression, desaturation indexes and insulin resistance. Diabetologia 51: 328–335. [Pubmed]

26. Webb SJ, Geoghegan TE, Prough RA, Michael Miller KK (2006) The biological actions of dehydroepiandrosterone involves multiple receptors. Drug Metab Rev 38: 89–116. [Pubmed]

27. Imai K, Kudo N, Koyama M, Shirahata A, Kawashima Y (2001) Effects of Dehydroepiandrosterone on Oleic Acid Formation in the Liver of Rats, Mice and Guinea Pigs. Jpn. J. Pharmacol 86: 437 – 447. [Pubmed]