Cancer Association of South Africa (CANSA)

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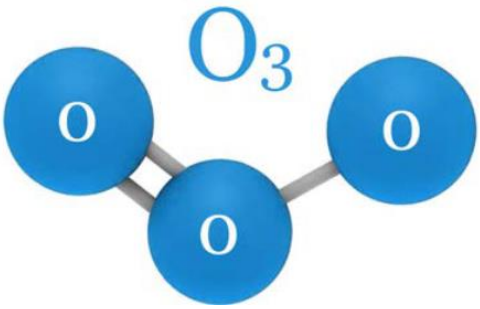
Fact Sheet
And Position Statement
on
Ozone Therapy

Introduction

Ozone (O_3) is a highly reactive gas composed of three oxygen atoms. It is both a natural as well as a man-made product that occurs in the earth's upper atmosphere (the stratosphere) and lower atmosphere (the troposphere). Depending on where it is in the atmosphere, ozone affects life on earth.



[Picture Credit: Ozone]

Ozone forms an energetic molecule that readily donates its third oxygen atom to free radicals that are usually causing damage to one's body through oxidation. If there is Ozone present in one's body, then the oxidation damage caused by these free radicals is halted because the free radicals are made stable and, therefore, non-destructive by the extra oxygen atom given off by the Ozone.

Clavo, B., Navarro, M., Federico, M., Borrelli, E., Jorge, I.J., Ribeiro, I., Rodríguez-Melcon, J.I., Caramés, M.A., Santana-Rodríguez, N. & Rodríguez-Esparragón, F. 2021.

Background: Chronic pain secondary to treatment in cancer survivors without tumor evidence is not unusual. Its management often requires specific approaches that are different from those applied for cancer patients with advanced disease and short life expectancy. Some studies have described clinical benefit with ozone therapy (O_3T) in the management of pain and side effects secondary to cancer treatment.

Objective: We present our preliminary experience with O_3T in the management of refractory pelvic pain syndromes secondary to cancer treatment.

Design: Case series.

Subjects and Methods: Six cancer patients (without tumor evidence) who had been treated previously with radiotherapy, chemotherapy, or endoscopic procedures and were suffering persistent or severe pelvic pain (median 14 months) received O_3T using ozone-oxygen gas mixture insufflation as a complementary therapy in addition to their scheduled conventional treatment.

Results: All cases, except one, showed clinically relevant pain improvement. Visual analog scale score with the standard treatment was 7.8 ± 2.1 before O_3T, 4.3 ± 3.4 (p = 0.049) after one month, 3.3 ± 3.7 (p = 0.024) after two months, and 2.8 ± 3.8 (p = 0.020) after three months of O_3T. The median value of "pain symptom" according to the U.S. National Cancer Institute Common Terminology Criteria for Adverse Events v. 5.0 showed a decrease from 3 (range: 2-3) to 1 (range: 0-3) (p = 0.046).

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Conclusions: Following unsuccessful conventional treatments, O_3T provided significant benefit in our patients with refractory pelvic pain secondary to cancer treatment. These results merit further evaluation in blinded, randomized clinical trials.

Clavo, B., Martínez-Sánchez, G., Rodríguez-Esparragón, F., Rodríguez-Abreu, D., Galván, S., Aguiar-Bujanda, D., Díaz-Garrido, J.A., Cañas, S., Torres-Mata, L.B., Fabelo, H., Téllez, T., Santana-Rodríguez, N., Fernández-Pérez, L. & Marrero-Callico, G. 2021.

(1) **Background**: Chemotherapy-induced peripheral neuropathy (CIPN) decreases the quality of life of patients and can lead to a dose reduction and/or the interruption of chemotherapy treatment, limiting its effectiveness. Potential pathophysiological mechanisms involved in the pathogenesis of CIPN include chronic oxidative stress and subsequent increase in free radicals and proinflammatory cytokines. Approaches for the treatment of CIPN are highly limited in their number and efficacy, although several antioxidant-based therapies have been tried. On the other hand, ozone therapy can induce an adaptive antioxidant and anti-inflammatory response, which could be potentially useful in the management of CIPN.

(2) **Methods**: The aims of this works are: (a) to summarize the potential mechanisms that could induce CIPN by the most relevant drugs (platinum, taxanes, vinca alkaloids, and bortezomib), with particular focus on the role of oxidative stress; (b) to summarize the current situation of prophylactic and treatment approaches; (c) to describe the action mechanisms of ozone therapy to modify oxidative stress and inflammation with its potential repercussions for CIPN; (d) to describe related experimental and clinical reports with ozone therapy in chemo-induced neurologic symptoms and CIPN; and (e) to show the main details about an ongoing focused clinical trial.

(3) **Results**: A wide background relating to the mechanisms of action and a small number of experimental and clinical reports suggest that ozone therapy could be useful to prevent or improve CIPN.

(4) **Conclusions**: Currently, there are no clinically relevant approaches for the prevention and treatment of stablished CIPN. The potential role of ozone therapy in this syndrome merits further research. Randomized controlled trials are ongoing.

Non-Medical Uses of Ozone

Ozone is used for non-medical purposes, for example:

- In the food industry as a decontaminating agent
- Pest control in the grain industry
- Water purification where it kills bacteria and viruses much more potent than chlorine and with no side effects
- Disinfection of air and removal of odours
- Disinfection in the field of plants and vegetables
- Disinfection in poultry farming
- Disinfecting swimming pools

Brodowska, A.J., Nowak, A. & Smigielski, K. 2018.

"The food contamination issue requires continuous control of food at each step of the production process. High quality and safety of products are equally important factors in the food industry. They may be achieved with several, more or less technologically advanced methodologies. In this work, we review the role, contribution, importance, and impact of ozoneas a decontaminating agent used to control and eliminate the presence of microorganisms in food products as well as to extend their shelf-life and remove undesirable odors. Several researchers have been focusing on the ozone's properties and applications, proving that ozone treatment technology can be applied to all types of foods, from fruits, vegetables, spices, meat, and seafood products to beverages. A compilation of those works, presented in this review, can be a useful

tool for establishing appropriate ozone treatment conditions, and factors affecting the improved quality and safety of food products. A critical evaluation of the advantages and disadvantages of ozone in the context of its application in the food industry is presented as well."

Amoah, B.A. & Mahroof, R.M. 2019.
"Gaseous ozone, an oxidizing agent used as a disinfectant in food processing and preservation, has potential for the control of stored product insects. In this study, we investigated ozone for the management of the rice weevil, Sitophilus oryzae (L.) (Coleoptera: Curculionidae), a serious stored product insect pest. We exposed eggs, immature stages within wheat kernels, and adults of the rice weevil to 200-ppm ozone for 12, 24, 36, 48, and 60 h. Insects were placed at 5, 15, or 25 cm depth within a wheat mass in PVC pipes (10 cm in diameter, 30 cm in height) and exposed to ozone. Egg eclosion was recorded 10 d after treatment (DAT), and immature stages were observed for adult emergence 28 DAT. Adults were observed for survival immediately after ozone exposure and again at 1 and 2 DAT. Egg eclosion was significantly lower at 5 cm compared with 25 cm at all exposure times, but not the 12-h exposure time. For each exposure time tested, significantly lesser adults developed from kernels and none of the adults survived at the 5 cm depth compared with the 15 and 25 cm depths. Survival rate of adults was significantly higher at 25 cm depth than at 15 cm depth at the 24-60 h. The deeper the insect in the grain mass, the higher the survival rate. The work reported suggests that ozone is effective in killing all life stages of S. oryzae; however, the efficacy of the gas is dependent on the concentration, exposure time, depth, and gas loss."

Ozone Therapy
Ozone therapy can be described as a form of therapy to improve the body's intake and use of oxygen and to activate the immune system. In medicine, ozone is used to disinfect and treat diseases by limiting the effects of bacteria, viruses, fungi, yeast, and protozoa.

Historically Ozone was found to be a useful treatment for people with HIV before pharmaceutical medication was available.

Today it is used for treating the following:

- infected wounds
- activation of the immune response
- disinfection and the treatment of diseases by limiting the effects of bacteria, viruses, fungi, yeast, and protozoa.
- circulatory disorders
- geriatric disorders
- macular degeneration
- viral diseases
- rheumatism and arthritis
- cancer
- severe acute respiratory syndrome (SARS)
- Aids

Although ozone is a gas, developments in technology mean it can be used in several forms and different ways, including:

- ozonated olive oil applied directly to the body
- insufflation, a risky therapy where ozone is blown into the rectum
- ozonated water, which is drunk
- injections, which are often used in dentistry
- autohemotherapy, where blood is withdrawn, mixed with ozone, and put back into the bloodstream
- gas bath or sauna

Oldoini, G., Frabattista, G.R., Saragoni, M., Cosola, S., Giammarinaro, E., Genovesi, A.M. & Marconcini, S. 2020.
"Chemotherapy usually causes complications affecting several tissues such as oral mucosa. In this case report, a soft palate oral ulcer caused by chemotherapy was treated by ozone gas. This kind of treatment is known for its antimicrobial, regenerative and analgesic proprieties. The results show a complete resolution of the lesion within 2 weeks of treatment. Ozone therapy demonstrates greater effectiveness with respect to this kind of oral lesion compared to traditional therapy. Considering this evidence, ozone therapy should be considered as a useful tool for the adjuvant therapy of oral complications in oncologic patients.
"Learning points: Intensive chemotherapy can have side effects, particularly affecting tissue with higher turnover. Therefore, there is a clinical need to prevent or to treat such complications.Ozone therapy could improve oral mucosa healing and have anti-inflammatory, antioxidant and antibacterial effects to prevent suprainfections. To date, there are no reported cases of oral ulcers in oncologic patients being completely resolved using ozone in the literature.Medical and dental doctors should collaborate with regards to complex patients to prevent such types of complications, discovering these clinical cases that are unknown in the literature and treating patients in a more comprehensive way."

Hayashi, K., Takeshi, O., Honda, H., Ozawa, N., Ohata, H., Takano, N. & Shibahara, T. 2019.
No effective, reliable treatment for stomatitis associated with cancer therapy has been established. This study focused on the its effectiveness of ozone nano-bubble water (ONBW) for the treatment of chemotherapy-induced stomatitis. Oral mucositis was induced in 14-week-old male Sprague-Dawley rats (N = 21). The animals were randomly divided into 3 groups: 7 without treatment (control); 7 treated with physiological salt solution (saline); and 7 treated with ONBW. Animals were weighed on Days 7, 9, 11, and 16. Stomatitis grade evaluation and bacterial count measurements were performed before rinsing in all animals 3, 5, and 10 days after acetic acid irritation (Days 9, 11, and 17 respectively). Weight loss after stomatitis creation was observed in all groups, with significant differences between the control and ONBW groups and between the saline and ONBW groups on Day 16. The stomatitis grade did not worsen during the experimental period in any group, with the lowest grades in the ONBW group on Days 11 and 16. Significant differences were identified between the control and ONBW groups and between the saline and ONBW groups on Days 11 and 16. Oral bacterial counts tended to decrease over time in all three groups, with the greatest decrease in the ONBW group, followed by the saline group. The decrease in the bacterial count was steepest in the ONBW group. Rinsing out the oral cavity with ONBW decreased bacterial counts and encouraged the healing of oral chemotherapy-induced stomatitis. ONBW may be an effective treatment for chemotherapy-induced stomatitis.

Aydogdu, I., Ilbey, Y.O., Coban, G., Ekin, R.G., Mirapoglu, S.L., Cay, A., Kiziltan, H.S., Ekin, Z.Y., Silay, M.S. & Semerci, M.B. 2019.
OBJECTIVE: We investigate the protective and therapeutic effects of ozone therapy (OT) in radiotherapy (RT)-induced testicular damage.
METHODS: Thirty healthy adult male Wistar rats divided into five groups consisting of six animals each as follows: (1) Control (C), (2) RT, (3) OT, (4) OT + RT, and (5) RT + OT group. Histopathological findings, Johnsen scores, thiobarbituric acid-reactive substances (TBARS), glutathione (GSH), superoxide dismutase (SOD), catalase, and glutathione peroxidase (GPx) levels were evaluated.

RESULTS: RT caused a significant decrease in testicular weight and Johnsen score compared to the control group. In addition, TBARS level was significantly higher, whereas GSH, SOD, catalase, and GPx levels were significantly lower in the RT group when compared to the control group. Pre and postRT OT significantly increased GSH, SOD, catalase, and GPx levels and decreased TBARS level. Furthermore, testicular weight and Johnsen score were increased with OT.
CONCLUSIONS: The present study showed that OT is protective and therapeutic in radiation-induced testicular damage. OT may be beneficial to the patients who underwent RT.

Tirelli, U., Cirrito, C., Pavanello, M., Plasentin, C., Lieshi, A. & Taibi, R. 2019.
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.

CANSA's Position on Ozone Therapy
Following an extensive search of the scientific literature, the Cancer Association of South Africa (CANSA) has concluded that:

> It cannot yet support ozone therapy as a stand-alone treatment for any form of cancer.

From the international scientific literature it would appear that there may be a variety of medicinal uses of ozone therapy. However, CANSA strongly advises that:

> Cancer patients should refrain from using any form of ozone therapy without having discussed it with their respective treating physician and/or oncologist.
>
> If adjuvant ozone therapy has been approved or advised by an oncologist, CANSA advises that such adjuvant ozone therapy should be used under supervision of the treating oncologist.

Medical Disclaimer

This Fact Sheet is intended to provide general information only and, as such, should not be considered as a substitute for advice, medically or otherwise, covering any specific situation. Users should seek appropriate advice before taking or refraining from taking any action in reliance on any information contained in this Fact Sheet. So far as permissible by law, the Cancer Association of South Africa (CANSA) does not accept any liability to any person (or his/her dependants/estate/heirs) relating to the use of any information contained in this Fact Sheet.

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Ozone
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