Research Article

Effect of six weeks of interval training and curcumin consumption on apolipoprotein A and B in diabetic male rats

Negar Soleimani[1], Mohammad Gallehdari[2], Reza Sheikh[3*]

Abstract

The present study was conducted to investigate the effect of six weeks of intermittent exercise and curcumin consumption on plasma Apo A and Apo B concentrations in male Wistar rats. 30 male Wistar rats were randomly divided into six groups (5 rats in each group): control, diabetic, healthy intermittent exercise, intermittent exercise diabetes, curcumin diabetes and curcumin exercise diabetes. Diabetes was induced by intraperitoneal injection of streptozotocin poison (50 mg/kg). Intermittent training consisted of 5-12 bouts of intense work (75 to 100% of maximum speed) of 60 seconds with active rest intervals of 75 seconds, six days a week for six weeks. Curcumin was fed to animals by gavage at a dose of 50 mg per kilogram of body weight. The results demonstrated that diabetes induction significantly decreased plasma Apo A concentration ($p \leq 0.01$) and increased plasma Apo B concentration ($p \leq 0.01$). Intermittent training caused a significant increase in Apo A and a significant decrease in Apo B plasma in diabetic rats. Also, it was found that six weeks of curcumin consumption significantly increased the concentration of Apo A in plasma and decreased the concentration of Apo B and the ratio of Apo B to Apo A ($p \leq 0.01$). At end, the results of the present study showed that intermittent exercise, curcumin and the combination of two interventions improve the disorders caused by diabetes in apolipoproteins.

Key Words: **Apolipoprotein, Curcumin, Diabetes, Interval training**

1. Master's Degree in Sports Physiology, Sports Nutrition, Faculty of Physical Education, Islamic Azad University, Ahvaz Branch, Iran. 2. Ph.D. in Biochemistry and Sports Metabolism, Department of Physical Education, Faculty of Humanities, Islamic Azad University, Ahvaz Branch, Iran. 3. PhD student in sports physiology, Faculty of Sports Sciences, Shahid Chamran University of Ahvaz, Ahvaz, Iran

*Author for correspondence: dreza.sheikh@gmail.com

N S: 0009-0002-0963-4061; M G: 0000-0002-0414-6520; R SH: 0000-0001-5554-9250

Received 2 April 2023; Accepted 7 June 2023

Introduction

Diabetes is one of the most common metabolic and endocrine disorders characterized by insulin secretion defects, insulin resistance, or both (Balaji et al., 2019). The most common feature of this disease is the increase in blood glucose level, accompanied by long-term disturbances in glucose, fat, and protein metabolism (Ta, 2014). Low level of plasma HDL cholesterol is an independent predictive factor for the development of diabetes. There are several metabolic disorders of apolipoproteins in diabetes, such as high levels of plasma Apo B concentration and low levels of plasma Apo A1 concentration, which are associated with dyslipidemia and its complications. HDLs and ApoA1 increase insulin synthesis and secretion in pancreatic beta cells. The underlying mechanism of this effect is similar to that reported for gut-derived proteins such as glucagon-like peptide-1 and glucose-dependent insulinotropic polypeptide, both of which induce insulin secretion from pancreatic beta cells under hyperglycemic conditions (Li et al., 2019). Experimental evidence shows that HDL cholesterol level may help improve the pathophysiology of diabetes through a direct effect on plasma glucose level. In fact, HDL cholesterol induces insulin secretion from pancreatic beta cells and glucose uptake in skeletal muscles under different conditions in laboratory and human samples (Haase et al., 2015).

Plasma HDL concentration is determined by a part of the catabolic fraction of apoA1 and ApoA-II, as well as the reduction of HDL with ApoA1 deficiency. ApoA1 plays an important role in glucose stabilization and mitochondrial function in muscle (Lehti et al., 2013). Lipid-dependent and non-lipid-dependent ApoA1 and ApoA-II increase insulin secretion from beta cells and decrease plasma glucose levels (Fryirs et al., 2010). However, in patients with diabetes, the catabolic rate of ApoA1 is significantly higher and absolute production of ApoA1 is inhibited compared to healthy individuals. This inhibition leads to a decrease in the level of ApoA1 in the blood plasma, which may cause a decrease in HDL concentration (Bisoendial et al., 2015). Apo B exists in the structure of chylomicrons, low-density lipoprotein, medium-density lipoprotein, and LDL, since each particle of these lipoproteins contains one Apo B molecule (Jun et al., 2018; Li et al., 2019). In diabetes, the increase in the amount of free fatty acids causes the production of hepatic TG, which then causes the secretion of Apo B and VLDL (Shulman, 2014). Insulin plays a key role in regulating Apo B by increasing the degradation of Apo B in hepatocytes and reducing Apo B secretion (Haas et al., 2013; Pu et al., 2013). Apo A/Apo B ratio represents the balance between atrogenic particles rich in Apo B and antiatherogenic particles rich in Apo A, and this ratio is considered as an indicator of cardiovascular risk (Kaneva et al., 2015). Moreover, high-intensity exercises with a rest period between exercises (for example, 30 seconds of high-intensity exercise followed by 30 seconds of rest, and this cycle is repeated for 7 minutes) has been studies in diabetes (Eather et al., 2019). Intermittent high-intensity training increases insulin sensitivity, reduces abdominal fat and creates favorable changes in blood lipids, and reverses cholesterol removal and modulates the anti-inflammatory capacity of HDL in patients with diabetes, causing anti-inflammatory capacity. It inhibits the expression of anti-inflammatory cytokines and prevents the oxidation of LDL. These two roles are mainly due to Apo-A and other anti-inflammatory enzymes that are present in HDL (Adams & Erbs, 2014; Álvarez et al., 2016).

Furthermore, curcumin is a polyphenol that directly target several molecular signaling and has multiple health benefits (Hewlings & Kalman, 2017). Treatment of illness and maintenance of health/well-being using herbal medicines is the oldest and most popular form of healthcare known to humanity and practiced by all cultures in all ages throughout the history of civilization (Unegbu et al., 2022). Curcumin is the biologically active ingredient of turmeric, a natural compound derived in powder form from the underground stem of the medicinal plant Chroma longa (commonly known as turmeric). Pharmacological research shows that curcumin is effective, safe and non-toxic (Pulido-Moran et al. 2016). It has also been reported that curcumin effectively reduced the number of people who were suffering from diabetes and it also increases the function of pancreatic beta cells (Chuengsamarn et al., 2012). In a study, it was shown that curcumin increases plasma paraoxonase activity, the ratio of HDL to total cholesterol and Apo A to Apo B, and activation of hepatic fatty acid oxidation by inhibiting its inhibitors (Adams & Erbs, 2014). The evidence shows that most of the studies on the effect of curcumin and exercise were done separately on the concentration of Apo A and Apo B and the ratio of Apo B to Apo A in serum and diabetes, and a study that simultaneously evaluated both variables (HIIT and curcumin) has not been conducted. Therefore, the present study was conducted to investigate and compare the effect of intermittent exercise and curcumin supplementation on the concentration of Apo A and Apo B and the ratio of Apo B to Apo A serum in diabetic rats.

Materials and Methods

Animals

The statistical population of this study included 30 male Wistar rats with an age of 10 weeks and a weight range of 230-250 grams. Mice were obtained from the Center for Reproduction and Breeding of Laboratory Animals of Jundishapur University of Ahvaz. The animals were kept in a special room for keeping animals with a temperature of 22 ± 2 degrees Celsius and a relative humidity of 50 ± 5% in 25 x 50 cm cages (each 5 mice in one cage). The cycle of light and dark was 12:12, and the onset of light was at 7 am. During the period animals had free access to standard food and water. After a week of familiarization with the new environment, the animals were randomly divided into six groups, each group containing five mice. The groups include: 1) healthy control (n=5), 2) Diabetes (n=5), 3) Diabetes and curcumin (n=5), 4) Diabetes and interval training (n=5), 5) Diabetes, Curcumin, and exercise (n = 5), and 6) Healthy interval training. Table 1 summarizes the research plan of the study.

Induction of diabetes

Diabetes was induced through intraperitoneal injection of a single dose of streptozotocin. Streptozotocin (Sigma Aldrich, USA) was dissolved in sodium citrate and citric acid solution and immediately injected into the animals at a dose of 50 mg per kilogram of body weight. In order to homogenize the samples, all injections were done between 9 and 9:30 in the morning. To ensure the correctness of the protocol, 48 hours after the injection, fasting blood sugar was measured by making a scratch at the end of the mouse's tail and using a glucometer. Animals with blood sugar higher than 250 mg/dL were considered as diabetic. To equalize the stress in the group of non-diabetic rats, sodium citrate solvent was injected only for them. Next, to ensure the diabetes status of the rats, fasting blood sugar was measured every week using blood from the tail vein with a glucometer.

Maximum speed test

The rats were trained on the treadmill for three days. On the fourth day, the test for determining the maximum speed was performed at 11 am in the condition of 4 hours without food. Heating was done at a speed of 5 meters per minute for 5 minutes. Then, for 5 minutes at a speed of 9 meters per minute, the speed was increased by 2 meters per minute every 2 minutes until the animals stopped. The disability criterion was the inability to return to running on the treadmill within 10 seconds, and the final speed was considered as the maximum speed (Charrin et al., 2017).

Table 1. Research design from animal preparation to sampling.

Provision of Animals	Familiarization	Induction of Diabetes	Examination	Random Replacement	Duration and type of intervention	Sampling
30 Male Wistar rat	Determining and isolating untrained rats	20 mice got diabetes by inducing streptozotocin poison.	Performing the maximum running speed test	control group) healthy)	without activity	End of the sixth week
				Diabetes group	without activity	End of the sixth week
				Diabetes and curcumin group	without activity	End of the sixth week
				Diabetes group, curcumin and exercise	6 weeks Curcumin	End of the sixth week
				Exercise diabetes	6 weeks Curcumin and interval training	End of the sixth week
				Healthy interval training	6 weeks interval training	End of the sixth week

Exercise training protocol

Intermittent training including running on the rodent treadmill at a speed equal to 75-95% of the maximum oxygen consumption was performed six days a week for six weeks. In general, during six weeks, the animals performed 8-12 1-minute repetitions with an intensity of 24-34 m/min with 75-second active rest intervals. This protocol was designed based on the study of Little et al. (2010). The reason for choosing this exercise protocol was that it was very small in volume and the exercise started with a lower intensity than the original protocol and because the animals of the current study were obese. All training sessions were accompanied by 5 minutes of warming up and 5 minutes of cooling down at a speed of 5 meters per minute. The exercise protocol is given in Table 2.

Curcumin

Pure curcumin powder was obtained from Merck, Germany. Then it was prepared in phosphatidylcholine (Kurita & Makino, 2013) and as a suspension. Animals were gavage six days a week in the early morning (between 7 and 8 am) at a dose of 50 mg per kg of body weight (Wang et al., 2016).

Table 2. Interval training program.

Weeks	Repetition × (intensity of light work) duration of light work × (intensity of heavy work) duration of intense work
1	5×1min(24m/min) ×75sec (5m/min)
2	8×1min(24m/min) ×75sec (5m/min)
3	10×1min(28m/min) ×75sec (5m/min)
4	10×1min(30m/min) ×75sec (5m/min)
5	12×1min(30m/min) ×75sec (5m/min)
6	12×1min(34m/min) ×75sec (5m/min)

Laboratory measurements

48 hours after the last training session and after 12 hours of fasting, the animals were injected with ketamine (1 cc per kg of body weight) and xylazine (0.5 cc per kg of body weight). Bleeding and blood sampling from the right ventricle of the mouse heart was done in the amount of 5 cc. To minimize the effect of time of day and circadian rhythm, all blood samples were taken between 9 and 11 am. Blood samples were immediately centrifuged at 1200g at room temperature for 15 minutes and frozen at -80°C until analysis. Apo A and Apo B plasma concentrations using commercial ELISA kits made by Bioassay Technology Laboratory (made in China), respectively, with a sensitivity of 0.022 µg/ml and an internal measurement CV of less than 10% and an external measurement of less than 8%. Also, it was measured with a sensitivity of 0.02 mmol/L and an internal measurement CV of less than 10% and an external measurement of less than 8%. Plasma levels of blood sugar, HDL and LDL were measured using Pars Azmoun kits (made in Iran) according to the manufacturer's instructions.

Statistical analysis

One-way analysis of variance (ANOVA) was used to compare the studied groups. Then Bonferroni's follow-up test was used to test each hypothesis.

Results

Based on the results, there is a significant difference in the concentration of Apo A ($p = 0.0001$, $F(5) = 42.707$), Apo B ($p =$

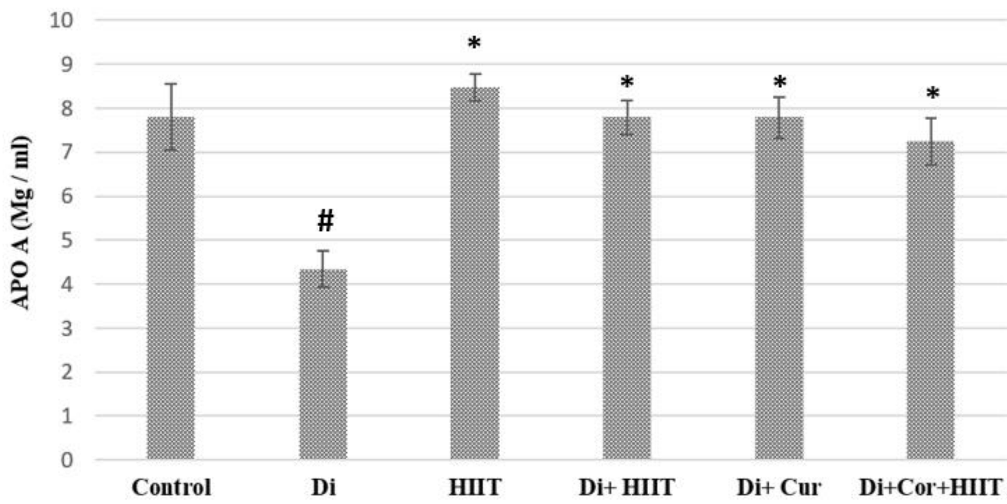

Figure 1. Comparison of mean and standard deviation of plasma Apo A between six groups. Di: Diabetes, HIIT: High Intensity Interval Training, Cur: Curcumin. #: Sign of significant compare to control group, *: Sign of significant compare to Di group.

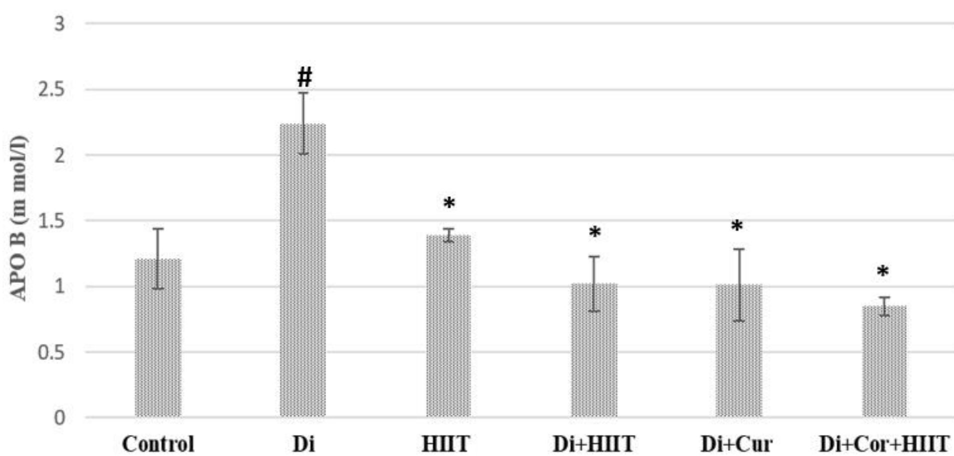

Figure 2. Comparison of mean and standard deviation of plasma Apo B between six groups. Di: Diabetes, HIIT: High Intensity Interval Training, Cur: Curcumin. #: Sign of significant compare to control group, *: Sign of significant compare to Di group.

0.0001, F (5) = 31.590) and the ratio of Apo B to Apo A (p = 0.0001, F (5) = 69.690) exists between the six studied groups. In the following, Bonferroni test was used to check the difference between the groups.

The results of the Bonferroni test showed that there was a significant difference between the concentration of Apo A in the diabetes group and healthy control groups (4.34 ± 0.41 vs. 7.8 ± 0.76 respectively) and diabetes exercise (34 ± 0.41 respectively There is a difference of 7.79 ± 0.39 (4.4 vs. 0.39). As can be seen in Figure 1, Apo A concentration in plasma has decreased significantly after diabetes induction compared to the control group. Then, six weeks of intermittent training in diabetic rats has caused a significant increase in Apo A concentration ($p \leq 0.01$). Also, the consumption of curcumin causes a significant increase in plasma Apo A concentration compared to the diabetic group.

The results of the Bonferroni test show that both exercise and curcumin significantly reduce the plasma Apo A concentration in diabetic rats, but there is no significant difference between the intervention groups.

The results of the Bonferroni test showed (Figure 2) that diabetes causes a significant increase in plasma Apo B concentration in diabetic rats compared to healthy rats (diabetic: 2.24 ± 0.23 versus healthy: 0.23 ± 0.23). Also, six weeks of intermittent training significantly reduced the concentration of Apo B plasma in diabetic rats (diabetic: 2.24 ± 0.23 versus diabetes training: 1.02 ± 0.21) and brought it to the levels of the control group. The consumption of curcumin also significantly reduced the plasma Apo B concentration in diabetic rats. Furthermore, the results of statistical analysis showed that the combination of curcumin and exercise in diabetic rats significantly reduces the plasma Apo B concentration. This means that the combination of exercise and curcumin is more effective than exercise or curcumin alone. Even the decrease in plasma Apo B concentration in the training and curcumin group was significantly higher than the healthy training group.

As displayed in Figure 3, there is a significant difference in the ratio of Apo B to Apo A in plasma between the diabetes group and the control group ($p \geq 0.01$). Moreover, the ratio of Apo B to Apo A plasma has increased significantly in the diabetes group ($p \geq 0.01$). However, interval training did not have a significant effect on the plasma Apo B to Apo A ratio. The results of the Bonferroni test showed that six weeks of curcumin consumption significantly increases the ratio of Apo B to Apo A in diabetic rats. The combination of exercise and curcumin significantly reduces the ratio of Apo B to Apo A in diabetic rats compared to the diabetic group, but there is no difference between the exercise group and curcumin alone.

Discussion

Diabetic patients typically have a pattern of abnormalities in plasma lipids and lipoproteins, including increased small dense LDL particles, increased triglyceride levels, and decreased HDL. Due to the fact that Apo A is the main apolipoprotein of HDL particles, in diabetes, the serum level of Apo A decreases and following the increase of LDL, the level of Apo B also increases. In addition, due to the fact that the ratio of Apo A / Apo B represents the balance between atherogenic particles rich in Apo B and anti-atherogenic particles rich in Apo A, this ratio is considered as an indicator of cardiovascular risk and blood lipid abnormalities (Kaneva et al., 2015; Mooradian, 2009). It is directly related to the increased risk of cardiovascular diseases and other side effects in diabetic patients (Gordon et al., 2008).

In the present study, six weeks of intermittent training significantly increased the concentration of Apo A in the plasma, which is in line with the results of the study by Deloui et al. (2015). They reported that eight weeks of aerobic training increases the concentration of apolipoprotein A. Another study reported that 12 weeks of combined training increased plasma Apo A concentration in middle-aged women with type 2 diabetes, which supports the results of the present study. Also, as intense interval training reduced Apo B and the ratio of Apo B to Apo A, the researchers claimed that interval training is a better way to improve blood apolipoprotein status than combined training (strength endurance) (Hosseinian et al., 2016). In the present study, it was observed that six weeks of curcumin consumption increases serum Apo A concentration and decreases Apo B concentration. Jang et al. (2008) reported that 10 weeks of curcumin intake increases plasma Apo A levels. They reported that curcumin leads to a decrease in plasma levels of free fatty acids, cholesterol and triglycerides and an increase in HDL. These results confirm the findings of the present study. However, Apo B did not show a significant change, which is not consistent with the results of this study. The lack of effect of curcumin on Apo B concentration is probably due to the negative regulation of cholesterol biosynthesis by curcumin. Curcumin reduces fatty acid syntheses activity and increases fat beta oxidation. Curcumin reduces hyperlipidemia by inhibiting fat storage (Jang et al., 2008).

Another study reported that curcumin reduces total cholesterol and LDL and increases HDL. It also increases the expression of Apo A and decreases the expression of Apo B and the ratio of Apo B to Apo A. The results of this study confirm the current findings (Elseweidy et al., 2015). In another study, eight weeks of aerobic training increases serum Apo A concentration in overweight and obese male adolescents, which confirms the res-

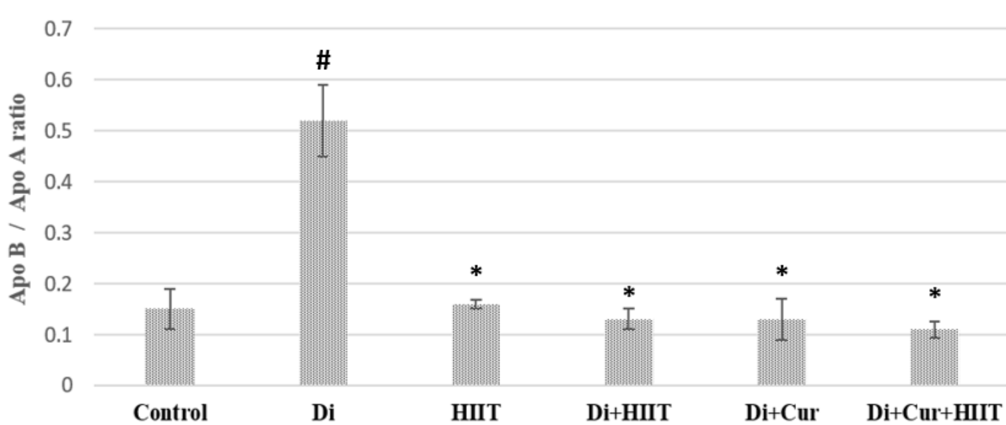

Figure 3. Comparison of mean and standard deviation of plasma Apo B to Apo A ratio between six groups. Di: Diabetes, HIIT: High Intensity Interval Training, Cur: Curcumin. #: Sign of significant compare to control group, *: Sign of significant compare to Di group.

-ults of the present study (Ghorbanian et al., 2015). Reverse transport of cholesterol is called the process of collecting excess cholesterol from peripheral tissues, including macrophages of the arterial wall, and returning them to the liver. The first step of the process of reverse transfer of cholesterol depends on its extracellular acceptor, namely Apo A; therefore, the suggested mechanism for increasing Apo A is increasing the activation of LPL, lecithin and cholesterol acyltransferase enzymes and decreasing liver lipase enzyme (Lennon et al., 2004). In the study by Adab et al. (2013) on the effect of turmeric consumption on anthropometric indicators, glycemic status and fat pattern in patients with type 2 diabetes with hyperlipidemia, it was found that aerobic exercise and the consumption of turmeric powder supplements have a direct effect on tissue fat and its oxidation can reduce serum concentrations of inflammatory index in non-athlete women. Aerobic exercise and turmeric powder decreased serum LDL and increased Apo A, which is consistent with the present study (Adab et al., 2013).

Curcumin in turmeric inhibits cyclooxygenase and lipoxygenase. These enzymes convert arachidonic acid into inflammatory mediators such as histamine, serotonin, bradykinin, cytokines and prostaglandins. Research in this field shows that curcumin prevents the production of free oxygen radicals due to its antioxidant properties (Adab et al., 2013). 18 weeks of curcumin consumption compared to lovastatin on the development of atherosclerosis and lipid profiles of the subjects showed that the plasma level of Apo A in the group receiving curcumin and lovastatin did not change compared to the control group, but the level of Apo A mRNA expression in the liver tissue showed a significant increase. Besides, the plasma level of Apo B in the group receiving curcumin and lovastatin significantly decreased compared to the control group. Also, the ratio of Apo A to Apo B increased in the group receiving curcumin and lovastatin compared to the control group, which is in line with the present study (Shin et al., 2011). The possible mechanism of turmeric in improving dyslipidemia deals with increasing cholesterol catabolism via increasing the activity of the liver enzyme cholesterol 7-hydroxylase, which in turn inhibits cholesterol synthesis by inhibiting the enzyme HMGCOA reductase. Curcumin also affects LDL receptors and inhibits dietary cholesterol absorption (Khajehdehi et al., 2012).

Conclusions

In general, the results of the present study showed that intermittent exercise, curcumin and the combination of two interventions improve the disorders caused by diabetes in apolipoproteins. Hence, periodic exercise as an option available and accepted by the public, and curcumin supplement as an anti-diabetic cheap and safe herbal drug, can be prescribed to control or improve complications caused by diabetes.

What is already known on this subject?

The evidence shows that most of the studies on the effect of curcumin and exercise were done separately on the concentration of Apo A and Apo B and the ratio of Apo B to Apo A in serum and diabetes.

What this study adds?

HIIT, curcumin and the combination of two interventions improve the disorders caused by diabetes at apolipoproteins.

Organ Cross-Talk Tips:

- Cross-talk is formed between skeletal muscle and blood apolipoproteins following interval training in diabetes.
- Curcumin may have an additional effect on the mentioned cross-talk.

Acknowledgements

The following article is taken from the master's thesis of Negar Suleimani, which was carried out at the reproduction and maintenance center of the Faculty of Veterinary Medicine, Shahid Chamran University, Ahvaz. We thank and appreciate all the people who helped us in the implementation of this research.

Funding

None.

Compliance with ethical standards

Conflict of interest The authors declare that they have no conflict of interest.

Ethical approval Experimental protocols were approved by the Ethics Committee of Islamic Azad University, Ahvaz, Iran (Ethcal code: IR.IAU.AHVAZ.REC.1400.056).

Informed consent Animal study.

Author contributions

Conceptualization: N.S., M.G., R.SH.; Methodology: N.S., M.G., R.SH.; Software: R.SH.; Validation: N.S., M.G.; Formal analysis: N.S., M.G.; Investigation: N.S., M.G.; Resources: N.S., M.G.; Data curation: N.S., M.G., R.SH.; Writing - original draft: N.S., M.G., R.SH.; Writing – review & editing N.S., M.G.; Visualization: N.S., M.G.; Supervision: N.S., M.G.; Project administration: N.S., M.G., R.SH.; Funding acquisition: R.SH.

References

Abbasi Deloui, A., Hedayatzadeh, S., Abdi, A., & Abbaszadeh Faki, H. (2015). The effect of eight weeks of aerobic training on serum levels of FGF21, apolipoprotein A-1 and the ratio of LDL-C to HDL-C in obese women. Physiology and Management Researches in Sports, 8(1). Retrieved from URL: https://www.sid.ir/fa/journal/ViewPaper.aspx?id=303115

Adab, Z., Eghtesadi, S., Vafa, M., Heydari, I., Shojaei, A., Haqqani, H., & Khorraminia, N. (2013). Effect of turmeric on body measurement indices, glycemic condition, and lipid profile in hyperlipidemic patients with type 2 diabetes. Iranian Journal of Nutrition Sciences & Food Technology, 8(3), 217-227.

Adams, V., & Erbs, S. (2014). Influence of exercise training on HDL function. Taylor & Francis.

Álvarez, C., Ramirez-Campillo, R., Martínez, C., Mancilla, R., Flores, M., Cano-Montoya, J., & Ciolac, E. (2016). Low-volume high-intensity interval training as a therapy for type 2 diabetes. Int J Sports Med, 37(9), 723-9. doi: https://doi.org/10.1055/s-0042-104935

Balaji, R., Duraisamy, R., & Kumar, M. (2019). Complications of diabetes mellitus: A review. Drug Invention Today, 12(1).

Bisoendial, R., Tabet, F., Tak, P. P., Petrides, F., Cuesta Torres, L. F., Hou, L., . . . Rye, K. A. (2015). Apolipoprotein A-I Limits the Negative Effect of Tumor Necrosis Factor on Lymphangiogenesis. Arterioscler Thromb Vasc Biol, 35(11), 2443-2450. doi: https://doi.org/10.1161/atvbaha.115.305777

Charrin, E., Dubé, J. J., Connes, P., Pialoux, V., Ghosh, S., Faes, C., . . . Martin, C. (2017). Moderate exercise training decreases inflammation in transgenic sickle cell mice. Blood Cells, Molecules, and Diseases. doi: https://doi.org/10.1016/j.bcmd.2017.06.002

Chuengsamarn, S., Rattanamongkolgul, S., Luechapudiporn, R., Phisalaphong, C., & Jirawatnotai, S. (2012). Curcumin extract for prevention of type 2 diabetes. Diabetes Care, 35(11), 2121-2127.

Eather, N., Riley, N., Miller, A., Smith, V., Poole, A., Vincze, L., & Lubans, D. R. (2019). Efficacy and feasibility of HIIT training for university students: The Uni-HIIT RCT. J Sci Med Sport, 22(5), 596-601. doi: https://doi.org/10.1016/j.jsams.2018.11.016

Elseweidy, M. M., Younis, N. N., Elswefy, S. E., Abdallah, F. R., El-Dahmy, S. I., Elnagar, G., & Kassem, H. M. (2015). Atheroprotective potentials of curcuminoids against ginger extract in hypercholesterolaemic rabbits. Nat Prod Res, 29(10), 961-965. doi: https://doi.org/10.1080/14786419.2014.957699

Fryirs, M. A., Barter, P. J., Appavoo, M., Tuch, B. E., Tabet, F., Heather, A. K., & Rye, K. A. (2010). Effects of high-density lipoproteins on pancreatic β-cell insulin secretion. Arteriosclerosis, Thrombosis, and Vascular Biology, 30(8), 1642-1648.

Ghorbanian, B., Kurdi, M., Ravasi, A. A., Hedayati, M., & Ghasem Nian, A. (2015). The effect of eight weeks of interval endurance training on lymphocyte ABCA1 protein expression, ApoA-I and blood lipid profiles in overweight and obese male adolescents. Sports Biology Journal, 7(3), 375-390. doi: https://doi.org/10.22059/jsb.2015.56253

Gordon, L. A., Morrison, E. Y., McGrowder, D. A., Young, R., Fraser, Y. T. P., Zamora, E. M., . . . Irving, R. R. (2008). Effect of exercise therapy on lipid profile and oxidative stress indicators in patients with type 2 diabetes. BMC Complementary and Alternative Medicine, 8, 21-21. doi: https://doi.org/10.1186/1472-6882-8-21

Haas, M. E., Attie, A. D., & Biddinger, S. B. (2013). The regulation of ApoB metabolism by insulin. Trends in Endocrinology and Metabolism: TEM, 24(8), 391-397. doi: https://doi.org/10.1016/j.tem.2013.04.001

Haase, C. L., Tybjaerg-Hansen, A., Nordestgaard, B. G., & Frikke-Schmidt, R. (2015). HDL Cholesterol and Risk of Type 2 Diabetes: A Mendelian Randomization Study. Diabetes, 64(9), 3328-3333. doi: https://doi.org/10.2337/db14-1603

Hewlings, S. J., & Kalman, D. S. (2017). Curcumin: A review of its effects on human health. Foods, 6(10), 92. doi: https://doi.org/10.3390/foods6100092

Hosseinian, M., Banitalebi, E., & Amirhosseini, S. E. (2016). Effect of 12 weeks of intensive interval and combined training on apolipoprotein A and B, visfatin and insulin resistance in overweight middle-aged women with type 2 diabetes. Quarterly of Horizon of Medical Sciences, 22(3), 237-245. doi: https://doi.org/10.18869/acadpub.hms.22.3.237

Jang, E. M., Choi, M. S., Jung, U. J., Kim, M. J., Kim, H. J., Jeon, S. M., . . . Lee, M. K. (2008). Beneficial effects of curcumin on hyperlipidemia and insulin resistance in high-fat-fed hamsters. Metabolism, 57(11), 1576-1583. doi: https://doi.org/10.1016/j.metabol.2008.06.014

Jun, J. E., Choi, Y. J., Lee, Y.-H., Kim, D. J., Park, S. W., Huh, B. W., . . . Choi, S. H. (2018). ApoB/ApoA-I ratio is independently associated with carotid atherosclerosis in type 2 diabetes mellitus with well-controlled LDL cholesterol levels. The Korean Journal of Internal Medicine, 33(1), 138.

Kaneva, A. M., Potolitsyna, N. N., Bojko, E. R., & Odland, J. Q. (2015). The apolipoprotein B/apolipoprotein AI ratio as a potential marker of plasma atherogenicity. Disease Markers, 2015.

Khajehdehi, P., Zanjaninejad, B., Aflaki, E., Nazarinia, M., Azad, F., Malekmakan, L., & Dehghanzadeh, G.-R. (2012). Oral supplementation of turmeric decreases proteinuria, hematuria, and systolic blood pressure in patients suffering from relapsing or refractory lupus nephritis: a randomized and placebo-controlled study. Journal of Renal Nutrition, 22(1), 50-57.

Kurita, T., & Makino, Y. (2013). Novel curcumin oral delivery systems. Anticancer Res, 33(7), 2807-2821.

Lehti, M., Donelan, E., Abplanalp, W., Al-Massadi, O., Habegger, K. M., Weber, J., . . . Hofmann, S. M. (2013). High-density lipoprotein maintains skeletal muscle function by modulating cellular respiration in mice. Circulation, 128(22), 2364-2371. doi: https://doi.org/10.1161/circulationaha.113.001551

Lennon, S. L., Quindry, J., Hamilton, K. L., French, J., Staib, J., Mehta, J. L., & Powers, S. K. (2004). Loss of exercise-induced cardioprotection after cessation of exercise. J Appl Physiol (1985), 96(4), 1299-1305. doi: https://doi.org/10.1152/japplephysiol.00920.2003

Li, X., Li, Z., Zhao, M., Nie, Y., Liu, P., Zhu, Y., & Zhang, X. (2019). Skeletal muscle lipid droplets and the athlete's paradox. Cells, 8(3), 249.

Little, J. P., Safdar, A., Wilkin, G. P., Tarnopolsky, M. A., & Gibala, M. J. (2010). A practical model of low-volume high-intensity interval training induces mitochondrial biogenesis in human skeletal muscle: potential mechanisms. The Journal of Physiology, 588(Pt 6), 1011-1022. doi: https://doi.org/10.1113/jphysiol.2009.181743

Mooradian, A. D. (2009). Dyslipidemia in type 2 diabetes mellitus. Nature Clinical Practice Endocrinology & Metabolism, 5, 150. doi: https://doi.org/10.1038/ncpendmet1066

Pu, L. J., Lu, L., Zhang, R. Y., Du, R., Shen, Y., Zhang, Q., . . . Shen, W. F. (2013). Glycation of apoprotein AI is associated with coronary artery plaque progression in type 2 diabetic patients. Diabetes Care, 36(5), 1312-1320.

Pulido-Moran, M., Moreno-Fernandez, J., Ramirez-Tortosa, C., & Ramirez-Tortosa, M. (2016). Curcumin and health. Molecules, 21(3), 264.

Shin, S. K., Ha, T. Y., McGregor, R. A., & Choi, M. S. (2011). Long-term curcumin administration protects against atherosclerosis via hepatic regulation of lipoprotein cholesterol metabolism. Mol Nutr Food Res, 55(12), 1829-1840. doi: https://doi.org/10.1002/mnfr.201100440

Shulman, G. I. (2014). Ectopic fat in insulin resistance, dyslipidemia, and cardiometabolic disease. New England Journal of Medicine, 371(12), 1131-1141.

Ta, S. (2014). Diagnosis and classification of diabetes mellitus. Diabetes care, 37(1), 81-90.

Unegbu, C. C., Ajah, O., Nnorom, C. M., Onwusonye, J. C., Duru, C. A., & Joel, O. M. (2022). Antidiabetes, antidyslipidemia, hemoprotective, nephroprotective and hepatoprotective effect of ethanol extract of Jatropha tanjorensis leaf against alloxan induced diabetes in rats. Journal of Medicinal Herbs, 13(1), 57-64.

Wang, L., Zhang, B., Huang, F., Liu, B., & Xie, Y. (2016). Curcumin inhibits lipolysis via suppression of ER stress in adipose tissue and prevents hepatic insulin resistance. Journal of Lipid Research, 57(7), 1243-1255. doi: https://doi.org/10.1194/jlr.M067397