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Evaluation of the Effects of High Intensity Interval Training on Cytokine Levels and Clinical Course in Treatment of Opioid Use Disorder

Pelin TAŞ DÜRMÜŞ[1], Mehmet Erdal VARDAR[2], Oktay KAYA[3], Pınar TAYFUR[4], Necdet SÜT[5], Selma Arzu VARDAR[6]

SUMMARY

Objective: Opioid use disorder (OpUD) is a biological and psychosocial disorder with limited treatment options. Addition of physical exercise to the pharmacological treatment has been proposed to be effective on reducing substance use and improving the quality of life. In this study we aimed to investigate the effects of a high-intensity interval training (HIIT) program on the serum levels of cortisol, insulin-like growth factor1 (IGF-1), interferon-gamma (IFN-γ), interleukin 17 (IL-17) and the clinical progress of inpatients with OpUD.

Method: Our study enrolled 22 male inpatients diagnosed with OpUD on the basis of the DSM-5 criteria. Two groups of 11 individuals were formed as the exercise (EG) and the control (CG) groups. The EG conducted 5 sessions of a HIIT. Participant data were collected with Sociodemographic Questionnaire, the Addiction Profile Index (API), and the Barratt Impulsiveness Scale (BIS-11). Also, the Hamilton Depression Rating Scale (HAM-D), the Hamilton Anxiety Rating Scale (HAM-A) and the Substance Craving Scale (SCS) were used before and after the treatment program in order to evaluate the clinical progress. Blood samples were collected on the 5th and the 21st days for estimation of the serum cortisol, IGF-1, IFN-γ and the IL-17 levels.

Results: Comparison of the pre- and the post- treatment performances of the two groups on the HAM-D, the HAM-A and the SCS indicated a significant drop in the respective scores of the EG. Also, a significant increase was observed in the post-treatment IGF-1 level of the EG as compared to the CG. No differences were observed between the cortisol, IFN-γ and IL-17 levels of the EG and the CG.

Conclusion: HIIT resulted in significant reduction in the symptoms of depression, anxiety and substance craving, and increased the serum IGF-1 levels. HIIT did not change serum cortisol, IFN-γ and IL-17 levels. We believe this research will contribute to the literature on the treatment of opioid depencence by emphasising the effects of HIIT on patients treated for OpUD.

Keywords: Dependence, exercise, heroin, opioid, cytokine, cortisol

INTRODUCTION

Opioid use disorder (OpUD) is an important public health problem involving comorbid psychiatric disorders, poor quality of life and excessive management costs (Weinstock et al. 2012). The 2018 Drug Report of the European Monitoring Centre for Drugs and Drug Addiction (EMCDDA) shows that 36% of the total number of treatment requests made for substance dependence in the European Union had been for opioid use. The same report emphasises that the mean 0.4% prevalence of opioid use among individuals of 15-64 years of age indicates the presence of 1.3 million high risk opioid users in European countries. In a research including 8483 high school students in Edirne-Turkey, the lifetime heroin use was found to be 0.2% (Sönmez et al. 2016).

The current opioid depence therapy uses pharmacological agents including methadone, buprenorphine, naltrexone and lofexidine backed up with motivational and cognitive therapies (Butler and Le Foll 2019, Mumba et al. 2018). Despite these treatment options, the post treatment recurrence for OpUD is in the 40-60% range (McLellan et al. 2000). Therefore, there is need for additional therapeutic approaches to reduce

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[1]MD., Besni State Hospital, Psychiatry Clinic, Adıyaman. [2]Prof., Trakya University School of Medicine, Department of Psychiatry, [3]Assis. Prof., [4]Research Assis., [6]Prof., Trakya University School of Medicine, Department of Physiology, [5]Prof., Trakya University, School of Medicine, Department of Biostatistics, Edirne, Turkey.

e-mail: erdalvardar@trakya.edu.tr

the recurrence rates as well as substance use and to improve life quality.

Physical exercise is a promising measure for treatment affecting the early and the late stages of substance dependence with secondary benefits such as preventing obesity and coronary heart disease (Lynch et al. 2013). Having a low side effect profile in comparison to pharmacotherapy presents an advantage next to its easy accessibility, flexibility, relatively low costs and easy integration with other therapeutic approaches (Thompson et al. 2018).

Although the biological basis of the effect of exercising on substance use has not been clarified there have been diverse proposals on the subject. The most important explanations have included the stimulation of the reward system by activation of the mesolimbic pathway, and the improvement in the striatal dopamine receptor deficits (Greenwood et al. 2011, Robertson et al. 2016), and the reduction of comorbidities such as depression and anxiety which underlie the substance use recurrence (Beiter et al. 2016, Colledge et al. 2017). Evaluation physical exercise from the behavioral perspective suggests that it may help avoiding reminders for desire and hence the recurrence (Linke et al. 2015). At the same time brain plasticity may be affected through the new structuring of chromatin in the brain locations with the brain derived neurotrophic factor (BDNF) gene (Gomez-Pinilla et al. 2011).

Researchers have argued that exercise, by leading to physical stress, induces hormonal and immunological responses which can be suppressed or increased in activity depending on the intensity of the exercise (Polat and Kasap 2003). The relationship between cortisol and immune function and between the activation of the hypothalamo-hypophyseal axis and immunosupression have been shown (de Wit et al. 2010). The immune system functions are impaired in substance dependence and craving phase. Cytokines are immunological factors affected by the craving syndrome (Heidarianpour et al. 2016). The IFN-γ is a proinflammatory cytokine increasing the resistance to viral infections (Moldoveanu 2001). Wang et al. (2015) have shown in 65 OpUD patients with an age range of 18-45 years that the IFN-γ levels had not reached normality even at the end of a 12-week craving period. The IL-17 is also a proinflammatory cytokine that can cause inflammation and tissue damage at excessive levels (Gu et al. 2013). An intensive exercise session has a strong effect on the cytokine balance (Tofighee et al. 2014). Exercise increases the IGF-1 uptake by the brain. IGF-1, supports the differentiation of neurons and increases the hippocampal BDNF expression (Cotman 2002). Study on animal models has shown that physical activity results in neurocyte neogenesis and long term neuroplasticity regulated by BDNF and IGF-1 (Schiffer et al. 2009). Exercise has not yet been given a place in the routine addiction treatment programs. Although a variety of physical acitivities are being practiced in some clinics, these are generally not structured and information on the frequency and intensity of application is not available (Flemmen et al. 2014). The type, intensity and and duration of exercising required for the treatment of individuals with OpDU is still uncertain and research is required on the subject.

High Intensity Interval Training is a type of exercise program consisting of short, intermittent and intense activity nearing the maximal effort of the individual to achieve 80-100% increase in the heart rate and interrupted by rest or low intensity exercise (Kong et al. 2018). HIIT has drawn attention as it is beneficial in a shorter term than aerobic exercising and increases the aerobic capacity (Baynaz et al. 2017). Our research has aimed at investigating in patients with OpDU the effects to HIIT on symptoms of depression, anxiety and substance craving and on the serum levels of cortisol, IGF-1, IFN-γ and IL-17.

METHOD

Participants

The participants of this research were male inpatients with an age range of 18-45 years, diagnosed on the DSM-5 criteria with OpUD and placed under treatment between February 2017 and May 2018 at the Alcohol and Substance Dependents Treatment and Research Center, briefly AMATEM, at Trakya University School of Medicine, Department of Psychiatry. The exclusion criteria for the study included having any psychiatric disorder other than opioid and tobacco use disorder, cognitive impairment preventing understanding the instructions of the program, hypertension and/or heart disease, musculo-skeletal system diseases, active infection, parents with heart disease diagnosed below the age of 55 years and a result of VO2 max<20 ml/kg/min on the Astrand test.

During the reseach program, 52 patients with OpUD diagnosis had been admitted to our clinic and 34 had completed the treatment course. Of these 34 patients, 9 were excluded on grounds of using synthetic cannabinoids as well as opioids (1), having active infection (1), a history of cardiac surgery (1), hypertension with dyslipidaemia (1), having VO2 max<20 ml/kg/min on the Astrand test (3), and having fathers with cardiac problems below 55 years of age (2). Also, 3 refused to participate, leaving only 22 patients to be included in the study meeting the inclusion, exclusion and the basic health assessments criteria before exercising. Depending on their motivation to join the study, 11 patients were assigned to the exercise group (EG) and 11 were included as the control group (CG).

Our research was given the approval of the Scientific Research Ethics Committee of Trakya University Medical School Deanery with the protocol number TÜTF-BAEK 2017/133

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Measurements and Evaluations Completed Before the HIIT Program

Detailed anamnesis and physical examination of all participants of the research were completed at the outset. As the symptoms of opiate craving are observed to be more pronounced in the first 48 hours, basic performance measurements were carried out on the 3rd day of the research program so as to ensure reliability of the results of the treatment program as well as the safety of the participants. Advice was given for avoiding heavy meals, caffein and nicotine consumption 2 hours before the assessments were made. Resting blood pressure, resting electorcardiography, body height and weight, body mass index (BMI), percentage of body fat were measured. Also, sports performances were assessed at the sports physiology laboratory by the Astrand test on the bicycle ergometer (Monark 894-E, Sweden). The test involved indirect assessment of maximal oxygen consumption (VO2 max) by maintaining the heart rate at a submaximal level during a 6-minute pedalling of 50 rpm under a 600 kpm/min work load suitable to the individual while the heart rate was measured continuously by the Polar 610i (Finland) heart monitör. Pedalling cycle ergometer was continued until the difference between two consecutive heart beats recorded during the test were maximally 4 beats or until the consecutive heart beats were the same. The test was terminated upon the participant's request or when the heart rate reached 150 beats/min (Astrand and Ryhming 1954, Ersöz 1997, Saremi 2018). The VO2 max values were calculated by using the Astrand-Rhyming nomogram. After the determination of VO2 max levels, the first HIIT application was carried out 2 days later, on the 5th day of the 21-day hospital stay of the participants (Figure 1).

Implementing the HIIT Program

The HIIT program was implemented by means of 3 consecutive Wingate anaerobic tests (Bar-Or 1987) on the Monark bicycle ergometer at the sports physiology laboratory. The procedure was carried out twice per week on nonconsecutive days similarly to that previously carried out for another study (Vardar et al. 2018). However, considering that the participants of this research were not active sports people and were also cigarette smokers, the work load was reduced to 0.050 kg body weight and the number of loading periods were limited to 3 repeats. At the start of the HIIT, the participants warmed up for 4 minutes on the 30W pedal. During the loading exercise the participants pedalled for 30 seconds as fast as they individually could while they were verbally motivated. Subsequently the participants worked on the 30W pedal for 4 minutes. This exercise session comprising 30 seconds of loading followed by 4minutes of resting on the 30W pedal was repeated 3 times. The participants rested 3 days between each of the 5 exercise sessions carried out during the 21-day HIIT treatment period when the detox treatment given in the hospital was also completed.

Obtaining and Analysis of the Blood Samples

Before the first loading exercise on the 5th day of the treatment and in the 5 minutes immediately after the last exercise on the 21st day, 5cc of venous blood samples were obtained from the EG participants. On the 5th and the 21st days of the treatment 5cc venous blood samples were also obtained from the CG participants. As the exercise sessions were held between 10:00 and 11:00 hours, blood samples were taken from both groups of participants at these hours. The blood samples taken were processed at the Physiology Laboratory of Trakya University Medical School. After centrifugation at 3000 G for 15 minutes, the serum samples obtained were kept at -80 0C; and analysed for the IGF-1 (Elabscience, USA), INF-γ (Bender MedSystems GmbH, Vienna, Austria) and IL-17 (Bender MedSystems GmbH, Vienna, Austria) levels by the Enzyme-Linked ImmunoSorbent Assay (ELISA) method as outlined by the kit; and the absrobance was read at 450 nm wavelength to evaluate the levels. The serum cortisol levels were analysed at the central laboratory of the Trakya University Medical School.

Data Acquisition and Evaluation

The sociodemographic data form (SDF): The sociodemographic and clinical features of the participants were recorded by means of the SDF prepared by the researchers for assessing information on the year of birth, marital status, years of education, employment, cigarette smoking, alcohol use, opioid and other substance use, history on psychiatric and physical disorders, family history of psychiatric disorders and the drugs used during the course of the treatment.

The Barratt Impulsiveness Scale (BIS-11): The BIS-11 is a self report scale used for evaluating impulsiveness on 3 subscales on not planning, motor impulsiveness and attention impulsiveness. The validity and reliability of the Turkish language version of the BIS-11 was carried out by Güleç et al. (2008).

The Addiction Profile Index (API): Developed and validated by Ögel et al. (2015), the API is a 58-query self report questionnaire with 11 subscales measuring the dimensions and severity of dependence and evaluating the mental conditions and personal characteristics that could be related to the dependence.

The participants were psychometrically tested on the 1st and the 21st days of the treatment program on.

The Hamilton Depression Rating Scale (HAM-D or HDRS): The Ham-D is a 17-item scale developed to assess the severity of depressive sysmptoms. It is conducted by a clinician and a score of 14 or above is indicative of depression. The validity and reliability analyses of the Turkish language version of the HAM-D were carried out by Akdemir et al. (1996).

The Hamilton Anxiety Rating Scale (HAM-A): The HAM-A is a 14-item scale developed to evaluate anxiety symptoms and each item is scored between 0 and 4. It is conducted by a clinician and scores of 15 and above are indicative of generalised anxiety. The validity and reliability analyses of the Turkish language version of the HAM-A were reported by Yazıcı et al. (1998).

The Substance Craving Scale (SCS): The SCS is the application of the Penn Alcohol Craving Scale to substances other than alcohol. It consists of 5 items each with a score between 0 and 6. The validity and reliability analyses of the Turkish language version of the SCS were reported by Evren et al. (2011).

Statistical Analyses

The data of this research were analysed on the Statistical Package for Social Sciences, version 22.0 (SPSS-22) (Licence No: 10240642). The quantitative data were expressed in terms of the arithmetic mean and the standard deviation, whereas the qualitative data were expressed in numbers and percentages. The normality of the quantitative data were tested by the Kolmogorov Smirnov Test. Comparison of the normally distributed qualitative data was carried out by the independent-samples t-test, and comparison of the non-normally distributed data was made by the Mann Whitney-U Test. The categorical data were compared using the Chi-Square Test. The Quade's Rank ANCOVA Test was used for comparisons of the differences in the pre- and post treatment data of the EG and the CG. In all statistical tests, the p value of <0.05 was accepted for statistical significance.

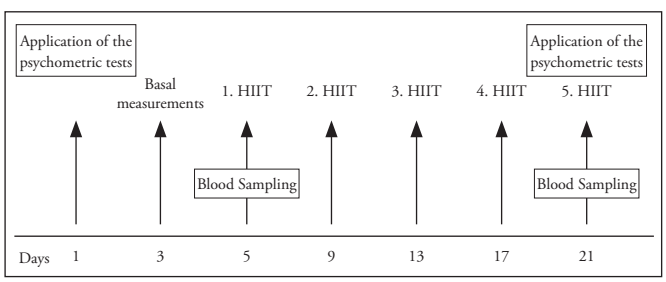

Figure 1. Timing Basis of the Study Plan

RESULTS

On the basis the SDF data, the mean age of the patients was 27.1 (range 21-42) years; 15 (68.1%) were primary school educated and 6 (27.2%) were lyceé educated; 3 (13.6%) were married and 19 (86.4%) were single; 10 (45.5%) were regularly employed and 12 (54.5%) were either unemployed or on irregular/precarious employment. The data of the EG and the CG on age, education, marital status, employment, body weight and height, BMI, fat content values and the Astrand scores (ml/kg/ming) are presented in Table 1.

Table 1. Comparison of the Groups with Respect to Age, Anthropomorphic Measurements and Astrand Scores

	Exercise Group (n=11)	Control Group (n=11)	Total (n=22)	p
	Mean±SD	Mean±SD	Mean±SD	
Age	27.0±7.3	27.1±5.2	27.1±6.2	0.270
Height (cm)	177.6±5.0	176.0±4.6	176.8±4.8	0.857
Weight (kg)	69.0±8.1	67.6±6.7	68.3±7.3	0.394
BMI (kg/m^2)	21.8±2.2	21.8±2.1	21.8±2.1	0.568
Fat (kg)	5.8±3.9	6.3±3.3	6.1±3.5	0.438
Fat (%)	8.1±4.7	9.1±4.2	8.6±4.4	0.588
Astrand Score	36.2±8.4	33.8±8.0	35.0±8.1	0.930

Independent groups t test. SD: Standard Deviation; BMI: Body Mass Index.

All 22 participants of the study were smoking cigarettes; this being 13.7±9.1 (n/day) for the EG and 14.9±7.5 (n/day) for the CG. Also, 3 participants in both the the EG and the CG were using alcohol with a frequency of less than once a week. The EG and the CG did not differ significantly on the basis of cigarette and alcohol use.

All patients were on buprenorphine-naloxone while being treated in the AMATEM clinic. The mean buprenorphine dosage used throughout the treatment period by the EG and the CG were, respectively, 8.9±4.3 mg/day and 12.9±6.0 mg/day, and the difference between these mean values was not statistically significant. The number of the participants on sedative medication quetiapine and mirtazapine varied, respectively, as 3 (27.3%) and 1 (9.1%), in the EG and as 7 (63.6%) and 1 (91%) in the CG. Statitically significant differences were not determined between the scores on the BIS-11 and the SCS of the EG and the CG.

On the first and the 21st days of the treatment, the HAM-D, the HAM-A and the SCS scores of the EG and the EC were very similar. However, when the changes in the pre- and posttreatment psychometric scores of the EG and the CG were evaluated by the Quade's Rank ANCOVA test, statistically significant reductions ($p<0.05$) were determined in the EG. The psychometric scores determined in the EG and the CG during the HITT program are shown in Table 2.

The serum cortisol, IGF-1, IFN-γ and the IL-17 levels at the start and at the end of the treatment program were evaluated. At the start of the treatment program, cortisol and the IFN-γ levels were similar in the EG and the CG; but statistically significant differences ($p<0.05$) were determined between the

Table 2. Comparison of the Changes in the HAM-D, HAM-A and SCS Scores Measured in the Course of Treatment

		Exercise Group (n=11)	Control Group (n=11)	p
		Mean±SD	Mean±SD	
HAM-D score	1st day	7.55±2.50	6.45±3.11	0.270#
	21st day	1.91±1.64	3.00±2.40	0.332#
	1-21day difference	5.63±1.20	3.45±1.29	<0.001##,*
HAM-A score	1st day	6.82±3.37	7.18±3.65	0.797#
	21st day	1.64±1.74	2.73±2.00	0.217#
	1-21day difference	5.18±2.18	4.45±1.86	0.021##,*
SCS score	1st day	18.55±5.12	18.09±5.90	0.847#
	21st day	3.73±2.57	5.36±2.54	0.171#
	1-21day difference	14.81±3.06	12.72±3.63	0.001##,*

#Mann-Whitney U test, ##Quade's Rank ANCOVA test. *p<0.05. HAM-D: Hamilton depression rateing scale; HAM-A: Hamilton anxiety rating scale; SCS: Substance Craving Scale; SD: Standard deviation

IGF-1 ve IL-17 levels of the EG and CG. Using the Quade's Rank ANCOVA to compare the changes in the levels of the serum parameters of both groups at the start and the end of the program demonstrated a significant increase (p<0.05) in the IGF-1 level of the EG, but not in the cortisol, IFN-γ and the IL-17 levels (Tablo 3).

Whereas 5 of the 11 participants of the EG completed the entire HIIT program, 4 did not continue with the program after the first session, 2 of these having personal reasons, 1 having been started on beta agonist therapy by the pulmonary diseases department and 1 having incurred muscle injury outside the treatment program. Comparison of the psychometric data of the 5 EG participants and the 11 participants of the CG at the end of the treatment program showed significant decreases in the HAM-D (p<0.001) and the SCS (p=0.014) scores of the EG; but a comparable decrease was not observed in the HAM-A scores (p=0.264). Also, a significant increase (p=0.027) was determined in the cortisol level of the 5 participants of the EG as compared to the CG; but similarly significant intergroup differences not demonstrated in the IGF-1 (p=0.073) and the IFN-γ and Il-17 Levels (p>0.05).

Table 3. Comparison of the Changes in Serum Cortisol, IGF-1, IFN- γ and IL-17 Levels in the Course of the Treatment

		Exercise Group (n=11)	Control Group (n=11)	P
		Mean±SD	Mean±SD	
Cortisol (µg/dl)	5th day	3.07±1.37	6.78±7.03	0.270#
	21st day	7.72±4.22	5.05±2.79	0.056#
	5th-21st day difference	-4.65±4.23	1.73±6.36	0.066##
IGF-1 (ng/ml)	5th day	37.89±18.07	55.69±21.40	0.047#,*
	21st day	60.86±26.58	56.56±20.39	0.652#
	5th-21st day difference	-22.96±16.10	-0.86±5.76	0.003##,*
IFN- γ (pg/ml)	5th day	6.71±3.85	5.07±0.30	0.478#
	21st day	7.45±3.65	5.16±0.31	0.270#
	5th-21st day difference	-0.73±2.08	-0.08±0.40	0.151##
IL-17 (pg/ml)	5th day	10.54±0.93	9.87±0.69	0.047#,*
	21st day	9.68±0.45	9.92±0.68	0.438#
	5th-21st day difference	0.85±0.90	-0.05±1.08	0.396##

#Mann-Whitney U test, ##Quade's Rank ANCOVA test. *p<0.05. IGF-1: Insulin-like Growth Factor, IFN-γ: Interferon-Gamma, IL-17: Interleukin-17; SD: Standard deviation

DISCUSSION

In this study, it was observed that implementing the HIIT treatment program in addition to the addiction treatment plan reduced depression, anxiety and substance craving symptoms and affected the serum cortisol and IGF-1 levels without changing the serum IFN-γ and IL-17 levels. Although none of the 22 patients included in this research had met the DSM-5 diagnostic criteria for depression, assessment of HAM-D scores in the course of the program demonstrated significant decreases in the EG as compared to the CG. It was reported in studies conducted with OpUD patients that a structured exercise program was effective in reducing depression and anxiety symptoms of substance craving (Haglund et al. 2015, Rawson et al. 2015). Results of a study evaluating the effects of regular exercising in adults under therapy for alcohol and substance dependence showed that the anxiery level of the exercise group was significantly reduced as compared to the controls (Ercan et al. 2016). It was concluded by Wang et al. (2014) in the meta-analysis of 22 studies that exercise reduced anxiety and depression and also alleviated the craving. The results of our research are in agreement with the previously reported evidence that exercising does reduce depression and anxiety related symptoms in substance dependent individuals (Hallgren et al. 2017, Palmer et al. 1995).

Decreased substance craving was shown in patients participating in exercise programs for the treatment of cannabinoid use disorder (Buchowski et al.. 2011). Experiencing the acute benefits of exercise programs such as improved mood and reduced dependence and craving reduces the risk of recurrence (Weinstock et al. 2017). The significant decrease in opioid craving in the EG demonstrated by our research is in agreement with the literature (Gimenez-Meseguer et al. 2015, Roessler 2010).

Comparing the metabolic and hormonal effects of the effects of moderate-intensity and high-intensity interval execise treatments, Peake et al. (2014) found out that cortisol levels were significantly raised immediately after high-intensity

interval exercise. Not observing significantly elevated serum cortisol after a single exercise treatment was attributed to not having implemented an adequately long and intense treatment (Meckel et al. 2009). Comparison of different types of endurance exercise protocols indicated that the highest increase in cortisol levels was achieved after a 4x30-second HIIT (Wahl et al. 2013). Evaluation of the change in cortisol levels after HIIT in our research showed that the increase was 4.65±4.23 in the EG as against the 1.73±6.36 decrease in the CG, the difference being close to statistical significance (p=0.066). Excluding the data on the patients leaving the study after the first session, the increase in the remaining EG participants was significant. The observed increase in cortisol levels with increasing number of sessions is compatible with the view that cortisol levels are correlated with exercise duration (Hill et al. 2008).

There may be elevated stress related to the withdrawal syndrome and biological stress of hypercorticolism and increased sensitivity to cortisol in the early stage detoxification treatment of heroin dependence. Research has also indicated that the increased cortisol response to craving for substance use is closely related to recurrence of dependence (Fatseas et al. 2011, Walter et al. 2013, Yang et al. 2016). However, it was reported that whereas the mediating role of glucocorticoids in craving or recurrence is not definitely known, treatment with a single dose of cortisol does reduce craving in patients using low doses of heroin (Walter et al. 2015). It has been demonstrated in our research that the increased cortisol levels after the exercise program is associated with reduced substance craving.

Studies on animal models have shown that exercising increased the peripheral signalling molecule IGF-1 that increases the BDNF level which strengthens the synaptic activity in the hippocampus (Nock et al. 2017). IGF-1 and the BDNF interact in modulating the exercise dependent cognitive functions (Carro et al. 2000, Ding et al. 2006). It has also been stated that IGF-1 is an important metabolic biomarker of outcomes of exercise and health (Nindl ve Pierce 2010).

Meckel eal. (2009) showed that a single session exercise did not change the peripheral IGF-1 level but increased the level of the IGF-1 binding protein-3 (IGFBP-3) and proposed that exercise effect on IGF-1 was implemented through effects on binding proteins. Higher elevations of IGF-1 and IGFBP-3 were demonstrated in the group undergoing HIIT as compared to controls (Schwarz et al. 1996). Comparison of moderate-intensity exercising and high-intensity interval exercising of 20-minute duration resulted in similarly raised IGF-1 and IGFBP-3 levels under both conditions (Copeland and Heggie 2008). It was shown in our research that the increase in the IGF-1 level of the HIIT EG group was 22.96±16.10 as compared to 0.86±5.76 in the CG, the difference being statistically significant in agreement with the literature.

OpUD may affect multiple physiological functions including those of the immune system which can be mediated directly on the lymphocyte and macrophage receptors or indirectly through the nervous system. Opioid dependence can modify the immune responses to stress through changes in cytokines and other mediators (Lashkarizadeh 2016). Changes can be observed during and after physical acitivity in the peripheral levels of differing cytokines. The effects of physical activity on the immune system may depend on the type and intensity of the exercise (Kruger et al. 2016). HIIT of long duration with high physical effort may result in changes in the blood concentrations of the lymphocyte subgroups and the inhibition of T-cell functions resulting in an inhibitory effect on immune functions (Engel et al. 2014).

The estimated changes in IFN-γ levels in respone to exercise vary in different investigations. The observed increase in IFN-γ levels immediately after exercising were reported to normalise only after two months of resting Zamani et al. 2017). Jahromi et al. (2014) reported a significant drop in the serum IFN-γ concentration following an 8-week endurance exercise program and this outcome was attributed to the inhibition of IFN-γ production by the increased cortisol and epinephrine response to the exercise. Changes were not observed in serum IFN-γ levels in a high-intensity interval exercise program after a single exercise session or a 2-week exercise program (Zwetsloot et al. 2014). In our research, statistically significant differences were not observed in the perpheral IFN-γ levels of the EG and the CG.

Research results on the peripheral level of IL-17 after exercise are conflicted. Having observed significant reduction in plasma IL-17 levels and its production in the peripheral mononuclear cells after an 8-week combined exercise program, Golzari et al. (2010) concluded that exercise had anti-inflammatory effects. Investigation of the changes in cytokine levels between the start and the end of endurance exercising showed that the IL-17A levels extimated 2, 4, 6, 8 and 24 hours after starting exercising were found increased only at the 8th hour (Kakanis et al. 2014). Investigating the IL-17 levels of different groups of sports people with a single session Wingate testing did not show any significant changes (Tofighee et al. 2014). Also, Düzova et al. (2018) did not demonstrate a significant alteration of IL-17 levels after a 12-week exercise program carried out with sedentary females. In our study a significant difference was not observed in the post HIIT levels of IL-17 in the EG and the CG.

Inclusion of only few participants in our study may be considered as a limitation. Evaluation of exercise effects on female patients was not included in our study and the results were based only on male patients. The effects of exercise on only 21 days of treatment were evaluated. It is believed that investigations with larger patient groups over longer periods

will be useful for assessment of the longterm effects of exercise treatment programs.

CONCLUSION

Our research on the HIIT program implemented in addition to buprenorphine-naloxon treatment on inpatients with OpUD resulted in reduction of depression, anxiety and substance craving symptoms, increased levels of IGF-1 but not of IFN-γ and IL-17 and an increase close to statistical significance in cortisol levels. To the best of our knowledge, this study is the first to investigate the effects of HIIT on peripheral cytokine levels in patients diagnosed with OpUD. There are uncertainties in the approaches to implement the optimal exercise treatments for individuals with OpUD which point out the necessity of further research in the field. It is beleieved that this research will contribute to the literature by emphasising the effects of HIIT on OpUD patients placed under detox treatment.

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The article was verbally presented at the 2019-International Alcohol and Substance Dependence Congress in Northern Cyprus Turkish Republic and was awarded the second place for the oral presentations. Complete text of presentation.

Before treatment commenced, patients were screened to ascertain that there was neither clinical evidence of growing brain tumor anywhere in the body, nor conrmed autoim-mune disease or chronic infections. Patients were also excluded if one of the following criteria applied: heart pacemakers, epileptic seizure within the last 3 years, photosensitive epilepsy as determined by EEG, mental diseases (schizophrenia), unstable diabetes, high blood pressure (.160/100 mm Hg), or instable or high level of intraocular pressure (i.e., .27 mm Hg).Â Changes of clinical parameters were compared after the rst stimula-tion course, at the beginning of the second course, and after the second course. Finally, we compared also results at baseline versus after the second treatment course. High intensity interval training is a time efficient way to induce physiological changes that occur with endurance training. Research specifically evaluating the effects of oral contraceptive use on HIIT adaptations is unknown and necessary for investigation as the results may clarify the effects of OC use on the physiological adaptations to exercise. Statement of Purpose The purpose of this study was to investigate the effects of seven high intensity interval training (HIIT) sessions over 2 weeks on sub maximal fat oxidation rates, body composition, hematocrit and VO2max in women taking oral contraceptives. Evaluation of the Effects of High Intensity Interval Training on Cytokine Levels and Clinical Course October 2020 Â· Turk psikiyatri dergisi = Turkish journal of psychiatry. Oktay Kaya.Â Objective: Opioid use disorder (OpUD) is a biological and psychosocial disorder with limited treatment options. Addition of physical exercise to the pharmacological treatment has been proposed to be effective on reducing substance use and improving the quality of life. In this study we aimed to investigate the effects of a high-intensity interval training (HIIT) program on the serum levels of [Show full abstract] cortisol, insulin-like growth factor1 (IGF-1), interferon-gamma (IFN-Î³), interleukin 17 (IL-17) and the clinical progress of inpatients with OpUD. 5.7 Treatment evaluation. 6 Patient level guidelines â€“ for clinicians 6.1 Diagnosis and assessment of opioid dependence. 6.1.1 urine drug screening 6.1.2 Testing for infectious diseases 6.1.3 Identifying the patient 6.1.4 Completing the assessment 6.1.4 Diagnostic criteria 6.1.5 Making the diagnosis 6.2 Choice of treatment approach 6.3 Opioid agonist maintenance treatment 6.3.1 Indications for opioid agonist maintenance treatment 6.3.2 Choice of agonist.Â Naltrexone produces no opioid effects itself, and blocks the effects of opioids for 24â€“48 hours. The short-acting opioid antagonist naloxone can be used to reverse the effects of opioid intoxication and overdose. for opioid agonist maintenance treatment, both medications provide good outcomes in most cases.