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Mechanism of hypogonadism in males of T2DM in eastern India: An original article

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Abstract
Male hypogonadism may be due to primary gonadal failure or secondarily from hypothalamic-pituitary causes. Diabetes contributes for a significant number of hypogonadism in males. In our study, it is shown that male patients with type 2 diabetes (T2DM) have hypogonadism due to primary gonadal failure as suggested by low serum testosterone and high serum FSH, LH levels.

Keywords: Hypogonadism, type 2 diabetes, testosterone, FSH, LH

1. Introduction

Male hypogonadism is a clinical condition comprising both symptoms and biochemical evidence of testosterone deficiency. It strongly affects the health of men especially causing reduced bone strength, decrease in muscle mass, hypertension, hyperlipidaemia, diabetes, asthma [1] etc. Deficiency of FSH and LH is the main cause of hypogonadotropic hypogonadism (HH), which may be a heritably condition [2] or an acquired cause. Whatever may be the cause, the primary symptoms of hypogonadism include lower libido, fatigue, depression, mood swings and erectile dysfunction [3].

The aim of our study was to find out the mechanism behind hypogonadism (primary or secondary) in T2DM patients from Eastern India, where very less number of studies are done yet to explore this aspect of diabetes and hypogonadism.

2. Materials and Methods

The study was carried out at the Department of Biochemistry, Calcutta National Medical college and Hospital, Kolkata, West Bengal. Total 360 subjects of age between 18 to 45 years constituted the study population. The research protocol was approved by the Ethics Committee of the institution.

Amongst them, 180 type 2 (non insulin dependent) diabetic patients were assigned to the case group and 180 non diabetic healthy individuals were assigned to the control group. A total 180 males and 180 females were involved in the study. These subjects of both sexes were categorized under three age groups of 18 to 26 years, 27 to 36 years and 37 to 45 years. Samples of venous blood were collected from all the individuals under aseptic technique and subjected to biochemical analysis after centrifuging at 3000 rpm for 10 minutes.

Fasting blood glucose and postprandial blood glucose were measured by GOD-POD method [4] and HbA1c% was measured by ion exchange resin method by coral clinical system kit [5]. The Calbiotech LH ELISA Kit was used for the quantitative measurement of LH in human serum or plasma [6]. The Follicle Stimulating Hormone (FSH) ELISA Kit (solid phase assay using streptavidin/biotin method) was used for the quantitative measurement of FSH in human serum [7]. Serum testosterone was measured by ELISA (Calbiotech) [8]. Data generated were analyzed using statistical package for social science (SPSS) version 20.00 and Microsoft Excel 2007. Comparison mean and standard deviation values were made for the various parameters for test and control subjects using student-t test. Results were considered statistically significant with a 95% confidence interval ($p<0.05$).

3. Results

Table 1: Age based comparison between cases & controls for LH, FSH, testosterone, FBS, PPBS and HbA1C% parameters among males.

Age group (years)	18 to 26		27 to 36		37 to 45	
Male	Case (Mean and SD)	Control (Mean and SD)	Case (Mean and SD)	Control (Mean and SD)	Case (Mean and SD)	Control (Mean and SD)
LH(mIu/ml)	8.17±1.23	5.25±0.60	8.12±0.51	5.85±0.53	11.14±0.76	6.29±1.48
FSH(mIu/ml)	9.28±0.73	6.25±0.106	9.21±0.79	7.35±0.09	14.04±1.00	10.68±1.10
Testosterone (pg/ml)	4.77±0.79	7.50±0.99	4.2±1.43	6.05±0.22	3.19±0.85	5.37±0.69
FBS (mg/dl)	175±5.45	78±5.63	201±7.40	88±5.34	167±8.58	98±7.01
PPBS(mg/dl)	254±16.99	102±13.51	236±8.23	110±8.44	210±9.35	115±6.09
HbA1C%	9.10±0.71	4.15±0.57	7.4±0.66	4.15±0.65	7.53±1.10	4.25±0.66
P value	≤0.05	≤0.05	≤0.05	≤0.05	≤0.05	≤0.05

4. Discussion

From FSH, LH and testosterone values of male cases and control groups of three age groups, it was found that the mean values of cases were more than that of control and the p value was significant (p value ≤ 0.05). Estimation of testosterone in males showed decreased testosterone levels and in all three age groups of cases compared to controls. Decreased levels of testosterone in male cases were associated with corresponding rise in FSH and LH levels. Our findings indicate a state of primary gonadal dysfunction in type 2 diabetes leading to emerging sexual dysfunction.

In the study of Rahmat *et al*. it was shown that level of testosterone was reduced in T2DM patients. Jat *et al*. showed the relationship with serum level of free and total testosterone amongst 80 males subjects of age 30 – 70 years with type 2 diabetes [9]. In study of Ernani *et al*. in 2005 and Fogari *et al*. in 2007, the level of serum total testosterone was found to be less in diabetic patients [10, 11].

The study of Onah *et al*. showed how the level of testosterone decreased with insignificantly high level of LH, which reflected abnormal feedback mechanism in hypothalamic pituitary testicular axis of diabetic men. This findings do agree with our study. Natah *et al*. and Ali *et al*. reported a significant higher FSH & LH levels in diabetics than in control [12, 13].

Hypogonadism in men with T2DM has become prevalent worldwide. In the recent study of Agarwal *et al*., the prevalence of hypogonadism in Indian males with T2DM and assessment of the primary and secondary hypogonadism along with androgen deficiency were done. It was evident from that study, that the incidence of hypogonadism is more in diabetic patients as compared to the general population. Hence, early screening for hypogonadism and application of testosterone replacement would be helpful [14]. Oxidative stress played an important role in the pathogenesis of cardiometabolic diseases and it was mostly found in the patients with hypogonadism. The study of Haymana *et al*., aimed to investigate possible differences in oxidative stress conditions between patients with hypogonadism and healthy controls [15].

5. Conclusion

In our study, it is shown that in male patients with T2DM, levels of testosterone were significantly lower than in non diabetic males, as well as FSH and LH levels were significantly higher than controls. These findings suggest that hypogonadism in males having T2DM is due mainly to primary testicular failure rather than hypothalamic-pituitary causes.

However, proper data and knowledge with regard to loss libido, sexual dysfunction due to lack of primary sex hormone were not readily available due to absence of structured patients' questionnaire pattern and feedback. Decrease serum testosterone level among men may be corrected by testosterone replacement. Moreover, whether hormone replacement among depleted T2DM subjects over a prolonged period of time is beneficial or not in terms of revival of libido is another subject of further research.

Increased oxidative stress may be one of the key factors for causing gonadal dysfunction. Serial measurement of various oxidant and antioxidant status of an individual during the course of progression from prediabetic to overt diabetic state may be done by simple standardized biochemical procedures. This shall be of great importance in assessment of chronic but silent complications of diabetes mellitus like sexual dysfunction, the symptoms of which can only be felt but can never be clearly defined.

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