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The Impact of Aerobic and Resistance Training on C-Reactive Protein (CRP) and Lipid Profiles in Methadone-Treated Addicted Men

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ABSTRACT

Introduction: The combined use of methadone and exercise training holds promise for promoting health. This study investigates the impact of resistance and aerobic training in conjunction with methadone consumption on lipid profiles and C-reactive protein (CRP) levels in addicted men.

Materials & Methods: Ninety addicted men (mean age 36.82 ± 4.32 years) undergoing prison treatment were randomly assigned to six groups (n=15 each): control, narcotics anonymous (NA), aerobic training + methadone, aerobic training + methadone reduction, resistance training + methadone, resistance training + methadone reduction. The 12-week exercise program, conducted thrice weekly, included aerobic training (4-8 sets, 3 minutes each, at 80-90% maximum heart rate on the ergometer bike) and resistance training (12 repetitions, 3 sets, at 70-85% of one repetition maximum). Blood samples collected pre- and post-intervention measured CRP and blood lipids using specialized kits. Data were analyzed with SPSS software, employing multiple analysis of variance (MANOVA) and Tukey's post hoc test ($P<0.05$).

Results: High-density lipoprotein (HDL) levels significantly increased in trained groups compared to the control ($P<0.001$). Moreover, trained groups exhibited significant decreases in low-density lipoprotein (LDL), triglycerides, total cholesterol, and CRP compared to the control group ($P<0.05$). Importantly, aerobic training was more effective than resistance training in improving the studied variables.

Conclusion: Exercise training, particularly aerobic training with methadone ingestion, yields positive effects, including reduced CRP levels and improved lipid profiles in addicted men. Exercise training with methadone reduction may be considered for empowering individuals with addiction issues.

Keywords: Exercise, Lipids, C-reactive Protein, Methadone, Substance-Related Disorders

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Introduction

Today, the challenge of addiction extends beyond the realms of health and treatment, evolving into a social crisis and an ominous phenomenon. Drug abuse, a contentious issue across various domains, has garnered the attention of experts. It is indisputable that the escalating use of addictive substances has emerged as a substantial and intricate problem in human societies, with a growing number of victims necessitating written interventions and programs (1).

Recent research in the scientific study of addiction and treatment challenges the prior belief that addicted individuals are morally flawed and weak-willed. In the past, punitive measures such as fines, imprisonment, and execution were favored over preventive approaches. However, advancements in science and technology have transformed societal perspectives, considering addicts as individuals afflicted by a medical condition (2). Managing addiction proves challenging due to withdrawal syndrome, but current chemical treatments, such as the use of methadone, appear as promising solutions (3).

Methadone, a μ-opioid agonist metabolized by the liver and gastrointestinal tract, boasts a slow metabolism and high fat tissue accumulation, prolonging its effects compared to morphine-based opioids (4). Despite its efficacy, reports in recent years highlight concerns about addiction, tissue damage, compromised immune function, and alterations in various hormones and factors, indicating potential inflammatory effects (5).

Intriguingly, methadone's oral activity, extended half-life, and reduced euphoria make it a viable alternative treatment, stabilizing patients' lives and curbing drug consumption (6). Nonetheless, drug abuse exerts widespread effects on the human body, impacting respiratory, cardiovascular, and lipid systems. Methadone addiction commonly leads to dyslipidemia, increasing the risk of cardiovascular diseases (7).

Traditionally, blood lipid profiles were indicative of cardiovascular risks; however, the American Heart Association, in 1998, recommended assessing inflammatory markers like plasma C-reactive protein (CRP). Evidence suggests heightened systemic inflammation in drug addicts, potentially elevating inflammatory indicators such as CRP (8).

CRP, regulated by cytokines, especially interleukin-6 (IL-6), serves as a sensitive indicator of systemic inflammation. Elevated CRP levels are associated with cell membrane damage, increased phagocytic cell activity, and activation of the classical complement pathway. Studies indicate higher CRP levels in drug addicts compared to control groups (9). Additionally, drug use has been linked to increased cytokine production, further elevating CRP levels (10).

On a positive note, there is compelling evidence supporting the use of regular physical activities as an effective method for both preventing and treating addiction in rehabilitation centers (11). Studies have reported that exercise plays a significant role in reducing C-reactive protein and inflammation (12). For instance, Mohammadi et al. (1401) found that eight weeks of resistance training led to a decrease in C-reactive protein

(CRP) and interleukin 18 levels (13). Similarly, another study demonstrated that regular aerobic exercises, with an intensity of 65 to 80% of the maximum oxygen consumption, improved plasma levels of C-reactive protein in young men (14). In a meta-analysis conducted by Michael et al. (2019), exercise was found to be associated with a decrease in CRP and BMI levels, irrespective of age or gender (15).

Furthermore, researchers have shown that engaging in sports activities can have positive effects on reducing dependence on substances such as morphine in animal samples and decreasing the consumption of cigarettes, cannabis, opium, and methamphetamine in addicted individuals (16). The practice of Bedwanjin, a type of yoga in China, has been reported to enhance the immune cells of individuals addicted to heroin (17). The belief that regular physical activity, with its low cost and attractiveness, contributes to increased cardiovascular health as a means to quit addiction is supported by studies highlighting improvements in aerobic fitness, muscle strength, insulin sensitivity, HDL, and reductions in triglycerides (TG) and LDL (18).

On one hand, addressing the issue of reducing cholesterol, LDL, and TG through structured exercise programs with appropriate intensity and duration, along with C-reactive protein measurements, is crucial in preventing cardiovascular diseases. Unregulated physical activity may lead to adverse consequences such as obesity, inflammation, increased protein catabolism, decreased sensitivity of cell receptors, disturbances in energy production pathways, destruction of contractile protein strands, excessive free radical increase, and lipid peroxidation (19). On the other hand, considering the limited research on the effects of sports training, particularly aerobic-resistance training, on inflammatory factors and lipid profiles, contradictory results have been reported (20, 21). The growing concern over the increasing prevalence of addiction and related diseases in the country prompted the researcher to employ a suitable, non-invasive, and cost-effective method in conducting the present research on methadone-addicted men. This study aims to not only contribute to the existing knowledge but also strengthen the background of research on how sports training is related to the function of inflammatory factors and the rehabilitation of methadone-addicted individuals. Consequently, the current research seeks to compare the effects of aerobic and resistance training with varying levels of methadone consumption on C-reactive protein and lipid profiles in addicted men undergoing methadone treatment.

Materials and methods

Subjects

This study employed an applied and semi-experimental research design with a pre-test-post-test structure, incorporating a control group. The target population consisted of male individuals undergoing methadone treatment within Ilam prisons. Inclusion criteria involved a daily methadone consumption of up to 30 mg, a positive urine test for methadone, and negative urine tests for morphine, hashish, and methamphetamine. Additional criteria included inactivity, absence of cardiovascular or metabolic conditions, normal blood pressure, no special diet, exclusive use of methadone without other drug involvement, and no regular physical activity over the previous six months, within an age range of 30 to 40 years. Ninety male participants meeting these criteria voluntarily enrolled in the study. The study interventions received approval from the Ethics Committee of Islamic Azad University, Science and Research Branch.

Procedure

To secure voluntary participation, potential participants were informed about the study's purpose, objectives, methods, and potential benefits through prison-wide communication. Initially, 214 individuals expressed interest in participating. After applying the inclusion criteria, 90 eligible individuals were selected. In a comprehensive briefing session, participants received detailed information about the research process, the test procedures, and associated risks. Subsequently, subjects provided informed consent by completing and signing consent forms. The 90 participants were then randomly assigned to six groups of 15 individuals each: control, NA, aerobic exercise + methadone, aerobic exercise + methadone reduction, resistance training + methadone, and resistance training + methadone reduction, using a random number table. The designated protocol was implemented over a 12-week period. Throughout the study, participants were instructed to maintain their usual eating and behavioral habits, including sleep and daily activities, while promptly reporting any physical issues to the researchers. Five individuals were excluded from the study due to irregular participation in the training program, resulting in a final cohort of 85 participants who completed the research.

Measurement Method

To assess inactivity, the Champs questionnaire based on MET (Metabolic Equivalent of Task) was employed (22). MET serves as a unit for estimating the metabolic cost associated with physical activity. A score of one indicates a sedentary level of physical activity, while a score exceeding one but less than three signifies low physical activity (inactivity). Scores equal to or greater than three and less than six indicate a moderate intensity of physical activity, and a score surpassing 6 signifies a high intensity of physical activity. The International Physical Activity Questionnaire (IPAQ) was utilized to measure the level of poor physical activity (23). According to IPAQ guidelines, if the total energy expenditure throughout the week is less than 600 Week/Cal/Met, the individual is classified as having poor physical activity (24).

To verify the absence of specific diseases and drug use, consultation with a specialist doctor in Methadone Maintenance Treatment (MMT) was conducted. The subjects' ages were determined using their birth certificates. Height was measured with a wall-mounted height meter model 4440, manufactured by Kaveh Company in Iran, with an accuracy of 5 mm. Weight was measured without shoes and with minimal clothing using a device from Kaveh company, made in Iran. Body Mass Index (BMI) was calculated by dividing the body weight (in kilograms) by the square of the height (in meters).

The body fat percentage was determined through the measurement of subcutaneous fat (triangles) using a Caliper (Yagami brand, made in Japan) (25). Waist circumference at the upper level of the pubic bone and hip circumference at the level of the gluteal cavity were measured with a tape measure, accurate to 5 mm. The Waist-to-Hip Ratio (WHR) was calculated by dividing the waist circumference by the hip circumference.

To calculate the maximum heart rate, the formula (220 - age) was applied, utilizing a heart rate monitor (Polar brand, made in Finland). Given the subjects' relatively poor physical fitness, determining the maximum oxygen consumption index using high exercise intensities was impractical. Therefore, VO2PEAK was calculated, representing the peak oxygen consumption of subjects in milliliters/kg/minute from the Rockport test. The calculation followed a specific formula (26).

Peak oxygen consumption = 100.5 + (8.344*gender) -(1663/*body weight) - (1.438*time) -(1938/. *Heart rate)

For the determination of maximum strength, participants selected weights based on an initial estimation of their maximum strength and executed the movement until reaching exhaustion. Subsequently, the Brzeski formula was applied by incorporating the weight moved and the number of repetitions. This calculation method allowed for the estimation of maximum strength (25).

$$Maximum\ Repetition = \frac{Weight\ Value}{1/0278 - (/0278)Repetition}$$

Aerobic Training Protocol

To ensure proper execution of the research, participants underwent a comprehensive orientation session led by a qualified bodybuilding instructor. Subsequently, the Rockport test was employed to estimate the subjects' peak oxygen consumption.

Following a thorough understanding of the prescribed exercise principles, the exercise protocol unfolded over 12 weeks, divided into three segments, each spanning four weeks. Under the supervision of an expert bodybuilding trainer, sessions took place on Sundays, Tuesdays, and Thursdays at 17:00 in the prison gymnasium. The ambient temperature in the facility was automatically regulated by a heating-cooling system during the training sessions.

The protocol adhered to the overload principle, with the first four weeks involving 4 repetitions of 3 minutes at 70% of the maximum heart rate. The subsequent four weeks increased the intensity to 85% of the maximum heart rate with 6 repetitions of 3 minutes. The final four weeks intensified further, comprising 8 repetitions of 3 minutes at 90% of the maximum heart rate, with 3 to 4-minute rest intervals (slow walking) on the treadmill between repetitions. The total training time was standardized across the 12-week period for the training group.

Each training session followed a structured format, including a 10-minute warm-up (involving slow running, stretching, and relaxation), the main training phase, and a 5-minute cool-down incorporating stretching and flexibility movements (25, 27).

Resistance Training Protocol

After comprehensive instruction on the correct execution of movements, encompassing leg press, chest press, knee extension, knee bend, front arm, and back arm (comprising 3 upper body and 3 lower body movements), a 12-week training protocol unfolded. Supervised by an expert bodybuilding trainer, the protocol consisted of three four-week cycles, conducted on Saturdays, Mondays, and Wednesdays at 17:00 in the Central Prison's gymnasium. Temperature conditions in the facility were meticulously regulated using an automatic heating-cooling system.

The circular protocol adhered to the overload principle, incorporating three sets in each session. The first set comprised 12 repetitions at 70% intensity of the maximum repetition, followed by the second set with 10 repetitions at 80% intensity of the maximum repetition, and the third set with 8 repetitions at 85% intensity of the maximum repetition. Two-minute passive rest intervals (slow walking) separated repetitions, with a strategic emphasis on large muscles before small muscles and multi-joint exercises preceding single-joint exercises.

Equalization of resistance training was achieved based on the formula: weight * number of repetitions * number of sets over the 12-week period. The training sessions encompassed three stages: a warm-up with 50% of the maximum repetition, the main exercise phase, and a 5-minute cool-down involving stretching and flexibility movements (25).

Methadone Consumption

Both the control and training groups, consisting of methadone users, adhered to a daily consumption of 30 mg of methadone in accordance with the established health and treatment protocol. Conversely, the NA and training groups, in conjunction with the methadone reduction plan, experienced a gradual decrease in methadone dosage, ranging from 1 to 2.5 mg per week. The methadone use was ultimately discontinued at the conclusion of the 12-week period (28,3).

Measuring the Investigated Variables

Following the categorization of subjects into the training, control, and NA groups, blood sampling was conducted during the pre-test phase. Participants were instructed to present themselves to the laboratory after a 12-hour fasting period, abstaining from sports or physical activity for two days prior to blood collection. In a seated and rested position, 10 ml of blood was drawn from the antecubital vein of the right hand from each subject.

Both pre-test and post-test blood sampling sessions occurred between 8 am and 10 am and were administered by a specialist in compliance with established protocols (26).

Following the initial blood sampling and measurement of the investigated variables during the pre-test stage, the research protocol spanned a 12-week period. At the conclusion of this research period, 48 hours after the last exercise session to mitigate the effects of the final session, all subjects were re-invited to the laboratory. Under the same conditions as the pre-test blood sampling, blood sampling and relevant measurements were once again conducted.

Upon immediate blood collection in both the pre-test and post-test phases, the obtained blood samples were divided into two parts. The first part was added to a vial containing citrate anticoagulant to determine C-reactive protein concentration. Simultaneously, the second part of the blood samples underwent centrifugation for 15 minutes at a speed of 3000 rpm to separate the plasma. Subsequently, tubes were removed from the device, and the serum was separated and stored in a freezer at a temperature of minus 80 degrees Celsius until the relevant tests were performed.

For the measurement of serum triglycerides and cholesterol (LDL, HDL), Pars Azmoun Iran kits, along with the photometric method, were employed. Total cholesterol was measured using the enzymatic method. C-reactive protein concentrations were measured and calculated using a commercial DBC kit model ELX888 from the United States. The Hanan Teb Pars kit was utilized for detecting urinary levels of drug use and methadone. All measurements strictly adhered to the manufacturer's instructions.

Statistical Data Analysis

The data from this research were analyzed using SPSS version 20 software. Initially, the normality of the research data was assessed using the Kolmogorov-Smirnov test, confirming normal distribution. Subsequently, the statistical test of multivariate analysis of variance (MANOVA) was employed to investigate changes in C-reactive protein and lipid profiles among the six groups. Tukey's test was then applied to examine specific changes between groups during the pre-test and post-test phases. A significance level of $P \leq 0.05$ was considered indicative of statistical significance. The presentation of data includes mean values and standard deviations.

Results

Baseline characteristics, encompassing age, height, body weight, addiction history, and duration of methadone consumption across different groups, are presented in Table 1, expressed as mean ± standard deviation.

Table 1. Baseline Characteristics of Participants in Different Groups (Expressed as Mean ± Standard Deviation).

Groups / Variables	C	NA+MR	AT+M	AT+MR	RT+M	RT+MR
Age (year)	37.53±3.67	38.3±3.05	34.92±4.93	37.02±3.39	39±2.25	34.5±3.24
Weight (kg)	80.34±2.94	82.89±3.14	78.07±2.20	80.34±3.49	80.25±1.73	77.61±4.32
Height (cm)	176.86±2.25	176.53±2.28	169.85±4.40	175.4±2.69	175.2±1.84	174.92±3.05
History of Addiction (years)	6.46±1.91	6.53±1.62	8.71±2.70	5.66±0.841	6.6±1.15	6.28±966

Methadone Consumption (months)	39±2.45	36±2.24	36±1.90	37±2.07	36±2.55	38±2.25

NA: Narcotics Anonymous, **MR**: Methadone Reduction, **AT**: Aerobic Training, **RT**: Resistance Training.

Present study findings show a significant increase in the maximum oxygen consumption (VO2max) in the trained groups compared to the pre-test ($P<0.05$). In addition, the body mass index (BMI) and subcutaneous fat significantly decreased in the trained groups compared to the pre-test. The mean levels of VO2max, subcutaneous fat thickness and BMI before and after 12 weeks interventions in the different training group were reported in the table 2 (mean±standard deviation)

Table 2. Pre-test and Post-test Levels of VO2max, Subcutaneous Fat Thickness, and BMI in the Different Training Groups (Mean ± Standard Deviation).

Variables Groups	VO2max		Subcutaneous Fat Thickness		Body Mass Index (BMI)	
	Pre-test	Post-test	Pre-test	Post-test	Pre-test	Post-test
Control	28.57±0.17	28.45±0.15	18.02±0.97	18.20±0.99	25.6±0.62	25.81±0.72
NA	28.55±14	28.48±0.13	18.44±1.05	18.49±0.99	26.47±0.70	26.63±0.72
AT+M	28.16±0.09	*28.83±0.16	18.3±0.85	18.15±0.85	24.04±1.74	*23.60±1.66
RT+M	28.34±15	*28.49±0.18	18.43±1.06	18.10±1.16	26.07±1.00	*25.85±0.99
AT+MR	27.67±26	*28.19±0.18	18.63±1.02	*18.46±0.92	25.93±0.51	*25.50±0.47
RT+MR	28.16±0.38	*28.35±0.38	18.59±1.2	18.54±1.3	25.45±1.03	*25.26±1.09

NA: Narcotics Anonymous, **MR:** Methadone Reduction, **AT:** Aerobic Training, **RT:** Resistance Training. * Indicate a significant change compared to pre-test.

The results of the MANOVA test revealed a significant between-group difference for CRP levels ($F=24.624$, $P<0.001$). Additionally, significant between-group differences were observed for HDL ($F=27.609$, $P<0.001$), LDL ($F=3.649$, $P=0.005$), triglyceride ($F=3.405$, $P=0.008$), and total cholesterol levels ($F=3.058$, $P<0.001$). Consequently, the 12-week exercise training (aerobic and resistance) alongside methadone consumption demonstrated a significant impact on CRP as an inflammatory factor (Table 3).

Table 3. MANOVA Test Results for Various Variables

Variable	Test Statistics	Degrees of Freedom	The Significance Level
CRP	24.624	5	P<0.001

HDL	27.609	5	P<0.001
LDL	3.649	5	P=0.005
TG	3.405	5	P=0.008
Cholesterol	3.058	5	P=0.014

The results of Tukey's post hoc test indicated that aerobic training following the reduction of methadone consumption was more effective in downregulating CRP levels compared to other trained groups (P<0.05). Additionally, the reduction in CRP levels was statistically significant in other trained groups compared to the control and NA groups. However, no significant difference was observed between the control and NA groups. The detailed findings of Tukey's post hoc test for CRP levels are presented in Table 4.

Table 5. Tukey's Post Hoc Test Findings for Observed Changes in CRP Levels

Groups	Control	NA	AT+M	RT+M	AT+MR
NA	0.717				
AT+M	<0.001	<0.001			
RT+M	<0.001	<0.001	1.000		
AT+MR	<0.001	<0.001	<0.001	<0.001	
RT+MR	<0.001	<0.001	<0.001	<0.001	0.027

NA: Narcotics Anonymous, **MR:** Methadone Reduction, **AT:** Aerobic Training, **RT:** Resistance Training

Discussion

The objective of this study was to compare the impact of aerobic and resistance training, combined with methadone consumption and its gradual reduction, on C-reactive protein (CRP) and lipid profiles in addicted men. The findings revealed a significant increase in blood HDL levels in the studied groups compared to the control group. Additionally, the training groups exhibited significant decreases in LDL, triglycerides (TG), and CRP levels compared to the control group.

Methadone, recognized as a synthetic opioid, serves as an effective pain reliever and alleviates symptoms of drug withdrawal, representing a preferred treatment for drug addicts in camps and prisons (28). While the benefits of physical activity in promoting health and mitigating inflammatory factors are well-established (29), the integration of sports interventions with methadone in the treatment of drug addiction is a subject of discussion.

In summary, this study demonstrated that a 12-week exercise regimen (aerobic, resistance) coupled with reduced methadone consumption in addicted men can yield varying effects on certain inflammatory factors. Regarding HDL levels, the exercised group exhibited a significant increase compared to the non-exercised groups. Furthermore, inter-group comparisons indicated that the most substantial increase occurred in the group that engaged in aerobic exercise alongside reduced methadone consumption. Consequently, it is suggested that aerobic training may exert a greater influence on HDL levels than resistance training.

Consistent with these results, Moradian et al. (1401) assert that high-density lipoproteins play a protective role against arterial atherosclerosis. Consequently, a higher ratio of high-density lipoproteins to low-density lipoproteins significantly reduces the likelihood of atherosclerosis (30). Numerous studies indicate that aerobic exercise contributes to an elevation in high-density lipoproteins in the blood. Moreover, LDL levels experienced a significant decrease in both the aerobic and resistance training groups. However, no significant difference was observed in the intra-group comparison between the training groups. These results align with previous findings (31, 32, 33) and differ from the study by Vakili et al. (2015), which reported no significant effect on the lipid profile of obese young girls following eight weeks of resistance and aerobic training. This inconsistency may be attributed to the absence of drug and methadone use or the gender-specific characteristics of the research subjects (34).

TG levels in both the aerobic and resistance training groups exhibited a significant decrease compared to the control and Narcotics Anonymous (NA) groups. Notably, this reduction was more pronounced in the aerobic groups than in the other groups. These outcomes align with findings from previous studies (26, 35, 36). Mirzai Pour et al. (2012) explored the impact of two methods of opium consumption on certain inflammatory and coagulation factors in golden hamsters. The results indicated a significant increase in C-reactive protein (CRP) due to drug consumption, although other research factors did not exhibit significant differences between the two groups. It is suggested that the sedentary lifestyle and reluctance of addicted individuals to engage in regular physical activity contribute to this increase.

In a study by Sheikh Saraf et al. (2013), the cardiovascular health structures of inactive men were compared before and after 8 weeks of combined sports activity following drug cessation. The findings revealed a significant decrease in CRP, leukocyte count, and LDL, accompanied by a significant increase in oxygen consumption and body mass index (BMI) (29).

The precise mechanism underlying the impact of exercise on CRP is not fully understood. Exercise activities elevate anti-inflammatory mediators, such as interleukin-1, while concurrently reducing TNF-α, leading to a decrease in interleukin-6 and, consequently, a reduction in CRP production in the liver. Simultaneously, sports activity diminishes the production of inflammatory factors by reducing fat mass and decreasing macrophage infiltration. Furthermore, sports activities exert an anti-inflammatory effect by channeling a substantial amount of free fatty acids into cells for energy production (20).

Abbaspour et al. (2017) demonstrated in their study that a 6-week simultaneous endurance training and Pilates regimen, conducted at an intensity of 60 to 80% of the maximum heart rate in inactive men, had a significant effect on reducing plasma C-reactive protein (CRP) levels and promoting weight loss (38). In a separate study, Basati et al. (2017) found that an 8-week aerobic exercise rehabilitation program, with an intensity of 70% of the maximum heart rate, led to a significant decrease in plasma levels of PTX3 and CRP biomarkers in both diabetic and non-diabetic coronary artery patients (39). Additionally, Khosravianfar et al. (2017) reported that 8 weeks of combined exercise, consisting of aerobic exercise (treadmill running for 20 minutes at 55-70% of the reserve heart rate) and resistance exercise (at an intensity of 55-70% of one repetition maximum), three times per week, resulted in a significant decrease in serum C-reactive protein and plasma interleukin-6 levels in obese women (40).

C-reactive protein, a product of the liver and coronary artery wall cells, serves as part of the immune system's response to infection or injury. In inflammatory reactions, its levels can surge up to three thousand times the normal amount. Furthermore, CRP levels exhibit direct associations with age, gender, body mass index, alcohol and drug consumption, and even the psychological state of individuals (41,42). According to the findings of the present study, a notable decrease in C-reactive protein was observed in the training groups.

Resistance exercises, by increasing protein synthesis and muscle mass, contribute to the reduction of body fat reserves. This, in turn, leads to the downregulation of the inflammatory cytokine gene in muscle tissue, reducing serum levels of the leukocyte adhesive molecule. Consequently, the inhibition of the reaction between monocytes and endothelial cells ultimately results in a decrease in inflammatory factors, including CRP (43). Meanwhile, regular aerobic activity enhances cardiorespiratory fitness, reduces catecholamine stimulation, LDL-c, and free radicals, potentially decreasing the secretion of TNF-α, a potent stimulator of interleukin-6 and CRP (44).

According to the findings of this research, C-reactive protein levels exhibit a direct relationship with high-density lipoprotein (HDL) and an inverse relationship with low-density lipoprotein (LDL), triglycerides, and cholesterol levels. Nevertheless, certain studies on drug addicts show no effect of exercise on blood parameters, presenting a disparity with the results of this research. For instance, Haddadi et al. (2015) reported that aerobic exercise had no impact on the lipid profile of individuals (45). Among the factors contributing to the disparities in findings are differences in the type of training protocol (intensity and duration), participant preparedness, nutrition, training environment, and the muscle volume engaged during training, in comparison to the protocol employed in the current research.

Conclusion

The findings indicate that engaging in 12 weeks of both aerobic and resistance training, while concurrently varying methadone consumption and gradually reducing its intake, significantly elevates high-density lipoprotein (HDL) levels in the bloodstream. Furthermore, the levels of low-density lipoprotein (LDL), triglycerides (TG), and C-reactive protein exhibit significant decreases in the training groups when compared to the control group. Notably, in the inter-group comparison, the results reveal that the methadone-aerobic exercise groups exerted a more pronounced effect on all measured variables than the other exercise groups.

These outcomes suggest that consistent exercise, particularly of the aerobic and resistance types, in conjunction with the reduction of methadone consumption, has a positive impact on inflammatory factors and, ultimately, on the health and well-being of individuals struggling with addiction.

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Authors' contributions

R CH and M GH conceived the study, designed and coordinated it. R CH, HM, and H AN were involved in data collection. F GH analyzed the research data. All authors participated in drafting the manuscript, read and approved the final version, and agreed with the order of authorship presentation.

Conflict of interest

The authors declare that no conflict of interest exists.

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