

Ozone therapy in 65 patients with fibromyalgia: an effective therapy

U. TIRELLI¹, C. CIRRITO¹, M. PAVANELLO¹, C. PIASENTIN¹, A. LLESHI², R. TAIBI²

¹Tirelli Medical Clinic, Pordenone, Italy

²Department of Medical Oncology, National Cancer Institute, Aviano (PN), Italy

Abstract. – **OBJECTIVE:** Fibromyalgia is a chronic disorder with a very complex symptomatology. Although generalized severe 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.

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.

PATIENTS AND METHODS: Sixty-five patients with fibromyalgia, according to the definition of the American College of Rheumatology (Arthritis Rheum 1990; 33: 160-172), were treated at the MEDE Clinic (Sacile, Pordenone, Italy) from February 2016 to October 2018. Females were 55 and males were 10; age ranged from 30 to 72 years, and the time from fibromyalgia diagnosis ranged from 0.5 to 33 years. Treatment was made by autohemotransfusion in 55 patients and by ozone rectal insufflations in 10 patients, according to SIOOT (Scientific Society of Oxygen Ozone Therapy) 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 45 patients (70%). 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.

CONCLUSIONS: At the moment, ozone therapy seems a treatment that, also because without any side effect, is possible to be proposed to patients with fibromyalgia that are not obtaining adequate results from other available treatments and it can be considered as complementary/integrative medicine.

Key Words:

Fibromyalgia, Ozone Therapy, Fatigue, Pain.

Introduction

Fibromyalgia is a chronic disorder with a very complex symptomatology¹. 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 pathophysiology of the disease. 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.

Due to ozone capability to control the oxidative stress, when administered in specific therapeutic doses, its therapeutic capacities have gained much attention in the last few decades. The first application of ozone as a antiseptic for operating rooms and to disinfect surgical instruments dates back to 1856, only 16 years after its discovery. Later, in 1892, an article was published describing the administration of ozone for the treatment of tuberculosis. During World War I, doctors used

ozone to treat soldiers wounds, trench feet and the effects of poisonous gases². No side effects other than coughing caused by accidental inhalation of the mixture are described, because ozone has irritating effects on the airways.

There are many routes of administration of the therapeutic mixture of ozone, they depend on the illness: subcutaneous; intramuscular; intra-articular; insufflative (vaginal, uterine, anal, urethral, joint); topical; hydropnic; major autohemoinfusion or minor autohemoinfusion. Ozone is an unstable molecule, and determines oxidative reactions generating a intended and transient oxidative stress that stimulates the intracellular antioxidant system.

A plethora of scientific evidence has demonstrated that the activation of hypoxia inducible factor-1 α (HIF-1 α), nuclear factor of activated T-cells (NFAT), nuclear factor-erythroid 2-related factor 2-antioxidant answer element (Nrf2-ARE), and activated protein-1 (AP-1) pathways are the most important molecular mechanisms following the valuable effects of the therapy with ozone, leading to the up-regulation of endogenous antioxidant systems, activation of immune functions together with suppression of inflammatory processes, which is essential for correcting oxidative stress in fibromyalgia.

Patients and Methods

Sixty-five patients with fibromyalgia, according to the definition of the American College of Rheumatology³, were treated at the MEDE Clinic, Sacile (Pordenone), Italy from February 2016 to October 2018⁴. Females were 55 and males were 10; age ranged from 30 to 72 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. Treatment was made by autohemotransfusion in 55 patients and by ozone rectal insufflations in 10 patients, according to SIOOT (Scientific Society of Oxygen Ozone Therapy) protocols, twice a week for one month and then twice a month as maintenance therapy.

This work has been performed in compliance with the Ethical values laid down by the Declaration of Helsinki, and informed consent doc-

umentation have been reviewed and agreed by the independent Ethics Committee at the Mede Clinic.

Results

Of the 65 patients with fibromyalgia we have treated, we found a significative improvement (>50% of symptoms) in 45 patients (70%). No patient reported important side effects. Differences according to age, gender, and adverse events were calculated using the Chi-square test. Univariate analyses was performed to match the study arms and the unadjusted logic regression method was used to assess crude odds ratios and 95% confident intervals. Logistic progression models adjusted for major confounders like age and gender were used to calculate adjusted odds ratios and 95% confident ratios. $p < 0.05$ was considered statistically significant.

Discussion

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 ineffective⁵⁻⁹.

The objective of the present work was to get a preliminary evaluation of the potential effectiveness of ozone therapy in the management of fibromyalgia. The encouraging clinical results obtained validate the ozone therapy in these patients. It is noteworthy that effectiveness of ozone therapy is due to its capacity of simultaneously activate many metabolic pathways that have gone astray. Seventy percent response rate obtained in our patients means that the ozone therapy is an effective therapy in 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. However, more patients are required and in particular a longer follow up is a required.

Conclusions

At the moment, ozone therapy seems a treatment that, also because without any side effect, is possible to be proposed to patients with fibromyalgia that are not obtaining adequate results from other available treatments and it can be considered as complementary/integrative medicine¹⁰⁻¹².

Conflict of Interests

All authors declare no commercial associations that might create a conflict of interest in connection with the submitted manuscript.

References

- 1) BENNETT RM, SMYTHE HA, WOLFE F. Recognizing fibromyalgia. *Patient Care* 1989; 23: 60-83.
- 2) LANDAY AL, JESSOP C, LENNETTE ET, LEVY JA. Chronic fatigue syndrome: clinical condition associated with immune activation. *Lancet* 1991; 338: 707-712.
- 3) WOLFE F, SMYTHE HA, YUNUS MB, BENNETT RM, BOMBARDIER C, GOLDENBERG DL, TUGWELL P, CAMPBELL SM, ABELES M, CLARK P, FAM AG, FARBER SJ, FIECHTNER JJ, FRANKLIN CM, GATTER RA, HAMATY D, LESSARD J, LICHTBROUN AS, MASI AT, MCCAIN GA, REYNOLDS WJ, ROMANO TJ, RUSSELL IJ, SHEON RP. The American College of Rheumatology 1990 Criteria for the Classification of Fibromyalgia. Report of the multicenter criteria committee. *Arthritis Rheum* 1990; 33: 160-172.
- 4) TIRELLI U, CIRRITO C, PAVANELLO M, DEL PUP L, LLESHI A, BERRETTA M. Oxygen-ozone therapy as support and palliative therapy in 50 cancer patients with fatigue - a short report. *Eur Rev Med Pharmacol Sci* 2018; 22: 8030-8033.
- 5) BERGMAN S. Psychosocial aspects of chronic widespread pain and fibromyalgia. *Disabil Rehabil* 2005; 27: 675-683.
- 6) CAMPBELL SM, CLARK S, TINDALL EA, FOREHAND ME, BENNETT RM. Clinical characteristics of fibrositis. I. A "blinded," controlled study of symptoms and tender points. *Arthritis Rheum* 1983; 26: 817-824.
- 7) LEAVITT F, KATZ RS, GOLDEN HE, GLICKMAN PB, LAYFER LF. Comparison of pain properties in fibromyalgia patients and rheumatoid arthritis patients. *Arthritis Rheum* 1986; 29: 775-781.
- 8) PELLEGRINO MJ. Atypical chest pain as an initial presentation of primary fibromyalgia. *Arch Phys Med Rehabil* 1990; 71: 526-528.
- 9) ROHLEDER N, SCHOMMER NC, HELLHAMMER DH, ENGEL R, KIRSCHBAUM C. Sex differences in glucocorticoid sensitivity of proinflammatory cytokine production after psychosocial stress. *Psychosom Med* 2001; 63: 966-972.
- 10) BERRETTA M, DELLA PEPA C, TRALONGO P, FULVI A, MARTELLOTTA F, LLESHI A, NASTI G, FISICHELLA R, ROMANO C, DE DIVITIIS C, TAIBI R, FIORICA F, DI FRANZIA R, DI MARI A, DEL PUP L, CRISPO A, DE PAOLI P, SANTORELLI A, QUAGLIARIELLO V, IAFFAIOLI RV, TIRELLI U, FACCHINI G. Use of Complementary and Alternative Medicine (CAM) in cancer patients: an Italian multicenter survey. *Oncotarget* 2017; 8: 24401-24414.
- 11) DEL BUONO A, D'ORTA A, TARRO G, ROSSI P, PAPA S, IODICE L, ABBADESSA A, MONTANO L, PORTALE G, BERRETTA M, DI FRANZIA R. "Terra dei fuochi, the starting point". The role of prevention and complementary medicine in the clinical practice *WCRJ* 2018; 5: e1112.