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Research Article

DEHYDROEPIANDROSTERONE LEVELS IN TYPE 2 DIABETES

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ABSTRACT

Background: Dehydroepiandrosterone (DHEA) is a steroid hormone secreted by the adrenal cortex. Recent research reports show that DHEA has various beneficial effects including, enhancing insulin sensitivity. This is still under study and yet to be proved in humans. **Aim**: To estimate the levels of DHEA and HbA_{1c} in men with Type 2 diabetes, in comparison with normal subjects of the same age group. **Materials and Methods**: A cross sectional comparative study of sixty participants (60 to 70 years of age), thirty men with uncomplicated Type 2 diabetes for at least five years duration and thirty non-diabetic controls was done. Informed consent was obtained. Serum levels of DHEA were estimated for all the participants by ELISA method. Their glycemic status was determined by HbA_{1c} levels. Statistical analysis was done using an unpaired T-test. Significance level was fixed at $p < 0.05$. **Results**: A significant decrease in the DHEA level was observed in Type 2 diabetes individuals (55.8 ± 11.9) compared with normal subjects (153.3 ± 49.7). A Significant increase in the HbA_{1C} level was observed in diabetic individuals (8.14 ± 0.66) compared to normal (6.01 ± 0.32). **Conclusion**: In cases with type 2 diabetes significantly lower levels of Serum DHEA was associated with significantly poorer glycemic control in comparison with normal subjects.

Keywords: Dehydroepiandrosterone sulphate, Glycosylated haemoglobin

INTRODUCTION

Dehydroepiandrosterone (DHEA) is a steroid, mainly of adrenal origin, that is found in relatively high concentrations in human plasma. It serves as a precursor of both androgenic and estrogenic steroid hormones. In the circulation, DHEA exists both free and bound to sulphate (DHEA-S). Thus, DHEA-S serves as the principal storage form of DHEA. DHEA-S has many intrinsic effects like anti aging, anti obesity, anti diabetic, anti atherogenic and neuroprotective effects.[1] A progressive decrease in circulating levels of DHEA with age has long been recognized, with peak levels occurring between the third and fourth decades of life and decreasing progressively thereafter by about 90% over the age of 85. The decline in circulating DHEA levels occurring with aging has been linked to the gradually increasing prevalence of atherosclerosis, obesity, and diabetes in elderly individuals.[2] Normal blood levels of DHEA-sulfate can differ by sex and age.[3]

Table 1: Typical normal ranges for Male & females

Age in years	Males (µg/dl)	Female (µg/dl)
18 – 19	108 - 441	145 - 395
20-29	280 - 640	65 - 380
30-39	120 - 520	45-270
40-49	95 - 530	32-240
50-59	70-310	26-200
60-69	42-290	13-130
Above 69	28-175	17-90

Insulin resistance is a major metabolic abnormality in obesity as well as in noninsulin-dependent diabetes mellitus (NIDDM) and is commonly observed in individuals with glucose intolerance, hypertension, dyslipidemia, and arteriosclerosis.[4, 5] Administration of DHEA has been reported to have striking beneficial effects on obesity, hyperlipidemia, diabetes, and atherosclerosis in obese rodents.[6] It has been demonstrated that DHEA reduces weight gain and food intake and ameliorates hyperinsulinemia in obese Zucker rats.[7] Short-term therapy with 50 mg per day of DHEA is safe for older women in relation to cardiovascular risk factors.[8] Another study showed improved insulin sensitivity, endothelial function and fibrinolytic activity for middle-aged men with high cholesterol taking 25 mg per day for 12 weeks.[9] A recent study found that DHEA supplementation may help reduce abdominal fat, which is associated with insulin resistance. Twenty eight men and 28 women, aged 65-78, supplemented with 50 mg per day of DHEA for six months, DHEA therapy induced significant decreases in visceral and subcutaneous fat. Insulin action was also improved.[10]

Dehydroepiandrosterone (DHEA) has been shown to modulate glucose utilization in humans and animals, but the mechanisms of DHEA action have not been clarified. We undertook the following study to find whether there is any link between DHEA levels and glycemic status in Indian population.

MATERIALS AND METHODS

The present study was conducted in the Institute of Physiology and Experimental medicine, Madras Medical College, Chennai after obtaining the approval of The Institutional Ethics Committee of Madras Medical College before starting the study. After obtaining informed consent, sixty male subjects aged between 60 and 70 years were selected for the study. The reason behind sample selection was that, DHEA-S levels show a considerable decline in many subjects above 60 years, though there is a huge inter-individual variation.[8,9] Thirty men with uncomplicated, well controlled Type 2 diabetes for at least five years duration, who were on oral hypoglycaemic agents and were on regular monthly follow-up and thirty non-diabetic, age and sex matched controls were selected from the population attending outpatient unit of Internal Medicine department, Govt. General Hospital, Chennai. We explained the scope and details of the study to the subjects. The subjects underwent routine clinical examination and biochemical tests to satisfy the selection criteria. Fasting blood samples of the subjects were obtained for estimation of DHEA-S and HbA_{1c} levels. Fasting blood samples were obtained under strict aseptic precautions, by venepuncture of the antecubital vein. The blood samples were drawn during the early hours of the day. The serum was separated and stored in the deep freezer at -20^0 C. The serum levels of DHEA-S was measured using ELISA kits based on the principle of competitive binding and microplate separation viz. serum Dehydroepiandrosterone sulphate estimation supplied by cal biotech Inc (California). HbA_{1c} levels were estimated by HPLC (high performance liquid chromatography). HbA_{1c} levels less than 6.0% was considered as good control.

Statistical analysis: The various parameters that were measured in this study were recorded and statistically analyzed using Microsoft office Excel and SPSS 7.0. Statistical analysis was done using unpaired t test and coefficient of correlation. Significance level was fixed at $p < 0.05$.

RESULTS

In our study, we observed a decrease in the DHEA level (µg/dl) in Type 2 diabetes individuals (55.8 ± 11.9) compared with normal subjects (153.3 ± 49.7) (graph 1). It was also observed that the decrease was significant ($p < 0.05$). A significant increase in the HbA_{1C} level (%) was observed in diabetic individuals (8.14 ± 0.66) compared to normal (6.01 ± 0.32) (Fig 2).

A significant negative correlation was observed between DHEA and HbA_{1C} levels (r = - 0.76) (Fig 3)

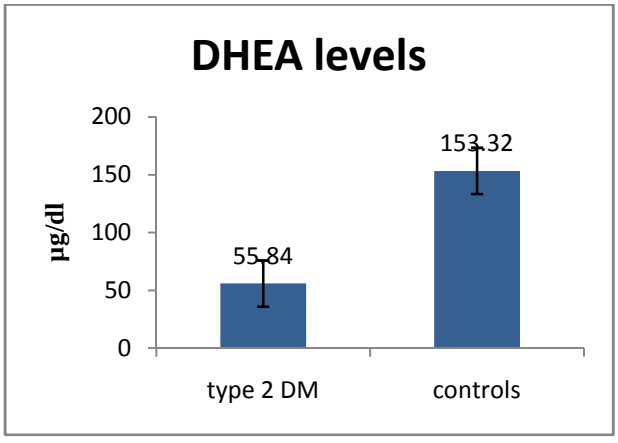

Fig 1: DHEA levels (µg/dl) in controlled Type 2 Diabetes in comparison with normal subjects.

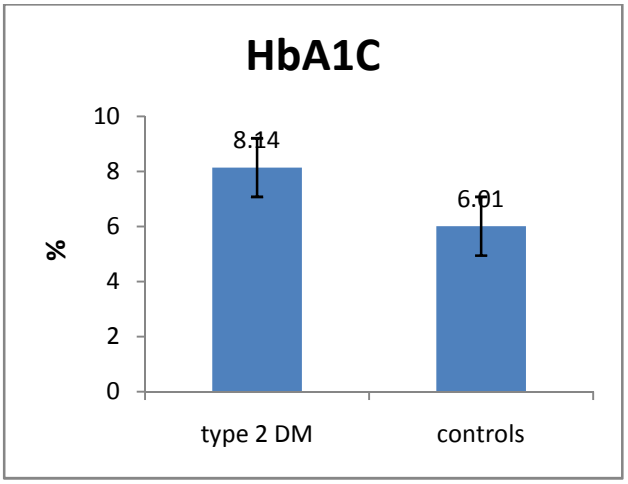

Fig 2: HbA_{1C} levels (in %) in controlled Type 2 Diabetes in comparison with normal subjects.

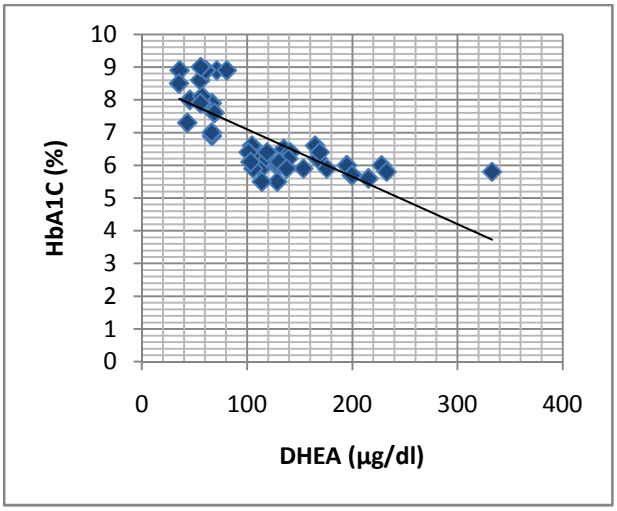

Fig 3: correlation between DHEA (µg/dl) and HbA_{1C} levels (%). A negative correlation (r = - 0.76) was observed.

Table 2: Showing Mean levels of DHEAS in µg /dl and HbA1C in %.

	TYPE 2 DM	CONTROLS	
	Mean		P value
DHEAS **(µg/dl)**	55.8 ± 11.9	153.3 ± 49.7	0.00**
HbA1C	8.1 ± 0.7	6.0 ± 0.3	0.00**

** Highly significant

DISCUSSION

In the early 1980s, Coleman ET al.[8, 10, 11] reported that dietary administration of DHEA to Mice induced remission of hyperglycaemia and largely corrected insulin resistance in these animals. More recently, DHEA was shown to protect against the development of visceral obesity and muscle insulin resistance in rats fed a high-fat diet. In addition, DHEA has been shown to restore insulin sensitivity in obese Zucker rats.[12] Oral administration of DHEA to insulin-resistant rats for 2 weeks resulted in increased glucose uptake by adipocytes compared with untreated animals.[13]

Genetically diabetic (db/db) mice develop obesity and glucose intolerance associated with insulin resistance, and subsequently exhibit β cell necrosis and islet atrophy. Supplementing their diet with DHEA prevented these pathologic changes and effected rapid remission of hyperglycaemia, β cell dysfunction, and insulin resistance[13]. Adiponectin gene expression in adipose tissue and serum adiponectin levels were elevated in DHEA-treated rats by activation of peroxisome proliferators activated receptor γ (PPAR γ).[14, 15]

Other recent studies have demonstrated that DHEA increases glucose uptake rates in human fibroblasts and rat adipocytes[16,17] and have suggested that this effect may be mediated by activation of PKC and PI 3-kinase. DHEA treatment of human adipocytes results in enhanced glucose transport rates through GLUT4 and GLUT1 transporter translocation to the cell surface. In vitro, the DHEA infusion is known to enhance insulin action[18].

Villareal and Holloszy reported a significant increase in an insulin sensitivity index in response to DHEA in the elderly. DHEA treatment can reduce body weight and serum TNF-α, and also may increase insulin sensitivity and slow progression of type 2 diabetes.[18]

In a recent study, enhanced insulin sensitivity and glucose disposal were found in hyperandrogenic women treated orally with DHEA, under conditions in which the treatment increased plasma DHEA and DHEAS.[19]

Insulin resistance is central to the metabolic syndrome, which has received increasing attention in the past few years as a concurrence of CVD risk factors including abdominal obesity, impaired glucose tolerance, dyslipidemia, and hypertension.[20, 21] Low DHEA concentrations are associated with development of central obesity, while decreased serum concentrations of DHEA may contribute to insulin resistance. Patients with type 2 diabetes mellitus often show clustering of risk factors, which puts them at particularly high risk for CVD. Low levels of DHEA seen in type 2 diabetes might be the triggering factor for these risk factors. Administration of metformin is reported to increase serum DHEA-S

secondarily to alleviation of hyperinsulinemia seen in insulin resistance.[22]

CONCLUSION

As an aim to find an association between DHEA levels and type 2 diabetes, we found that lower DHEA level was linked to poor glycemic control. Recently, there has been a resurgence of interest in DHEA, because it has been suggested that it might have anti-ageing effects. Hence, Type 2 diabetes and its associated complications which are considered as an expanded spectrum of accelerated ageing can attribute a part of its pathogenesis to lowering DHEA levels. Clinical trials on the effects of DHEA supplementation in humans with type 2 diabetes are still in their early stages. Further research on this topic can derive clues to pathogenesis of diabetes and ageing.

Competing interests: Nil

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