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	OXYGEN-OZONE THERAPY IS A POTENTIALLY EFFECTIVE THERAPY IN CHRONIC FATIGUE SYNDROME: RESULTS OF AN ITALIAN STUDY IN 65 PATIENTS.	
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ABSTRACT The Atlanta's Centers of Disease Control (CDC) first described the Chronic Fatigue Syndrom (CFS) at the end of 1980s. Since the last few decades, the therapeutic potential of oxygen-ozone therapy has gained much attention: in fact, when administered in precise therapeutic doses, oxygen-ozone therapy is active in many diseases.

At the MEDE Clinic of Sacile, Italy, from February 2016 to December 2017, we have treated 65 patients, with auto hemo transfusion (GAE), according to the SIOOT (Scientific Society of Oxygen Ozone Therapy) protocols, twice a week for one month and twice a month as maintenance therapy. Females were 50, males were 15; age ranged from 13 to 60 years and the time from CFS diagnosis ranged from 1 to 15 years. To assess the extent of fatigue we employed the Fatigue Severity Scale which is used to estimate the severity of the symptom with a score ranging from 1 to 7. Of the 65 patients with CFS we have treated, 52 patients (80%) showed a significant improvement in symptomatology (>50% improvement in symptoms). There have been no side effects to oxygen-ozone therapy.

In conclusion, at our knowledge this is the largest study of patients with CFS treated with oxygen-ozone therapy. Oxygen ozone therapy is an effective therapy in the treatment of CFS.

KEYWORDS : Ozone therapy, Chronic Fatigue Syndrome, Fatigue

## Introduction

Chronic fatigue syndrome (CFS), is a debilitating and complex disorder characterized by profound fatigue that is not improved by bed rest and that may be worsened by physical or mental activity. Persons with CFS most often function at a substantially lower level of activity than they were capable of before the onset of illness. In addition to these key-defining characteristics, patients report various nonspecific symptoms, including weakness, muscle pain, impaired memory and/or mental concentration, insomnia, and post-exertional fatigue lasting more than 24 hours. In some cases, CFS can persist for years. The cause or causes of CFS have not been identified and no specific diagnostic tests are available. Moreover, since many illnesses have incapacitating fatigue as a symptom, care must be taken to exclude other known and often treatable conditions before a diagnosis of CFS is made.

A great deal of debate has surrounded the issue of how best to define CFS. To resolve these issues, an international panel of CFS research experts convened in 1994 to draft a definition of CFS that would be useful both to researchers studying the illness and to clinicians diagnosing it. In essence, in order to receive a diagnosis of CFS, a patient must satisfy two criteria: to have severe chronic fatigue of six months or longer duration with other known medical conditions excluded by clinical diagnosis; and to concurrently have four or more of the following symptoms: substantial impairment in short-term memory or concentration; sore throat; tender lymph nodes; muscle pain; multi-joint pain without swelling or redness; headaches of a new type, pattern or severity; unrefreshing sleep; and post-exertional malaise lasting more than 24 hours. The symptoms must have persisted or recurred during six or more consecutive months of illness and must not have predated the fatigue.

In the last few decades, the therapeutic capacities of ozone have gained much attention thanks to its strong capacity, when administered in precise therapeutic doses, to control the oxidative stress. The first applications of ozone date back to 1856, just 16 years after its discovery, used as a disinfectant for operating theaters and to sterilize surgical instruments. In 1892, an article was published describing the administration of ozone for the treatment of tuberculosis. During World War I, doctors used it to treat wounds, trench feet and the effects of poisonous gases. [20] Side effects other than coughing caused by accidental inhalation of the mixture are not described, as ozone has an irritating effect on the airways.

The routes of administration of the therapeutic mixture are manifold and depend on the pathology: subcutaneous; intramuscular; intraarticular; insufflative (anal, vaginal, uterine, urethral, joint); topical; hydropinic; minor autohemoinfusion, major autohemoinfusion. Ozone, being an unstable molecule, determines oxidative reactions generating a calculated and transitory oxidative stress that stimulates the intracellular antioxidant system.

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

## Materials, Methods and Results

At the MEDE Clinic of Sacile, Italy, from February 2016 to December 2017, we have treated 65 patients, with auto hemo transfusion (GAE), according to the SIOOT (Scientific Society of Oxygen Ozone Therapy) protocols, twice a week for one month and twice a month as maintenance therapy. This study has been performed in compliance with the ethical values laid down by the Declaration of Helsinki, and informed consent documentation has been reviewed and agreed by the independent ethics committee at the MEDE

Clinic. Differences according to age, gender, and adverse events have been calculated using the Chi-square test. Univariate analyses have been performed to match the study arms and the unadjusted logic regression method has been used to assess crude odds ratios and 95% confident intervals. Logistic progression models adjusted for major confounders like age and gender have been used to calculate adjusted odds ratios and 95% confident ratios. P<0.05 has been considered statistically significant.

Female patients were 50, males were 15; age ranged from 13 to 60 years and the time from CFS diagnosis ranged from 1 to 15 years. To assess the extent of fatigue we used the Fatigue Severity Scale which is used to estimate the severity of the symptom with a score ranging from 1 to 7. Of the 65 patients with CFS we have treated, 52 patients (80%) showed a significant improvement in symptomatology (>50% improvement in symptoms). There have been no side effects to ozone therapy.

## Discussion

Standardized medical care (antidepressants, glucocorticoids, immunotherapy and metabolic drugs) is not beneficial and present some side effects in CFS patients. During the last seven years of clinical experimentation in vasculopathic and in age-related macular degeneration patients, we have consistently noted that ozonate autohemotherapy often yields a feeling of wellbeing and euphoria. This result is interesting, and we can only hazard that the reasons for these positive effects are the functional renewal of hormonal and neurotransmitter functions. Is than the "therapeutic shock" of ozone autohemotherapy helpful also in patients with fatigue and depression? Moreover, ozone therapy may change the vicious circle due to a chronic oxidative stress and deranged muscle metabolism. The positive clinical results obtained justify the ozone therapyin 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. Eighty percent response rate obtained in our patients means that the ozone therapy is an effective therapy in CFS. In conclusion, at our knowledge this is the largest study of patients with CFS treated with ozone therapy. Oxygen ozone therapy is an effective therapy in the treatment of CFS. However, more patients are needed and in particular a longer follow up is a necessary. In the meantime, ozone therapy seems a treatment that, also because without any side effect, is possible to be proposed to patients with CFS that are not obtaining sufficient results from available therapy.

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