



RESEARCH ARTICLE - MEDICAL TECHNIQUES

Role of leptin and inhibin B in infertile males with metabolic syndrome

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Abstract

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Harm of metabolic syndrome (MS) on male infertility is mostly attributed to the various problems related with overweight such as scrotal temperature, variation of serum testosterone levels or dyslipidemia. The current study was designed to determine the correlation of leptin with inhibin B and sex hormones in infertile men with metabolic syndrome. Forty five infertile male patients with a complete history and clinical examination were taken from the period from January to July 2017 with thirty fertile apparently healthy male volunteers. Blood samples were drawn from all patients subjects and healthy control in fasting state to measure the biochemical parameters which included fasting glucose levels (FBG), triglyceride (TG), high density lipoprotein HDL-c, concentrations. Also, follicle-stimulating hormone (FSH), luteinizing hormone (LH), total testosterone (tT) levels were estimated, while the levels of serum inhibin B and leptin were estimated. Additionally body mass index (BMI), waist circumference (WC) and blood pressure (BP) were recorded to all subjects. The results revealed a significant increase in the level of BMI, WC, SBP, DBP, FBG, triglyceride, high density lipoprotein level in the patients group when compared with the control group. Beside that, the levels of FSH, LH, tT, leptin and inhibin B were significantly highly different when comparing the patients group with the control group. Furthermore, a highly significant coefficients of correlation was observed between the leptin and FSH, LH, tT, inhibin B ($r = -0.46, -0.38, 0.28, -0.29$) respectively. This study suggests that increasing the levels of leptin associated with infertility in males with metabolic syndrome and the imbalance in reproductive hormone correlated with hyperlipidemia.

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Keywords: leptin, inhibin B; metabolic syndrome; infertility.

1. Introduction

Infertility is defined as the inability to conceive after one year of unprotective intercourse. About 30% of infertile cases are solely attributed to the male partner [1]. Infertility affects both men and women so that infertility usually appears if both partners have decreased fertility. Fertility in men can be reduced by abnormalities in congenital, endocrine disturbances, genetic abnormalities, malignancies and immunological factors [2]. Metabolic syndrome (MS) include dyslipidemia, elevated blood pressure, accumulated abdominal obesity and insulin resistance, also MS is related to proinflammatory, prothrombotic state, and reproductive disorders [3]. The harm of MS on male infertility is mostly attributed to the various problems related with overweight such as scrotal temperature, variation of serum testosterone levels or dyslipidemia [4]. Leptin hormone a non-glycosylated peptide of 146 amino acids, secretion of this hormone is by the adipose tissue and made also by the placenta, skeletal muscles and stomach. Leptin acts in a dual way at the central nervous system and modulates blood glucose homeostasis in which these effects are mediated by several mechanisms so that, leptin is considered as an indicator of the body fat mass [5]. Beside of the function of leptin as a body weight regulator it has effects on the reproductive system function [6]. Receptors of leptin are existent in testicular tissue and detection of leptin in semen has been confirmed [7] which links the male reproductive function with this hormone. A Sertoli cells are a kind of sustentacular cells in the testicle, located in the walls of the seminiferous tubules. The sertoli cells are important for the control of spermatogenesis and supplies nutrients to sperms, in addition it is consider the major source to secrete inhibin after puberty [8]. Inhibin is a gonadal dimeric glycoprotein composed of an α subunit and either β A subunit (inhibin A) or β B subunit (inhibin B) linked by disulphide bridges. The biological active form of inhibin A and B are synthesized by the ovary, testis, placenta and fetoplacental unit. Only inhibin B is present in the circulation of men. Inhibin correlates inversely with follicle stimulating hormone (FSH) in adult men,

work together with activins protein to regulate FSH secretion. Inhibin has an important role in hormone feedback regulation between gonads and the pituitary gland in both females and males; inhibin inhibits FSH production but does not inhibit the secretion of GnRH from the hypothalamus [9]. Serum inhibin B concentrations is represented as a diagnostic parameter in male subfertility and reflect sertoli cells function. In adult life, production of inhibin B is proportional to spermatogenesis amount, by the direct correlation between sperm count and serum inhibin [10]. The current study aimed to find a correlation between leptin with inhibin B, and with sex hormones in infertile men suffering from metabolic syndrome.

2. Material and methods

From the consult clinic of high institute for infertile diagnosis and assisted reproductive technologies, Al- Nahreen University in Baghdad consultant of male infertility evaluated forty five infertile male patients with completed history and clinical examination were taken for the period from January to July 2017 with thirty volunteers' fertile healthy male. Infertile patients with metabolic syndrome were chosen according to the National Cholesterol Education program adult treatment panel III criteria [11]. Males were considered as patients who have at least three of the following components: waist circumference (WC) ≥ 102 cm, triglyceride (TG) ≥ 150 mg/dl, HDL < 40 mg/dl, blood pressure $\geq 130/85$ mmHg and fasting glucose (FBG) ≥ 100 mg/dl. For all participants, waist circumference (WC), body mass index BMI was calculated for each male in patients and control groups [12]. A venous blood sample was drawn at fasting state to assay fasting glucose levels [13], triglyceride [14], HDL-c [15], concentrations were determined by enzymatic methods. Also, follicle-stimulating hormone (FSH), luteinizing hormone (LH), total testosterone (tT) [16] levels were estimated by radioimmunoassay, while the levels of inhibin B and leptin were estimated by ELISA technique [17]. Any male with any testicular pathology, pituitary disease, thyroid disorder, patients receiving steroids and diuretics treatment were excluded.

Permission from institutional ethics committee (Al- Nahreen University, high institute for infertile diagnosis and assisted reproductive technologies) and informed consent was obtained from all participants.

Statistical test: All data of this study was submitted as (mean \pm SD). Student's T-test was applied to compare patient groups with healthy group also Pearson's coefficient was used for correlation analysis.

3. Results

Results in Table (1) summarized the anthropometric and metabolic characteristics of all participants. The average age of volunteers group (34.21 ± 1.87) was similar to the average age of patients group (34.30 ± 2.40) therefore, no significant difference was noticed when comparing between studied groups. As expected patients with metabolic syndrome had significantly higher ($p < 0.001$) BMI, WC systolic and diastolic blood pressure (SBP and DBP), triglyceride (TG), fasting blood glucose (FBG) and high-density lipoprotein (HDL) levels as compared to controls group.

Table 1: Descriptive parameters for the patients and control groups.

	Patients group (Mean \pm SD)	Control group (Mean \pm SD)	P-value
Age (Yrs)	34.30 ± 2.40	34.21 ± 1.870	>0.05
BMI(kg/m ²)	33.07 ± 4.45	24.01 ± 1.32	<0.001
WC (cm)	96.90 ± 7.40	70.10 ± 6.40	<0.001
SBP (mmHg)	143.50 ± 12.40	118.50 ± 8.80	<0.001
DBP(mmHg)	94.60 ± 6.50	77.10 ± 4.50	<0.001
FBG (mg/dl)	142.83 ± 25.49	87.36 ± 12.11	<0.001
TG (mg/dl)	169.03 ± 22.34	153.40 ± 0.40	<0.001
HDL-c (mg/dl)	35.40 ± 4.30	46.50 ± 14.24	<0.001

Statistical significance was considered when P-values was <0.05 and highly significant difference was considered when P-values was <0.001 .

The result on Table (2) showed that the average level of FSH, LH, tT, leptin and inhibin B was significantly highly different when comparing patients group with the control group.

Table (2): Hormonal levels in control and patients groups

	Patients group (Mean± SD)	Control group (Mean± SD)	P value
FSH (mIU/ml)	5.33 ± 0.58	7.11 ± 0.07	<0.001
LH (mIU/ml)	4.31 ± 0.49	6.21 ± 0.30	<0.001
tT (ng/dl)	344.2 ± 61.82	447.3 ± 72.69	<0.001
Leptin(ng/dl)	23.5± 4.3	10.8 ± 1.9	<0.001
InhibinB (pmol/L)	112.11± 34.3	162.53 ±22.5	<0.001

P-values <0.05 was considered statistically significant.

Also, data in Table (3) describe a highly significant coefficients of correlation observed between leptin and FSH, LH, tT, inhibin B (r = -.46, -0.38, 0.28, -0.29) respectively.

Table 3: Correlation of leptin with some variables

	r	P-value
Leptin & FSH	- 0.46	<0.001
Leptin & LH	-0.38	<0.001
Leptin & tT	0.28	<0.001
Leptin & inhibin B	-0.29	<0.001

P-values <0.05 was considered statistically significant.

4. Discussion

Each part of metabolic syndrome definition has impacts on male fertility independently, when put together; these metabolic components can have additional effects on fertility. Metabolic syndrome was characterized by insulin resistance, dyslipidemia and obesity, all that associated with low testosterone levels so that, metabolic syndrome was supposed as a risk factor for hypogonadism in males and that agree with the results of this study which show decreased levels of the reproductive hormones; testosterone, LH, FSH and inhibin B in infertile men with metabolic syndrome [18]. Decreasing level of testosterone causes increased activity of lipoprotein lipase and triglyceride uptake leading to increased insulin resistance, obesity and androgen deficiency. Obesity possibly impaired sertoli cells function and that lower the synthesis of inhibin B so that gonadotropin response will be inadequate [19]. Inhibin B is a marker to sertoli cells function predicting semen quality and male factor infertility; decreasing levels of inhibin B was noticed in patients group and that is in agreement with other researches [20- 22]. Many studies indicate some of adipose tissue regulates reproductive function and effectiveness to each other by some mechanisms directly or indirectly [23-25]. Leptin an adipocyte-derived hormone have significant roles in numerous physiological functions, including reproduction, it is necessary for normal sexual function, but when present in excess, leptin can have an effect on sperm count, increased sperm abnormalities, and oxidative stress in obese men [26]. In the present study, there was a significant increase in leptin levels in patients group and there was a correlation between leptin and inhibin B and testosterone levels, suggesting that leptin could affect inhibin B secretion and may be the function of sertoli cells. The relation between leptin and inhibin B levels in infertile patient with metabolic syndrome has not yet been reported to the best of our knowledge.

5. Conclusion

The current study indicates that increasing leptin levels was related with infertility in males with metabolic syndrome and suggesting that leptin might affect testicular function. Additionally, imbalance in reproductive hormone correlates with hyperleptinemia.

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