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Biochemical Parameters Response to Treadmill Exercise Training in Patients with Chronic Hepatitis C Virus Infection

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Chronic hepatitis C virus infection is usually associated with abnormal liver enzymes, lipid profile and glucose hemostasis. The beneficial effects of aerobic exercise have been a matter of controversy in the field of CHC virus infection management. Objective: The aim of this study was to measure the impact of aerobic exercise training on glucose hemostasis, liver enzymes and lipid profile abnormalities among patients with CHC virus infection. Sixty non-cirrhotic CHC virus infection patients with abnormal lipid profile & non diabetic with insulin resistance. Patients were divided in to two equal groups. The first group received aerobic exercise training, three sessions per week for three months in addition to their antiviral treatment. The second group (B) received only their antiviral treatment. The mean values of alkaline phosphatase (ALP), alanine aminotransferase (ALT), aspartate aminotransferase (AST), gamma– glutamyltransferase (GGT), insulin, homeostasis model assessment-insulin resistance- index (HOMA-IR), total cholesterol (TC), low density lipoprotein cholesterol (LDL-c) and triglycerides (TG) were significantly decreased in group (A), where the mean value of the quantitative insulin-sensitivity check index (QUICKI) and high density lipoprotein cholesterol (HDL-c) were significantly increased, while there were no significant changes in group (B) Also; there was a significant difference between both groups at the end of the study. Treadmill walking exercise training modulates glucose hemostasis, liver enzymes and lipid profile abnormalities among patients with CHC virus infection.

Keywords: Liver Enzymes; Glucose Hemostasis; Blood Lipids; Chronic Hepatitis C; Aerobic Exercise.

Chronic hepatitis C (CHC) is a major health problem with almost 160 million people infected worldwide[1]. The available treatment for HCV which consists of a combination of pegylated interferon (IFN) and ribavirin[2] . Chronic hepatitis C virus infection is considered as an independent risk factor for insulin resistance and diabetes[3-6] , serum level of lipoproteins of varying triglyceride and cholesterol composition determines the level of plasma HCV RNA[7], also sustained virological response (SVR) to antiviral treatment is dependent on the blood lipids concentration[8-11].

Hypertriglyceridemia, increased serum level of LDL-C, decreased serum level of HDL-cholesterol and insulin resistance are closely related in non-diabetic subjects[12]. Also, degree of obesity , hyperglycemia and blood lipid profile abnormalities are associated with insulin in older subjects[13] and in obese adolescents[14].

The aim of this study was to measure the impact of aerobic exercise training on glucose hemostasis, liver enzymes and lipid profile abnormalities among patients with CHC virus infection.

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MATERIALS AND METHODS

Subjects

Sixty non-cirrhotic CHC virus infection patients (mean age 42.59 ± 3.56 year) with abnormal lipid profile & non diabetic with insulin resistance were selected from patients of Gastroenterology and Hepatology Department, King Abdulaziz University Teaching Hospital. All these patients were anti HCV positive detected by ELISA. None of the patients included in this study had other potential causes of liver disease, such as alcoholism or autoimmune phenomena. Only patients diagnosed with chronic HCV mono-infection and have anti HCV antibodies by ELISA were selected to undergo Real-Time polymerase chain reaction (RT-PCR) treated with combined pegylatedinterferon--alfa (PEG-IFN±)-ribavirin therapy. All participants signed a consent form before sharing in the study.

Measurements

Real-Time polymerase chain reaction (RT-PCR)

Ten milliliter venous blood samples were collected from each participant. The blood samples were withdrawn and kept in heparinized vacuum syringes and stored at –70°C. Serum samples of all participants were tested for RT-PCR to detect serum HCV RNA levels using the COBAS TaqMan HCV test, v2.0 (Roche Diagnostics, Indianapolis, NJ, USA).

Blood lipid profile and liver enzymes measurements

The fasting venous blood samples were withdrawn and dropped in clean tubes had few mg of K2EDTA, centrifugation and separated plasma was stored at -20° for f plasma lipid profile analysis (Total cholesterol (TC) , Triglycerides (TG), High density lipoprotein (HDL) and Low density lipoprotein (LDL)). However, Liver enzymes (aspartate aminotransferase, AST; alanine aminotransferase, ALT; alkaline phosphatase, ALP and Gamma – Glutamyltransferase, GGT were measured by the colorimetric enzymatic method using an automatic spectrophotometer and respective kits for analysis (Bioclin, Quibasa, Belo Horizonte, MG, Brazil). All samples were assayed in duplicate, and the mean of the paired results was determined.

Glucose hemostasis measurements

Human insulin was measured with an insulin kit (Roche Diagnostics, Indianapolis, IN, USA) using a cobas immunoassay analyzer (Roche Diagnostics). Insulin resistance was assessed by homeostasis model assessment (HOMA-IR) . HOMA-IR = [fasting blood glucose (mmol/l) _ fasting insulin (mIU/ml)]/22.5 [15]. However, insulin sensitivity was assessed by The quantitative insulin-sensitivity check index (QUICKI) using the formula: QUICKI=1/[log(insulin) + log(glucose)] [16]. All serum samples were analyzed in duplicates.

Procedures

Following the previous evaluation , all participants were enrolled into two study groups:

Patients in study group (A) received their antiviral treatment and practiced aerobic treadmill exercise for forty minutes , with an initial five minutes of warming up that was performed on the treadmill (Enraf Nonium, Model display panel Standard, NR 1475.801, Holland) with low work load, actual training time was thirty minutes with an intensity of 70–80% of HRmax and finally five minutes of cooling down that was done in the form of running or walking.

Patients in Group (B) received only their antiviral treatment.

Statistical analysis

Mean values of the investigated parameters was compared by student paired “t” test. While, the unpaired” test was be used to compare between the two groups ($P<0.05$).

RESULTS

Both study groups were considered homogeneous regarding the demographic variables (table 1). The mean values of insulin, alkaline phosphatase (ALP), alanine aminotransferase (ALT), aspartate aminotransferase (AST), gamma–glutamyltransferase (GGT), homeostasis model assessment-insulin resistance- index (HOMA-IR), triglycerides (TG), total cholesterol (TC) and low density lipoprotein cholesterol (LDL-c) decreased significantly after aerobic exercise training in the study group (A), where the mean value of The quantitative insulin-sensitivity check index (QUICKI) and high density lipoprotein cholesterol (HDL-c) increased significantly, while there were no significant changes in group (B) (Table 2 and 3)

.Also; there was a significant difference between both groups at the end of the study (Table 4).

Insulin Resistance (HOMA-IR) index. (*) indicates a significant difference between the two groups, $P < 0.05$.

DISCUSSION

As exercise is a low-cost, reliable and sustainable therapy for many chronic diseases[17-20]. Increased exercise duration and intensity has been evaluated as an important therapeutic intervention in treating patients with non-alcoholic fatty liver disease (NAFLD) and chronic liver disease[21]. As a result of the CHC virus interaction with glucose and lipid metabolism leads to insulin resistance, type 2 diabetes, hypercholesterolemia and hepatic steatosis in patients with CHC virus infection[22]. However , there is close relationship between CHC virus infection and abnormal glucose

Table 1. Mean value of demographic data for participants in both groups

	Group (A)	Group (B)	Significance
Age (year)	41.73 ± 6.41	42.45 ± 7.21	P > 0.05
Gender (M/F)	55/45	57/43	P > 0.05
BMI (kg/m2)	30.81 ± 5.22	30.16 ± 5.78	P > 0.05
Hip circumference (cm)	117.68 ±10.14	115.44 ± 11.36	P > 0.05
Waist circumference (cm)	103.83 8.65		
104.83 7.92			
P > 0.05			
waist hip ratio	0.921± 0.043	0.917± 0.036	P > 0.05
Hb (gm/dl)	11.74 ± 1.61	12.83 ± 1.94	P > 0.05
Albumin (gm/dl)	3.86 ± 0.92	3.61 ± 0.85	P > 0.05
Total Bilirubin (mg/dl)	1.52 ± 0.66	1.45 ± 0.51	P > 0.05
HCV-RNA (KIU/mL)	1000946.53± 317.22	1000782.49± 281.85	P > 0.05

BMI : Body Mass Index; Hb : Hemoglobin.

Table 2. Mean value and significance of ALP, ALT, AST, GGT, TC, LDL, HDL, TG, insulin, QUICKI and HOMA-IR of group (A) before and at the end of the study

	Mean ± SD Before	T-value After	Significance	
ALP (U/L)	68.13 ± 6.41*	51.72 ± 5.19	8.22	P < 0.05
ALT (U/L)	44.52 ± 4.63*	33.11 ± 4.25	7.36	P < 0.05
AST (U/L)	43.17 ± 5.32*	34.28 ± 4.57	7.71	P < 0.05
GGT(U/L)	28.93 ± 3.65*	20.76 ± 3.14	6.25	P < 0.05
TC(mg/dL)	261.11 ± 18.24*	235.24 ± 15.26	10.15	P < 0.05
LDL (mg/dL)	178.23 ± 10.51*	150.21 ± 8.32	8.94	P < 0.05
HDL (mg/dl)	31.44 ± 4.16*	38.95 ± 4.68	7.51	P < 0.05
TG (mg/dl)	90.23 ± 7.12*	74.52 ± 6.87	8.22	P < 0.05
Insulin (mU/l)	15.17 ± 3.12*	9.16 ± 2.76	6.14	P < 0.05
QUICKI	0.126 ± 0.018*	0.171 ± 0.029	5.82	P < 0.05
HOMA-IR	5.74 ± 1.62*	4.06 ± 1.43	5.48	P < 0.05

ALP: Alkaline Phosphatase; ALT: Alanine Aminotransferase; AST: Aspartate Aminotransferase; GGT: Gamma – Glutamyltransferase; TC: Total Cholestrol ; LDL: Low Density Lipoprotein; HDL: High Density Lipoprotein; TG: Triglycerides; QUICKI : The Quantitative Insulin-Sensitivity Check Index; HOMA-IR: Homeostasis Model Assessment-Insulin Resistance (HOMA-IR) index. (*) indicates a significant difference between the two groups, $P < 0.05$

hemostasis[23]. Our study was a designed to detect the impact of aerobic exercise on liver enzymes, glucose haemostasis and blood lipid profile in patients with CHC virus infection . Results of this study indicated that the mean values of alkaline phosphatase (ALP), alanine aminotransferase (ALT), aspartate aminotransferase (AST), gamma–glutamyltransferase (GGT), insulin, homeostasis model assessment-insulin resistance- index (HOMA-IR), total cholesterol (TC), low density lipoprotein cholesterol (LDL-c) and triglycerides (TG) were significantly decreased in group (A), where the mean value of the quantitative insulin-sensitivity check index (QUICKI) and high density lipoprotein cholesterol (HDL-c) were significantly increased, while there were no significant changes

Table 3. Mean value and significance of ALP, ALT, AST, GGT, TC, LDL, HDL, TG, insulin, QUICKI and HOMA-IR of group (B) before and at the end of the study

	Mean ± SD Before	T-value After	Significance	
ALP (U/L)	66.32 ± 7.42	67.51 ± 7.47	0.93	P > 0.05
ALT (U/L)	43.71 ± 5.31	45.23 ± 5.42	0.94	P > 0.05
AST (U/L)	41.95 ± 4.16	43.42 ± 4.31	0.88	P > 0.05
GGT(U/L)	27.14 ± 3.22	28.93 ± 3.46	0.79	P > 0.05
TC(mg/dL)	257.32 ± 16.98	260.14 ± 17.15	1.21	P > 0.05
LDL (mg/dL)	174.85 ± 9.67	178.12 ± 9.84	1.14	P > 0.05
HDL (mg/dl)	32.11 ± 3.85	31.47 ± 3.61	0.98	P > 0.05
TG (mg/dl)	88.54 ± 6.42	90.21 ± 6.85	1.16	P > 0.05
Insulin (mU/l)	14.71 ± 3.09	15.28 ± 3.24	1.12	P > 0.05
QUICKI	0.128 ± 0.019	0.115 ± 0.018	0.97	P > 0.05
HOMA-IR	5.67± 1.41	5.89 ± 1.52	0.86	P > 0.05

ALP: Alkaline Phosphatase; ALT: Alanine Aminotransferase; AST: Aspartate Aminotransferase; GGT: Gamma – Glutamyltransferase; TC: Total Cholestrol ; LDL: Low Density Lipoprotein; HDL: High Density Lipoprotein; TG: Triglycerides; QUICKI : The Quantitative Insulin-Sensitivity Check Index; HOMA-IR: Homeostasis Model Assessment-Insulin Resistance (HOMA-IR) index.

Table 4. Mean value and significance of ALP, ALT, AST, GGT, TC, LDL, HDL, TG, insulin, QUICKI and HOMA-IR of group (A) and group (B) at the end of the study

	Mean ± SD Group (A)	T-value Group (B)	Significance	
ALP (U/L)	51.72 ± 5.19*	67.51 ± 7.47	7.19	P < 0.05
ALT (U/L)	33.11 ± 4.25*	45.23 ± 5.42	6.14	P < 0.05
AST (U/L)	34.28 ± 4.57*	43.42 ± 4.31	6.48	P < 0.05
GGT(U/L)	20.76 ± 3.14*	28.93 ± 3.46	5.11	P < 0.05
TC (mg/dL)	235.24 ± 15.26*	260.14 ± 17.15	8.78	P < 0.05
LDL (mg/dL)	150.21 ± 8.32*	178.12 ± 9.84	7.23	P < 0.05
HDL (mg/dl)	38.95 ± 4.68*	31.47 ± 3.61	6.14	P < 0.05
TG (mg/dl)	74.52 ± 6.87*	90.21 ± 6.85	6.82	P < 0.05
Insulin (mU/l)	9.16 ± 2.76*	15.28 ± 3.24	5.93	P < 0.05
QUICKI	0.171 ± 0.029*	0.115 ± 0.018	4.76	P < 0.05
HOMA-IR	4.06 ± 1.43*	5.89 ± 1.52	4.19	P < 0.05

ALP: Alkaline Phosphatase; ALT: Alanine Aminotransferase; AST: Aspartate Aminotransferase; GGT: Gamma – Glutamyltransferase; TC: Total Cholestrol ; LDL: Low Density Lipoprotein; HDL: High Density Lipoprotein; TG: Triglycerides; QUICKI : The Quantitative Insulin-Sensitivity Check Index; HOMA-IR: Homeostasis Model Assessment-Insulin Resistance (HOMA-IR) index. (*) indicates a significant difference between the two groups, P < 0.05.

in group (B) Also; there was a significant difference between both groups at the end of the study , these findings agreed with many previous studies in this field.

Eizadi etal. and Konishi etal. proved that aerobic exercise able to modulate abnormalities of blood lipid profile and glycemic control in obese subjects[24,25]. Similarly, Jiménez and Ramírez-Vélez found that insulin sensitivity was improved associated with reduction in LDL-C and increase in HDL-C levels following eight weeks of strength training for obese patients[26]. Also, Durstine et al and Kelley meta- analysis, reported that aerobic exercise training for 8 weeks significantly increase HDL-C levels in adults[27,28]. The possible mechanism by which insulin sensitivity can be improved by exercises is that active muscle contraction causes membrane depolarization that increased cytoplasmic calcium concentration and causes activation of 52 -adenosine monophosphate–activated protein kinase that causes translocation of glucose transporter protein–4 (GLUT-4) to the plasma membrane[29] or changing the energy state of the cell as a result of high intracellular ratio of adenosine monophosphate to adenosine triphosphate[30]. Also, the improved effects on fatty acid metabolism due to changed expression of a number of lipogenic and glycolytic enzymes in the liver caused by 52 - Adenosine monophosphate–activated protein kinase activation[30,31]. Finally, the anti-inflammatory effects of aerobic exercise reduces the level of serum IL-6 which may inhibit insulin resistance[32].

The benefit of exercise on the liver is supported by other multicentre studies or meta-analyses showing its favourable effect on ALT levels and steatosis[33-35]. A ret-rospective analysis by Kistler et al., which evaluated the association between physical activity intensity and histological severity of NAFLD, demonstrated a signifi-cant decrease in histological severity with vigorous exercise (P = 0.04) but no differ-ence in ALT levels[33].Two systematic reviews by Musso et al. and Thoma et al., albeit both with small sample sizes, showed that exercise reduces levels of liver enzymes and steatosis regardless of weight loss[34, 35]. Also, Nasif etal., conducted a study on 40 patients with chronic HCV who were randomly assigned into two groups, exper-imental group (Group I), who received aerobic exercise of moderate intensity for two months, two sessions a week, 30 minutes for each session, and a control group (Group II), who did not receive exercise. Their mean age was (40±5 years) and aerobic exercise training of moderate intensity led to decrease serum levels of liver enzymes (AST and ALT) which means protection of hepatic cells and restoration of its function[36].

CONCLUSION

Treadmill walking exercise training modulates glucose hemostasis, liver enzymes and lipid profile abnormalities among patients with CHC virus infection.

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