Ozone therapy in 40 patients with fibromyalgia: an effective therapy

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Abstract

Fibromyalgia is a chronic disorder with a very complex symptomatology. There is evidence that oxidative stress is increased in fibromyalgia, although it is not known whether this increase is involved as a causative factor in the development of the disease, or whether it is secondary to the patients' unfit condition. Ozone therapy is thought to act by exerting a mild, transient, and controlled oxidative stress that promotes an up regulation of the antioxidant system and a modulation of the immune system. The objective of the present study was to get a preliminary evaluation of the potential effectiveness of ozone therapy in the management of fibromyalgia. At our knowledge, this is the largest study of patients with fibromyalgia treated with ozone therapy reported in the literature and it demonstrates that the ozone therapy is an effective treatment for fibromyalgia patients without significant side effects.

Introduction

Fibromyalgia is a chronic disorder with a very complex symptomatology. Although generalized pain is considered to be the cardinal symptom of the disease, many other associated symptoms, especially non restorative sleep, chronic fatigue, anxiety, and depressive symptoms also play a relevant role in the degree of disability characteristic of the disease. Fibromyalgia pathogenesis is also complex, and both genetic and environmental factors seem to play a role in the patho-physiology of the disease.[1-34] There is evidence that oxidative stress is increased in fibromyalgia, although it is not known whether this increase is involved as a causative factor in the development of the disease, or whether it is secondary to the patients' unfit condition. Ozone therapy, is thought to act by exerting a mild, transient, and controlled oxidative stress that promotes an up regulation of the antioxidant system and a modulation of the immune system.[35-62] According to these mechanisms of action, it was hypothesized that ozone therapy could be useful in fibromyalgia management. The objective of the present study was to get a preliminary evaluation of the potential effectiveness of ozone therapy as add-on treatment in the management of fibromyalgia.

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Materials and Methods

Forty patients with fibromyalgia, according to the definition of the American College of Rheumatology,[34] were treated at the MEDE Clinic, Sacile (PN), Italy, from February 2016 to December 2017. Females were 35 and males were 5; age ranged from 22 to 68 years, and the time from fibromyalgia diagnosis ranged from 0.5 to 33 years. The evaluation of pain was made by the Numeric Rating Scale, in which the patients chooses from 0 (no pain) to 10 (maximum pain) and the evaluation of the fatigue was made by the Fatigue Severity Scale, which is used to estimate the severity of the symptom with a score from 1 to 7.[2,10,21,31,34,63] Treatment was made by auto hemo transfusion in 30 patients and by ozone rectal insufflation in 10 patients, according to the Scientific Society for Oxygen-Ozone Therapy (SIOOT) protocols, twice a week for one month and then twice a month as maintenance therapy.

Results

We found a significative improvement (>50% of symptoms) in 32 patients (80%). No patient reported important side effects. In conclusion, at our knowledge, this is the largest study of patients with fibromyalgia treated with ozone therapy reported in the literature and it demonstrates that the ozone therapy is an effective treatment for fibromyalgia patients without significant side effects.

Discussion and Conclusions

Ozone therapy, which is used to treat a wide range of diseases and seems to be particularly useful in the treatment of many chronic diseases, is thought to act by exerting a mild, transient,

and controlled oxidative stress that promotes an up-regulation of the antioxidant system and a modulation of the immune system. According to these mechanisms of action, it was hypothesized that ozone therapy could be useful in fibromyalgia management, where the employed therapies are very often ineffective.

The objective of the present study was to get a preliminary evaluation of the potential effectiveness of ozone therapy in the management of fibromyalgia. In conclusion, at our knowledge, this is the largest study of patients with fibromyalgia treated with ozone therapy reported in the literature and it demonstrates that the ozone therapy is an effective treatment for fibromyalgia patients without significant side effects.

References

1. Age.Na.S., Tirelli U. Chronic Fatigue Syndrome "CFS"; 2014. Available from: www.stanchezzacronica.it/documento__indirizzo_CFS.pdf
2. Annunziata MA, Muzzatti B, Mella S, et al. The revised piper fatigue scale (PFS-R) for Italian cancer patients: a validation study. Tumori 2010;96:276-81.
3. Arpino C, Carrieri MP, Valesini G, et al. Idiopathic chronic fatigue and chronic fatigue syndrome: a comparison of two case-definitions. Ann Ist Super Sanità 1999;35:435-41.
4. Bergman S. Psychosocial aspects of chronic widespread pain and fibromyalgia. Disabil Rehabil 2005;27:675-83.
5. Canadian Expert Consensus Panel. Clinical case definition for ME/CFS. J Chronic Fatigue Syndr 2003;11:7-116.
6. Carruthers BM, van de Sande MI, De Meirleir KL, et al. Myalgic encephalomyelitis: International Consensus Criteria. J Intern Med 2011;270:327-38.
7. Conti F, Priori R, De Petrillo G, et al. Prevalence of chronic fatigue syndrome in Italian patients with persistent fatigue. Ann Ital Med Int 1994;9:219-22.
8. Fukuda K, Straus SE, Hickie I, et al. The chronic fatigue syndrome: a comprehensive approach to its definition and study. International Chronic Fatigue Syndrome Study Group. Ann Intern Med 1994;15:953-9.
9. Giacalone A, Berretta M, Spina M, Tirelli U. Is long-term fatigue in patients with cancer an infrequent symptom? J Clin Oncol 2012;30:4175.
10. Giacalone A, Polesel J, De Paoli A, et al. Assessing cancer-related fatigue: the psychometric properties of the Revised Piper Fatigue Scale in Italian cancer inpatients. Support Care Cancer 2010;18:1191-7.
11. Giacalone A, Quitadamo D, Zanet E, et al. Cancer-related fatigue in the elderly. Support Care Cancer 2013;21:2899-911.
12. Giacalone A, Spina M, Berretta M, Tirelli U. Two types of fatigue in cancer patients. Br J Cancer 2012;106:424.
13. Holmes GP, Kaplan JE, Gantz NM, et al. Chronic fatigue syndrome: a working case definition. Ann Intern Med 1988;108:387-9.
14. Jain KA, Carruthers M, Van De Sande MI, et al. Fibromyalgia syndrome: canadian clinical working case definition, diagnostic and treatment protocols – a consensus document. J Musculoskeletal Pain 2003;4:3-107.
15. Kroenke K, Wood DR, Mangelsdorff AD, et al. Chronic fatigue in primary care. Prevalence, patient characteristics, and outcome. JAMA 1988;206:929-34.
16. Kruesi MJP, Dale J, Straus SE. Psychiatric diagnoses in patients who have chronic fatigue syndrome. J Clin Psychiatry 1989;50:53-6.
17. Leavitt F, Katz RS, Golden HE, et al. Comparison of pain properties in fibromyalgia patients and rheumatoid arthritis patients. Arthritis Rheum 1986;29:775-81.
18. Manu P, Lane TJ, Matthews DA. Somatization disorder in patients with chronic fatigue. Psychosomatics 1989;30:388-95.
19. Manu P, Matthews DA, Lane TJ. Panic disorder among patients with chronic fatigue. South Med J 1991;84:451-6.
20. Masuda A, Nozoe SI, Matsuyama T, Tanaka H. Psychobehavioral and immunological characteristics of adult people with chronic fatigue and patients with chronic fatigue syndrome. Psychosom Med 1994;56:512-8.
21. Russell IJ. Fibrositis/fibromyalgia. In: Hyde BM, Goldstein J, Levine P, eds. The clinical and scientific basis of myalgia encephalomyelitis/chronic fatigue syndrome. Ottawa, Canada: The Nightingale Research Foundation; 1992.
22. Spazzapan S, Bearz A, Tirelli U. Fatigue in cancer patients receiving chemotherapy: an analysis of published studies. Ann Oncol 2004;15:1576.
23. Swartz MN. The chronic fatigue syndrome-one entity or many? N Engl J Med 1988;319:1726-8.
24. Tavio M, Milan I, Tirelli U. Tumor-correlated asthenia. Recenti Prog Med 2002;93:610-6.
25. Tavio M, Milan I, Tirelli U. Cancer-related fatigue (review). Int J Oncol 2002;21:1093-9.
26. Tavio M, Tirelli U. [Astenia correlata ai tumori]. In: Bonadonna G, Robustelli Della Cuna G, Valagussa P, ed. [Medicina oncologica]. [Book in Italian] 7th ed. Milano: Elsevier; 2003.
27. Tirelli U, Chierichetti F, Tavio M, et al. Brain positron emission tomography (PET) in chronic fatigue syndrome: preliminary data. Am J Med 1998;105:54S-8.
28. Tirelli U, Lleshi A, Berretta M, et al. Treatment of 741 Italian patients with chronic fatigue syndrome. Eur Rev Med Pharmacol Sci 2013;17:2847-52.
29. Tirelli U. [La stanchezza quando diventa una malattia: La sindrome da fatica cronica (CFS)]. [Book in Italian]. Ravenna, Italy: SBC Edizioni; 2014.
30. Walker EA, Katon WJ, Jemelka RP. Psychiatric disorders and medical care utilization among people in the general population who report fatigue. J Gen Intern Med 1993;8:436-40.
31. Wessely S, Nimnuan C, Sharpe M. Functional somatic syndromes: one or many? Lancet 1999;354:936-9.
32. White KP, Speechley M, Harth M, Ostbye T. Coexistence of chronic fatigue syndrome with fibromyalgia syndrome in the general population - a controlled study. Scand J Rheumatol 2000;29:44-51.
33. Wolfe F, Clauw DJ, Fitzcharles MA, et al. Preliminary diagnostic criteria for fibromyalgia and measurement of symptom severity. Arthritis Care Res 2010;62:600-10.
34. Wolfe F, Smythe HA, Yunus MB, et al. The American College of Rheumatology criteria for the classification of fibromyalgia. Report of the Multicenter Criteria Committee. Arthritis Rheum 1990;33:160-72.
35. Glaser R, Padgett DA, Litsky ML, et al. Stress-associated changes in the steady-state expression of latent Epstein-Barr virus: implications for chronic fatigue syndrome and cancer. Brain Behav Immun 2005;19:91-103.
36. Arnett SV, Alleva LM, Korossy-Horwood R, Clark IA. Chronic fatigue syndrome – A neuroimmunological model. Med Hyp 2011;77:77-83.
37. Bansal AS, Bradley AS, Bishop KN, et al. Chronic fatigue syndrome, the immune system and viral infection. Brain Behav Immun 2011;26:24-31.
38. Barker E, Fujimura SF, Fadem MB, et al. Immunologic

abnormalities associated with chronic fatigue syndrome. Clin Infect Dis 1994;18:S316-41.
39. Bennett RM, Smythe HA, Wolfe F. Recognizing fibromyalgia. Patient Care 1989;23:60-83.
40. Broderick G, Fuite J, Kreitz A, et al. A formal analysis of cytokine networks in chronic fatigue syndromes. Brain Behav Immun 2010;24:1209-17.
41. Caligiuri M, Murray C, Buchwald D, et al. Phenotypic and functional deficiency of natural killer cells in patients with chronic fatigue syndrome. J Immunol 1987;139:3306-13.
42. Campbell SM, Clark S, Tindall EA, et al. Clinical characteristics of fibrositis. I. A "blinded," controlled study of symptoms and tender points. Arthritis Rheum 1983;26:817-24.
43. Cannon JG, Angel JB, Abad LW, et al. Interleukin-1beta, interleukin-1 receptor anatagonist, and soluble interleukin-1 receptor type II secretion in chronic fatigue syndrome. J Clin Immunol 1997;17:253-61.
44. Carlo-Stella N, Badulli C, De Silvestri A, et al. A first study of cytokine genomic polymorphisms in CFS: positive association of TNF-857 and IFN γ874 rare alleles. Clin Exp Rheumathol 2006;24:179-82.
45. Fletcher MA, Zeng XR, Barnes Z, et al. Plasma cytokine in women with chronic fatigue syndrome. J Transl Med 2009;7:96.
46. Häuser W, Akritidou I, Felde E, et al. Steps towards a symptom-based diagnosis of fibromyalgia syndrome. Symptom profiles of patients from different clinical settings. Z Rheumatol 2008;67:511-5.
47. Hudson JI, Pope HG Jr. Affective spectrum disorder: does antidepressant response identify a family of disorders with a common pathophysiology? Am J Psychiatry 1990;147:552-64.
48. Konstantinov K, von Mikecz A, Buchwald JJ, et al. Autoantibodies to nuclear envelope antigens in chronic fatigue syndrome. J Clin Invest 1996;98:1888-96.
49. Kuczmarski RJ. Prevalence of overweight and weight gain in the United States. Am J Clin Nutr 1992;55:495-502.
50. Landay AL, Jessop C, Lennette ET, Levy JA. Chronic fatigue syndrome: clinical condition associated with immune activation. Lancet 1991;338:707-12.
51. Lerner AM, Beqai SH, Deeter RG, Fitzgerald JT. Valacyclovir treatment in Epstein-Barr virus are subset chronic fatigue syndrome: thirty-six months follow-up. In Vivo 2007;21:707-13.
52. Moss RB, Mercandetti A, Vojdani A. TNF-alpha and chronic fatigue syndrome. J Clin Immunol 1999;19:314-6.
53. Natelson BH, Haghighi MH. Evidence for the presence of immune dysfunction in chronic fatigue syndrome. Clin Diagn Lab Immunol 2002;9:747-52.
54. Nishikai M. Antinuclear antibodies in patients with chronic fatigue syndrome. Nippon Rinsho 2007;265:1067-70.
55. Pellegrino MJ. Atypical chest pain as an initial presentation of primary fibromyalgia. Arch Phys Med Rehabil 1990;71:526-8.
56. Rohleder N, Schommer NC, Hellhammer DH, et al. Sex differences in glucocorticoid sensitivity of proinflammatory cytokine production after psychosocial stress. Psychosom Med 2001;63:966-72.
57. Rohleder N, Wolf JM, Piel M. Impact of oral contraceptive use on glucocorticoid sensitivity of proinflmmatory cytokine production after psychosocial stress. Psychoneuroendocrinology 2003;28:261-73.
58. ter Wolbeek M, van Doornern LJ, Kavelaars A, et al. Longitudinal analysis of pro- and anti-inflammatory cytokine production in severity fatigue adolescents. Brain Behav Immun 2007;21:1063-74.
59. Tirelli U, Marotta G, Improta S, Pinto A. Immunological abnomarlities in patients with chronic fatigue syndrome. Scand J Immunol 1994;40:601-8.
60. Tirelli U, Pinto A, Marotta G, et al. Clinical and immunologic study of 205 patients with chronic fatigue syndrome: A case series from Italy. Arch Intern Med 2003;153:116-20.
61. Wessely S, Powell R. Fatigue syndromes: a comparison of chronic post-viral fatigue with neuromuscular and affective disorders. J Neurol Neurosurg Psychiatry 1989;42:940-8.
62. Wolfe F, Hawley DJ. Measurement of the quality of life in rheumatic disorders using the EuroHRQoL. Br J Rheumatol 1997;36:786-93.