Research Article

Evaluation of Insulin like growth factor 1 (IGF-1) and selected Biochemical markers in Iraqi Patients with Multiple Sclerosis

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ABSTRACT

The objective of the study is to assess serum IGF-1, Vit. D and other clinical parameters in multiple sclerosis (MS) patients and to evaluate the severity of the disease and to compare between the studied parameters before and after treatment. Thirty Iraqi newly diagnosed patients with MS and follow them after one month of treatment (Beta interferon inj. I inj./ week) and compare the results with 20 healthy control. Serum IGF-1, Vit.D, S.GOT, S.GPT, Total Cholesterol and Uric acid were measured. In MS patients, there was a significant increase in IGF-1 level in pretreatment patient group when compared to control. [P<0.001], as well as post treatment group also shown a significant increase when compare to healthy group [<0.006]. Serum VIT.D significantly decrease in pretreatment patient group when compared to control [p<0.001] and Serum Vit. D mean values were found to be significantly decreased [p<0.001] in post treatment patients group compared to control. Both GOT and GPT not affected by the disease also there was no significant difference in Total cholesterol when compared between two patients groups and control. Serum Uric acid levels did not show a significant variation [P>0.05] between pre-treatment MS patients and control. In contrast uric acid demonstrated a significant (P ≤ 0.001) increased geometric mean in post-treatment MS patients as compared to controls. The increase in circulating IGF-I and a reduction its level after one month of INF-β treatment in MS patients. The observed increase in IGF-I in patients treated with IFN-beta being of most significance as a potential therapeutic biomarker.

Keywords: Insulin, biochemical marker, Iraqi patients.

INTRODUCTION

Multiple sclerosis (MS) involves an immune-mediated process in which an abnormal response of the body's immune system is directed against the central nervous system (CNS), which is made up of the brain, spinal cord and optic nerves. The exact antigen — or target that the immune cells are sensitized to attack — remains unknown, which is why MS is considered by many experts to be "immune-mediated" rather than "autoimmune." Insulin-like growth factor-1 (IGF-1) is of considerable interest because it is not only a potent neuro protective trophic factor but also a survival factor for cells of the oligo dendrocyte lineage and possesses a potent myelinogenic capacity. However, the IGF system is complex and includes not only IGF-1 and IGF-2 and their receptors but also modulating IGF-binding proteins (IGFBPs), of which six have been identified. Insulin-like growth factor.

1 stimulates regulatory T cells and suppresses autoimmune disease reports the beneficial effects of a systemic delivery of insulin-like growth factor-1 (IGF-1) in suppressing autoimmune diseases.[1]

Vitamin D is a fat-soluble secosteroids responsible for increasing intestinal absorption of calcium, iron, magnesium, phosphate, and zinc.[2]

There is a connection between vitamin D and MS could be tied to the positive effects vitamin D has on the immune system.[3]

The current study aimed to assessed IGF-1 and vitamin D in newly diagnosed MS patients and monitors the development of disease after treatment.

MATERIALS AND METHODS

The study was done in (SHAR 400 BED Hospital) between (July 2015- May 2016). Thirty Iraqi MS patients; aged (20 - 50) years. The medical history was taken. All patients had been already diagnosed and the diagnosis had been confirmed according to The 2010 McDonald Criteria for Diagnosis of MS. For comparison with twenty apparently healthy subjects with no inflammation, no infection, non-diabetic, non-hypertensive, no chronic diseases, non-smokers, non-drinking with normal healthy subjects. Patients samples were taken before treatment and after one months of treatment (Beta-interferon injection one per week). Serum insulin like growth factor-1, Vit.D, Liver function test, total cholesterol and uric acid were measured.

Statistical Analysis

Data were analyzed using General Linear Model (GLM) in SAS program (2010) to investigate the effect of treatments (pretreatment, post treatment and control), the effect of sex and age within treatment on cholesterol, SGOT, SGPT, Uric acid, IGF-1 and Vit. D.

SPSS-21 (Statistical Packages for Social Sciences- version 21) and Microsoft Office Excel (Microsoft Office Excel for windows; 2010) were also used to conduct the figures. Means were compared by using least significant

difference (LSD) while Fisher exact test was used to compare the differences among proportions because when 25% of the cells have expected counts less than 5. Chi-Square may not be a valid test and the alternative test is Fisher exact test. As such case was found in the present data; hence this test was used to compare the difference between proportions for all cases.

Pearson Correlation Coefficients were estimated for all groups. $P < 0.05$ considered statistically significant.

RESULTS

The mean serum level of IGF-1for newly diagnosis patients with MS was [35.95±3.52ng/ml] and for the control group was [9.72±0.8ng /ml].

Table 1: The Clinical characteristics of all studied groups.

Parameters	Pre N=30	Post N=30	Control N=20	P
Chol. Min-Max	179.50±24.57 126.00-230.00	170.36±18.15 113.00-198.00	172.15±27.06 126.00-230.00	0.28
SGOT Min-Max	26.36±6.32 15.00-38.00	30.06±5.45 18.00-42.00	26.25±6.07 15.00-38.00	0.02
SGPT Min-Max	24.06±7.83 15.00-43.00	28.70±9.05 3.00-42.00	24.70±8.54 15.00-43.00	0.08
Uric acid Min-Max	4.37±0.42 3.20-5.30	4.40±0.40 3.60-5.30	4.45-0.39 3.90-5.30	0.80
IGF_1 Min-Max	35.95±19.29 16.00-64.90	20.58±9.87 11.40-60.00	9.72±3.70 1.40-15.50	<0.0001
Vit_D Min-Max	7.80±2.39 5.01-13.40	11.10±2.55 6.80-15.20	29.89±8.66 15.40-56.20	<0.0001

There was significantly elevated [P<0.001] in pre-treatment patients when compared with that found in control group, table 3.1.There was a significant difference [P<0.001] in patients between pre and post treatment in MS patients, figure 1. Figure 1, also shown that there was a significant difference when compare between post treatment patients and healthy group [<0.006].
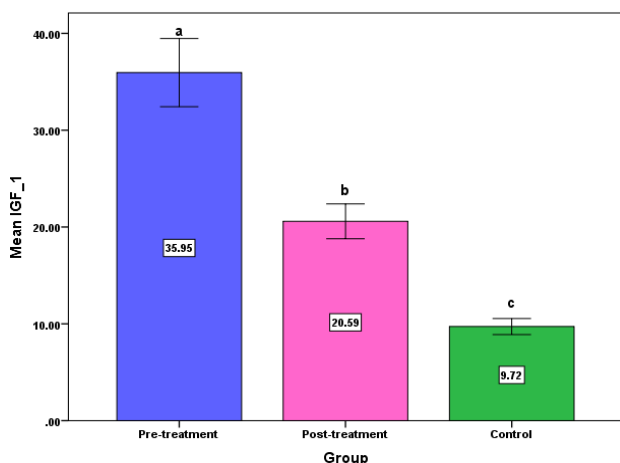

Figure 1: Comparison among means of IGF_1 according to group

The present study noticed that the serum vitamin D mean values were [7.80±0.43pg/ml] for pre-treatment MS patients and [2.75±0.66 pg/ml] for control as shown in figure 2. Serum Vit. D mean values were found to be significantly decreased [p<0.001] in patients group

compared to control Figure 2, also shown that Serum Vit.D mean values were found to be significantly elevated [p<0.001] in patients group compared to control.
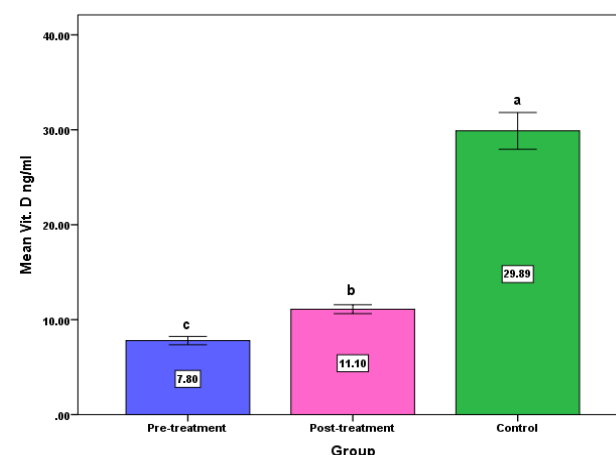

Figure 2: Comparison among means of Vit.D according to group.

The difference in the mean serum level of SGOT mean values were [26.37±1.15 IU/L] for pre-treatment MS patients and in control [9.53±1.78 IU/L] and in post-treatment patients group was [30.07±0.99IU/L] as shown in Table.1& Figure3., There was no significant difference [P>0.05] in SGOT between healthy and pre-treatment patients group in MS patients, while there was a significant difference between pre and post treatment groups.
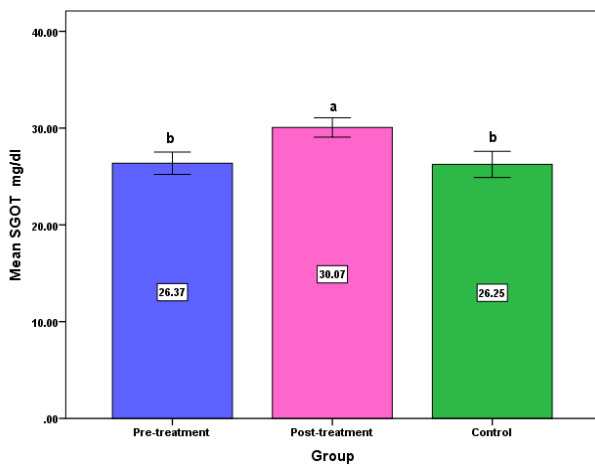
Figure 3: Serum level of SGOT in pre and post treatment compare with control.

For SGPT serum level, The mean values were [24.07±1.43IU/L] for pre-treatment MS patients and in post-treatment patients group was [28.70±1.65IU/L] and in control [24.7±1.91 IU/L] as shown in Table.1& Figure.4, There was no significant difference [P>0.05] in SGPT between healthy and pre-treatment patients group in MS patients, also there was no significant difference between pre and post treatment groups [P>0.05]
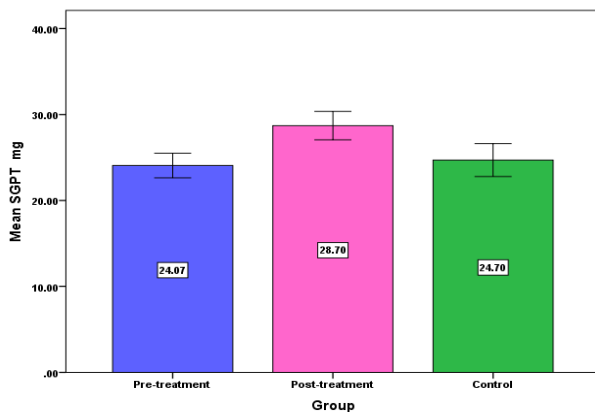

Figure 4: Serum level of SGPT in pre and post treatment compare with control.

It was found that the mean of uric acid serum levels did not show a significant variation [P>0.05] between pre-treatment MS patients [4.37±0.07mg/dl] and controls [4.45±0.08 mg/dl]. In contrast uric acid demonstrated a significant (P ≤ 0.001) increased geometric mean in post-treatment MS patients [4.8±0.09 mg/dl] as compared to controls as shown in table 1& figure 5.

The present study found that the difference in the mean serum level of Serum Total Cholesterol, The MS patients (pre-treatment group) showed a slightly increased mean of total cholesterol in comparison with controls (179.5*vs* 172 mg/dl) and the difference was not significant. Also there was no significant difference between post-treatment patients group when compared to control (170.37vs 172 mg/dl). As well as, there was no significant difference between pre and post-treatment

groups in the mean of serum total cholesterol [P>0.05] as shown in table .1 & Figure.6.
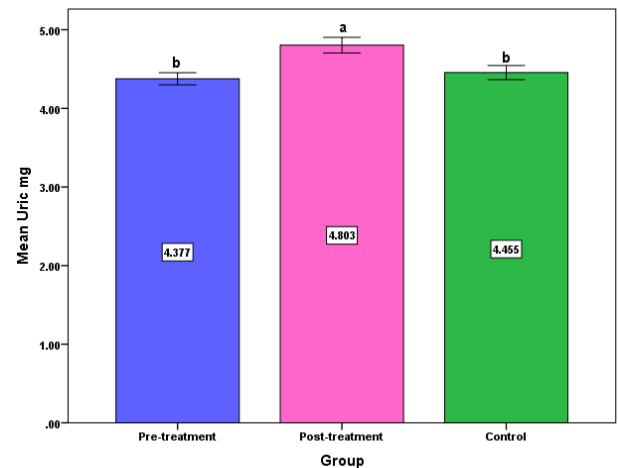

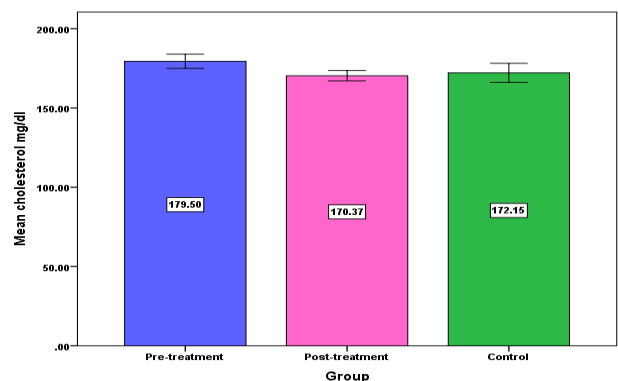**Figure 5:** Serum level of UA in pre and post treatment compare with control.

Figure 6: Serum level of Cholesterol in pre and post treatment compare with control.

DISCUSSION

The present study design to evaluate serum IGF-1, Vit D and other parameters in the patients with multiple sclerosis (MS) and Follow-up of patients after treatment for one month and one year.

The present study showed that there is a significant increase in serum IGF-1 levels in MS patients when compared to control group. Recent study reports the beneficial effects of a systemic delivery of insulin-like growth factor-1 (IGF-1) in suppressing autoimmune diseases. This new finding suggests a novel approach for toning down the immune system so that in a disease like MS, destruction of myelin can be slowed down or even halted.[4] According to the recent report, IGF-1 may be useful for treating autoimmune disease because it stimulates the proliferation of T regulatory cells. T regulatory cells are responsible for suppression of immune and inflammatory responses, and assist in the self-regulation of the immune system.[5]

IGF-1 is a naturally occurring protein that causes cell division and protects from immune system-induced stress. Also known as somatomedin, it is already an

approved medication, used to increase growth in people with certain types of dwarfism

In autoimmune diseases such as MS, T-effector cells launch an immune attack on myelin. At the same time, T-regulatory immune cells also fail. T regulatory cells normally stop the T-effector immune response.[6] Investigators from the European Molecular Biology Laboratory (EMBL) in Monterotondo, Italy, examined both mouse and human T cells in vitro, and found that recombinant human (rh) IGF-1 increased the number of T regulatory cells when delivered via a miniature pump. The rhIGF-1 specifically affected T regulatory cells and no other immune cell types. The scientists also found that delivering rhIGF-1 into affected tissues in a mouse model of MS—known as experimental autoimmune encephalomyelitis (EAE)— increased T regulatory cells and suppression of immune responses specifically in the spinal cords of the animals. It also improved the movement problems that are normally induced in the EAE model.[4] Other study that designed to find a therapeutic strategies for MS reduce inflammation and its destructive consequences, but are not effective in the progressive phase of the disease. There is a need for neuro protective and restorative therapies in MS. Insulin-like growth factor-1 (IGF-1) are of considerable interest because it is not only a potent neuro protective trophic factor but also a survival factor for cells of the oligo dendrocyte lineage and possesses a potent myelinogenic capacity. However, the IGF system is complex and includes not only IGF-1 and IGF-2 and their receptors but also modulating IGF-binding proteins (IGFBPs), of which six have been identified. [7]

Serum vitamin D significantly decrease in pre-treatment MS patients when compared to control group, but its level increase slightly in post treatment group, these results were in agreement with Speer G. at (2013) who suggest that the low serum vitamin D level has an increased association with risk of multiple sclerosis (MS).[8]

Vitamin D deficiency is very common among MS patients. Multiple preclinical studies have shown that vitamin D is a potent regulator of inflammation in MS. Most observational studies support an association between high vitamin D levels and a reduced risk of developing MS. However, conflicting results have been reported by observational studies on the correlation between vitamin D and MS severity and by interventional studies using vitamin D as a therapeutic agent for MS.

There was no significant difference in SGOT between healthy and pre-treatment patients group in MS patients, while there was a significant difference between pre and post treatment groups. There was no significant difference in SGPT between healthy and pre-treatment patients group in MS patients, also there was no significant difference between pre and post treatment groups. Usually it conducted of liver function

tests in MS patients to evaluate the liver performance because the treatment effects on its efficiency. Jeri Burtchell reported that elevated liver enzymes are a regrettably common complication of multiple sclerosis and its treatments.[9] The mean of uric acid serum levels did not show a significant variation between pre-treatment MS patients and controls. In contrast uric acid demonstrated a significant increased geometric mean in post-treatment MS patients as compared to controls; these results were in agreement with[10]. This observation may favor the view that, although a concomitant disease activity-related effect is present, low UA levels might represent a primary "MS-specific" deficiency.[11]

The MS patients (pre-treatment group) showed a slightly increased mean of total cholesterol in comparison with controls and the difference was not significant. Also there was no significant difference between post-treatment patients group when compared to control.

Dyslipidemia can potentiate inflammatory processes at the vascular endothelium, lead to the induction of adhesion molecules, and the recruitment of monocytes. Associations between dyslipidemia and increased inflammation are well established in conditions such atherosclerosis, cardiovascular disease, metabolic syndrome and obesity.[12]

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