

Ozone therapy in the management of cancer patient toxicity and our works in lung diseases.

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Introduction:

The aim of this work is to show the potential beneficial effects of Ozone therapy in the management of some side effects related to cancer treatment and to mention our related experimental researches and next clinical studies.

Material and methods:

First, it will be shown a summary of clinical and preclinical studies about the successful effect of Ozone therapy in different adverse events related with cancer treatments.

Later, it will be shown a short description of our recent experimental researches and upcoming clinical studies.

Presentation:

1) Mechanisms of action.

The effects of Ozone in this field are mediated by three well documented mechanisms of action:

- The effect on blood flow and oxygenation. This is the field where our group has carried out deeper clinical studies and we will describe with a little more extension.
- Modulation of immune system which is mediated by cytokine induction by ozone therapy. This effect supports additional role of ozone during cancer treatment as well as during inflammation process related with toxicity of cancer treatment,
- Improvement of the “free radical/antioxidant” balance which has been demonstrated to protect for further damage induced by chemotherapy and radiotherapy.

Using polarographic probes (the Eppendorf device) as a well validated technique, ozone therapy can lead to an improvement in tissue-pO₂ as demonstrated in our first study about oxygen modification in healthy tissue (tibialis anterior muscle) by ozone therapy (1). However, we should note that this was not a homogeneous effect: tissue oxygenation was increased only in previously worse oxygenated tissues.

Ozone does not significantly increase arterial pO₂. Then: How is ozone able to increase tissue-oxygenation? Several mechanisms have been proposed, several of them linked to increase of blood flow. This way, in a Doppler study we found a blood flow improvement in common carotid artery and middle cerebral artery after ozone therapy, supporting data about oxygen modification (2). Additionally, studies using SPECT (single photon emission computed tomography) to assess loco-regional blood flow modification in brain tissues (3).

2) Clinical and experimental studies

All above mentioned effects of Ozone therapy could be useful to treat different side effects of Radiotherapy, Surgery, Chemotherapy and related drugs, as it has been well described by several studies.

- A potential and relevant contribution of Ozone therapy to cancer treatment could be to avoid delays in the commencement of Radiotherapy and Chemotherapy. These treatments can decrease or prevent the scaring capacity. When delayed wound-healing after cancer surgery happens, usually Radiotherapy and Chemotherapy are also delayed until wound-healing. This delay can increase the risk for local tumor relapse. Local Ozone application (with or without systemic Ozone treatment) can improve scaring process.
- In our hospital, we have treated many other side effects of cancer treatments: delayed healing after chemotherapy extravasation, radiation-induced dermatitis, fistula and fibrosis after Chemotherapy, Surgery and Radiotherapy (4), radiation-induced hematuria (5), radiation-induced proctitis (6, 7) and radiation-induced brain injury (3). We have also used ozone therapy in some patients with diarrhea, mucositis, wound infections.
- Other institutions have also described beneficial effects of Ozone therapy in the treatment of mucositis, wound infections or bisphosphonate-related jaw osteonecrosis in cancer patients.
- Additionally, a growing number of preclinical studies have shown "protective" effect of Ozone preconditioning against selective toxicity induced by different chemotherapy drugs and radiation: nephrotoxicity by cisplatin, intestinal injury by Methotrexate, cardiotoxicity

by Doxorubicin and radiation induced toxicity in rectum, ileum, liver and lung. These works suggest the potential clinical application to prevent toxicity.

3) Our experimental research in lung diseases

We would like to show two related animal studies carried out by our group about the effect of Ozone preconditioning.

- One of them showed the potential decrease of lung-fibrosis induced by Bleomycin (another Chemotherapy drug).
- the other showed the capacity to avoid acute and chronic rejection after lung transplantation (8).

Both studies led to a Ph.D. degree at Las Palmas University, and they could be useful for further clinical studies and treatments in cancer patients.

4) Upcoming clinical research

Finally, we would like to comment the clinical trials with ozone therapy we are trying to carry out in collaboration with near 20 other Departments in our Hospital:

- Randomized Clinical Trials:
 - o Patients with disc herniation waiting for surgery (microdiscectomy).
ClinicalTrials.gov Identifier: NCT00566007
<https://clinicaltrials.gov/ct2/show/NCT00566007>
Closed. Waiting for publication.
 - o Ictus. (Waiting for funding).
 - o Diabetic foot. (Waiting for funding).
 - o Pelvic radiation induced toxicity. (Waiting for funding).
- Prospective post-authorization study as standard practice:
 - o Patients with disc herniation waiting for surgery (microdiscectomy)
Commencement: January-2017.

Conclusions:

Ozone therapy as adjuvant treatment in Oncology, could be useful to prevent or to treat different side effects of Radiotherapy and Chemotherapy and to accelerate the commencement of cancer treatments in patients with delayed wound healing. Several

experimental and clinical studies support these sentences, although the final demonstration will depend of well addressed clinical trials.

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