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The effect of aqua-therapy on plasma and interleukin-12 and 17 in patients with multiple sclerosis

El efecto de la terapia acuática en el plasma y la interleucina-12 y 17 en pacientes con esclerosis múltiple

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Abstract: Cytokines such as Interleukin 12 (IL-12) and Interleukin 17(IL-17) influence the function of the immune system and different tissues and are studied due to the role they play in Multiple Sclerosis (MS). The aim of the study was to investigate the effect of aqua-therapy on plasma IL-12 and IL-17 in patients with MS. 25 men with MS were divided into two groups: exercise and control. Blood sample was taken before and after the intervention protocol. The exercise group carried out three exercise sessions per week during eight weeks. The beginning and final parts of each session included warming up and cool down, and were carried out in shallow areas. These activities were designed and implemented by a researcher under the supervision of a sports physiologist and an experienced neurologist. During the training sessions, the first 10 minutes were for warming up, and the last 5 minutes of training were for cool down. Exercise intensity was approximately 75% of heart rate reserve. The data demonstrated that both IL-12 and IL-17 decreased significantly from pre-test to post-test in the exercise group. We conclude that aqua-training may reduce risk factors regarding multiple sclerosis, including IL-12 and IL-17.
Keywords: water, exercise, multiple sclerosis, interleukin.

Resumen: Las citocinas como la interleucina-12 (IL-12) y la interleucina-17 (IL-17) influyen en la función del sistema inmune y los diferentes tejidos, siendo estudiadas debido al papel que desempeñan en la Esclerosis Múltiple (EM). El objetivo de este estudio fue investigar el efecto de la terapia acuática en la IL-12 y la IL-17 en pacientes con esclerosis múltiple. Participaron 25 hombres con esclerosis múltiple, los cuales fueron divididos en dos grupos: ejercicio y control. Se tomó una muestra de sangre antes y después de la intervención. El grupo de ejercicio llevó a cabo tres sesiones por semana durante ocho semanas. Las partes inicial y final de cada sesión incluyeron calentamiento y vuelta a la calma, llevadas a cabo en zonas poco profundas. Las actividades fueron diseñadas y llevadas a cabo por un investigador bajo la supervisión de un fisiólogo deportivo y un neurólogo experimentado. Durante las sesiones de entrenamiento, se dedicaban los primeros 10 minutos al calentamiento y los últimos 5 minutos a la vuelta a la calma. La intensidad del ejercicio fue aproximadamente del 75% de la frecuencia cardíaca máxima. Los datos demostraron que tanto IL-12 como IL-17 disminuyeron significativamente entre el pre-test y el post-test. Por tanto, se concluye que la terapia acuática puede reducir los factores de riesgo con respecto a la esclerosis múltiple, incluidas la IL-12 y la IL-17.
Palabras clave: agua, ejercicio, esclerosis múltiple, interleucina.

Introduction

Multiple sclerosis is characterized by triple inflammation, myelination, and gliosis (Chae & Bothwell, 2018). The course of the disease may be recurring and progressive. MS scans are typically published in terms of time and position. MS has involved around 350,000 Americans and 1.1 million people around the world (Stamatelos & Anagnostouli, 2017). In Western societies, MS is ranked second only to neurologic disabilities in the early to mid-adult years after trauma. MS demonstrations range from a benign disease to a rapidly progressive and debilitating disease that requires a significant change in lifestyle. According to the studies, exercise and therapeutic exercises play an important role in treating MS, and exercise exercises improve the symptoms of the disease, given that it is unclear what kind of exercise and how intensive and time it takes to improve MS patients. Therefore, the present study intends to investigate whether the aqueous exercises affect some motor disorders of autistic patients with MS (Panitch, Hirsch, Schindler, & Johnson, 1987).

Cytokines impress the role of the immune system, the cardiovascular system of the body and various tissues and are studied due to the role they play in MS (Segal & Shevach, 1996). A change in the cytokine secretion pattern, often secreted by immune cells, is features that can help experts predict the condition. Injection of interferon gamma into MS causes an attack. Research has proven that the level of interferon-gamma serum levels increases before relapse, and it is affirmed that activity and recurrence of the disease are primarily related to Th1 activity (Li et al., 2006). Interleukin 12, 17, and 23 are also effective factors in the incidence of MS. Researchers have associated interleukin-12 with changes in MRI. It is believed to be effective in patients with a lower level of IL-12 mRNA, a disease novel with interferon

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beta (Bryan, 2018). The level of IL-17 production has a direct relation with the patient's activity and is reduced by the treatment with interferon beta. A notable point is that in people who have recently been diagnosed with their disease, they have more levels of interleukin 17 than the other patients (Komiyama et al., 2006).

Several reports have reported the reduction of interferon and interleukins in the development of MS (Moller et al., 1996). In an under-medication and double-blind, subcutaneous increase in interferon beta-1, the severity of deterioration reduced the severity of brain damage in MRI images (Chtara et al., 2005). Accordingly, the US Food and Drug Administration used it somehow in the treatment of MS. It has also been suggested that elevated beta levels due to diet can improve motor distress in MS patients. Based on the results, caloric restriction can prevent unknowns from the occurrence of MS and affect its early levels (Gendelman& Benner, 2017). Since physical activity and exercise are some of the limitations of calories, the researchers question the question of whether physical activity can reduce interferon-gamma and interleukin 12, 17 and 23 (Deshpande, King, & Segal, 2006). Jiang & Pernis conducted a 3-month training program on MS patients and observed a relative improvement in EDSS in MS patients (Jiang & Pernis, 1992). Kraemer et al. (2002) concluded that a relative improvement in EDSS in MS patients occurs after six weeks of training (Kraemer et al., 2002). In another study, Frzovic et al (2000) found that an aerobic and therapeutic activity period had a significant effect on EDSS in MS patients (Frzovic, Morris, & Vowels, 2000; Panitch et al., 1987). Hesse et al. (2011), after one year of training on MS patients, concluded that interleukin-12 was slightly reduced and cortisol concentrations increased (Arnason et al., 1999; Hesse et al., 2011). Research in 2016 states that after eight weeks of aerobic training in the MS group, IL-6 decreased and these exercises may improve the body's defensive mechanisms in resting state on MS patients (Arnason et al., 1999). Hydrotherapy is a combination of exercise and exercise therapy in physiotherapy, it is a comprehensive examination therapeutic approach that assists with several rehabilitation treatments using water exercises (Hauser et al., 2008). Nowadays, water is conceived as a therapeutic and rehabilitation method. Education for rehabilitation in many diseases with symptoms of pain, muscle stiffness and balance imbalance, reduced range of movement, motor growth retardation and even the relief of some psychological symptoms are used (Chae & Bothwell, 2018; López, Nicolás, & Díaz, 2018). As it has been reported that aqua therapy may improve inflammation and function of patient with multiple sclerosis, we are interested to clarify if it improve via reduction in interferon gamma and interleukin 23. Hence the aim of this study was to investigate the effect of aqua-therapy on plasma interferon gamma and interleukin-23 in patient with multiple sclerosis.

Methods

Participants

The statistical population of this study was the patients with multiple sclerosis with EDSS2.5 to 5 with a degree of Ataxia and referred to the MS Society of Mashhad. The Expanded Disability Status Scale (EDSS) is a method of quantifying disability in multiple sclerosis and monitoring changes in the level of disability over time. It is widely used in clinical trials and in the assessment of people with MS. EDSS of patients were already assigned by the neurologist. After that Ataxia was diagnosed by the neurologist. Patients with orthopedic problems, patients with underlying illnesses such as diabetes, heart problems and blood pressure, and those who used tobacco, and other neurological diseases were excluded from the group through a form of information that was provided from the patient's history. In addition to the above, patients who participated in regular exercise programs were also excluded from the research group. Then the patients filled the conditions, the consent form and the cooperation. Finally the subjects of this study were twenty-five men with multiple sclerosis (EDSS 2.5 to 5), who had a Ataxia degree introduced by the Mashhad MS Society. There was no significant difference between the groups in this regard. The 25 selected subjects were divided into two groups of exercise and control. The samples were taken before and after the protocol.

Aqua training program

At the first session of training, the subjects were accustomed to the circumstance of the pool. Recommendations about Safety were commented to lower any risk during operation of the protocol, such as fall. To floating the patients easily, exercise belts was utilize for maintaining balance and benefiting from deep water. The belt was first taught to patients. The first few exercises were performed to patients' familiarization with aqua training in shallow water. The beginning and final stages of each session included warming up and cool down, carried out in shallow areas. These operations were designed and carried out by a researcher under the supervision of a sports physiologist and an experienced neurologist. During the training sessions, 10 minutes of warming up, and the last, 5 minutes of training to cool down were operated. Exercise intensity was approximately 75% of heart rate reserve. The men were asked to rest for 5 minutes between each stage of their training, which felt tired, and then resume exercise again.

Variables Measurement

ELISA kits specific for the human were utilized to assess plasma Interleukin 12 and 17 (Hangzhou, Eastbiopharm Co., Ltd., China).

Statistical analyses

Shapiro-Wilk test was used to determine distribution normality which was found to be distributed normally. One-way analysis of variance (ANOVA) with repeated measures was applied to determine the differences in variables among the groups. Significant differences were identified using (LSD) post-hoc test by using SPSS version 16. All data were expressed as mean ± SD and significance was set at the alpha level $p < 0.05$.

Results

There was no significant difference between the pre-test and post-test scores in the control group and interleukin 12 remained unchanged in this group, while the difference in the exercise group is completely significant at the 5% error level. In other words, in the exercise group, Interleukin 12 with a mean of 1.30 in post-test was significantly less than the pre-test mean. It is clear that the values of IL-12 in exercise group decreased significantly from pre-test to post-test. Also there was no significant difference between the pre-test and post-test scores in the control group and interleukin 17 remained unchanged in this group, while the difference in the exercise group is completely significant at the 5% error level. In other words, in the exercise group, interleukin 17 with a mean of 2.29 in post-test was significantly less than the pre-test mean. It is clear that the values of interleukin 17 in exercise group decreased significantly from pre-test to post-test. (Table 1).

Table 1. Differences between pre-test and post-test.

Variables	Groups	Pre Mean ±SD	Post Mean ±SD
Interleukin 12	Exercise group	1.50±0.28	1.30±0.12
	Control	1.88±0.54	1.97±0.69
Interleukin 17	Exercise group	4.62±1.37	2.29±1.34
	Control	3.92±2.67	3.97±1.69

Discussion

Several studies have reported the reduction of interferons and interleukins in the development of MS. In an under-medication and double-blind, subcutaneous increase in interferon beta-1, the severity of deterioration reduced the severity of brain damage in MRI images. Accordingly, the US Food and Drug Administration used it somehow in the treatment of MS (Brok et al., 2002). It has also been suggested that elevated beta levels, due to the appropriate diet, can improve motor distress in MS patients. Based on the results, caloric restriction can prevent unknowns from the occurrence of MS and affect its early levels. Because exercise and exercise are one of the forms of calorie restriction (Komiyama et al., 2006).

Jiang & Pernis (1992) conducted a 3-month training program on MS patients and observed a relative improvement in EDSS in MS patients (Jiang & Pernis, 1992). Kraemer et al. (2002) concluded that a relative improvement in EDSS in MS patients occurs after six weeks of training (Kraemer et al., 2002). In another study, Frzovic (2000) found that an aerobic and therapeutic activity period had a significant effect on EDSS in MS patients (Deshpande et al., 2006; Frzovic et al., 2000). Hesse et al. (2011), after one year of training on MS patients, concluded that interleukin-12 was slightly reduced and cortisol concentrations increased (Hesse et al., 2011). The Interleukin 12 and 17 dimer consists of two subunits, P 4235, because the unit before the game unit P19 interleukin 23 forms a complex that together with the formation of a unique subset of Interleukin 17 and the differentiation of th17 cells (Grifka-Walk & Segal, 2017).

As noted earlier, researchers have found that interleukin-12 levels are related to the disease's activity and alterations in MRI. In patients with MS who have a lower level of transcription of the p35 and IL-12 gene, treatment with interferon beta is more effective than this marker. Prognosis is accurately predicted in 81% of patients and patients, and it is also clear that after treatment with certain drugs, the level of interleukin 12 also decreases significantly (Moller et al., 1996).

The level of IL-17 production has a direct relation with the disease activity and is lowered by treatment with interferon beta. The novelty 3 is considered here in patients who have recently been diagnosed with MS, compared to patients who have long been exposed to this The disease has been interfering with the level of interleukin 17 production, which can be attributed to the high level of interleukin 17 with activity and severity of the disease (Kleinschmidt-DeMasters & Tyler, 2005). It is worth noting that the activity and severity of the disease are in patients who have long been involved in MS. It reaches to the equilibrium Ten people who do not respond to treatment with beta interferon has high serum levels of IL-17 (Pravenec et al., 2003).

Many of the subsequent studies showed an increase in the concentration of different cytokines after a long-term exercise. Increases in circulating concentrations of pro-inflammatory cytokines (such as IL-1β and TNFα and IL-12), anti-inflammatory (such as IL-6 and IL-10), cytokine inhibitors (such as IL-1 and TNF receptors α), chemokine's

(e.g., tetrafluorine gamma-IL-8, inflammatory macrophage protein, and chemo-monocyte-1 protein and colony stimulants after endurance exercise have been reported (Donges, Duffield, & Drinkwater, 2010). However, the increase in IL-6 concentration in circulation after long-term exercise is fully characterized and sustained, but the response from exercise to any other cytokine requires a lot of research. Release of cytokines during and after exercise may be a protective mechanism for coping with general inhibition of post-exercise safety responses. In addition, many of the acute phase proteins released in response to increased levels of cytokines, and protease inhibitors or free radical cleansers, limit the tissue lesions resulting from toxic molecules and free radicals of active neutrophils (Giannopoulou et al., 2005; Kadoglou et al., 2007).

Conclusion

The result of this study suggests that aqua-training may reduce risk factors regarding multiple sclerosis, including interleukin-12 and 17.

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Conflict of interests:

The authors declare there is no conflict of interests.

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