



RESEARCH PAPER

OPEN ACCESS

Effect of hydrotherapy on serum TNF α and IFN γ in the women with multiple sclerosis**Zohre Afsharmand¹, Vahid Imanipour², Fatemeh Mahdi², Mehdi Sadeghi³, Alireza Naderi⁴, Sokhanguie Yahya^{5*}, Behboodi Laleh¹**¹*Faculty of physical education, Islamshahr Branch, Islamic Azad University, Islamshahr, Iran*²*Department of physical education, Parand Branch, Islamic Azad University, New City of Parand, Iran*³*Fars Science & Research Branch, Islamic Azad University, Fars, Iran*⁴*Faculty of physical education and sport sciences, Borujerd Branch, Islamic Azad University, Borujerd, Iran*⁵*Department of Physiotherapy, University of Social Welfare and Rehabilitation Sciences, Tehran, Iran***Key words:** Sclerosis, Hydrotherapy, TNF α , IFN γ , EDSS, Womendoi: <http://dx.doi.org/10.12692/ijb/3.8.168-173> Article published on August 20, 2013**Abstract**

Aquatic exercise can refer to pool therapy, hydrotherapy, or balneotherapy. Hydrotherapy is frequently applied to patients with painful neurological or musculoskeletal alterations, because the heat and floatability of the water can block nociceptors by acting on thermal receptors and mechanoreceptors and exert a positive effect on spinal segmental mechanisms (Bender, 2005). Warm water can also increase the blood flow, helping to dissipate allogeneic chemicals and enhance muscle relaxation. The present study aims to explore the effect of 10 weeks hydrotherapy on EDSS, TNF α and IFN γ in female MS patients. The statistical population consists of 30 MS patients whose MS has been confirmed by a neurologist. They divided into two groups based on inclusion criteria. Experimental group consisted of 15 and the control group consisted of 15 people with ages ranging from 22 to 51 and the weight of 58.9 ± 9.3 kg - Height of 153.5 ± 15.6 cm. Hydrotherapy program for the experimental group was implemented for 10 weeks, 3 sessions per week. Control group participated in none activity program in this period. According to the descriptive statistics, EDSS decreased in the experimental group after 10 weeks hydrotherapy. But no significant different was seen in TNF α and IFN γ in two groups. Results showed that endocrine and proinflammatory immune responses to physical exercise are not significantly altered in MS. So EDSS decreased in experimental group. In the other hand, participating in hydrotherapy programs led to benefit in the MS patients.

* **Corresponding Author:** Sokhanguie Yahya ✉ vhim918@yahoo.com

Introduction

Multiple sclerosis (MS) is a complex neuron-generative autoimmune disease, characterized by dissemination of inflammatory lesions in the central nervous system (CNS). The localization and severity of MS lesions within the brain and spinal cord is unpredictable and, therefore, a wide range of body systems can be adversely affected to a variable degree. Consequently, there is a myriad of symptoms and comorbidities associated with MS that can impact negatively on patient quality of life. Several theories of the symptom experience have identified symptoms as direct and indirect influences on performance and behavioral outcomes in persons with chronic diseases. (Armstrong, 2003; Teel, 1997). Indeed, symptoms have been inversely associated with activities of daily living (e.g. work, personal care, and social interaction) in individuals with MS. (Aronson, 1997, Hemmett, 2004) for example, motor symptoms (e.g. arm and leg weakness, spasms, and balance problems) were moderately and inversely correlated with activities of daily living associated with fine and gross motor tasks (e.g. eating, dressing, bathing, and walking) in individuals with MS. (Gulick, 1989).

Secondary analysis of data from 686 persons with MS indicated that emotional symptoms exhibited a moderate and inverse relationship with over-all activities of daily living, and the effect was partially mediated by personal attributes and social support. (Gulick, 2001). Recent guidelines from the National Institute of Health and Clinical excellence (NICE) affirmed that MS patients should be informed of findings on the benefits of certain approaches but declared that insufficient evidence is available to make a firmer recommendation (NICE, 2003). Named techniques include reflexology, massage, fish oils, magnetic field therapy, neural therapy, massage plus body work, Tai-Chi, and multi-modal therapy (Esmonde, 2008). MS patients also report the therapeutic use of exercise, vitamins, herbal and mineral supplements, relaxation techniques, acupuncture, cannabis, and massage, mainly for the treatment of pain, fatigue and stress (Olsen, 2009). Maloni (Maloni, 2000) reported that Tai-Chi,

meditation and hypnotherapy may improve the quality of life and reduce pain in MS patients by interfering with pain conduction, producing analgesia through nociceptive pathways. Aquatic exercise can refer to pool therapy, hydrotherapy, or balneotherapy (Kamioka, 2010). Hydrotherapy is frequently applied to patients with painful neurological or musculoskeletal alterations (Hall, 2008), because the heat and floatability of the water can block nociceptors by acting on thermal receptors and mechanoreceptors and exert a positive effect on spinal segmental mechanisms (Bender, 2005). Warm water can also increase the blood flow, helping to dissipate allogeneic chemicals and enhance muscle relaxation.

Finally, the hydrostatic effect of water can alleviate pain by reducing peripheral edema and sympathetic nervous system activity (Gabr and Elsen, 2000). A systematic review on crenobalneootherapy in patients with limb osteoarthritis found that it reduced pain and improved function and quality of life (Forestier, 2008). CAM is frequently used in spa therapy in situ without exercise for various chronic diseases, with highly positive effects in middle-aged and elderly patients (A. Franc, on 2009). Recently, endocrine and immune responses to experimental psychological stress have been investigated showing no clear-cut regulatory changes in MS patients (Ackermann *et al.*, 1998; Heesen *et al.*, 2002a). However, the perception of experimental psychological stressors varies considerably between individuals. One study (Fassbender *et al.*, 1998) did not find correlations with IL-1, IL-6, and TNF levels in serum and CSF. Taken together, these studies indicate that hypothalamo-pituitary-adrenal (HPA) axis dysregulation is rather a secondary phenomenon than primarily involved in the disease pathogenesis. Alterations have also been described in the sympathetic nervous system regulation of immune function including increased β -adrenoreceptor expression on peripheral blood lymphocytes (Zoukos *et al.*, 1992), altered catecholamine levels (Consentino *et al.*, 2002; Rajda *et al.*, 2002), and decreased sensitivity of cytokine

production after terbutaline administration (Heesen *et al.*, 2002b).

Our intention was to investigate whether MS patients show alterations during moderate physical stress in water as part of a hydrotherapy.

We hypothesized that MS patients would show an altered stress response with attenuated immune response in comparison to healthy individuals. Against the back-ground of the beneficial effect of exercise training reported in MS, we further hypothesized that training might partially normalize this dysregulation.

Materials and methods

The present study aims to explore the effect of 10 weeks hydrotherapy on EDSS, TNF α and IFN γ in female MS patients. The type of research is applied research, and the methodology is semi-experimental, which due to the limitations, the research plan included testing the experimental and control groups before and after the tests the results of which were analyzed.

The statistical population consists of 30 MS patients whose MS has been confirmed by a neurologist. They divided into two groups based on inclusion criteria. Experimental group consisted of 15 and the control group consisted of 15 people with ages ranging from 22 to 51 and the weight of 58.9 ± 9.3 kg - Height of 153.5 ± 15.6 cm. Patients had no Cardiovascular disease history- final diagnosis of MS confirmed by a neurologist - no history of epilepsy - no history of metabolic diseases - not pregnant -no history of regular exercise during the past three months - All participants had physical disability scale (EDSS) between 1-5. One day before starting the hydrotherapy program the patients involved in the study came together in the desired location and were briefed on how to do the exercise – the intensity of exercise - the number of repetitions in each session and then the experimental and control groups participated in the pretest and at this stage, physical disability scale test developed by a specialist neurologist, and gave blood sample for analyzing

IFN γ and TNF α . Hydrotherapy program for the experimental group was implemented for 10 weeks, 3 sessions per week. Control group participated in none activity program in this period. After completing the training the program both groups were given tests and the results were analyzed.

Results

The main purpose of this research was the effect of 10 weeks hydrotherapy on TNF α , IFN γ and EDSS in MS patient. This study found that ten weeks of hydrotherapy had a significant impact on the EDSS among M.S patients. According to the descriptive statistics, EDSS decreased in the experimental group after 10 weeks hydrotherapy (table 1). But no significant different was seen in TNF α and IFN γ in two groups (tables 2 and 3).

Table 1. Statistical indices of EDSS in the experimental and control groups.

	Post-test	Pre-test	Post-test	Pre-test	
	3.5 \pm 0.6	3.4 \pm 0.3	3.1 \pm 0.2	3.8 \pm 0.8	EDSS

Table 2. Statistical indices of TNF α in the experimental and control groups.

Control	Experimental	Variable
Post-test	Pre-test	Post-test
33.8 \pm 12.6	33.73 \pm 12.1	33.70 \pm 10.1
		33.75 \pm 9.6

Table 3. Statistical indices of IFN γ in the experimental and control groups.

Control	Experimental	Variable
Post-test	Pre-test	Post-test
39.1 \pm 8.6	38.2 \pm 8.9	38.2 \pm 9.9
		37.3 \pm 10.1

Discussion and conclusion

In this study we showed that endocrine and proinflammatory immune responses to physical exercise are not significantly altered in MS. Cytokines findings (TNF- α and INF γ) were consistent in

experimental group in this research as well as another investigation (Ostrowski *et al.*, 1999). Stepkard showed that after the exercise IFN γ was strongly induced in all 2 groups (experimental and control). Data on IFN γ indicate elevations in response to suppression after exhausting exercise (Stepkard and Skek, 1997).

But we found no significant different in our study because exercise in this study was very mild. IFN γ is a crucial cytokine to control infection. On the other hand it governs counter regulatory immunosuppression and endotoxin tolerance (Northoff *et al.*, 1998). Thus its modulation might explain the differential effects on the immune system during moderate and exhausting exercise, a protective effect of moderate training and an increased rate of infections after exhaustive training. The moderate correlation of IFN γ production with disease duration might indicate that in later disease stages MS patients may produce a stronger IFN γ response to exercise. TNF α and INF γ were not significantly induced during the hydrotherapy in any group. Baseline values in experimental group did not differ to controls in this study. The discrepancy of these findings to another studies might be explained by the different exercise intensity and sampling time and the different patient characteristics (Petrovsky, 2001).

Studies on TNF α levels during and after exercise in healthy individuals have led to conflicting results (Ostrowski *et al.*, 1998; Rhind *et al.*, 1995). Elevated glucocorticoid levels are thought to mediate the suppressive effects of exercise on TNF (Rhind *et al.*, 1995). Cortisol induction has been demonstrated mainly during prolonged exercise (Howlett, 1987). This might explain divergent TNF results of studies with different exercise paradigms. Differences in cytokine production might be explained by a genetically determined ability to respond to mitogen challenge which varies strongly even in healthy individuals (Santamaria *et al.*, 1989). This fact leads to large standard variations which make it difficult to obtain significant findings. Several authors have shown that changes of immune parameters might occur hours after the exercise (Drenth *et al.*, 1998).

Sampling times differed largely between studies which further complicate the search for consistent results on immune alterations during exercise. Another variable in this investigation was EDSS.

Result showed that EDSS decreased in experimental group. In the other hand, participating in hydrotherapy programs led to benefit in the MS patients.

References

Ackermann KD, Martino M, Heyman R, Moyna NM, Rabin BS. 1998. Stressor-induced alteration of cytokine production in multiple sclerosis patients and controls. *Psychosomatic Medicine*. **60**, 484-491.

Gabrielsen A, Videbek R, Johansen LB. 2000. Forearm vascular and neuroendocrine responses to graded water immersion in humans. *Acta Physiologica Scandinavica*. **169 (2)**, 87-94.

Francon A, Forestier R. 2009. Spa therapy in rheumatology. Indications based on the clinical guidelines of the French national authority for health and the European league against rheumatism, and the results of 19 randomized clinical trials. *Bulletin de l'Academie Nationale de Medicine*. **193(6)**, 1345-1358.

Armstrong TS. 2003. Symptoms experience: a concept analysis. *Oncology Nursing Forum*. **30**, 601-606.

<http://dx.doi.org/10.1188/03.ONF.601-606>

Aronson KJ. 1997. Quality of life among persons with multiple sclerosis and their caregivers. *Neurology*. **48**,74-80.

<http://dx.doi.org/10.1212/WNL.48.1.74>

Consentino M, Zaffaroni M, Marino M, Bombelli R, Ferrari M, Rasini E, Lecchini S, Ghezzi A, Frigo G. 2002. Catecholamine production and tyrosine hydroxylase expression in peripheral blood mononuclear cells from multiple sclerosis patients: effect of cell stimulation and

possible relevance for activation-induced apoptosis. *Journal of Neuroimmunology*. **133**, 223-240.

Drenth JP, Krebbers RJ, Bijzet J, Vandermeer JW. 1998. Increased circulating cytokine receptors and ex vivo interleukin-1 receptor antagonist and interleukin-1 β production but decreased tumor-necrosis factor- α production after a 5-km run. *European Journal of Clinical Investigation*. **28**, 866-872.
<http://dx.doi.org/10.1046/j.1365-2362.1998.00366.x>

Fassbender K, Schmidt R, M€ooßner, Kischka R, K€uuhnen U, Schwartz J, Hennerici AM. 1998. Mood disorders and dysfunction of the hypothalamic–pituitary–adrenal-axis in multiple sclerosis. *Archives of Neurology*. **55**, 66-72.
<http://dx.doi.org/10.1001/archneur.55.1.66>

Heesen C, Schulz H, Schmidt M, Gold S, Tessmer W, Schulz KH. 2002a. Endocrine and cytokine responses to acute psychological stress in multiple sclerosis. *Brain, Behavior and Immunity*. **16**, 282-287.
<http://dx.doi.org/10.1006/brbi.2001.0628>

Heesen C, Gold SM, Raji A, Schulz KH, Wiedemann K. 2002b. Cognitive impairment correlates with hypothalamic–pituitary–adrenal axis dysregulation in multiple sclerosis. *Psychoneuroendocrinology*. **27**, 505-517.
[http://dx.doi.org/10.1016/S0306-4530\(01\)00071-3](http://dx.doi.org/10.1016/S0306-4530(01)00071-3)

Gulick EE. 1989. Model confirmation of the MS-Related Symptom Checklist. *Nursing Research*. **38**, 147-153.
<http://dx.doi.org/10.1097/00006199-198905000-00012>

Gulick EE. 2001. Emotional distress and activities of daily living functioning in persons with multiple sclerosis. *Nursing Research*. **50**, 147-154.
<http://dx.doi.org/10.1097/00006199-200105000-00004>

Hemmett L, Holmes J, Barnes M, Russell N. 2004. What drives quality of life in multiple sclerosis. *Q journal of Medicine*. **97**, 671-676.
<http://dx.doi.org/10.1093/qjmed/hch105>

Kamioka H, Tsutani K, Okuizumi H. 2010. Effectiveness of aquatic exercise and balneotherapy : a summary of systematic reviews based on randomized controlled trials of water immersion therapies. *Journal of Epidemiology*. **20(1)**, 2-12.
<http://dx.doi.org/10.2188/jea.JE20090030>

Kamioka H, Nakamura Y, Yazaki T. 2006. Comprehensive health education combining hot spa bathing and lifestyle education in middle-aged and elderly women: one-year follow-up on randomized controlled trial of three- and six-month interventions. *The American Journal of Epidemiology*. **16(1)**, 35-44.
<http://dx.doi.org/10.2188/jea.16.35>

Howlett TA. 1987. Hormonal responses to exercise and training: a short review. *Clinical Endocrinology*. **26**, 723-742

Maloni HW. 2000. Pain in multiple sclerosis: an overview of its nature and management. *Journal of the American Association of Neuroscience Nurses*. **32(3)**, 139-152.
<http://dx.doi.org/10.1097/01376517-200006000-00004>

Hall J, Swinkels A, Briddon J, McCabe CS. 2008. Does aquatic exercise relieve pain in adults with neurologic or musculoskeletal disease? A systematic review and meta-analysis of randomized controlled trials. *Archives of Physical Medicine & Rehabilitation*. **89(5)**, 873-883.
<http://dx.doi.org/10.1016/j.apmr.2007.09.054>

Esmonde L, Long AF. 2008. Complementary therapy use by persons with multiple sclerosis: benefits and research priorities. *Complementary Therapies in Clinical Practice*. **14 (3)**, 176-184.

- National Institute of Clinical Excellence.** 2003. Multiple Sclerosis. Understanding NICE Guidance-Information for People with Multiple Sclerosis, Their Families and Care r s, and The Public (Clinical Guideline-8). National Institute for Clinical Excellence, London, U K.
- Northoff H, Berg AS, Wrinstock C.** 1998. Similarities and differences of the immune response to exercise and trauma: the IFN- c concept. Canadian Journal of Physiology and Pharmacology. **76**, 497-504. <http://dx.doi.org/10.1139/y98-052>
- Ostrowski K, Hermann C, Bangash A, Schjerling P, Nielsen JN, Pedersen BK.** 1998. A trauma-like elevation of plasma cytokines in humans in response to treadmill running. Journal of Physiology. **513**, 889-894. <http://dx.doi.org/10.1111/j.1469-7793.1998.889ba.x>
- Ostrowski K, Rohde T, Asp S, Schjerling P, Pedersen BK.** 1999. Pro- and anti-inflammatory cytokine balance in strenuous exercise in humans. Journal of Physiology. **515**, 287-291. <http://dx.doi.org/10.1111/j.1469-7793.1999.287ad.x>
- Petrovsky N.** 2001. Whole blood assay and the influence of circadian rhythmicity on human cytokine measurement. In: O Neill, LAJ, Bowie, A. (Eds.). Methods in molecular medicine. **60**, 163-174.
- Rajda C, Bencsik K, Vecsei L, Bergquist J.** 2002. Catecholamine levels in peripheral blood lymphocytes from multiple sclerosis patients. Journal of Neuroimmunology. **124**, 93-100. [http://dx.doi.org/10.1016/S0165-5728\(02\)00002-4](http://dx.doi.org/10.1016/S0165-5728(02)00002-4)
- Rhind SG, Shek PN, Shepard RJ.** 1995. The impact of exercise on cytokines and receptor expression. Exercise Immunology. **1**, 97-148.
- Forestier R, Francon A.** 2008. Crenobalneootherapy for limb osteoarthritis: systematic literature review and methodological analysis. Joint Bone Spine. **75 (2)**, 138-148. <http://dx.doi.org/10.1016/j.jbspin.2007.06.009>
- Santamaria P, Gherz RC, Bryan MK.** 1989. Involvement of class II MHC molecules in LPS-induction of rIL-1/TNF secretion by human monocytes; quantitative differences at polymorphic level. Journal of Immunology. **143**, 913-919.
- Olsen SA.** 2009. A review of complementary and alternative medicine (CAM) by people with multiple sclerosis. Occupational Therapy International. **16(1)**, 57-70. <http://dx.doi.org/10.1002/oti.266>
- Bender T, Karagulle Z, Alint GPB, Gutenbrunner PVB.** 2005. Hydrotherapy, balneootherapy, and Spa treatment in pain management. Rheumatology International. **25(3)**, 220-224. <http://dx.doi.org/10.1007/s00296-004-0487-4>
- Teel CS, Meek P, McNamara AM, Watson L.** 1997. Per-spectives unifying symptom interpretation. Image the journal of nursing scholarship. **29**, 175-181. <http://dx.doi.org/10.1111/j.1547-5069.1997.tb01553.x>
- Zoukos Y, Leonard JP, Thomaidis T, Thompson AJ, Cuzner ML.** 1992b. Adrenergic receptor density and function of peripheral blood mononuclear cells are in-creased in multiple sclerosis: a regulatory role for cortisol and interleukin-1. Annals of Neurology. **31**, 657-662. <http://dx.doi.org/10.1002/ana.410310614>