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Comparative Study of Aromatase Activity Level in Male Patients with Active Acromegaly

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Abstract : Aromatase activity in the acromegaly is a critical marker of decided sexual behavior. There is a confirmation demonstrated that aromatase activity is associated with testosterone and estradiol levels. The goal was to explore the relationship between GH, IGF-1, testosterone, estradiol and aromatase activity in patients with active acromegaly. In this study sixty male (age 20-60) years were enrolled. Serum of testosterone, estradiol, GH, IGF-1 and aromatase activity measured in both groups. The results revealed that mean of serum aromatase activity and estradiol levels were significant differences decrease in active acromegaly when compare with the control group and aromatase activity important correlate with IGF-1and estradiol necessary correlate with GH/ IGF-1and T/E_2.While GH, IGF-1-1, GH/ IGF-1, testosterone and T/E_2 were significant differences increase in active acromegaly when compare with the control group and GH was necessary to correlate with GH/ IGF-1 in patients group.
Keywords : GH, aromatase activity, testosterone, E_2, IGF-1, active acromegaly.

Introduction:

Acromegaly is severe hormonal disorder and uncommon portrayed by progressive somatic deformation involving mainly face and extremities and from variant growth hormone secretion and subsequent increment of IGF-I, most created by benign pituitary adenomas, and can characterized as a hormonal disorder that most typically happens in moderately aged men and women [1]. At the time of diagnosis, systemic complications are also common, including cardiovascular, changes in the physical, gastrointestinal, endocrine and metabolic systems, catabolic states, renal failure, malnutrition, and diabetes mellitus[1]. Excessive growth hormone production in children can prompt to gigantism, and in adults, it can prompt to acromegaly. Various variables are known to influence GH secretion, such as sex, diet, age, stress, exercise, and other hormones[2]. Lack of sleep suppresses GH release, especially after early adulthood [3.] An increase of GH secretion causes the liver to produce more than the usual amount of (IGF-I).Then this new IGF-I that causes the growth of the organs and soft tissues and swelling.A successive result of acromegaly is developed a web-based acromegaly patient registry and utilized it to demonstrate that hypogonadism, even in male patients with microadenomas, who are not at hazard from hypopituitarism because of local mass impacts. Additionally showed that hypersecretion of prolactin and GH contribute to the pathogenesis of hypogonadism in acromegaly and that may happen in macroadenoma patients even without of hyperprolactinaemia[4].

Aromatase is the enzyme that's considered as a rate-limiting in the conversion of androgens into estrogens and is an individual from the P450 cytochrome superfamily. Through successive cytochrome P450-catalyzedoxidations the one central pathway that converts progesterone to its derivative (17-hydroxy, 17-hydroxyprogesterone,and then to Δ^4-androstenedione) [5]. The activity of aromatase on Δ^4-androstenedione createdestrone, and activity of a dehydrogenase on this gives the main compound, 17β-estradiol. Instead, Δ^4-androstenedione can be converted into the androgen and then into testosterone, which can be transformed straightforwardly into 17β-estradiol https://en.wikipedia.org/wiki/Estradiol - cite_note-7 [6].Factors knew to increment aromatase activity incorporate age, insulin, weight, liquor andgonadotropins. Diminished aromatase activity is by an anti-Müllerian hormone, prolactin. Its shows to be Strengthen in particular estrogen-dependent local tissue next to endometrial cancer, endometriosis, uterine fibroids and breast tissue [7].

Likewise sometimes alluded to as familial gynecomastia or familial hyperestrogenism, is an endocrine syndrome and rare hereditarywhich is featuringby aromataseoverexpression, thus resulting in excessive levels of circulating estrogens [8].Physiological observed variations of the condition include overexpression of aromatase and, accordingly, excessive estrogens levels including estradioland estrone, and the greater rate of peripheral conversion of androgens to estrogens[7].

The goal of this study was to estimate the variant in the aromatase activity levels in acromegaly patients compare with control and some related parameters, GH, IGF, Testosterone hormone, estradiol hormone and whether aromatase level can potential use to follow up the active acromegaly patients.

Patients and Methods

In this study sixty male (age 20-60) years were registered, (30) active acromegaly patients who have attended the National Diabetes Center and Specialist Center for endocrinology and diabetes, Baghdad for the period from month (12/ 2015) to month (6/ 2016) and (30) healthy as a control group. Since physicians diagnosed all patients. Blood was collected, and the sera were separated. GH, IGF-1and levels of aromatase activity estimated by (ELISA) enzyme-linked immune sorbent assay kits. MiniViduse is used for hormonal Testosterone and estradiol hormones investigations for all the patients and control. The principle test combines a final fluorescent detection with an enzyme immunoassay sandwich method (ELFA). All steps of the assay are achieved automatically by the instrument VIDAS® estradiol, VIDAS® Testosterone. BMI was determined by used this equation (BMI)=mass (kg)/(height)^2 (m^2).

The Statistical Analysis

Statistical analyses were done using SPSS program version 19 which includes: Mean ± standard deviation, independent t-test, P-value equal or less than 0.05 be considered significant, we used Pearson's Correlation coefficient to test between (aromatase activity) and different parameters.

Discussion and Results

Mean ± SD of IGF-1, GH, ratio of GH to IGF-1 and BMI for active acromegaly patients and control were seen in table (1) was manifested that: In patients with active acromegaly the mean of GH, IGF-1 and ratio of GH to IGF-1 were significant differences greater than control group, while BMI was non-significant differences and greater than the control.

Table 1. Mean±SD of GH, GH/ IGF-1 ,IGF-1 and BMI

p-value	t-test	The patients	The controls	Parameters
		Mean ± standard deviation	**Mean±standard deviation**	
0.000*	9.776	11.173±4.601	1.065±0.458	**GH** ng/mL
0.000*	5.429	493.417±183.506	274.478±73.153	**IGF-1** ng/mL
0.000*	8.058	0.005±0.003	0.027±0.012	**GH/IGF-1**
0.000*	4.839	30.032±2.744	25.436±2.628	**BMI** kg/m^2

Table 2.Mean±SD of Testosterone, Estradiol, and Testosterone/Estradiol

p-value	t-test	The patients	The controls	Parameters
		Mean ± standard deviation	**Mean±standard deviation**	
0.000*	15.207	14.173±2.168	5.2947±1.33228	**Testosterone** ng/mL
0.000*	-24.363	25.748±6.989	69.313±4.969	**Estradiol** Pg/mL
0.000*	10.639	591.802±210.064	77.069±18.634	**Testosterone/Estradiol**

Table(2) showed that mean of testosterone, estradiol and ratio of testosterone to estradiol were a higher significant difference in patients with active acromegaly when contrasted with the control group.

Table(3) showed that mean of aromatase activity was a significant difference greater in patients with active acromegaly when contrasted with healthy control group.

Table 3. Mean±SD of Aromatase activity

p-value	t-test	The patients	The controls	Parameters
		Mean ± standard deviation	**Mean±standard deviation**	
0.000*	-34.807	2.836±1.095	11.209±0.364	**Aromatase activity** ng/mL

Table 4. Correlation between parameters for male active acromegaly patients

P-value	Correlation (r)	Parameters	
.030*0	.5110	GH/IGF-1	**GH**
.008**0	-0.605	GH/IGF-1	**IGF-1**
.016*0	.7320	Aromatase activity	
.026*0	.5220	Estradiol	**GH/IGF-1**
.000**0	-0.789	Testosterone/ Estradiol	**Estradiol**

Table (4) demonstrated the correlation between GH and(GH/ IGF-1) positively significant difference in active acromegaly patients In male patients with acromegaly keeps that significant negative correlation between IGF-1and(GH/ IGF-1) and positive correlation with aromatase activity. (GH/ IGF-1) was a positive correlation with estradiol while its negative correlation with Testosterone/Estradiol**.**

In this study, we determined aromatase activity and some hormones such as testosterone, estradiol and some parameters such as IGF-1, GH and BMI in Iraqi active acromegaly patients and compared with control group.

Serum GH level was very highly significant increase (P≥0.0000) was seen in this study in active acromegaly patients when contrasted with control groups. Acromegaly disorders created by increased secretion of growth hormone on account of tumor in the pituitary. GH activities anabolic on numerous organs systems very much recorded. GH invigorates bone growth during the childhood, and its induces skeletal maturation during early adulthood and adolescence [9]. Most investigate, for example, the outcome which acquired by Johan *et al.* [10]. In this study found the GH stimulates longitudinal bone growth and body mass index and expanded in patients with acromegaly, because of positively correlated with the body weight with bone mineral density ,the obese is not the reason, The outcome in our study is conformity with the outcome which acquired by Reid [11] was demonstrated that difference seen inter alia both acromegaly and healthy control group and no variance particularly active acromegaly and control, but the result was dispute with the outcome acquired via Berg *et al.*, [12] who demonstrated that no significant variance when contrasted with levels of physiological.

In the present study was seen the serum IGF-1 level was very highly significant (P=0.0000) in patients with active acromegaly when compared with control groups, due to GH secretion by the pituitary into the circulation that's motivated to make another hormone called insulin-like growth factor-I from the liver then lead to tissue growth in the body. Elevated levels of IGF-I, similar to this, signal the pituitary to decrease GH generation. If the pituitary continues to make GH-independent of the conventional regulatory mechanisms, the level of IGF-I continues rising, stimulated to bone overgrowth and organ enlargement. Furthermore, also in the present study was seen increase significant increment of level GH/IGF-1 ($P \geq 0.0000$) in serum patients with active acromegaly when contrasted control groups, The result in our study is inter alia with the outcomes acquired via Julie M Silverstein[13]proposes that the utilization of the last available values for GH/IGF1 assessments, which have invariably utilized in most clinical studies, may not accurately estimate mortality hazard in patients with acromegaly.

A very highly significant increment of serum testosterone and the ratio levels (P=0.0000) and the significant decrease of serum estradiol(p=0.0000) were seen in this study in patients with active acromegaly when contrasted with control groups.Other than making a healthier person, inhibiting aromatase creation will also apparently increment testosterone levels because less testosterone will be converted into estrogen[14].Testosterone /estrogen ratio controlled by the activity of aromatase and intracellular presented. The testosterone /estrogen proportion has been seemed to essential for apoptosis of the oocytes and the induction of ovulation [15, 16]. From the clinical studies was discoveries on the estrogen deficiency significance in men [17,18], the actions of estrogen and its necessity in males also has turned into an acknowledged idea these days[19,20].

A very highly significant decrease of serum aromatase activity levels (P=0.0000) The outcome of our review is concurrence with the findings got by[21,22]demonstrates the 28yearsold XX, followed since childhood, showed the essential elements of the aromatase deficiency syndrome as newly characterized. The patient at birth had no adrenal female pseudohermaphrodism and undergone reform of the external genitalia, such as a clitorectomy. Since at the puberty, created following indications of pubertal failure, virilization without any estrogen action signs, hypogonadotropic polycystic ovaries and hypogonadism lead to increase the plasma androstenedione concentrations, 17-hydroxyprogesterone and testosterone, while low plasma of estradiol. Polycystic ovaries that a strikingly unusual proportion of testosterone and androstenedione to estrone and estradiol. Hormone surrogate therapy prompted to menses, breast development, determination the growths of ovarian, and extinction of the increased LH and FSH amounts. Regulate the P450arom gene by tissue-specific promoters at the levels of transcriptional in the brain, adipose tissues, placenta , gonads[23,24] the authors control of aromatase gene expression not just for the breast cancer treatment[25], additionally in males, for example, in the instances of gynecomastia [26,27]or prostate cancers [28]The outcome of our study is agreement with the results acquired by [29]that suggested aromatase blockade brought about a fall in E2 with a with a relating increment in T levels.

Conclusions :

we conclude that there is positively significantly association between levels of (GH/ IGF-1) with GH in active acromegaly patients. While (GH/ IGF-1) is negatively significantly association with IGF-1. Positively associated with aromatase activity with IGF-1in patients with acromegaly. Estradiol is positively significantly association with (GH/ IGF-1) while it's negatively significantly association with T/E_2. Aromatase activity can play a role to estrogen level in patients with acromegaly

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