Study of Lipid Profiles levels in Iraqi children with GH Deficiency Before and after 6 Months GH Replacement Therapy

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Abstract

This present study aimed to quantify serum lipid levels [Total cholesterol (TC), Triglyceride (TG), Low Density Lipoprotein –cholesterol (LDL-c), Very Low Density Lipoprotein –cholesterol(VLDL-c), High Density Lipoprotein–cholesterol (HDL–c)] quantified before and after 6 months of treatment in Iraqi children with HGH deficiency

This study was conducted at the National Center for Diabetes Treatment and Research of the Mustansiriya University in Baghdad and for the period from, (October 2016 to July 2017). The study included 200 samples divided into two groups. The patient group included 100 children with short stature including 52 males and 48 females with their age ranged from 5 to 12 years . For comparison, 100 samples (50 females and 50 males) of healthy children corresponding to patients with sex, age were selected as control group.

The results of the study showed Serum (TC), (TG), (LDL-C) and (VLDL) levels had a highly significantly increased in children GHD group when compared with controls group (P<0.001).

Regarding serum (HDL-C) levels there was a highly significantly decreased in children GHD group when compared with healthy children (P<0.001) before treatment, and after 6 months of treatment a decrease in fat levels was observed in patients [(TC), (TG) and (LDL-C), (VLDL), very significantly (p <0.001), while their HDL-C level was higher than before treatment .

To distinguish between GHD patients and the control group, the Receiver Operator Curve (ROC) analysis showed a descending order of significance for the indicators that showed significant differences before treatment. The serum level of LDL-C was 0.77, followed by (TG) (0.637) ,(VLDL-C) (0.637),(TC) (0.626), and (HDL-C) (0.614) respectively [this means that all variables managed to occupy a significant region of ROC

It was concluded from this study that there was a significant increase (P <0.001) in serum TG, TC, LDL-C and VLDL-C, while the level of HDL-C in the blood decreased significantly in GHD children compared with healthy children. After 6 months of treatment rhGH has improved the lipid profile of children with growth hormone deficiency.

Keywords: *Growth hormone deficiency , GH therapy, lipid profile.*

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Introduction

Human Growth hormone (hGH) A polypeptide protein hormone on a single base of protein containing two sulfuric bonds (disulfide bonds -S-S) the hormone is

produced and stored and then secreted by somatotropin cells in the frontal lobe of the pituitary gland [1] , GH necessary for normal growth during childhood and adolescence and influences bone mineralization and body composition in children and adults [2] . Growth hormone helps Consumption of stored fat in the body as a source of energy because The amount of carbohydrates stored in the body is small and insufficient to produce the necessary energy, so the hormone helps prevent the destruction of protein for use as an energy source[3, 4] . Cholesterol (TC), a waxy substance produced by the liver and found in certain foods, is needed to make vitamin D and some hormones, build cell walls, and create bile salts that help to digest fat[5] . Triglycerides (TG) are another class of fat or lipids, a mixture of fatty acids and glycerol circulated in the bloodstream. Triglycerides (TG) are necessary for life itself . they contain chains of high energy fatty acids providing much of the fuel needed for body cells to function . thus the cells remove TG from the VLDLs only when they need them as energy source , People with high triglycerides (TG) often have a high total cholesterol (TC) ,high low density lipoprotein (LDL-c) (bad) cholesterol and a low High Density Lipoprotein–cholesterol(HDL-c) (good) cholesterol level[6]. HDL is a class of lipoproteins produced by the liver and intestines , Sometimes it is referred to as 'good cholesterol' lipoprotein The High density lipoprotein level it normal or decrease in severe hypothyroidism because of a decrease in activity of cholesteryl-ester transfer protein (CETP) and hepatic lipase (HL),which are enzymes regulated by thyroid hormones[7].Very Low Density Lipoprotein –cholesterol (VLDL) particles have a diameter of 30-80 nm. VLDL transports endogenous products while chylomicrone transports exogenous (dietary) products. low density lipoprotein (LDL-C) is a type of lipoprotein that carries cholesterol from the liver to cells of the body. Sometimes it is referred to as bad cholesterol lipoprotein [8]

Materials and Methods

This study was conducted at the National Center for Diabetes Treatment and Research of the Mustansiriya University in Baghdad and for the period from October 2016 - July 2017)

The study included (200) samples divided into two groups. The patient group included 100 samples (52 males and 48 females) of children with growth hormone deficiency Informed consent was obtained from parents, 100 samples (50 females and 50 males) of healthy children corresponding to patients with sex, age, nutritional behavior and geographical area were selected as control group Informed consent was obtained from parents ,The study also included age groups for both sexes between (5-12) years and for both infected samples and control group. Serum (TC) , (TG) , (HDL-C), (LDL-C) and (VLDL-C) at baseline and after 6 months of treatment were measured.

Samples collection: Ten milliliters (10 ml) of peripheral venous blood was aspirated from each patient and control subject at time (8.30 – 10.30 a.m.) in the fasting state, and after an overnight's fast, venous blood samples was collected in plain tubes for serum collection.

Lipid Profile the [TC, TG, HDL-C, LDL-C and VLDL-C] were measured by enzymatic colorimetric method . (LDL-C), and (VLDL-C) were calculated according to the (Friedewald formula) [9].

Statistical Analysis

Statistical analysis done according to [10]

Results

METABOLISM OF LIPID

Table (1) summarizes the differences between healthy and HGH deficient children. The result indicates a significant increase ($p < 0.0001$) in serum(TG, TC, LDL-C and VLDL-C). (163.7± 15.2,90.9 ± 15.4,100.2 ± 7.8 and18.2 ± 3.1 mg/dl)respectively compared to healthy controls (156.8± 13.2,82.3 ± 16.9 ,92.4 ± 6 and16.5 ± 3.4 mg/dl)respectively compared to healthy controls (156.8± 13.2,82.3 ± 16.9 ,92.4 ± 6 and16.5 ± 3.4 mg/dl)respectively.

Regarding serum high density lipoprotein (HDL-C) levels there was a highly significantly decreased ($P<0.001$) in children GHD group (45.4 ± 5.3mg/dl) when compared with controls (48 ± 4.8 mg/dl) before treatment.

A 6 months of treatment with growth hormone has revealed a dramatic increase in levels of serum (HDL-C) (47.4 ± 4.4 mg/dl) in children with growth hormone deficiency. As presented in table (2), the effect of GHD

on increase the serum concentration of Serum HDL was also evaluated as a strong effect (Cohen's d = 1.33) , so the treatment with growth hormone has contributed to improved levels of serum HDL compared to what they were before treatment

To distinguish between GHD patients and the control group, the Receiver Operator Curve (ROC) analysis showed a descending order of significance for the indicators that showed significant differences before treatment. The serum level of LDL-C was 0.77, followed by (TG) (0.637) , (VLDL-C) (0.637),(TC) (0.626), and (HDL-C) (0.614) respectively [this means that all variables managed to occupy a significant region of ROC as shown in the table (3) and figure (1)below .

Table 1: parameters differences between growth hormone deficiency patients and Controls group.

HDL-high density lipoprotein, LDL-Low density lipoprotein, VLDL-Very Low density lipoprotein

Parameters	Area ROC	P value
Serum LDL (mg/dl)-before treatment	0.778	<0.001
Serum Triglycerides (mg/dl)-before treatment	0.637	<0.001
Serum VLDL (mg/dl)-before treatment	0.637	<0.001
Serum Total Cholesterol (mg/dl)-before treatment	0.626	0.002
Serum HDL (mg/dl)-before treatment	0.614	0.005

Table 2: parameters differences between growth hormone deficiency patients befor and after

Parameters	before treatment Mean ± SD	after treatment Mean ± SD	changes after 6 months of treatment Mean ± SD	Cohen's d	P Value
Serum total Cholesterol (mg/dl)	163.7 ± 15.2	160.1 ± 13.7	3.6 ± 1.5	-1.28	p<0.001
Serum Triglycerides (mg/dl)	90.9 ± 15.4	87.4 ± 14.9	3.5 ± 0.5	-1.94	p<0.001
Serum HDL (mg/dl)	45.4 ± 5.3	47.4 ± 4.4	-2 ±0.9	1.33	p<0.001
Serum LDL (mg/dl)	100.2 ± 7.8	95.2 ± 6.8	5 ± 1	-1.56	p<0.001
Serum VLDL (mg/dl)	18.2 ± 3.1	17.5 ± 3	0.7 ± 0.1	-1.75	p<0.001

Table(3): ROC area for selected measurements at baseline (before treatment) when used as test to diagnose GH deficiency differentiating it from healthy control. (Larger values of the measurement is associated with higher probability for having GH deficiency).

Parameters	Control group Mean ± SD	Patients group Mean ± SD	P Value
Serum total Cholesterol (mg/dl)	156.8± 13.2	163.7± 15.2	p<0.001
Serum Triglycerides (mg/dl)	82.3 ± 16.9	90.9 ± 15.4	p<0.001
Serum HDL (mg/dl)	48 ± 4.8	45.4 ± 5.3	p<0.001
Serum LDL (mg/dl)	92.4 ± 6	100.2 ± 7.8	p<0.001
Serum VLDL (mg/dl)	16.5 ± 3.4	18.2 ± 3.1	p<0.001

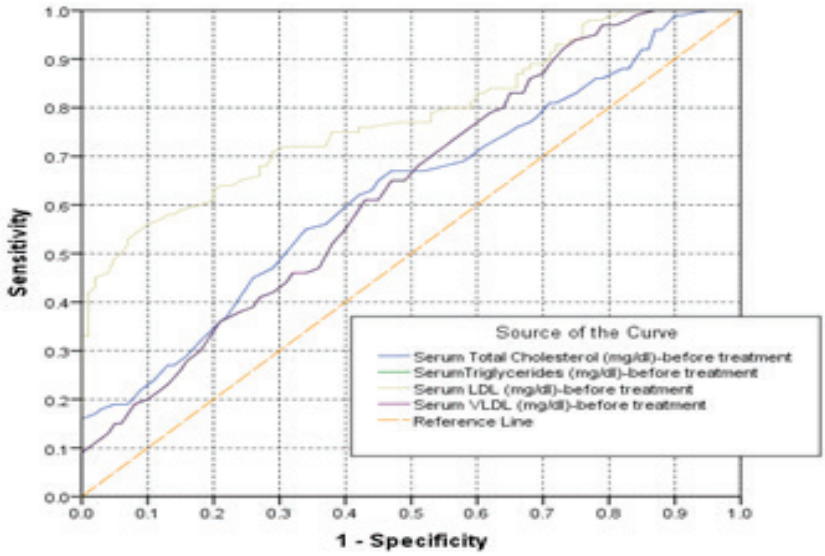

Figure 1. ROC Curve Showing the Trade-off between sensitivity and specificity for LDL, TG, VLDL, HDL and Cholesterol at baseline (before treatment) when used as test to diagnose GH deficiency differentiating it from healthy control

Discussion

Growth hormone deficiency (GHD) is a endocrine disease which could affected onto individual's life with childhood, adolescence while adulthood [11] . (GH) could boosts linear growth, quicken protein synthesis and catalyze bone growth; in addition to , it has determined effects onto the body formation, bone density, muscle strength and blood lipid level [12]. Growth hormone deficiency has a global incidence of 1: 4000 - 1: 10,000 worldwide [13]. HGH helps to consume fat stored in the body as an energy source. The amount of carbohydrates stored in the body is small and insufficient to produce the necessary energy, so this hormone helps prevent the destruction of protein to be used as an energy source[14] . Growth hormone deficiency (GHD) is a pathological condition it is caused by a lack of pituitary secretions where the body does not produce sufficient growth hormone. The most common cause of growth hormone

deficiency is pituitary tumors [15]. The origin of the disease may be fungal or acquired. For acquired causes: (15% unknown, 50% higher tumors of the pituitary gland, 5% of inflammatory wounds)[16] .

Previous studies suggest that the development of cardiovascular disease (CVD) and atherosclerosis begins in early childhood [17] . Children with growth hormone deficiency (GHD) patients are at risk of developing heart disease and atherosclerosis, including blood lipid disorder, impaired heart function and abnormalities in body composition due to their growth hormone deficiency [18] .

Dyslipidaemia during childhood with adolescence is an strong sign onto atherogenic risk to can contribute in evolution coronary heart disease (CHD) at adulthood[19]. Childhood atherosclerosis cannot be obvious, moreoer, atherosclerosis is a multifactorial disease with its roots during childhood[20] .

RhGH according to the reports in 1985 first prouction released , which able to support the final solution as treatment for all patients with GHD. Since while after that the rhGH has been approved in the rapid clinical application, the therapeutic effects of rhGH were demonstrated in wide way, as well as considered the predominant drug of the treatment GHD[21] , an effect rhGH therapy onto lipid metabolism became a centre from interest during these years [22] .

The results of Lipid profile study agreed with other studies The result indicate the presence of significant increase ($p < 0.001$) in serum TG, TC, LDL-C, and VLDL-C. Serum HDL-C levels were significantly decreased ($p < 0.001$) in GHD patients.

Patients with GHD frequently have an abnormal blood lipid profile which increase in(TC), (TG), (LDL–C) and (VLDL–C),while (HDL–C) showed decrease in patient with GHD compared to control.

where GHD children suffer from metabolic disorder for fats and RhGH therapy can improve blood lipid levels because GH promotes lipolysis regulates the rate of lipolysis in adipocytes by activating adrenergic receptors in adipocytes, thereby reducing the fat content in tissues [23]. GH had a significant effect in reducing fat by increasing blood lipid metabolism [24], and regulating the level of mRNA expression of hepatic LDL-C receptors, enhancing the liver's ability to absorb LDL-C and reducing the rate of LDL-C production [25].

moreover, some studies had observed that improvements at atherogenic danger factors are the poorerest following the withdrawal of GH therapy , which supports the beneficial effect of GH treatment onto cardiovascular danger. at 2015, an European Society of Paediatric Endocrinology emphasized that GH can improve a blood lipid levels with reduce a carotid intimal thickness, as supported by a results of our study . also , these results suggest that rhGH therapy has preventive monuments onto cardiovascular features at GHD children [26].

Our results agreed with a previous study conducted by [26] which noted this Children with untreated GHD carries a range of early cardiovascular risk factors, RhGH alternative therapy in GHD children can improve the image of blood lipids .

It was concluded from this study that there was a significant increase ($P < 0.001$) in serum TG, TC, LDL-C and VLDL-C, while the level of HDL-C in the blood decreased significantly in GHD children compared with healthy children. but After 6 months of treatment rhGH has improved the lipid profile of children with growth hormone deficiency.

In conclusion, GHD children develop lipid metabolic disorder, and rhGH therapy can improve the blood lipid levels.

Ethical Clearance: The Research Ethical Committee at scientific research by ethical approval of both environmental and health and higher education and scientific research ministries in Iraq**.**

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