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RESEARCH ARTICLE

Lipid Profile Response to Electroacupuncture in Non-Alcoholic Fatty Liver Patients with Hyperlipidemia

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Background: Non-alcoholic fatty liver disease (NAFLD) is estimated to be one of the most common diseases affecting the liver because of its high prevalence worldwide. Abnormal lipid profile between NAFLD patients has been reported in several studies.
Objectives: This study aimed to evaluate the lipid profile response to electroacupuncture in NAFLD patients.
Methods: A total of 60 female patients with NAFLD were included in the study with ages ranged from (30-55) years old. They were divided equally into two groups, group A received electroacupuncture (EA) stimulation at points of; LR14, LR3, ST36, and GB34. And group B received sham acupuncture application in non-acupuncture points. The demographic data and lipid profile such as total cholesterol (TC), serum triglycerides (TG), serum high-density lipoprotein (HDL), serum low-density lipoprotein (LDL) were recorded before and after the study.
Results: The study results revealed a significant decrease ($p < 0.05$) of LDL, TC, TG after 6 weeks of non-interrupted treatment sessions in group A, However HDL showed no significant improvement ($p > 0.05$). A significant difference was found between post-treatment values of LDL, TC, and TG between both groups.
Conclusion: Electroacupuncture can be an effective, simple, and applicable method for the improvement of elevated lipid profiles in NAFLD patients.

Keywords: Electroacupuncture, Non-alcoholic fatty liver disease, Lipid profile, Hyperlipidemia

INTRODUCTION

Non-alcoholic fatty liver disease (NAFLD) is a disease where the lipids are precipitated inside the liver tissue by a percentage of (5-10%) in the absence of chronic alcohol abuse. Numerous patients experiencing NAFLD have just raised liver fat content (simple steatosis), while others experiencing inflammation of hepatic tissue which is called nonalcoholic steatohepatitis (NASH) [1].

Hepatic steatosis is a developing health concern in industrialized nations. Despite increasing awareness in recent years, the prevalence is increasing and its prevalence varies relying upon the country, age, sex, ethnicity, and related risk factors. NAFLD is believed as one of the most well-known reasons for chronic liver disease all over the world [2,3].

In clinical settings, laboratory assessment of blood lipids, insulin resistance, and aminotransferases are regularly utilized for recognizing of NAFLD [4]. NAFLD is characterized by apparent disturbance of lipid metabolism and storage. A thorough assessment of lipid species in the advanced phases of NAFLD can give insights into the mechanism for disease progression and could be non-invasive biomarkers of various stages [5].

Hyperlipidemia is a main risk factor of NAFLD and it has an important role in the appearance of NAFLD [6]. Souza et al. [7] demonstrated that 20-80% of NAFLD cases accompanied by dyslipidaemia and most commonly in the form of hypertriglyceridemia, increased levels of low-density lipoprotein (LDL), and there is a direct relationship between hepatic steatosis and alterations in blood lipid and body mass

index (BMI).

In clinical settings for detection of NAFLD, laboratory measurements of blood lipids, aminotransferases, and insulin resistance are often used [4]. Gorden et al. [5] explained that concise "signatures" of lipids could be a useful indication of reaction to treatment in the management of NAFLD and may serve as biomarkers for its progression.

As a medical treatment for dyslipidemia, lipid-lowering drugs that are clinically used, contain statins, niacin, resins, fibrates, intestinal cholesterol absorption inhibitors, and other different compound preparations [8]. However, most of the major drugs for lowering lipid levels have side effects [9].

In traditional Chinese medicine, acupuncture has an important role and it is used to treat many diseases and is considered as a new different alternative method to medical treatment [10].

One of the advanced types of conventional acupuncture treatment is electroacupuncture (EA) where the needles are connected to small electrical currents using EA stimulator. It has a more acceptable treatment effect and results [11].

In a clinical setting, acupuncture has distinguished outcomes on several liver diseases. Acupuncture treatment helps in decreasing blood lipids in patients with fatty liver disease and plays a significant role in improving the immunity system in patients with hepatitis in addition to improving their clinical symptoms [12]. Previous clinical studies in China indicated that acupuncture able to decrease total cholesterol (TC), triglycerides (TG), LDL, and elevate high-density lipoproteins (HDL) in patients suffering from dyslipidemia [13-15].

Acupuncture has been used previously in the treatment of hyperlipidemia which is considered the main focus in the treatment of NAFLD. However, its efficacy on hyperlipidemia has not been evaluated in fatty liver disease. Moreover, Because of the unequal quality of research, the difference in the methodology, and quality levels included in the trials and different acupoints used, there is wide significant heterogeneity in the results of the clinical studies. Based on this, this study aimed to evaluate the effect of electroacupuncture on the lipid profile in patients with NAFLD.

MATERIALS AND METHODS

1. Ethical approval

Before the study commencement, the authors obtained ethical approval from the Institutional review board at the faculty of physical therapy, Cairo University. No: P.T REC/012/001579_1. The study was conducted according to the "World Medical Association Declaration of Helsinki". This study was registered as a randomized clinical trial at ClinicalTrials.gov in August 2019 (ref. NCT04046718). Before participating in this study, all patients signed an informed consent form before data collection.

2. Inclusion and exclusion criteria

Sixty female patients suffering from NAFLD were included in the study. They were recruited from the Department of Internal Medicine, Cairo University Hospital. They were first diagnosed as a fatty liver patient using abdominal ultrasonography. Patients with hepatitis B and C, severe ventricular arrhythmia, and patients who participated in any form of acupuncture therapy in the past 6 months were excluded from participating in this study.

3. Outcome measures and intervention

Out of 72 subjects who were assigned to the trial, a total of 60 subjects (electro acupuncture n = 30 vs. sham acupuncture n = 30) completed the study (Fig. 1). Block randomization was conducted and the patients were assigned to group A (n = 30) or group B (n = 30) randomly. The primary outcome measure includes laboratory measurements of total cholesterol, high-density lipoprotein, triglycerides, and low-density lipoprotein. The secondary outcome measure includes BMI that calculated form obtained height and weight measurement. The outcome measures were calculated before and after the end of the treatment sessions (non-interrupted six weeks), the safety of interventions was assessed at every session. Documentation of any clinical symptoms or adverse events or reactions were recorded by researchers and addressed and analyzed properly.

Acupuncture treatment was applied in accordance with the Standards for Reporting Interventions in acupuncture guidelines in clinical trials [16]. In group A, single-use sterile acupuncture' stainless steel needles (35 mm in length and 0.20 mm in diameter) were inserted at a depth of 3-30 mm in patients' skin according to the basic character of each selected point, with the direction of meridian energy flow. Using the stimulator wires, the needles were connected to an EA stimulator device, model (KWD-808). The session duration was about 20 min. The frequency was set to be 5 Hz with intensity tolerable to each patient. The treatment sessions were applied three times per week for 6 weeks. The acupuncture points were described according to the international nomenclature [17] using the following points: LR3: "located in the dorsum of the foot, in the depression anterior to the junction of the first and second metatarsals" [18]. LR14: "located at the mamillary line, in the sixth intercostal space, 4 cun (width of the patient's thumb used to detect acupuncture point) lateral to the midline" [18]. GB 34: "located on the lateral aspect of the lower leg, in the depression anterior and inferior to the head of the fibula" [18]. ST36: "located on

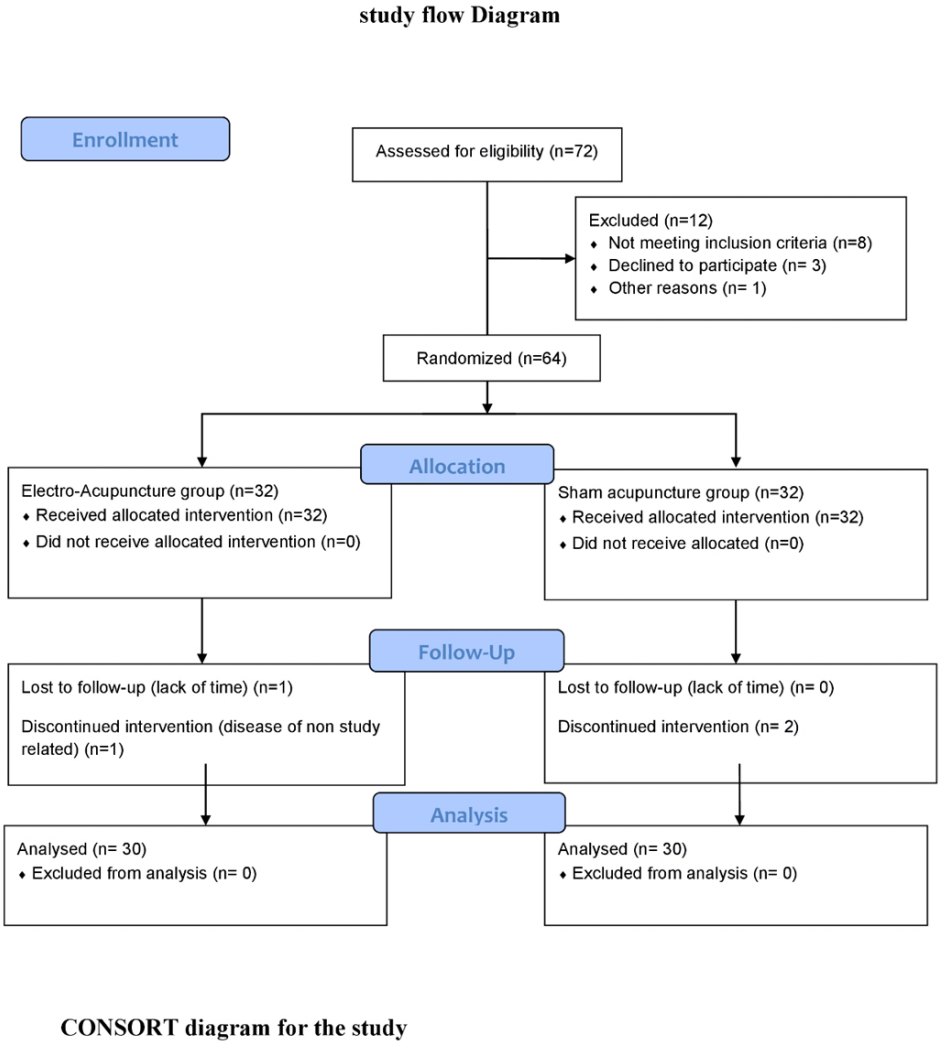

Fig. 1. The flow diagram of the study.

the anterior aspect of the lower leg, 3 cun below ST 35, one fingerbreadth (middle finger) from the anterior crest of the tibia" [18].

In group B, the selected insertion points were 1.5 cm outside the selected real acupuncture points for applying the study EA stimulation. In addition, a disconnection occurred between the cables attached to the needles and the electrical stimulator; furthermore, the needles were inserted superficially for avoiding the (de qi) sensation. The participants were informed about the treatment schedule to treat each separately at different times to avoid any sharing of experiences while applying the sessions.

4. Power analysis of the study.

The sample size was calculated before study commencement using G*power version 3.1.9.2. Sample size calculation was based on t-test two independent groups, type I error a = 0.05, and the effect size 0.778 of the main outcome variable HDL and LDL and type II error b = 80%. The suitable minimum sample size was 44 patients (22 patients in each group as a minimum).

5. Statistical analysis

Results are expressed by the mean and standard deviation. Pre-treatment data were assessed for normal distribution using the Kolmogorov–Smirnov test. Unpaired t-test was used to compare variables between the two groups and a paired t-test was used to compare variables before and after treatment in the same group. Analysis of data was done using SPSS Statistics ver. 18.0 (IBM Co., Armonk, NY). $p < 0.05$ was considered significant.

RESULTS

The Anthropometric characteristics of both groups were obtained before starting the sessions including age and body mass index BMI. As shown in Table 1 and Table 2, there were no statistically significant differences in age, weight, height,

Table 1. Anthropometric characteristic of patients

Items	Age (year)	Weight (kg)	Height (cm)	BMI (kg/m^2)
Group A (n = 30)	45.30 ± 7.32	104.20 ± 5.23	164.93 ± 3.56	38.077 ± 1.57
Group B (n = 30)	45.93 ± 6.86	105.67 ± 7.87	166.10 ± 4.85	38.41 ± 1.47
p	0.73	0.40	0.29	0.40

SD = standard deviation; *p* = probability value.

Table 2. Outcomes of the study

Variable	Group A (EA)	Group B (sham)	*p* between groups
TC pre-treatment	212.63 ± 59.03	214.27 ± 50.66	0.909
TC post-treatment	169.37 ± 31.27	213.10 ± 51.45	0.0001
p within group	0.0001	0.129	
TG pre-treatment	169.50 ± 47.34	171.8 ± 47.66	0.852
TG post-treatment	125.87 ± 42.79	173.23 ± 46.72	0.0001
p within group	0.0001	0.096	
LDL pre-treatment	143.77 ± 46.55	152.13 ± 48.05	0.496
LDL post-treatment	110.27 ± 29.28	151.27 ± 47.77	0.0001
p within group	0.0001	0.160	
HDL pre-treatment	40.20 ± 8.72	38.20 ± 7.45	0.344
HDL post-treatment	40.53 ± 8.18	38.57 ± 7.01	0.322
p within group	0.077	0.19	

p = probability; S = significant; NS = non-significant; TC = total cholesterol; TG = triglycerides; LDL = low-density lipoproteins; HDL = high-density lipoproteins.

BMI, TC, TG, LDL, and HDL between the two groups at pre-treatment. However, post-treatment, there were statistically significant differences in values of TC, TG, and LDL except for HDL between both groups in favor of group A.

In group A: There was a statistically significant improvement in the mean value of TC, TG, and LDL with a percentage improvement of 20.34%, 25.74%, and 23.3%, respectively, but there was no significant difference in the mean value of HDL post-treatment when compared with pre-treatment. Whilst there was no significant difference in the mean value of all study variables in group B post-treatment when compared with pre-treatment, as demonstrated in Table 2. No adverse events were reported during the study period.

DISCUSSION

Abnormal lipid profile and dyslipidemia in NAFLD patients had been found in several studies [19,20]. This dyslipidemia and abnormal lipids profile can be considered at least partially responsible for the elevated cardio vascular diseases (CVD) risk in patients suffering NAFLD [21].

EA was found to be a potent modality that can improve the liver functions in patients who suffered from NAFLD [22,23].

This randomized trial aimed to judge the effect of EA on the lipid profiles in patients with NAFLD. The study results showed a significant improvement in the mean value of TC, TG, and LDL with a percentage improvement of 20.34%, 25.74%, and 23.3%, respectively, after 6 weeks of non-interrupted treatment sessions in group A, However HDL showed no significant improvement ($p > 0.05$).

The results of this study have coincided with the results of many other studies, as the study of Cabioğlu and Ergene [24], 2005 which reported a significant improvement in total cholesterol, triglyceride, and LDL levels in EA group $p < 0.05$ in their study when intended to evaluate the effect of acupuncture treatment on body weight and the serum TC, TG, HDL. and LDL levels in obese women.

Moreover, the study by Wang et al. [25], 2008 revealed that High-frequency EA is effective in decreasing fat accumulation and improve the abnormal lipid metabolism in obese rats through a significant decrease in fat weight, adipose cell area, serum TG, TC, LDL, serum leptin, and insulin levels.

It had been observed that EA can be considered as a simple, high significant modality for improvement of liver functions and lowering triglycerides in patients suffering nonalcoholic fatty liver when applied on acupuncture points of LR14, LR3, ST36, and GB34 [22].

In addition, the findings of this study were also supported by a study conducted by Kim [26], 2006 who assessed the effect of acupuncture treatment on the body weight and serum lipids levels. He noticed a significant decrease in TG and TC levels in EA and diet groups when compared to the

control group.

Another study supporting the use of EA in metabolic syndrome cases [27], with observing its therapeutic effect by stimulation of GB26 acupoint, The authors reported that EA stimulation of GB26 acupoint can reduce insulin resistance, regulate blood lipid, and lower blood glucose in metabolic syndrome rats.

In agreement with the results of our study, by investigating the influence of EA on liver function and blood lipid in non-alcoholic fatty liver rats, Feng et al., [23] 2010 found a significant improvement in serum TC ratio, LDL, TG, liver index, and Aspartate aminotransferase in NAFLD group $p < 0.05$. They concluded that EA can significantly lower their blood lipids, improve their liver function, and thus have effective treatment for non-alcoholic fatty liver.

Against our results, in a trial study conducted in the Health Science Center at Peking University in Beijing, they reported no significant differences in the plasma levels of glucose, cholesterol, and triglyceride before and at the end of the EA treatment. But this may be due to a temporarily stopping of the treatment program for 4 weeks in the winter vacation of the Chinese New Year [28].

1. Study limitations and future recommendations

This study was limited by these reasons. (1) It was conducted on female patients only. Other researches need to be conducted in different settings to confirm the results of these findings in both sexes. (2) Many patients were not interested to follow a regimen protocol for 6 weeks. This may be due to the wide gap in patients' knowledge about nonchemical interventions as a safe treatment for NAFLD.

CONCLUSIONS

Electroacupuncture stimulation can be considered an effective, simple, and applicable method for improvement of abnormal lipid profiles in patients who suffered from NAFLD with hyperlipidemia.

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CONTRIBUTIONS OF AUTHORS

All authors contributed to the original trial design, acquisition, and reviewing of data, statistical analysis, interpretation, writing, and revision of the article. They approved the final version, and agree to be accountable for all aspects of the work.

CONFLICT OF INTEREST

The authors declare no conflict of interest.

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