Effects of eight weeks of resistance training and cucumber juice consumption on the liver enzymes status of type 2 diabetic patients

Running title: Effects of exercise and nutritional interventions on the liver enzymes of type 2 diabetic patients

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Abstract

Background: Type 2 diabetes is a serious chronic disease associated with hyperglycemia, overweight, and metabolic syndrome. The prevalence of this disease is constantly increasing. This trial aimed to investigate the separate and combined effects of resistance training and cucumber juice consumption on liver indicators in women with type 2 diabetes.

Methods: Type 2 diabetic women aged 35 – 70 years (N = 40) were selected. Subjects were randomly placed into four groups (three experimental groups and one control group). The Training+placebo group implemented resistance training and consumed a placebo. The Training+ Supplement group implemented resistance training and consumed cucumber juice, the Supplement consumed cucumber juice, and the control group consumed a placebo for eight weeks. 48 hours before and after the research, blood sampling was done, and the changes in liver enzyme levels were investigated and compared among the groups. Data were analyzed using one-way analysis of variance and Tukey post hoc test at the significance level of 0.05.

Results: The results of the present study showed that eight weeks of separate or combined resistance training and consumption of cucumber juice led to a significant reduction in the levels of liver (ALT, AST, and ALP) indices ($P \leq 0.05$).

Conclusion: In the present study, liver enzyme levels decreased. Therefore, separate or combined implementation of resistance training and consumption of cucumber juice can be used as therapeutic aids to control the levels of liver enzymes in women with type 2 diabetes.

Keywords: Training, Cucumber juice, Type 2 diabetes

Introduction

One of the most common types of diabetes, which includes more than 90% of the entire diabetic population, is type 2 diabetes (1). This is a serious illness that is related to hyperglycemia, overweight, and metabolic syndrome. The prevalence of type 2 diabetes is constantly increasing. Sedentary lifestyle and overweight have been identified as key risk factors for type 2 diabetes (2). This disease is associated with hyperglycemia, insulin resistance, and relative insulin deficiency with a slow onset. Type 2 diabetes is a silent disease that affects different organs of the body. One of the organs of the body that is strongly affected by type 2 diabetes is the liver (3). In fact, the liver is directly affected by type 2 diabetes and indirectly by reactive oxygen species and oxidative stress. The liver plays an important role in the transfer of lipids and metabolism and probably participates in the occurrence and development of diseases such as atherosclerosis, type 2 diabetes and obesity (4). Maintaining the stability of the blood glucose level by harvesting and storing glucose in the form of glycogen, glycogenesis, glycogenolysis, and gluconeogenesis is one of the functions of the liver (5). In fact, one of the organs of the body that helps maintain blood sugar in the normal range is the liver. An increase in blood sugar leads to an imbalance of oxidation-reduction reactions in liver cells. Among the predictors of diabetes, we can mention an increase in the levels of liver enzymes (6). Diabetes increases liver enzyme levels in the blood, the main reason of which is the increase in oxidative stress in tissue areas. In fact, the plasma concentration of liver enzymes is the best indicator to evaluate the condition of the liver, and it is one of the indicators through which one can find out the presence of diabetes in a person (7). Cucumber has antioxidant activity and can possibly help in the treatment of liver disease (8). Ezodili et al. (2017) showed that cucumber consumption does not cause significant changes in the levels of liver enzymes (aspartate aminotransferase and alanine aminotransferase) (4). This is despite the fact that performing sports training leads to significant changes in the levels of liver enzymes. Researchers have reported that performing resistance training for eight weeks leads to a decrease in plasma levels of liver enzymes AST and ALT in men with non-alcoholic fatty liver disease (9, 10). Although regular physical activity may play a role in controlling diabetes and its complications, including fatty liver, most people with type 2 diabetes are inactive. On the other hand, despite the importance of sports activity in improving the conditions of diabetes, there are many discussions about the prescription of sports program along with the effect of supplement consumption for the health of these people. In recent decades, sports activities along with diets have been recommended as a suitable solution for the management of diabetes treatment. Considering the exorbitant costs of the drugs used in the treatment of type 2 diabetes and the side effects caused by their use, In this research, we sought to see whether we can help diabetic patients by combining exercise and diet or not. To our extent of research, there is no data about effects of resistance training and cucumber juice consumption on the liver enzyme levels in women with type 2 diabetes, and this issue should be comprehensively investigated. Therefore, the aim of this research is the assessment of implementing resistance training and consumption of cucumber juice on the liver enzymes status of women with type 2 diabetes.

Methods

Study design

This trial utilized a randomized double-blind pretest-posttest design and focused on women with type 2 diabetes who were referred to the Kermanshah Diabetes Research Center. The inclusion criteria for the research focused on women aged 35 to 70 with type 2 diabetes who had a valid coronavirus vaccination card, fasting blood sugar levels between 140 and 280 mg/dl, no regular physical activity in the past six months, and a health certificate from a physician allowing them to participate in sports activities. Conversely, participants were excluded if they voluntarily withdrew from the study, sustained an acute injury while performing resistance exercises, or missed two consecutive sessions or three non-consecutive sessions during the research period.

A total of 40 women with type 2 diabetes were selected for the study. Subjects were randomly placed into four groups (three experimental groups and one control group). The population of each group was 10. This research lasted for eight weeks (24 sessions). Anthropometric measurements of the subjects were done by the researcher before the trial and are demonstrated in Table 1. Before and after each session, a glucometer was used to evaluate the blood sugar levels of the subjects. It should be noted that none of the subjects were under insulin therapy.

Supplementation protocol

This trial was double-blind. The placebo was prepared to be similar in color and taste to cucumber (C. sativus L.) juice. Subjects did not know what they received (cucumber juice or placebo). In addition, the researcher did not know about this process. The research assistant gave cucumber juice to the (Training+Supplement and Supplement) groups**,** and a placebo to the (Training+Placebo and control) groups in a double-blind manner. The research assistant ensured that the entire volume determined (240 mL) for each person was consumed.

Resistance training protocol

This protocol was implemented in the gym. Participants were tested for 1Repetition Maximum (RM) to determine muscle strength. The resistance training program consisted of 40-minute sessions (three times per week for 8 weeks). Each movement consisted of 2 sets with 8-10 repetitions. The rest between sets was 2 minutes. The intensity of training was considered between 60-75% of 1RM.

Laboratory assessments

48 hours before and after the research, blood sampling was done and the changes of liver enzyme levels were investigated and compared among the groups.

Blood samples (7ml) were collected from the antecubital vein by a laboratory specialist 48 hours before and after the trial. Liver indicators (ALT, AST, ALP) were investigated before and after the trial in the four groups. Liver enzyme levels are shown in Table 2.

Statistical analysis

All data were analyzed using SPSS version 22. One-way ANOVA and Tukey's post hoc test were used for data analysis, with a significance level set at ($P \leq 0.05$).

Results

Anthropometric measurements are shown in Table 1. The liver enzymes (ALT, AST, and ALP) showed a significant reduction from the pre-test stage to the post-test stage ($P < 0.05$) in all three groups (training + placebo, training + supplement, and supplement). No significant changes were observed in all the control group variables from the pre-test to the post-test ($P \geq 0.05$). The liver enzymes (ALT, AST, and ALP) were decreased significantly after eight weeks of resistance training ($P < 0.05$).

Additionally, the enzymes were significantly reduced after eight weeks of cucumber juice consumption ($P < 0.05$). Combined resistance training and cucumber juice consumption reduced liver enzymes (ALT, AST and ALP) significantly ($P \leq 0.05$).

The results of the one-way ANOVA test indicated a significant difference in the changes in the levels of liver (ALT, AST and ALP) enzymes was significant difference between the Training+placebo, Training+supplement, supplement and control groups ($p=0.0001$).

Tukey's post hoc test demonstrated that there was a significant difference between training + placebo and training + supplement groups, training + placebo and supplement groups, supplement and control groups, training + placebo and control groups, training + supplement and control groups in the levels of liver indices (ALT and ALP enzymes). Also, there was a significant difference in the levels of liver indices (ALT and ALP enzymes) in the supplement and training+ supplement groups ($p \leq 0.05$).

The test showed a significant difference in AST levels between the training + placebo and training + supplement groups, training + placebo and control groups, training + supplement and supplement groups, and training + supplement and control groups ($p \leq 0.05$). There were no significant differences in the levels of liver index (AST) between training+ placebo and supplement groups and supplement and control groups ($p \geq 0.05$).

Discussion

The research carried out in the field of the effects of cucumber consumption on the levels of liver enzymes is limited to the following. Ezodili et al. (2017) showed that 21 days of consuming 400 grams of cucumber in the fasting state did not result in a significant change in aspartate transaminase and alanine transaminase levels compared to the pre-test state in healthy undergraduate students (4). The results of their research are not consistent with the present study. Mohammad et al. (2021) evaluated the effect of aqueous extract of cucumber fruit on liver enzymes (aspartate transaminase and alanine transaminase) in healthy rats and rats that developed diabetes with streptozotocin. The results of their research showed that this extract has no toxic effect and leads to the reduction of AST and ALP levels and may be used to manage the treatment of diabetes (11). Egbirmahon et al. (2022) investigated the comparative effect of cucumber leaves and juice on the liver of albino rats. Their findings showed that cucumber leaf and juice extracts are safe and non-toxic for the liver (12).

Cucumber juice is rich in antioxidants, vitamins, minerals, and other bioactive compounds. One of these compounds is cucurbitacin. Cucumber bitterness is mainly caused by cucurbitacin C, but in very small amounts (much less than 1 mg/100 g) (13). Cucurbitacin in cucumber has been shown to have anticancer activity. In addition, cucurbitacins also showed a wide range of pharmacological effects *in vitro* or even *in vivo* and are used as clearing and anti-inflammatory agents (14). Cucurbitacins have been shown to have anti-inflammatory and hepatoprotective properties. When ingested, these compounds can trigger a series of cellular and molecular events in the liver. Studies have shown that cucurbitacin inhibits the activity of certain liver enzymes involved in the metabolism of toxins and drugs, such as cytochrome P450 enzymes. By inhibiting these enzymes, cucumber juice may improve liver detoxification processes, reduce liver cell load, and modulate liver enzyme activity. In addition, cucumber juice is a diuretic, and by increasing urine production and helping to eliminate toxins from the body, it can indirectly affect liver enzymes by reducing exposure to harmful substances. The mechanism of the hepatoprotective effect of cucumber can be due to the reduction of the production of reactive oxygen species and antioxidant properties (15). At the cellular level, antioxidants in cucumber juice, such as vitamin C and beta-carotene, can scavenge free radicals and reduce oxidative stress. It helps protect liver cells from damage and maintains their normal function. Oxidative stress is known to release liver enzymes into the bloodstream. With vitamins such as vitamin C and beta-carotene, cucumber reduces oxidative stress, increases the total antioxidant capacity, and consequently reduces the levels of liver enzymes (AST, ALT, and ALP) (7). At the molecular level, cucumber juice may also affect the expression of liver enzymes. Research shows that cucurbitacin can modulate gene expression, specifically targeting genes involved in inflammation and liver function. By reducing pro-inflammatory genes and resetting anti-inflammatory genes, cucumber juice may help reduce liver inflammation and improve liver enzyme levels. In addition, the protective function of the liver has been confirmed due to the presence of saponarin in the cucumber (16). Under the influence of sports activities, the activity of liver enzymes is intensified (17). High-intensity prolonged trainings has a significant effect on the activity of liver enzymes(18). The study conducted in the field of serum enzyme activities due to training shows that intense training increases liver aminotransferase enzymes. According to this research, training fatigue caused by increasing the duration and intensity of training increases membrane permeability and also increases the levels of ALT, ALP and AST enzymes (19). Ruiz et al. (2014) concluded that moderate-to-vigorous physical activity causes a significant increase in AST and the AST/ALT ratio (20). These researchers concluded that training intensity is an effective factor in creating significant changes in the activity of liver enzymes. Therefore, the intensity of training, both aerobic and resistance, as the most important component of training, can have positive or negative effects on body tissues. Therefore, the correct design of training intensity can increase the function of different body tissues, including the liver tissue. It has been stated that the mechanism involved in the reduction of liver fat and correspondingly improving the activity of liver enzymes and optimal blood supply to the liver tissue, improving the metabolism of liver lipids due to physical activities and lifestyle interventions (21). Some studies have concluded that people with regular physical activity have lower levels of ALT, AST, and GGT (22).

Long-term endurance activities, which predominantly rely on aerobic metabolism, affect the activity of AST and ALT enzymes due to the increased demand for energy production through the aerobic system. Since AST and ALT are key enzymes in liver metabolism, and the liver contributes more significantly during endurance exercise, the risk of liver cell membrane damage is higher in such activities. In contrast, heavy resistance training primarily depends on anaerobic pathways for energy supply; thus, liver cells and their enzymes are less involved, resulting in a lower likelihood of enzyme-related damage (23). Therefore, resistance training is considered the best type of training for women with type 2 diabetes who have high levels of liver enzymes ALT, AST, and ALP.

Conclusion

In conclusion, integrating resistance training with cucumber juice consumption presents a promising non-pharmacological strategy for managing type 2 diabetes in women, effectively aiding in the reduction of liver enzyme levels while offering a cost-effective and natural alternative to traditional medications. This dual approach not only enhances physical health but also empowers women to take control of their diabetes management.

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Ethical statement

This study was approved by the Ethics Committee in Biomedical Research at Razi University, Kermanshah, Iran (code: IR.RAZI.REC.1400.092).

Conflicts of interest

There are no conflicts of interest to declare by any of the authors.

Author contribution

"ML and NB analyzed and interpreted the patient data regarding the assessment of implementing resistance training and consumption of cucumber juice on the liver enzymes status of women with type 2 diabetes. ML performed this project and was a major contributor to writing the manuscript. NB checked the prepared manuscript. All authors read and approved the final manuscript."

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Data availability statement

The data that support the findings of this study are available from the corresponding author upon reasonable request.

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Table 1. Anthropometric measurements (Age, Weight, Height, BMI)

Group	Age (Yr)	Weight (kg)	Height (m)	BMI (kg/m^2)
Training+Placebo	49.30±4.64	76±12.82	1.58±0.04	30.50±5.66
Training+Supplement	48.90±4.30	77.08±9.94	1.56±0.04	31.69±3.76
Supplement	49.50±4.30	80.12±10.48	1.55±0.04	33.23±5.73
Control	49.40±4.35	82.67±10.53	1.57±0.04	33.35±4.86

Table2. The data of liver enzymes levels before and after the trial

Variable / Groups	ALT (U/L)		AST (U/L)		ALP (U/L)	
	Before	**After**	**Before**	**After**	**Before**	**After**
Training+Placebo	37.70±5.22	31.10±5.42	32.30±3.83	26±3.80	179.60±52.10	111.60±36.18
Training+Supplement	42.90±7.53	29.70±6.21	47.90±9.63	27.50±5.19	243±31.51	127±27.74
Supplement	29.40±5.31	26.60±4.99	33.40±6.85	30±6.49	170.10±37.66	135.70±36.67
Control	28.40±7.01	28.60±7.01	25.50±4.14	25.70±4.11	147.80±23.03	148.10±23.34