Comparing the effect of high-intensity functional training with and without L-carnitine supplementation on glucose metabolism in obese women

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مقارنة تأثير التدريب الوظيفي عالي الكثافة مع وبدون مكملات الكارنتين على عملية التمثيل الغذائي للجلوكوز لدى النساء البدينات

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الملخص:

لقد أدى انتشار السمنة وانتشارها كواحد من أهم عوامل الخطر القلبية الوعائية في العصر الحالي إلى دفع الباحثين إلى محاولة إيجاد طريقة للسيطرة عليها من خلال نمط حياة صحي. لذلك، كان الهدف من هذه الدراسة هو التحقيق في تأثير ٨ أسابيع من التمارين الوظيفية المكثفة وإعطاء الكارنتين على توازن الجلوكوز والدهون في الدم لدى النساء البدينات. وفقًا لذلك، تم تقسيم ٢٠ امرأة بدينة (ن = ٢٠) إلى مجموعتين من HIFT + الكارنتين و HIFT +دواء وهمي في تجربة سريرية شبه تجريبية قبل الاختبار وبعده. تم تطبيق التدخل على كلتا المجموعتين لمدة ٨ أسابيع و ٣ أيام في الأسبوع؛ تلقت مجموعة المكملات أو الدواء الوهمي الكارنتين ٥ مرات يوميًا لمدة ٨ أسابيع. تم قياس عينات الدم قبل وبعد ٨ أسابيع من التدخل لقياس نسبة الجلوكوز في المصل والأنسولين ومستوى الدهون. ومن أجل اختبار الفرضيات، تم استخدام اختبار t التابع لتقييم القياسات داخل المجموعة وتم استخدام اختبار التباين لاختبار الاختلافات بين المجموعات. أظهرت النتائج أن نسبة الجلوكوز في المصل (p = 0.001) والأنسولين (p = 0.001)و HOMA-IR (p = 0.001)انخفضت بشكل ملحوظ بعد ثمانية أسابيع في كلتا المجموعتين، على الرغم من عدم ملاحظة أي اختلاف بين المجموعات. أظهرت نتائج الدراسة الحالية أيضًا أن نسبة الدهون في المصل (LDL) (p = 0.03)و (p = 0.01) و HDL (p = 0.001)و TG (p = 0.002) و (p 0.02) والكوليسترول (p = 0.03) والكوليسترول (p = 0.01) انخفضت بشكل ملحوظ بعد ٨ أسابيع من التدخل. وأظهرت نتائج تحليل التباين أيضًا عدم وجود فرق كبير في دهون الدم بين المجموعتين. لذلك، أظهرت الدراسة الحالية أنه على الرغم من تحسن عوامل الخطر القلبية الوعائية مثل مقاومة الأنسولين ومستوى الدهون بعد ٨ أسابيع من التدريب عالي الكثافة، إلا أن استهلاك إل- كارنيتين لم يؤثر بشكل كبير على هذا التغيير.

الكلمات المفتاحية: تأثير التدريب الوظيفي، مكملات الكارنتين، التمثيل الغذائي، الجلوكوز، النساء البدينات، التجربة السريرية.

Abstract:-

The spread of obesity and its prevalence as one of the most important cardiovascular risk factors in the present age has led researchers to try to find a way to control it through a healthy lifestyle. Therefore, the aim of this study was to investigate the effect of 8 weeks of intense functional exercise and L-carnitine administration on glucose homeostasis and blood lipids in obese women. Accordingly, 20 obese women (n = 20) were divided into two groups of HIFT + L-carnitine and HIFT + placebo in a quasi-experimental pretest-posttest clinical trial. The intervention was administered to both groups for 8 weeks and 3 days per week; the supplement or placebo group received L-carnitine 5 times daily for 8 weeks. Blood samples were measured before and after 8 weeks of intervention to measure serum glucose, insulin and lipid profile. In order to test the hypotheses, the dependent t-test was used to evaluate intra-group measurements and the covariance test was used to test for group differences. Results showed that serum glucose (p = 0.001), insulin (p = 0.001), and HOMA-IR (p = 0.001) significantly decreased after eight weeks in both groups, although the difference No intergroups were seen. The results of the present study also showed that serum lipids (LDL) (p = 0.03) and (p = 0.01), HDL (p = 0.001), TG (p = 0.002) and (p 0.02) Cholesterol (p = 0.03) and cholesterol (p = 0.01) were significantly decreased after 8 weeks of intervention. The results of covariance analysis also showed that there was no significant difference in blood lipids between the two groups. Therefore, the present study showed that despite the improvement of cardiovascular risk factors such as insulin resistance and lipid profile after 8 weeks of HIFT, consumption of L-carnitine did not significantly affect this change.

Key words: Effect of functional training, carnitine supplementation, metabolism, glucose, obese women, clinical trial.

Introduction:-

One of the consequences of technological progress is a decrease in physical activity. Those who are not physically active are twice as likely to develop cardiovascular disease. For example, people who are inactive have a higher prevalence of dyslipidemia and high blood pressure. According to the World Health Organization, 39% and 13% of people over the age of 18 are overweight and obese, respectively (World Health Organization, 2019). Evidence suggests that the prevalence of obesity will increase by 33% over the next two decades (Finkelstein et al., 2014). Evidence suggests that increasing physical activity levels and eating a healthy diet can help reduce calorie intake by improving abdominal obesity indicators such as waist-to-hip ratio, visceral fat, and glucose metabolism (Gariballa et al., 2023; Kim and Kwon., 2024). One of the metabolic problems that inactive, obese, and postmenopausal women face is insulin resistance, which is closely related to type 2 diabetes. This condition is a pathophysiological disorder that occurs due to defects in the pathways through which insulin stimulates glucose uptake (8, 9). Today, unlike major public health factors, such as smoking and childhood malnutrition, whose prevalence appears to have decreased over time (Steven et al., 2012; Ng et al., 2014), obesity interventions have not led to a significant reduction in its prevalence worldwide and may have even increased it. As such, it is important to find strategies that reduce the disease and encourage individuals to be and stay active (Fieto et al., 2019). HIFT emphasizes functional, multi-joint movements that can be adapted to any fitness level, induces greater muscle recruitment with aerobic and strength-muscle activities (Fieto et al., 2018; Henrich et al., 2015), and may affect glucose utilization, insulin, and insulin resistance in individuals with type 2 diabetes (Church et al., 2010; Amini-Lari et al., 2017). Recently, Fieto et al. reported a significant reduction in body fat percentage (approximately 65%) after 16 weeks of training among healthy individuals (Fieto et al., 2018). In addition to a lifestyle based on exercise, the use of a healthy diet and, in particular, the use of various supplements has become increasingly popular among obese and diabetic individuals. L-carnitine is an essential nutrient that is widely used and added to a variety of important food products, including weight loss formulations, infant formula, and sports bars

and drinks. Carnitine is known to be a key factor in the regulation and transport of active fatty acids into mitochondria for oxidation (Brass and Hiatt, 1998), and as a result, many human studies have attempted to increase skeletal muscle fatty acid oxidation with carnitine supplementation (Berwood et al., 2005; Novakova et al., 2016). In a study by Galloway et al., which examined the effects of 3 g of L-carnitine per day on fasting glucose, glucose tolerance, insulin, insulin resistance, and glucan-like peptide in obese and overweight individuals and lean individuals after glucose ingestion, they found significant differences between groups in body mass, fat percentage, and body mass index (BMI) in the L-carnitine group compared to placebo. Plasma glucose concentrations at 30 minutes were lower in the lean group after L-carnitine ingestion compared to placebo. Conversely, plasma glucose concentrations at 30 minutes did not differ between groups but were significantly higher at 90 minutes in the obese/overweight group after L-carnitine ingestion. Also, Ramadanpour et al. showed that daily consumption of 500 mg of L-carnitine along with aerobic exercise for 4 weeks significantly reduced fasting blood sugar in the experimental group compared to the control group, while no significant change was observed in serum triglyceride, cholesterol, LDL, and HDL levels between the two groups (Ramazanpour et al., 2015). So far, no study has compared the effects of HIFT and fat-burning supplements on glucose, insulin, insulin resistance index, and lipid profile in obese and overweight individuals. In a study by Newwood et al., significant reductions in body fat (-1/) and non-significant changes in body weight were observed. Although non-significant changes were seen for any of the markers associated with glucose homeostasis (i.e. glucose, insulin, insulin resistance, etc.), researchers did report improvements in beta-cell function after 6 weeks of training (Newwood et al., 2017), so longer interventions with diet and fat-burning supplements may be needed to produce statistically significant changes in glucose markers and lipid profiles. Meanwhile, Feely et al. reported a significant improvement in insulin sensitivity of 15% (Feely et al., 2018), while reducing total and regional fat mass and preserving lean body mass, which is important in blood glucose regulation (Kirwan et al., 2018). Therefore, given the limited number of recent studies that have examined HIFT programs in conjunction with nutritional supplements, the researcher sought to answer the question of

whether short-term HIFT programs in conjunction with L-carnitine supplementation have an effect on serum levels of glucose, insulin, triglycerides, total cholesterol, LDL-C, HDL-C, and insulin resistance index (HOMA-IR) in healthy, inactive overweight and obese women.

Research method

Participations

The present study is of a semi-experimental and laboratory type, and is cross-sectional in terms of the length of time and in terms of the use of applied results, which was conducted as a pre-test-post-test, with a control or placebo group. The subjects of this study were human samples and were randomly divided into 2 groups (10 people in each group).

The statistical sample of the present study consisted of 20 obese and overweight women in Saravan city, who were selected purposefully and conveniently and randomly divided into 2 groups. In this study, women aged 35 to 45 years volunteered to participate in this study. After calculating BMI, those with a BMI of 30 kg/m2 and above were selected. After screening, people with specific diseases and those taking medication were excluded, and finally 20 people were selected and randomly divided into 2 groups: high-intensity functional training (HIFT)-L-carnitine (LC) supplementation (HIFT-LC) (10 N), high-intensity functional training (HIFT)-placebo (Pla) (HIFT-Pla) (10 N). All subjects selected for inclusion in the study were in good physical health and had no history of bone, cardiovascular, respiratory, liver, kidney, brain, or hormonal diseases. All subjects were married and also followed a nutritional program. After selecting the statistical sample, the participants' primary and personal information such as name and surname, age, occupation, and level of education were recorded. Finally, the working conditions and implementation of the research project were fully explained to the volunteers, and the subjects were assured that taking the desired supplement or doing sports activities would not have any side effects for them and would even be very beneficial for their health and fat loss and weight. Finally, they signed the consent form alone or in the presence of one or two witnesses. Throughout the research period, they were given the option to leave the study and cancel it at any time and for any reason, and they were free and had no obligation in

this regard. Also, during the research period, transportation and movement conditions, appropriate nutrition on the day of their activity were provided by the researcher to the extent possible. Also, after the research period, the subjects, especially the control group, were given the opportunity to use the research protocol after the activity, and free consultations were provided to them.

The study consisted of two stages: pre-test and post-test. Between these two stages, the subjects performed the relevant activities for 8 weeks. The purpose and program of the study were explained to the subjects. The variables of age, weight, height, blood pressure, and health were examined by a doctor, then blood was drawn. Biochemical indices were measured after 48 hours of overnight fasting at 8 am by a specialized laboratory. The initial blood sample of 15 cc was taken from the subjects' anterior brachial vein by the laboratory's blood collection specialists and frozen at -35°C.

HIFT Protocol

After the necessary coordination with the gym officials and trainers, the main protocol began for 8 weeks. All participants were also asked to maintain their usual diet throughout the study and, depending on the group they were in, not to change their physical activity or participate in other sports activities. High-intensity functional training (HIFT) was performed according to the study by Feito et al. (2019), the total training period of the subjects was 24 sessions (8 weeks) and each session was about 60 minutes of activity. CrossFit was used as the HIFT program in this study. All HIFT sessions were supervised and led by a level 2 instructor, and the first and second sessions used common HIFT movements (squats, deadlifts, presses, barbells, dumbbells, medicine ball exercises, pull-ups, kettlebell swings, etc.); no additional exercises were performed on these two days. Beginning on the third day, each HIFT class consisted of 10–15 min of stretching and warm-up, 10–20 min of training and instructional movements and techniques, and 5–30 min of a work-of-the-day (WOD), which was performed at a very high intensity and relative to the individual's ability. The main components of the training included aerobic activities (e.g., running, jumping rope), bodyweight activities (e.g., pull-ups, squats), and weightlifting (front squats, kettlebell swings), always performed in the format of CrossFit exercises in single, double, and triple sets for time,

repetitions, or weight. Each weight and movement performed was recorded according to the individual's understanding and ability in each exercise session. Based on the WOD characteristics, the time to complete the WOD, the repetitions and rounds completed in the WOD, the weights used, and any equipment needed to perform a workout program, the daily workout amount was recorded. The average time for each WOD and the average total WOD during the week for the entire training group were recorded. In general, this workout program was performed for 8 weeks, 3 days per week.

L-carnitine supplementation

The subjects in the L-carnitine supplement group with placebo also received two grams of L-carnitine (8 250 mg tablets) in three meals with meals (three tablets in two meals and two tablets in one meal). The supplements were delivered to the subjects every two weeks and to measure their compliance with the supplement, they were asked to hand over the supplement packet each time. The dosage and method of administration were implemented using the study by Rafraf et al. (2012).

Blood sampling

Blood sampling was performed in two stages, 48 hours before the start of the first training session (pre-test) and 48 hours after the last training session (end of the eighth week). The collected blood was placed in sterile tubes and then centrifuged (for 20 minutes at 2000 to 3000 rpm) to separate the plasma serum and frozen at 35°C until measurement. After 8 weeks of training, similar blood sampling was performed. All blood samples were removed from the freezer on the same day and the desired tests were performed to measure CRP by ELISA using the CRP laboratory kit model CK-E10873 from Pars Azmoun Company, Iran, and insulin manufactured by Metwayand Company, USA, with a sensitivity of 0.5 U/MI, and by a fully automatic ELISA device manufactured in Germany. Fasting blood sugar levels were also measured by enzymatic colorimetry using a glucose oxidase peroxidase kit manufactured by Pars Azmoun Company, Iran. Insulin resistance was also calculated and evaluated using the homeostasis model assessment of insulin resistance and based on the following equation:

HOMA = (FBS (mmol/L) × FBI (IU per ml) ÷ 22.5)

Where HOMA is the homeostasis model of insulin resistance, FBS is fasting blood glucose values, and FBI is fasting blood insulin values.

After data collection, SPSS version 22 statistical software was used to analyze them; in a way that the values of central tendency and mean dispersion and standard deviation were used to estimate descriptive statistics of the research. The Shapiro-Wilks statistical test was used to examine the distribution of data and the t-test was used to compare means within groups and the analysis of covariance (ANCOVA) test was used to compare between groups. The significance level was considered to be P<%5. All data analysis was performed using SPSS22 software.

Result

Twenty-nine participants were enrolled, 7 participants withdrew due to health complications unrelated to the study (HIFT+LCAR: N = 4; HIFT+PLA: N = 3) and 2 dropped out due to unforeseen family and work interruptions (HIFT+LCAR: N = 1; HIFT+ PLA: N = 1). Twenty participants completed the full intervention (HIFT+LCAR: N = 10; HIFT+ PLA: N = 10). with an adherence rate between 85-100%. Participant characteristics from the eligibility screening (Table 1) and all baseline outcome variables were similar between groups ($p > 0.050$). A Wilcoxon test revealed no differences in pre-to-post SLIQ for each group ($p > 0.050$) indicating participants maintained their current lifestyle behaviors throughout the intervention period.

Table 2 present the baseline (Pre) and 8-week follow-up (Post) data for each of the frequency dose groups, and includes the within group effect sizes and 95% confidence intervals. The preliminary t test and ANCOVA and mixed-effects p-values are also included.

Discussion

One of the most important findings of the present study was the improvement in insulin resistance index, insulin, and glucose in both groups after 8 weeks of intervention, while no significant difference was observed between the two groups. Recently, Nieuwedot et al. (2017) examined changes in beta cell function after six weeks of HIFT among 12 sedentary adults with type 2 diabetes. After performing 10–20 min sessions 3 days a week, participants showed

significant improvements in beta cell function along with decreased body fat and maintenance of lean mass. In a second study, Flei et al. (2018) evaluated the effectiveness of their 6-week HIFT intervention on cardiometabolic risk factors and reported improvements in blood pressure, body composition, fat oxidation, plasma triglycerides, and very low-density lipoprotein. In addition, insulin sensitivity was increased after exercise, although the downward change in glucose was not statistically significant after the intervention. These two studies provide initial insight into the benefits of HIFT among people with type 2 diabetes and support the idea that this type of exercise is beneficial, even if the total exercise volume is lower than usual (American College of Sports Medicine, 2017). To date, no other study has examined metabolic changes associated with HIFT. Similarly, no studies have compared HIFT with and without various fat-burning supplements in obese women, so the design of this study seems timely and necessary. On the other hand, high-intensity functional training has been shown to reduce body weight in obese individuals, thereby improving insulin and glucose resistance. Olsen et al. (2005) observed a decrease in glucose uptake in the legs, which was improved by increasing lean body mass. Although no significant differences were found between groups, the present study is the first to compare HIFT with and without a fat-burning supplement (L-carnitine) on glucose control and body composition markers, the exact mechanisms of which are not known.

Several investigators have shown that 8–12 weeks of training may not be sufficient time to produce significant improvements in glucose metabolism after endurance and resistance training programs in nondiabetic individuals (Craig et al., 1999; Fenischia et al., 2004). For example, Craig et al. (1999) reported the effect of a 12-week resistance training program among a group of males (23 years) and older (63 years) participants. They showed that although all participants showed significant improvements in lean mass and body composition, no group showed a response in glucose concentrations despite a reduction in insulin after a glucose load. Similarly, Finicchia et al. (2004) examined the effects of an acute resistance training session and a six-week training program in women with type 2 diabetes and showed that, despite the effect of resistance training on increasing strength, glucose concentrations improved immediately after the acute period, but no change was

observed after six weeks of training. In addition, no improvement in insulin concentrations was observed.

Previous research has shown that insulin secretion is inhibited by exercise due to increased norepinephrine levels. It is also possible that the decrease in insulin due to exercise is due to glucose sparing, which limits the use of blood glucose by muscles and makes more blood glucose available to the brain. Among the possible causes of the decrease in insulin resistance due to exercise, we can also point to insulin-independent mechanisms such as the increase in GLUT-4 levels due to muscle contractions (Haghighi et al., 2005). Several studies have been conducted on the effects of L-carnitine supplementation and insulin resistance. Hassani and Ghorbani (2018) showed improvement in insulin resistance after a week of L-carnitine and omega-3 supplementation and stated that L-carnitine leads to improvement in insulin, glucose, and insulin resistance by increasing fat oxidation and weight loss. Alipour et al. (2015) also stated that increasing irisin improved insulin resistance in obese individuals, which was a limitation of the present study.

Conclusion

1. According to the findings of the present study, it seems that performing intense functional training along with L-carnitine supplementation improves blood lipids, glucose homeostasis, and ultimately reduces metabolic complications of obesity among young and middle-aged individuals.

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Table 1.

Participant baseline characteristics from eligibility screening. Data are means (±SD).

	HIFT+ LCAR (n=10)	HIFT+ Pla (n=10)	p-value
Age (yrs)	33.50 (5.48)	32.60 (5.42)	0.52
High (cm)	161.40 (1.23)	160.20 (1.74)	0.84
Body weight (kg)	76.42 (9.33)	76.60 (7.53)	0.65
BMI (kg/m2)	31.01 (1.70)	30.70 (2.08)	0.62

Table 2.

Within-group change and ANCOVA results in blood analysis markers.

		HIFT+LCAR			HIFT+PLA			ANCOVA	
	Pre means (±SD)	Post means (±SD)	sig	Pre means (±SD)	Post means (±SD)	sig	F	P value	EF
GLU (mg/dL)	120.10 (7.22)	115.10 (2.05)	0.001	112.7 (8.38)	109.8 (20.40)	0.001	0.192	0.66	0.01
INS (mcIU/mL)	37.57 (0.7)	29.57 (0.7)	0.001	19.53 (0.7)	12.52 (0.7)	0.001	0.568	0.46	0.03
HOMA-IR (mg/dL)	29.20 (0.2)	27.07 (0.2)	0.001	21.00 (0.2)	22.92 (0.1)	0.001	2.137	0.16	0.11