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1

OZONE AND EVIDENCE BASED OZONE THERAPY

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The medical evidence (in any science) evolves from simple clinical observation to well structured evidence, through the rumor, empiricism and structured scientific studies including experimental and clinical trials.

Evidence Based Medicine (EBM) is a process to making decisions in health care, with the best scientific evidence available and adjustable for a patient clinical setting. Therefore it seeks into scientific databases, research related about problem to be solved. The most important and best-designed work is selected. Then this is analyzed by comparison with efficacy and safety parameters, finally the cost.

There are different scales for measuring the quality of scientific evidence, which vary according to the context you have: prevention, treatment or prognosis. Also very situations there are several rating scales. Treatment case is the most commonly used, such as: recommended by the US Preventive Services Task Force (USPSTF), the Scottish Intercollegiate Guidelines Network (SIGN), the scale of Centre for Evidence-Based Medicine (EMBC) Oxford Scale, among others.

According to MBE, ozone therapy and indications have to date few publications in internationally indexed journals. The most widely used database in the world is the MEDLINE (PubMed): http://www.ncbi.nlm.nih.gov/PubMed (access October 20, 2015) that shows from 1985-2010 has a rise of publications (overall) about ozone (any type of publication) reaching a peak: 630 publications in 2007, among 11,550 publications since 1945.

When selected any publication on ozonetherapy is fewer, with peak in 2008 with 90 publications, among 1,429 publications since 1945. Filtering by clinical trials only, 146 publications are obtained since 1979 (first published clinical trial). And finally, filtering by systematic reviews and meta-analysis we have 6 and 4 publications, respectively, since 2004 (first publication).

Conclusion: There are relatively few and poorly quality controlled clinical studies about ozonetherapy, dosages are varied and there are very much indications.

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SCIENTIFIC BASES OF THE OXIDATIVE STRESS AND THEIR APPLICATION IN OZONE THERAPY

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Oxidative stress is a biological phenomena that has become the angular stone in biomedicine. Two centuries ago, the scientists started investigations in this field trying to guess the intrinsic mechanisms and their relationship with many different pathologies and recently, with different metabolic pathways.

The concept of oxidative stress has changed in time according to he results of the investigations. The recent research shows that it is a complex process whose knowledge is basic for the health professionals. However, presently we cannot only speak about oxidative stress, but also about antioxidative stress., that shares the same pathways that oxidative one; transient and chronic situations, that can lead to pathological situations.

Ozone therapy is deeply related to both situations, oxidative and antioxidative. The base of this therapy is inducing a low and controlled oxidative stress that arises a postive effect on the target cells. Measuring its effect is important to know the real effectiveness of this therapy.

In this presentation we will see the relationship between all these concepts explained here.

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OZONE THERAPY. TOXICITY VERSUS TERAPEUTIC EFFECTS

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We want to clarify that ozone has therapeutic effects when used in a therapeutic range following the scientific based protocols.

In this paper we show the possible side effects of ozone rectal insufflation, major autohemotherapy and breathing.

In order to get official authorization, ozone molecule needs security studies, both clinical and preclinical.

In Cuba, CNIO together CENPALD we developed these studies for these different ways of application.

Rectal insufflation.

- Teratogenic effect in rats: pregnant Wistar rats without side effects on fetus or uterus.

- Acute toxicity in rats: 5 mg/Kg was evaluated without side effects in the toxicity laboratory - CENPALAB.

- Mutagenic effect in mice: we used SPRD mice (weight: 180-200 g) and demonstrated the absence of chromosoma's damage.

- Other studies have been developed to check Chronic Tocicity in rats: we used dosage of 160-1000 mcg/Kg. 98% of the animals survived the study; we registered no evident side effect. We did not observed any anatomo-pathological damage, only increase in linfocytes and monocytes in cecum; no side effect was detected in the rest of the organs. Studies on Chronic toxicity in rabbits (462-2000 mcg/Kg) neither showed any toxicity.

Major autohemotherapy.

- Acute toxicity in rats: no side effect with 3 different dosage (168-512 mcg/Kg)

- Mutagenic effect on linfocytes: in 21 volunteers with a 50 mcg/mL concentration in 100 mL of peripheral blood without side effects. Other study on leucocytes showed DNA reversible damage. Other studies measuring micronuclei did neither find any changes at normal dosages.

Only breathing ozone even at very low doses produce a well known series of side effects. In case of accidental ozone breathing, oxigen inhaled and ascorbic acid endovenous can be very useful. Professionals working with ozone should have a periodical examination in blood of oxidative stress levels to check for possible pulmonary damage.

Conclusions: Ozone therapy is toxic by inhalatory way.

In Cuba, we have checked the security of ozone in ozonized water, ozonized oil, rectal insufflation, major autohemotherapy, intramuscular and intraperiteonal ways.

Due to inhalatory toxicity, a periodical examination of health professionals working with ozone is advisable.

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OZONE THERAPY IN DERMATOLOGY AND COSMETICS

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NO ABSTRACT AVAILABLE

5

OZONE THERAPY AND INTESTINAL BACTERIA. TOOLS TO RECOVER HEALTH

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Guts contain 50% of the immunity system through spectific Mucosae Associated Limphoid Tissure (MALT) that is present in all mucosae tissue in order to protect our body from malicious bacteria. However, not only MALT help us to defend from potential damage; gastric acid, IgA, peristalsis, enzymes, bile, also help us to maintain a healthy status. Even saprophytes bacteria block the growth of malicious ones in order to keep us without disease.

Gut mucosae not only control molecule absorption but also prevent the pass of malicious bacteria into the blood circulation. Apart from this, our evolution with our saprophytes bacteria has produced a deep connection with our immune system, so the changes in the first induce a modification in the second, many times, pathological. Fortunatelly,only 3-5% of the bacteria are pathological. Keeping our saprophytes bacterial in all mucosae tissues and their interaction with our immune system produce a safe health status and avoid general and local mucosae pathology such as atopy, liver inflammation, arthritis, autoimmune diseases, cardiovascular problems.

The use of rectal ozone insufflations can help to normalize the microbiota of the guts and, together other tools like diet, probiotics, etc., can help to restore the normal flora of our mucosae and, so our own health.

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MODULATOR EFFECT OF OZONE THERAPY IN RESPIRATORY DISEASES

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Abstract: Bronchial asthma and emphysema are non transmitted chronic diseases, which can compromise the patient's life if not treated. They occupy an important place in the world within respiratory conditions due to its high prevalence. Ozone, applied therapeutically, is able to modulate the immunological system, to improve the oxygen metabolism and blood circulation, to stimulate the antioxidant defense systems and has anti-inflammatory capacity, among other effects. Two studies where is evaluated the ozone therapy effectiveness in patients with asthma and emphysema is presented. In the first study, 113 patients with moderate asthma were treated with 3 cycles (5 to 6 months between each cycle) with different ozone therapy protocols. The first two were applied ozone by major autohemotherapy (M-AHT), at doses of 4 and 8 mg (each cycle of 15 sessions). In the third group, ozone was applied by rectal insufflation (RI), at a dose of 10 mg and cycles of 20 sessions. IgE and HLA-DR figures diminished after the three different treatments, while glutathione peroxidase, glutathione reductase, glutathione S transferase and reduced gluthathione increased. Pulmonar function and symptoms significantly improve, achieving better results in this order: M-AHT 8 mg > RI 10 mg > M-AHT 4 mg. Another study in 36 patients with severe asthma is presented. They were divided at random into two groups: ozone (15 patients), 20 sessions by rectal insufflations at a dose of 10 mg and control (18 patients), as ozone group but applying oxygen. In the ozone group there was a trend in the improvement of the respiratory functional tests, as well as a trend in IgE decrease ($p = 0.059$). In the patients treated with ozone, a marked reduction in the consumption of anti asthmatic drugs, as well as an improvement in the clinical response were achieved. In the oxygen group, no beneficial effects were obtained. In the emphysema study, the sample was divided at random in three groups: Group 1- 20 patients with their conventional treatment plus 20 sessions of ozone (one daily) by rectal insufflations (dose = 6 mg). This ozone cycle was repeated at 3 months. Group 2 – as group 1, but applying oxygen instead of ozone. Group 3 – 10 patients with only the conventional treatment. The ozone group was the only one that achieved significant improvements in the pulmonary function tests and the oxygen partial pressure. Also, clinical symptoms were reduced in 40 % of patients, permitting refer an improvement according to their self assessment. No modifications were observed in CT scan and X-rays at the end of the treatment in all the groups. No side effects were observed in any of the studies performed. Ozone therapy may be a beneficial therapeutic option in patients diagnosed with asthma and emphysema

Keywords: Ozone therapy, bronchial asthma, emphysema, oxidative stress, pulmonary function

test.

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OZONE THERAPY IN TUBERCULOSIS

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Introduction: Tuberculosis causes 1.5 million deaths per year, 4 times more than AIDS. Is the third cause of death in the world in women between 15 and 44 years old. Its incidence is 9 million new cases each year. Most cases appear in the South-East Asia (35%), Africa (30%) and West Pacific (20%). We are far from eradication, not because lack of access to drugs but resistant strains of bacteria, drugs side effects and patients abandoning the treatments.

One of the new factors associated with the disease and the resistant strains of Mycobacterium is oxidative stress. This is why we decided to study the possible benefit of using ozone to treat tuberculosis patients. We can find the first references in Lancet (1892).

We have reviwed the papers and have found several references. We would like to point out three most significant done by Bellanin in Russia.

In the first paper, Mycobacteria (MB) of the clinical strain resistant to streptomycin, isoniazid (IN), rifampicin and kanamycin were injected intravenously into 68 BALB/c mice. The animals were divided into 5 groups: two control groups 0 and 1 (intact and infected without subsequent treatment), group 2 (treated with IN), group 3 (treated with IN and injected intraperitoneally with dissolved ozone, or dO3), group 4 (injected with dO3). The animals started to die by month 4 after the infection. By month 5 all mice died with the exception of intact mice and those treated with dO3). By month 4 the study of MB cultures isolated from the lungs revealed a decrease in their resistance to IN in the groups undergoing treatment with dO3. Hepatic and splenic lesions were observed after treatment with IN only were greater than in the absence of treatment. After the use of IN + dO3 such lesions were the least. The mechanism of a decrease in the medicinal resistance of MB under the action of dO3 and the expediency of the simultaneous use IN and dO3 in cases of the unknown medicinal resistance of MB are discussed.

In the second paper, for 60 minutes, a mycobacterial (MBT) clinical strain resistant to streptomycin (S), rifampicin (R), isoniazid (I) was treated with dissolved ozone (PO3) at the concentration used for intravenous injection in the clinic. Then the strain was added to the Löwenstein-Jesen solid medium containing different concentrations of antituberculous agents. Following 3 weeks, drug sensitivity was determined by the number of grown colonies. Then MBT were retreated with PO3 in the same fashion, by repeating the cycle three times. At week 3, a growth of over 100 colonies was recorded in all control cultures. After each PO3 treatment of the strain, there was a reduction in its resistance to I and R. After triple treatment, MBT sensitivity to I completely recovered. In the R-containing media, there was also decrease in drug resistance, but the latter remained high (640 mu/ml). S resistance substantially lowered after the second PO3 treatment, but it restored after the third one. A mechanism responsible for lower MBT resistance to I and R under the action of "therapeutical" concentrations of PO3 is analyzed. The paper discusses whether MBT resistance can be changes at the phenotypic level rather that at the genetic one.

In the third paper, the outcomes of treatment were analyzed in 56 patients with ever-progressive multidrug-resistant pulmonary tuberculosis who had been long isolating Mycobacterium tuberculosis (MBT). The patients were divided into 2 groups. In the study group (n = 36), 75% isolated MBT resistant to streptomycin (S), isoniazid (I), rifampicin (R), and kanamycin (K). In this connection, 41.7% of them received only 2 second-line antituberculous drugs and 27.8% took 3 drugs. The control group (n = 20) was comparable with

the study group in the rate of bacterial isolation and in the drug resistance of the causative agent. In addition to chemotherapy (CT), dissolved ozone (pO3) was intravenously injected to the patients of the study group twice a week. They received a total of 12 to 55 infusions. Four-month addition of pO3 infusions to CT eliminated the resistance of isolated MBT to I and/or R. MBT became susceptible to I in 38.9% of the patients, R in 16.7%, and to K in 11.2%. By month 4, the isolated MBT became susceptible to I, R, and K in 47.2%. The mechanisms responsible for lowering drug resistance in MBT are discussed. The clinical example shows that patients with multidrug-resistant tuberculosis may be treated with first-line drugs provided that systemic intravenous injection of pO3 is performed.

Conclusions: There is enough evidence to start a pilot program in our Hospital to treat this kind of patients. We have only treated one patient yet.

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OZONE THERAPY IN THE VESTIBULOCOCHLEAR SYNDROME

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Introduction: It is named vestibulocochlear syndrome to a group of affections characterized by hearing and equilibrium disturbances. They are frequent caused of medical consultation and working absence. Vertigo is the main symptom, though hearing loss, tinnitus, pain and humid sensation can also be presented. This affection has an important prevalence and represents high economical expenses, due to the range of medicaments and long treatments that are used. Taking into account the different ozone therapeutical effects, as: improvement in the oxygen deliver to tissues, the calcium homeostasis, the stimulation of the antioxidant defence system, the immunological modulation, the vasodilation, among others, the aim of this study was to evaluate the efficacy of ozone therapy in the treatment of patients with peripheral vestibulocochlear syndrome.

Patients and methods: Sample was of 50 patients, with diagnose of mild peripheric vertigo-MPV (34), labyrinthitis (4), MPV + acoustic trauma (2), Menière´s disease (7), MPV + otosclerosis (3). Ozone (at a concentration of 20 mg/L and a volume of 5 mL) was injected into the points localizable in the paravertebral muscle, corresponding to the cervical region C2-C3, at 2 cm calculated bilaterally to the spinal process (twice per week, for 20 sessions). The evaluation criteria was based in the evolution of nystagmus, tinnitus, hearing loss (audiometric test) and vertigo (by means of the Romberg, Babinsky Star and Osterhamser tests) at the beginning, after fifth and tenth sessions and at the end of the treatment. Also, as an evaluation criterion, it was taken into account the behaviour of different biochemical parameters as: reduced glutathione (GSH), glutathione peroxidase (GPx), catalase (CAT), superoxide dismutase (SOD) and thyobarbituric acid reactive substances (TBARS).

Results: Females (55 %) and the range between 46 and 55 (42 %) years old were predominant. Vertigo was the main symptom. Patient evolution, according to vertigo, hearing loss, tinnitus and nystagmus and respect to the number of ozone sessions showed, after the 20th session, the disappearance of these symptoms in 90, 62, 61 and 100 %, respectively. The results demonstrated that patient improvements, according to vertigo, hearing loss, tinnitus and nystagmus, were of 90, 80, 65 and 100 %, respectively. Respect to vertigo, that was the main symptom, in 90 % of patients disappeared. It can be observed that patients with vestibulocochlear syndromes were, at the beginning of the treatment, under condition of systemic oxidative stress. Therefore, there exists a kind of dangerous central and systemic presence of reactive molecules, aimed toward the polyunsaturated fatty acids and homeostatic complex enzymes that are not compensated by the natural antioxidant

defence. However, after the ozone treatment they achieved a redox homeostasis. TBARS that presented increased values, at the beginning of the treatment, reduced significantly its figures even below the control group. GSH, GPx, SOD activities were increased after the ozone sessions and also respect to control group, preventing oxidative damage. CAT activity increased significantly with respect to the initial value, being similar to the control group. GPx and CAT increase were enough to overcome lipid peroxidation.

Conclusions: Ozone was able to maintain an adequate cellular redox balance. High SOD, GSH, GPx and CAT levels and low lipid peroxidation were obtained. Improvements in vertigo, hearing loss, tinnitus and nystagmus of 90, 80, 65 and 100 %, respectively, were achieved. Ozone therapy, in patients with peripheral vestibulocochlear syndrome, is effective, ease to perform, no structural damage is produced and can be used in outpatients with a minimum recovery time. No side effects were observed during the study.

Keywords: ozone therapy, peripheral vestibulocochlear syndrome, vertigo, nystagmus, hearing loss, ear noise.

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OZONE THERAPY IN PANCREAS CANCER

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Pancreas cancer is the 8th cause of death in men and the 9th on women. Only 20% survive one year after the diagnosis and less than 5% after 5 years. It is related with tobacco, helicobacter and meal rich diet. Risk factors are obesity, periodontal disease, solvents, asbestos and nickel. Most frequent presentation is the ductal carcinoma. The usual treatment is surgery + chemotherapy.

The use of ozone can be considered because the references support the decrease in chemotherapy side effects with it; also, the enhance in the immune system can also be potentially positive.

We are participating in a multicentric study in which we use rectal, endovenous and intraperitoneal ozone, together with alfa-lipoic acido, anti-homotoxic drugs, special diet, supplements and dental control. The preliminary results are very promising.

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OZONE THERAPY IN IMMUNOLOGICAL DISEASES

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The basic hypothesis of this work is whether ozone therapy has an immunomodulation effect checked through different parameters.

In the past 10 years, Dr Velio Bocci has been studying the effect of ozone therapy on the immune system; in one of his early papers, he showed that, in vitro, concentration over 50 mcg/mL increased the levels of IL–1, IL–2, IL–6, TNFα , IFNγ, GM–CSF TGF-1. This effect is mediated by the Nuclear Factor κβ.

Other interesting topic is that Th CD4+ immature cells can be induced into Th1 (cellular immunity), Th2 (humoral immunity), Th17 (chronic tissue damage) and Th reg (immunomodulation) depending upon local cytokines (Rossetal, 2013).

Some disease appear because of an excess of cellular immunity (Artritis Reumatoidea, Síndrome de Sjogren, Esclerosis Múltiple, Diabetes Mellitus tipo I, Psoriasis); others are due to an excess of humoral immunity (Lupus Eritematoso Sistémico, Asma Bronquial, Progresión de HIV a SIDA, Dermatitis Atópica y Cáncer Gástrico)

Dr Bocci published that concentrations below 40 mcg/mL induce a Th1 differentiation. We developed a clinical model of bronchial hiperreactivity in ginea pigs in which we used two dosage with rectal insufflation for 15 days (0.2 mg/kg and 1,2 mg/kg). We tested IgG levels in the bronchial tissue. Low dose achieved a decrease in IgG levels, but high dose produced the contrary. This fact advice us to use not very high dose in asthma patients.

Other study about renal damage in ischemia-reperfusion model, we also used two different dosage (0,5 mg/kg and 1,1 mg/kg) and measured the level of IL-6. Also low dose achieved the expected results and high level induced an increase in IL-6 levels.

In AIDS (Th2 model) we have achieved positive results using dosage of 3-7 mg in systemic application. In Lupus, also minimal dosage is recommended (2-4 mg). However, in malabsortion syndrome by Giardia, usually associated to immunodeficiency, medium to high dose are advisable to stimulate the immune system.

Regarding cancer, the optimal moment for treating is in the early stages were the immune system is still fighting against the tumor.

Conclusions: Ozone modulates the immune system through T cells by regulating the synthesis of cytokines.

Ozone can induce release of IL-10 and TGF,

Concentration of 20-35 mcg/mL increase Th1 pattern so Th1 diseases can be negatively affected with these dosages.

Cytokines synthesis increases over 50 mcg/mL but decreases over 75 mcg/mL due to the ozone toxicity on the leukocytes.

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OZONE THERAPY IN DIABETIC FOOT

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Introduction: The ozone is an allotropic from oxygen, considered as a "superoxygen" one of the biggest oxidants of the nature, which gives bacteria and fungi properties, applied to the local treatment of infected wounds.

Objective: To evaluate the efficiency of the ozone in wounds located in diabetic foots neuroinfected.

Methods: Retrospective comparative study in patients with diabetes type 2, at the Medical Centre "Vida Diabetica" (Diabetic Life), Lima, Peru; between June 2012 and June 2015.

- Sample: 282 patients treated. All of them older than 50 years old.
- Patients treated with ozonetherapy: 132
- Groups with no-ozonotherapy: 150
- Men: 163
- Women: 110

The ozone was applied as:

Cuvette: (70 ugr/ml) for 21 days in a row, then each 4 – 5 days according to the healing turn.

Rectally: (20- 30 ug/ml) only for 21 days in a row and if they exceeded 03 months, the process and the perilesional infiltration was repeated at each time healing turn (60 ug/ml).

Results: the time of wound healing of a diabetic foot treated with ozone was less than 60% at deep minor wounds of less than 10cms and 20% at deep major wounds of 10cms. No difference was found at the evolution rate of diabetic foot treated with or without ozone.

Conclusions: The ozonetherapy is a complementary treatment for a diabetic foot type 2 neuroinfected and it reduces the time of wound healing.

Key words: Ozonetherapy , diabetic foot, neuroinfected.

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OZONE THERAPY IN ALTITUDE SICKNESS

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Many inhabitants from Southamerica live above 2500 m. Many of them will suffer from chronic altitude sickness; 5-10% will suffer pulmonary artery hypertension. We have studied the systemic ozone therapy with major autohemotherapy (MAHT), based on the studies of the Russian group on the effect of ozone over red blood cells. We compiled 24 patients between 2012 and 2014. Patients received 1 session of MAHT per week during 10 weeks using progressive doses from 2,5 mg up to 9 mg. All patients had a decrease in hemoglobin and an improvement in the altitude sickness score. We are sure that MAHT with ozone

can be a useful tool to treat the chronic altitude sickness.

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PERIRADICULAR OZONE IN RADICULOPATHY

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Several kind of ozone injections have been proposed as effective in the treatment on lumbar disc herniation. We decided to study the possible benefit of peri-radicular injections in patients with radiculopathy of different causes (lumbar spondylosis, disc herniation, post-surgical fibrosis, spondylolisthesis) with a clinical and electromiographic assessment; moreover, we studied the side effects of the antineuritic drugs alone or associated with ozone injections.

We studied 39 patients between 2013 and 2015 with the protocol of weekly injections of ozone: 4 intraforaminal with fluoroscope guide and 16 deep paravertebral injections close to the nerve root with external anatomical references.

Our results showed a 60% of patients with full recovery of the radiculopathy ant the end of the treatment, compared to 50% in the antineuritic group. Side effects were lower in the ozone group.

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OZONE THERAPY IN DIABETES: A PRECLINICAL AND CLINICAL STUDY

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Background: In Diabetes mellitus, long-term complications, that cause morbidity and premature mortality, is characterized by microvascular and macrovascular diseases. A more frequent concomitant of distal anesthesia is the development of neurotropic ulceration, particularly on the plantar aspect of the foot. All these events characterize the underlying mechanisms that may lead to rapid gangrene after foot injury. Vascular endothelium appears to be a vulnerable target for hyperglycemia-induced metabolic changes. Activation of polyol pathway, non-enzymatic glycosilation of proteins and the increase of reactive oxygen species (ROS) play an important role in diabetes complications. Ozone has been used as a therapeutical agent and beneficial effects have been observed. However, so far only a few biochemical and pharmacodynamic mechanisms have been elucidated. We demonstrated that controlled ozone administration may promote an oxidative preconditioning or adaptation to oxidative stress, preventing the damage induced by ROS. Aim. Taking into account that diabetes is a disorder associated with oxidative stress, we postulate that ozone treatment might protect antioxidant systems and maintain, at a physiological level, other markers of endothelial cell damage associated with diabetic complications. In this study we evaluate ozone efficacy in a preclinical diabetes animal model and in a clinical trial with type 2 diabetes patients suffering of diabetic foot complications.

Patients and Methods: Diabetes animal model: Five groups of rats were classified as follows: (1) control group treated only with physiological saline solution; (2) positive control group using streptozotocin (STZ) as a diabetes inductor; (3) ozone group, receiving 10 treatments (1.1 mg / kg), one per day after STZ-induced diabetes; (4) oxygen group (26 mg /kg), one per day, as in group 3, but using oxygen only and (5) control ozone group, as in group 3, but without STZ. The following parameters were evaluated: plasma glucose concentration; in pancreas homogenates: levels of aldose reductase, fructolysine, advanced oxidation protein products, nitrite/nitrates (as an index of nitric oxide), glutathione (GSH), total hydroperoxides (TH), malondialdehide concentration (MDA), catalase (CAT), superoxide dismutase (SOD) and glutathione peroxidase (GSH-Px) activities as indicators of redox balance. Pancreas morphology was evaluated by light microscopy. Clinical assay: Randomized controlled clinical trial where all patients provided a signed informed consent before being enrolled was perdormed. Adult hospitalized patients of both sex of any ethnic, with diagnosis of neuroinfectious diabetes foot suffering of ulcers of the feet and lower extremities were eligible to participate in the study. These patients must not meet any of the

following criteria: severe septic conditions, hypersensibility to the medication that will be used, hepatic dysfunction, renal failure (serum creatinine level > 1.32 mmol/L), pregnancy, cancer, current therapy with any immunosuppresive agent or anticonvulsant. Patients were randomized to two different groups of treatment: 1-, control, 50 patients treated with antibiotic therapy, systemic and topically in the lesion (during 20 days), and 2-, ozone, 52 patients treated daily with ozone, 20 sessions, by rectal insufflation (with an ozone dose of 10 mg, ozone concentration: 40 mg/L) and locally. The same biochemical parameters that were taking into account in the preclinical study were measured in plasma, at the beginning and at the end of the treatments, as well as the clinical evaluation of the lesions and length of hospitalization.

Results: In both studies, ozone treatment improved glycemic control, and prevented oxidative stress, the increase of fructolysine content and advanced oxidation protein products. However, high plasma glucose figures and oxidative stress were maintained in the antibiotic group. In the animal model, ozone treatment also improved pancreas integrity. In the clinical assay, at the end of the treatments, a decrease of the area and perimeter of the lesions, for both groups, was obtained, but the expected total recovery showed that patients treated with ozone needed half of the time to achieve it, with regard to the antibiotic group. No significant differences between both treatments were obtained for the variable clinical evaluation (qualitative clinical evaluation), but with a trend to increase the number of cured patients and to decrease the non-cured patients in the ozone group, in comparison with the antibiotic group. Ozone therapy not only reduced the number of patients submitted to amputation, but also decreased the area to be amputated. The length of hospitalization decreased in patients treated with ozone with regard to the antibiotic group.

Conclusions: The results of this study showed that repeated administration of ozone in non-toxic doses played a role in the control of diabetes and its complications. It is important to emphasize the ozone treatment effect in the increase of SOD, as well as to consider it a molecular target in this syndrome. This is an interesting explanation, since it has been recognized anion superoxide radical as the link of four pathogenic pathways associated to micro and macro vascular complications in diabetes. The ozone treatment, in patients with diabetes type 2 suffering of neuroinfectious diabetic foot, improved glycemic control and prevented oxidative stress associated to diabetes mellitus and its complications, maintaining a cellular redox balance, in agreement with the excellent results obtained clinically in these patients. No side effects were observed. Ozone therapy could be a future alternative in the therapy of diabetes and its complications.

Keywords: Ozone therapy, diabetes, oxidative preconditioning, oxidative stress.

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15
OZONE THERAPY IN STETIC MEDICINE

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Peru.

Due to the well known biological effects of the ozone therapy, we use it in:

1. Aesthetic Medicine: ozonized water and oil; ozone sauna and hidrosauna;
2. Plastic Surgery: to avoid infections and enhance cicatrization. Also decreases pain and inflammation. We use local and system applications.
3. Aesthetic Surgery: idem
4. Burns: idem.
5. Hand surgery
6. Anti-Aging: to enhance chronic oxidative stress and brain and muscular fatigue.

We show several examples in our presentation.

16

ROLE OF THE OZONE THERAPY IN THE REDOZ BALANCE OF AUTIST CHILDREN. ONGOING INVESTIGATION PROJECT

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Centro de Salud Integral Dra. Yaisy Picrin. Santiago. Chile
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In this investigation we show a detailed description of the metabolic factors related to the redox unbalance present in autism, and a revision of previous papers that has made us develop an hypothesis about the possibility to use ozone in these patients.

The factors involved in autism are genetic and environmental; both produce a neural development disfunction. There are many references about redox unbalance in autism, due to decrease in the metilation path due to failures in the transmetilation and transulfuration and an increased toxicity for metals.

Most used treatments today are atypical antipsycotics, selective serotinine inhibitors and psycostimulants that have been associated with significat side effects, apart from nutritional modifications and supplements of vitamins and minerals. In our investigation project we have established a treatment protocol with systemic ozone therapy using rectal inssuflation , orthomolecular treatment and metilcobalamin to surpass the defective ways and chelation to eliminate the metals.

In the first child treated, the preliminary examinations showed hig level of Cesium, Plumb and Uranium, and also a moderate oxidative stress. After the first cycle of treatment we observed a decrease in the metal levels (with normalization) and in the oxidative stress. We observed a clinical improvement in language and family interaction.

This investigation has just started and, so, the results are very weak to see a definitive effect, but this preliminary findings are very encouraging to go on with this project of treating autism.

17

CLINICAL BEHAVIOUR OF CHILDREN WITH CEREBRAL PALSY, BEFORE OZONE THERAPY BY RECTAL INSUFFLATIONS

Benjamin Arenas-Falcon, Jose Luis Calunga-Fernandez, Silvia Menendez-Cepero, Carmen Vera-Yoshimoto, Olga Franco-Alvarado.

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Taking into account the biological properties of ozone, especially the well know action mechanism in the improvement of vascular endothelial restoration and the cerebral functions, is possible to think in the positive result to improve the quality of life in children with cerebral palsy. For all mentioned reasons it was decided to carry out a non-controlled clinical trial study at the International Clinic of Ozone Therapy in Havana, Cuba in the period from January of 2013 to January of 2014. The objective of the study was to determine the effectiveness of ozone therapy in the treatment of cerebral palsy. The sample was obtained from patient refereed to pediatric consultation at the Ozone Clinic. Inclusion and exclusion criteria were considered. The study group consisted of 43 patients from 1 to 8 years old, with hypoxic- ischemic causes of cerebral palsy. The evaluation criteria were: Evolution of motor disorder following the criteria of Gross Motor Function Classification System; modification of muscle tone using the modified Ashworth scale and the respond to treatment according to the modified O'Brien scale. The administration of ozone was by rectal insufflations at concentrations of: 15-18-20-25 mg/L, and volumes according to age group. Twenty sessions (representing 1 cycle) are indicated every three months to reach 4 cycles in the period of one year. The patients were evaluated following the mentioned clinical scales at the end of each cycle. The best answer to treatment was obtained in the group from 1 to 4 years old. The results at the end of treatment were significant in all analyzed variables; 65% of the group improved the motor disorder, the group of children below 4 years old had the better answer regarding muscle tone. The respond to treatment following the family criteria was of very significant improved in 70% of the study group (remarked improvement in tone and muscle function). No adverse effects were reported during the study.

Keywords: Ozone therapy, cerebral palsy, rectal insufflations, tone and muscle functions, O'Brien scale.

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OZONE THERAPY AND POSTUROLOGY

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Some of the pitfalls of the ozone treatment of spinal pathology are due to mistaken diagnoses. It is very important to study the postural aspect of the joints involved in the problem in order to detect possible postural defects that can lead to a pitfall and are easy to solve with simple orthopedic measures.

We show in these presentation some examples of postural disorders that can be treated easily with inlays and other devices and not with ozone therapy, in spite of having problems that could make us indicate ozone injections.

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OZONE THERAPY IN THE ISCHEMIC BRAIN STROKE PENUMBRA

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Introduction: The aim of this paper is analyze the results of treating brain ischemic stroke (BIS) (acute or chronic) with ozone therapy during the past 7 years.

Patients and methods: We included all patients treated with systemic ozone therapy using great autohemotherapy, after suffering a (BIS), whether supra or infratentorial. We evaluated the motor function, Barthel index and quality of life post-brain stroke. Regarding imaging, we used functional MRI (diffusion-perfusion).

Results: In acute BIS, 75% improved the motor function and the mental status; the ICP decreased in less than 72 hours and the good results were related with a soon treatment. No BIS turned into hemorragic. In MRI all showed a wall-edema, not observed in patients not treated with ozone.

In chronic BIS, Barthel index and mental status improved globally.

Conclusions: In patients with BIS, acute or chronic, the use of systemic ozone therapy seems useful. In acute BIS, the sooner the better result. In chronic BIS, there is a global improvement in patients that usually don't improve anymore with standard treatments.

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OZONE THERAPY IN SPORT MEDICINE

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Sports medicine is the medical specialty that studies the effects of exercise, sport and physical activity in the human body and its relation to the speed of recovery from injuries, prevention and improvement of physical performance of athletes or sportsmen.

The practice of moderate and intense exercise generates oxygen consumption is 10-15 times higher than at rest and increased muscular level reaches up to 100 to 200 times ; The body produces an increased free radical production due to hypoxia suffered in multiple tissues and systems that will produce an increase in lactic acid production, increased lipid peroxidation related substances, increase of catecholamines, self- hemoglobin oxidation , etc.

These reactions cause a physiological oxidative stress, because energy needs are covered by oxidative phosphorylation that generates energy and, secondary, reactive oxygen species (ROS). ROS exert a role in the effectiveness of muscle contraction, including promoting tissue remodeling and constituting a natural stimulus that leads to an improvement of antioxidant defenses, provided there is a good antioxidant system that reacts properly.

In order to maintain in perfect condition the antioxidant system, ozone therapy opens the possibility of an oxidative pre-conditioning in athletes to improve their skills and physical performance, by having an optimal physiological response to oxidative stress induced by the exercise.

21
EXPERIENCE IN PAIN THERAPY AND OZONE THERAPY UNIT OF THE SOLIDARITY METROPOLITAN SYSTEM (SISOL)

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The Solidarity Metropolitan System (SISOL) Is s a public agency of the Metropolitan Municipality of Lima, Sisol manages 20 hospitals in Lima city and 7 hospitals in provinces.

In1998 started working in Hospital Solidarity, in the center of town, the Pain and Ozone Therapy Unit.

From 1998 until August 2015, 9.392 patients have been treated with ozone therapy having made 27.828 attentions, fifty-four percent of treated

patients were women and fourty-six were men; in terms of the average age of the patients treated, 50 percent had between 45 and 70 years old.

The most common diseases treated with chronic pain were: back pain (43.6%), gonarthrosis (14.62%), neck pain (8.53%) and coxarthrosis (7.82%)

In our experience, we considered these treatment protocols as the most appropriate to ease the pain of our patients:

Lumbar hernia discal

- 20 paravertebral ozone injections
- 10 cc volume
- concentration of 20-25 mcg/mL

50 percent of patients resolve the pain between the 7th to 10th session

Gonarthrosis

- 15 - 20 intra-articular injection
- 10 cc volume
- concentration 20-25 mcg/mL

50 percent of patients resolve the pain of the tenth session

Coxarthrosis

- 15 - 20 intra-articular injection
- 15 – 20 cc volume
- concentration 20-25 mcg/mL

50 percent of patients resolve the pain of the tenth session

When neuropathic pain is present, we include major autohemotherapy once or twice per week, up to 8 sessions.

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THE STUDY OF OZONETHERAPY EFFECTS IN LUMBO-SACRAL PAIN DISORDERS

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Based on medical data on our own clinical observation upon a consistent lot of patients we have describe the beneficial effect of ozonetherapy on different cases of acute lumbago and sciatica, developing either a retrospective study or a prospective longitudinal study with patients suffering from L4-L5-S1 radiculopathy, post neurosurgical painful sequel (lumbar disc herniation) and non specific low-back pain.

The patients were evaluated upon a number of clinical and functional parameters such as: pain, sensitive troubles, physical disabilities, disabilities, use of medical drugs and the quality of life, according to the requests of Evidence based Medicine.

The results of these studies confirm the beneficial either on the pain or on some disabilities, as well as the reducing of drug use after three-four week of ozonetherapy.

A continuous monitoring of all these patients for a longer period is mandatory, for the aim of better evolution of the lasting effects and of possible falls.

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OZONE THERAPY IN THE CHRONIC SPINE PATHOLOGY

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Chronic spine pathology is a very common disease after the sixties. 90% of the radiological examinations in these patients show narrowing of the lumbar spinal canal, facet joint osteoarthritis, flavum ligament hypertrophy, spondylolisthesis, multiple disc degeneration, bone spurs and/or scoliosis.

These findings can be painful and maybe associated with radiculopathy.

The symptomatic patients can be advised to undergo a surgical decompression and stabilization; however, this is impossible in many of them due to surgery contraindications or personal preferences.

In these situations, minimal invasive procedures are very valuable for the surgeon.

We have treated with ozone injections, both paravertebral and/or intradiscal these kind of patients in the last 10 years, in order to improve pain and quality of life. We show our results along these years, that have been very positive regarding relief of pain, improve in walking and the chance to repeat the treatment if needed. We think it is a very valuable tool for these patients when surgery is disregarded.

OCTOBER 23TH

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OZONE INJECTIONS IN FOOT AND ANKLE INJURIES

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We study the most common, both conservative foot and ankle pathologies and their treatment that successfully use medical ozone, such as surgical.

ANKLE PATHOLOGIES

The most frequent pathologies of the ankle are:

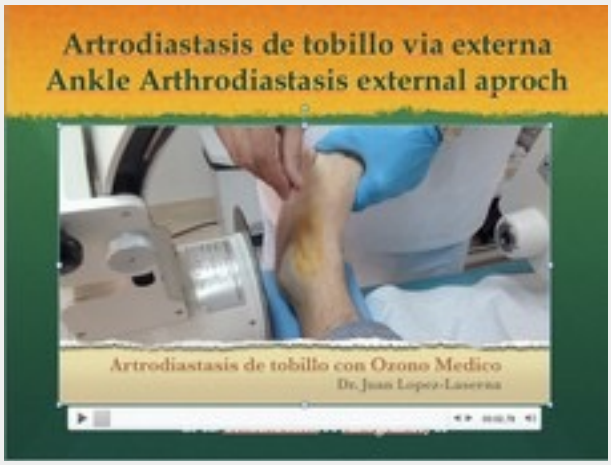
- osteoarthritis
- rheumatic arthritis
- Osteocontritis.
- Posterior impingement syndrome
- Impingement syndrome above
- ankle sprains.

Ankle osteoarthritis

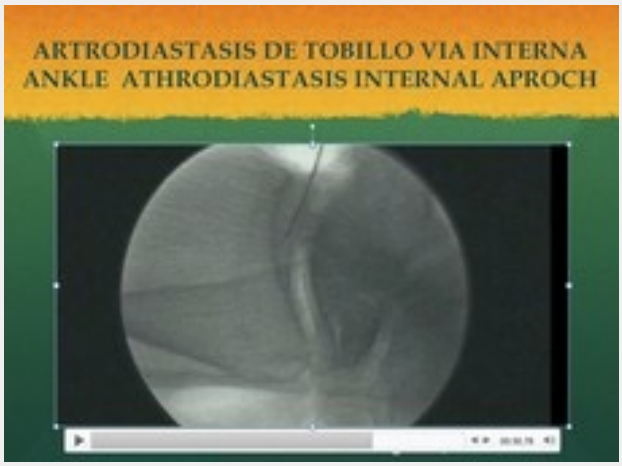
- Uncommon. The primary form is rare and usually secondary to fractures, repeated trauma, rheumatic processes, etc.
- Mechanical pain to flexo brand extension affectation to tibiotalar level
- The pain supination (while walking on uneven ground) usually marks involvement of the subtalar joint.

Ankle infiltrations can do for the internal or external via, use the tracks of previous approach of arthroscopy.

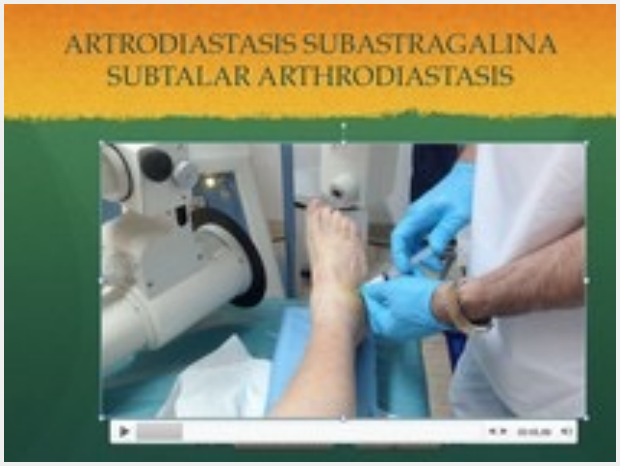
Ankle Arthrodiastasis extenal aproch.



Ankle Arthrodiastasis internal aproch.



Subtalar arthrodiastasis



SUBTALAR JOINT PATHOLOGIES

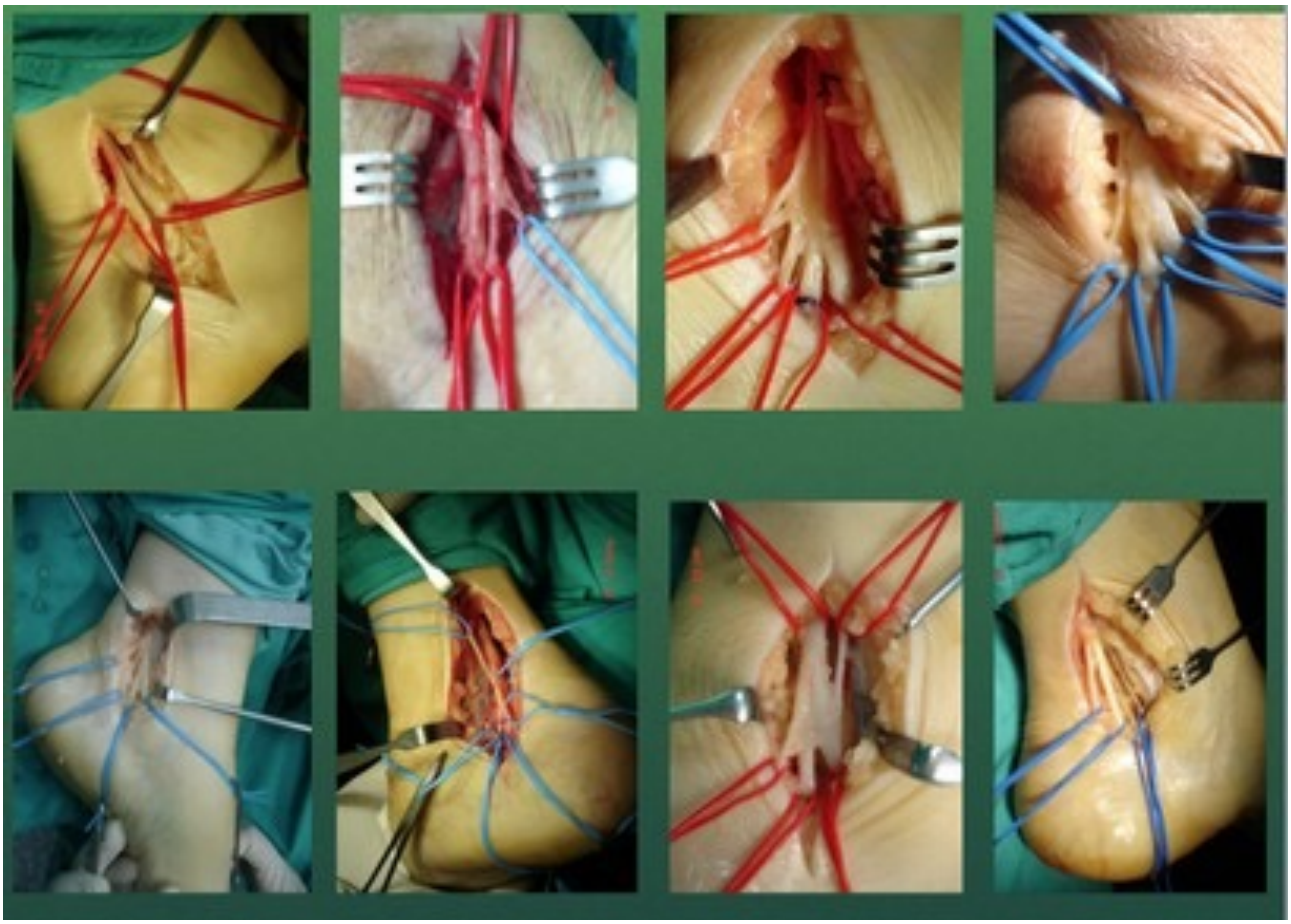
1. Subtalar arthrosis.
2. Breast pathologies tarsus (tarsal sinus syndrome)
3. Syndrome posterior impingement.
4. Arthritis.

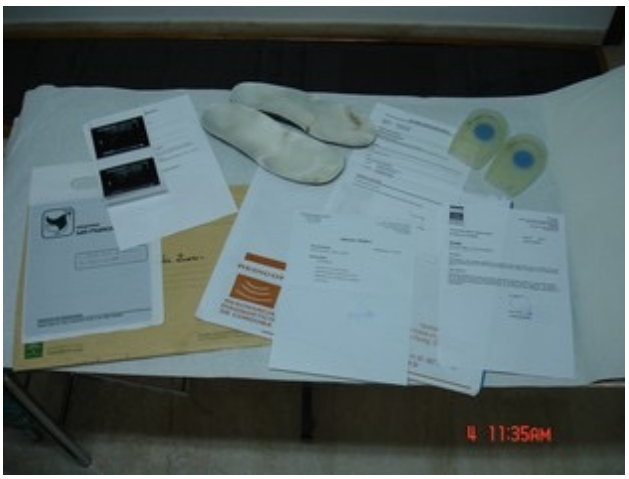
Posterior tarsal tunnel syndrome (TTS)

The TTS is an extrinsic or intrinsic foot neuropathy secondary to compression of the tibial nerve (TN) or one of its terminal branches (Plantar medial,Plantar side, Medial calcaneus branch and Baxter's nerve) in the tarsal tunnel or Richet's channel.

There are a large number of anatomical variations tibial nerve.

We think about a TTS when a patient refers pain in the talus. He usually arrives at our office with many





complementary examinations, several treatments but no improvement.

Symptomatology:

1. Burning pain in the foot: It is the main symptom, and its intensity, pace, location and irradiation, vary according to the different clinical forms
2. Paresthesias: Feeling clumsy gait, tingling, pricking or burning. Similarly the characteristics thereof change according to the clinical forms.

Exploration:

Valleix phenomenon.
Tinel sign.
Mandel test.
The dorsiflexion-eversion test.
Windlass test.

Clinical forms:

Posttraumatic. Biomechanics *(Frequent foot flat-valgus, very common in functional hallux limitus, very fecunte associated with hallux rígidus, in this group we can include many of the cases described as idiopathic)*. Neuritis of pronation. Trophic. Tumor y Topographic.

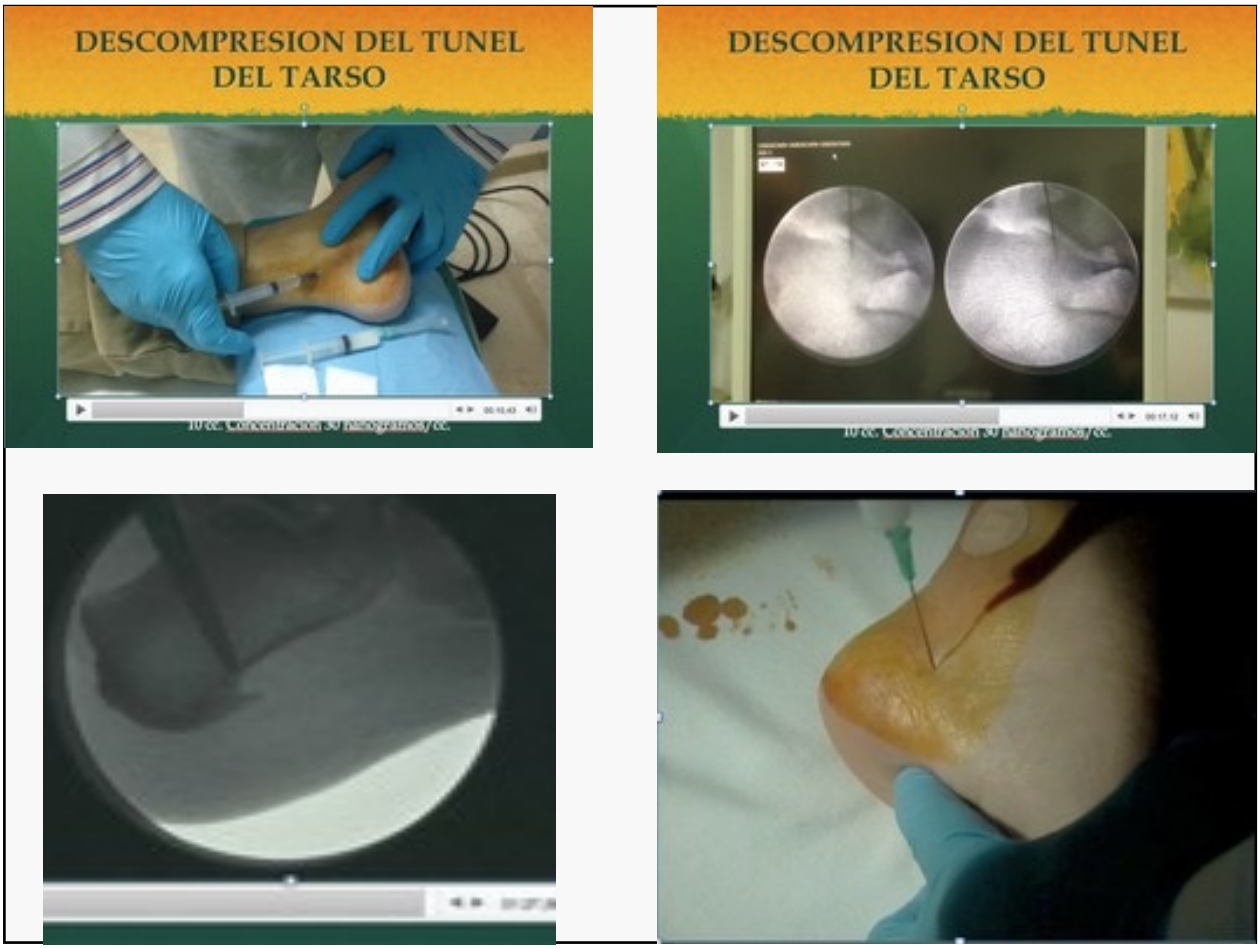
Treatment:

Conservative

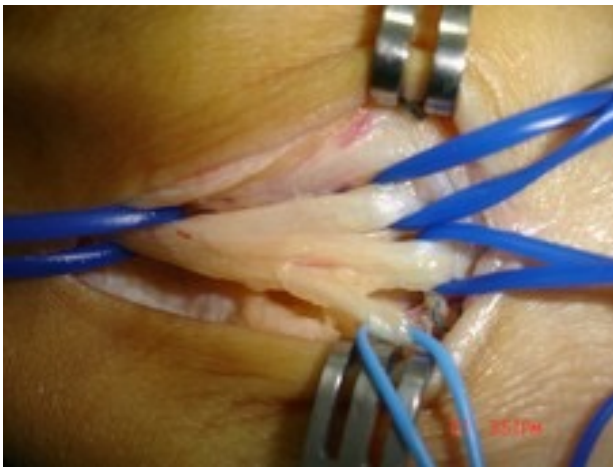
- Antineuritic, NSAIDs, etc.
- Orthopedic measures
- Physiotherapy
- Local infiltrations of O2-O3

Surgical

ANTERIOR TARSAL TUNNEL SYNDROME (ATTS)



ATTS is an extrinsic or intrinsic foot neuropathy



secondary to compression of the deep peroneal nerve or some of its branches under the extensor retinaculum and the extensor finger

Etiopathogeny

Biomechanics: Cavus Foot.
Traumatic: Fractures, microtrauma by tight shoes (ballet).
Rheumatic; Rheumatoid arthritis.
Degenerative: Impigement talus, talo-navicular bone spur.
Iatrogenic: Ankle surgery.

Sintomatology:

- The patient complains of constant pain and numbness that radiates from the back of the foot to the first and second toe.
- Weakness of the extension of the first finger.
- Pain with high-heeled shoes.
- Severe pain at night in some more severe cases.
- Hallux loss of mobility and strength of his short extensor.
- Paresthesia and dysesthesia in the first and second toes.
- Tinel + the deep peroneal nerve at the anterior tarsal tunnel.

Treatment:

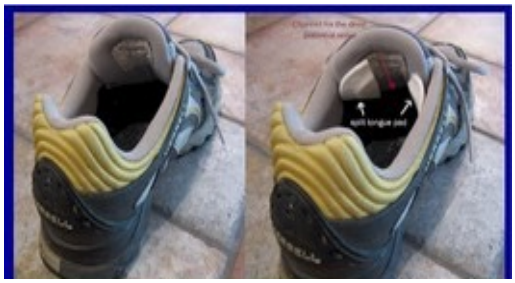
Conservative

- Antineuríticos, NSAIDs, etc.
- Orthopedic measures
- Physiotherapy
- Local infiltration with corticosteroids and O2O3.

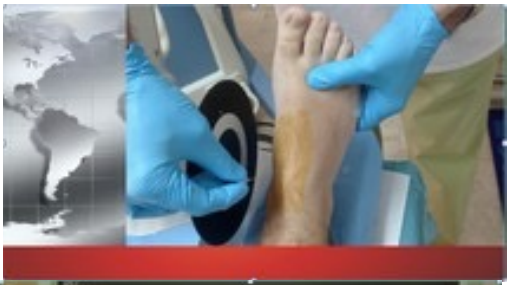
Surgical.

Conclusions

Conservative

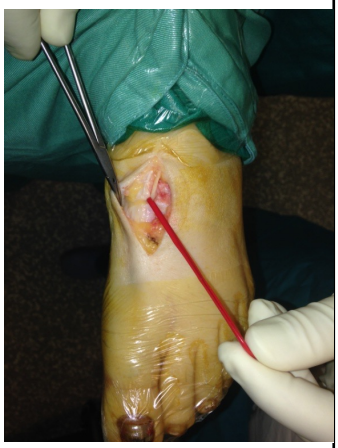


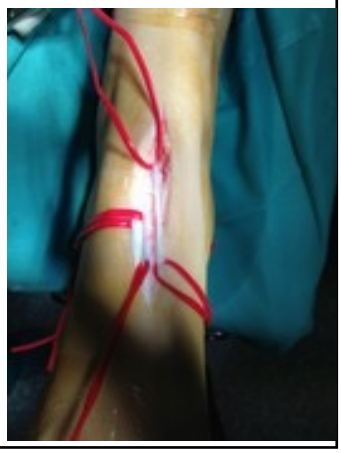
Orthopedic measures



Local infiltration with corticos-teroids and O_2O_3

Surgical





William James (January 11, 1842 – August 26, 1910) was an American philosopher and psychologist who was also trained as a physician :

Every new theory passes through three phases:

1. It is attacked and declared absurd.
2. Then it is admitted that it is true and obvious, but insignificant.
3. To the end it is recognized the real importance and its detractors demand the honor to have discovered it.

Medical ozone therapy gives good results in the treatment of pathologies of the ankle and foot.
In tarsal tunnel syndrome have cures 80% of cases with three injections, we also have good results with the surgical treatment.

The ankle osteoarthritis improve with medical ozone infiltrations by their arthrodiastasis effect, allowing us to defer surgery to year.
We have not had any infectious complication or skin with Medical Ozone infiltrations.

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ARTHRODIASTASIS AND NERVE ENTRAPMENT DECOMPRESSION WITH OZONE INJECTIONS

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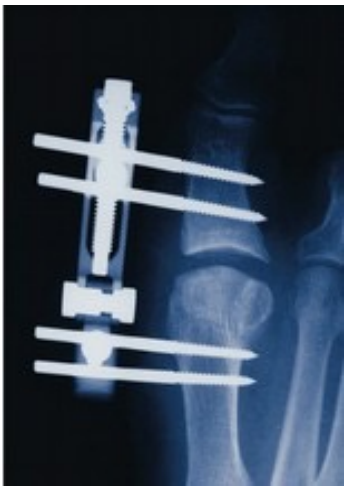
Since successfully we employ 1,999 medical ozone by infiltration osteotarticulares conditions for their antioxidant effects, anti-inflammatory, etc.

We define arthrodiastasis:

- Distraction is a degenerative joint pathologies to improve it.
- Improves joint mobility.
- Decreases pain.
- This method described as an alternative to arthrodesis or prosthesis in ankle joint.



The arthrodiastasis external fixator has been applied in pathologies ankle, knee, Perthes disease, etc. Alone or associated with arthroscopic synovectomy and cleaning. The joint distraction is a technique commonly used by European surgeons for handling ankle osteoarthritis. European orthopedic surgical literature provides examples of results that show how this procedure increases the range of motion and decrease the symptoms of pain when walking.

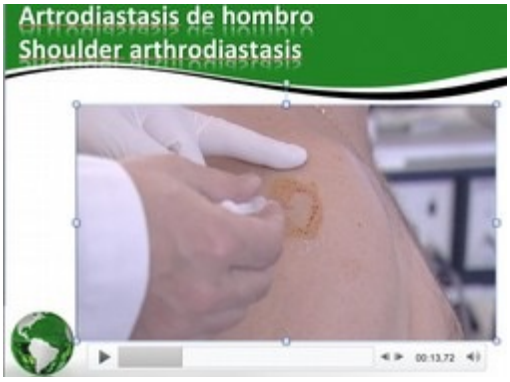
Arthrodiastasis with medical ozone

- The infiltration of articulation with Medical Ozone produces arthrodiastasis effect.
- This depends on the type of joint and the amount of gas We breathed.

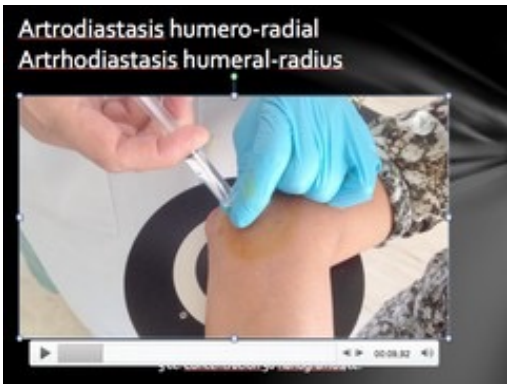
In this paper we will share our experience in the treatment of osteoarthritis with Medical Ozone infiltrations, with images showing the arthrodiastasis effect, especially in tight joints such as the ankle, the metatarsophalangeal first, radio-humeral, etc.

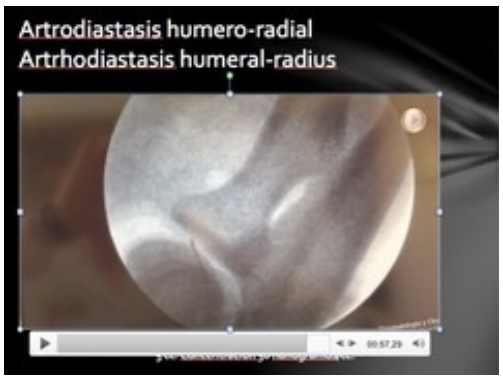
Acromioclavicular artrhodiastasis

Shoulder arthrodiastasis



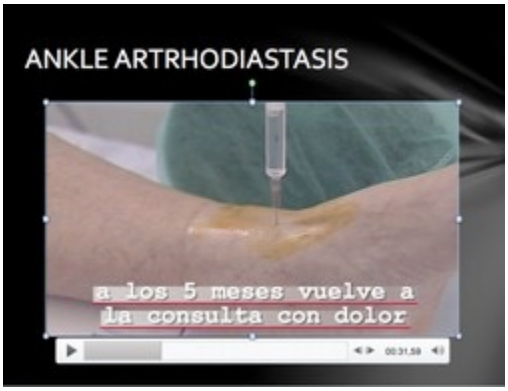
Artrhodiastasis humeral-radius

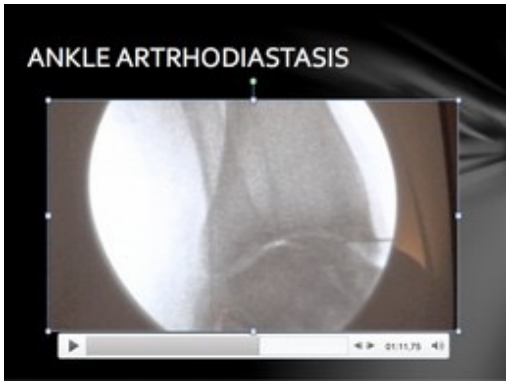




Rizartrhosis Artrhodiastasis

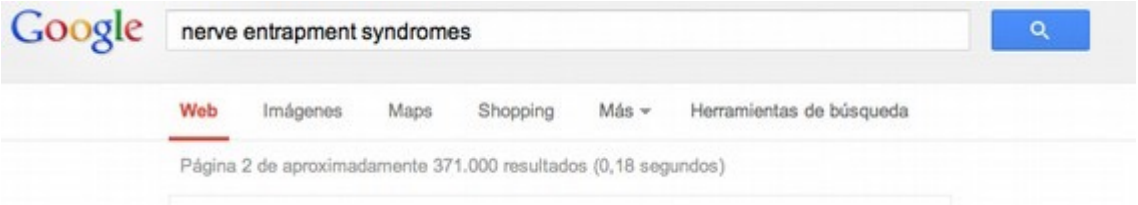
Ankle Artrhodiastasis





CANALICULAR DESCOMPRESSION

The canalicular syndromes include neurological manifestations assembly shown by compression of a nerve in a channel or anatomical gorge. The most common cause is the mismatch between the mainland (channel or gorge) and the content (nerve).



nerve	place	usually referred to as
common peroneal	fibular neck	peroneal nerve compression
tibial	tarsal tunnel	tarsal tunnel syndrome
lateral cutaneous nerve of thigh	inguinal ligament	meralgia paraesthetica
sciatic	piriformis	piriformis syndrome [not always due to entrapment]
iliohypogastric	lower abdomen	iliohypogastric nerve entrapment
obturator	obturator canal	obturator nerve entrapment
pudendal	pelvis	pudendal nerve entrapment
abdominal cutaneous nerves	abdominal wall	abdominal cutaneous nerve entrapment syndrome

nerve	place	usually referred to as
median	carpal tunnel	carpal tunnel syndrome
median (anterior interosseous)	proximal forearm	anterior interosseous syndrome
median	pronator teres	pronator teres syndrome
median	ligament of Struthers	ligament of Struthers syndrome
ulnar	cubital tunnel	cubital tunnel syndrome
ulnar	Guyon's canal	Guyon's canal syndrome
radial	axilla	radial nerve compression
radial	spiral groove	radial nerve compression
radial (posterior interosseous)	proximal forearm	posterior interosseous nerve entrapment
radial (superficial radial)	distal forearm	Wartenberg's Syndrome
suprascapular	suprascapular notch	suprascapular nerve entrapment

The term open decompression is used in the treatment of these syndromes.

Infiltration with medical ozone produces a closed decompression effect canalicular syndromes. This explains coupled with improved anti-inflammatory effect of these pathologies.

We study the most common canalicular syndrome, its diagnosis and conservative treatment with ozone both medical and surgical.

Fhrose arcade decompression

Compression terminal motor branch of the radial nerve: posterior interosseous nerve in the short supinator tunnel fibroosseous

Closed carpal tunnel decompression

It is an entrapment of the median nerve in the carpal canal.

It is the most common entrapment neuropathy, 3% population.

Entrea more common in women 40 to 60 years.

Exploration:

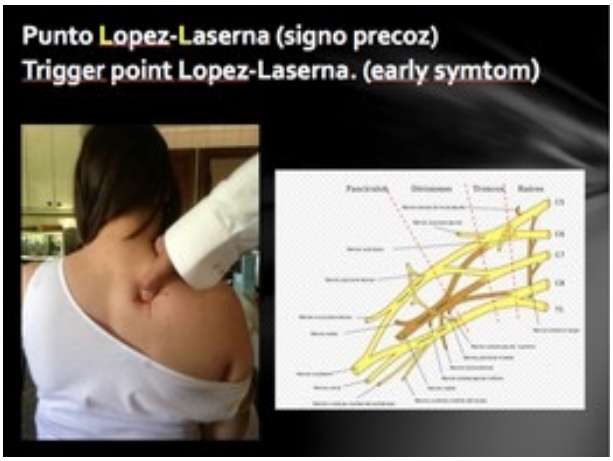
Phalen sign: The palmar flexion of the wrist at 90 degrees for one minute the crawl space is reduced, triggering paresthesias in the hand when there is studied prior commitment or narrowness of it.

Tinel sign: percute annular ligament of the wrist with a reflex hammer. If there is channel commitment a cramping sensation on the second and third fingers (innervated by the n. Medium) occurs.

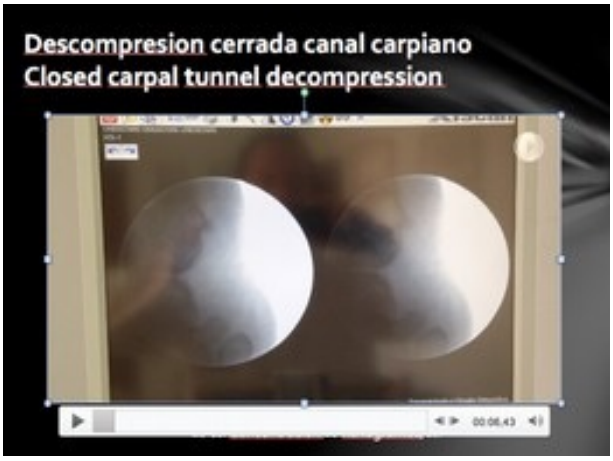
Circle sign: When the patient tries to oppose the first finger to the second (running the figure of a circle, or the international sign of OK) is not able to flex correctly you phalanges drawing a "clip" or "duckbill" in instead of a circle.

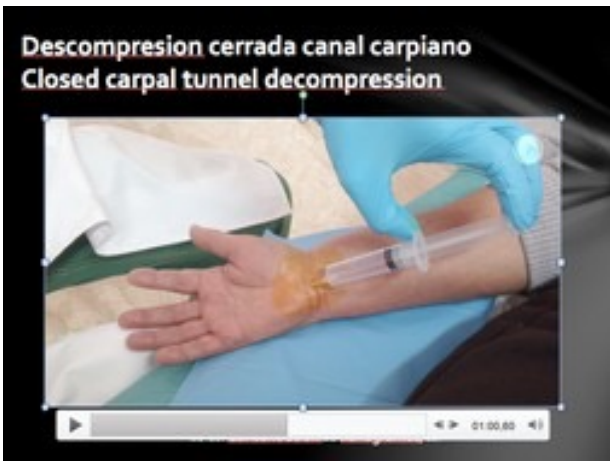
Durkan sign: The explorer presses with the thumb the palm side of the wrist, in the area between the thenar and hypothenar eminences (area of greatest narrowing of the canal), triggering the symptoms if there narrowness of Step.3

Pyse-Phillips sign: Disappearance of the annoyances with the elevation of the affected limb.



Trigger point Lopez-Laserna





Closed decompression of Morton´s neuroma

At the foot and ankle conference we will see other canalicular syndromes of the foot and ankle.

Conclusions

Middle Ozone has a mechanical effect of diastasis in closed joints, nerve and tendon passes on its way through the retinacula synovial sheaths.

This is in addition to its other effects on the improvement of the musculoskeletal pathologies we treat.

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OZONE THERAPY FOR CHONDROMALACIA PATELLA

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Introduction: Chondromalacia patella is a common cause of pain in patients between 15 and 50 year, frequently woman. If it is not corrected it evolves into knee osteoarthritis.

Usually, chondromalacia is due to abnormalities in the mechanics of the patello-femoral joint. Without solving theses external problems, chondromalacia problem cannot be solved.

We have references about ozone injections in knee osteoarthritis, but no paper about this topic.

Study Desing: This is an open prospective study that started in October-2008, not yet finished: We compile the preliminary results of patients that were treated until September 2014.

Inclusion criteria were:

- Patello-femoral pain for more than 2 months
- MRI diagnose of chondromalacia and grade
- Residual pain after correcting mechanical factors
- Informed consent

Exclusion criteria were:

- Previous surgery or indication for surgery due to severe misalignment or joint defects
- Osteoarthritis in plain XRay image
- Rheumatic pathology
- Treatment with NSAIDs

We used WOMAC questionnaire in the first day of the treatment and 1, 2, 3, 6 and 12 months after.

Ozone Technique

All patients were injected intrarticular under the patella with strict asepsy and the knee in extension position; once a week, using a siliconized plastic syringe and a 27G x 30 mm needle; at least during three weeks with a maximum of six weeks. Dosage was 15 mL at 20 mcg/mL concentration. Some patients needed periarticular injections for concurrent pain of anserine, patellar or cuadricipital tendons; we used 5 mL at 20 mcg/mL concentration for each painful point.

Results: We treated 47 knees of 41 patients (6 bilaterally). Only 8 knees (17%) did not improve significantly (WOMAC improvement of 25%). No patient relapsed in the first year. Periarticular injections, age, gender or chondromalacia grade were not related with the result.

Discussion: We have not found papers on this topic, so we cannot compare our findings. Comparing with knee osteoarthritis, our results are slightly better.

Conclusions: According to WOMAC scales, 83% of the patients treated has a good response that was stable at least 12 months.

It is mandatory to treat first the mechanical factors that produce chondromalacia patella.

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KNEE OSTOARTHRITIS. OZONE VS. OZONE + PRP

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Introduction: The use of ozone in knee osteoarthritis is clearly justified by the references. Other papers support the use of platelet rich plasma (PRP) to treat this pathology. The combination of both techniques could be potentially positive, so we design this study to test it.

Study Desing: We did a two cohort comparative study. The first group (only ozone) was treated from 2002 to 2010 and had been compiled in a prospective study already published.

We designed a second group as a prospective study starting in 2010 and not yet finished. We show here preliminary results. To make both groups comparable, we used the same inclusion/exclusion criteria and used the same valutation scale, WOMAC. The patients received ozone and PRP in alternate weeks.

Ozone Technique

All patients received an injection under the patella in strict asepsy with the knee in extended position, once each two weeks, with a siliconized plastic syringe and a 27G x 30 mm, up to 4 times. Dosage was 15 mL at 20 mcg/mL concentration. Some patients needed periarticular injections for concurrent pain of anserine, patellar or cuadricipital tendons; we used 5 mL at 20 mcg/mL concentration for each painful point.

PRP Techique

We used DISPRAS® technique from PROTEAL® to obtain PRP. The intermediate weeks between the ozone injections, we did a 6 mL PRP injection also under the patella bone, 3 weeks.

Results: We have treated in the new cohort 151 knees. In the ozone cohort, we treated 225 knees. Good results (WOMAC improvement over 25%) were 94% versus 80,5% in the ozone cohort. Global results comparision showed better results in the new cohort, but without statistical significance. Relapse and complication rates were similar in both groups.

Discussion: PRP for knee osteoarthritis is still under discussion:

- What exactly is PRP
- Volume of injection
- Intrarticular or periarticular

In Spain, DISPRAS® technique is approved by the Health Ministry to treat knee osteoarthritis.

We have get better results with ozone+PRP cohort, but without statistical significance; we think that the different size of the sample can justify this fact.

Conclusions: The combined treatment with ozone and PRP seems to be better than ozone alone, after one year follow up. The difference is important but without statistical significance.

Good results group in both cohorts showed significant differences in favor of ozone+PRP cohort.

Complications were similar for both treatments.

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ANATOMICAL AND RADIOLOGICAL CONSIDERATIONS FOR THE TREATMENT OF LUMBAR RADICULOPATHY. PERSONAL EXPERIENCE

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We describe the pathophysiology of disc herniation and the anatomical details that are related with this problem. We think this knowledge is basic to indicate the best treatment.

The author details his personal experience in an observational retrospective study on 153 patients with cervical, thoracic and lumbar disc herniation treated with ozone injections since 2003 with a combination of intradiscal and paravertebral infiltrations. 71 were asimptomatic, 15% are better and do not need any treatment. The rest needed other treatment. Only 4 relapses were registered during 5 years. We did not registered any side effect that needed any treatment. We think that ozone therapy is an extraordinary method to treat disc herniation.

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OZONE THERAPY IN THE CHRONIC INFLAMMATION OF THE DEGENERATIVE DISC DISEASE

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Introduction: Back pain is one of the most common chronic diseases and has a lot of personal, social and economical consequences. Most frequent cause is the disc degeneration. This degeneration is a multifactorial process, involving mechanical, genetic and biological factors.

In the degenerated disc there is decrease in water and proteoglycans in the nucleus pulposus that leads to the degeneration process. The exact molecular changes are still unknown, but it has been proved that a mechanical stress induces a release of inflammatory mediators like nitric oxide (NO), matrix metalloproteinases (MMPs), Tumoral Nechrosis Factor α (TNF α) and interleukines.

Until now, in the IAOT, we have studied the results of the treatment of the accute LDH. However, in this paper we have compiled the results of patients with crhonic degenerative disc disease (CDD) treated with ozone therapy, until February 2012, before we started to use platelet rich plasma in order to improve our results.

One of the main mechanism of action of the ozone in this pathology is the activation of the celular antioxidation system that induces a decrease in the mediators of this chronic inflammation.

Patients and methods: We included patients with lumbar (L4-5-S1) degeneration confirmed with MRI. All patients fulfilled the treatment protocol of 10 paravertebral lumbar injections and 2 intradiscal injections in each level affected. We checked the VAS. We considered a successful situation an improvement of 4 or more points in VAS.

Results: Until February 2012, 63% of the treated patients showed had a positive result (improve in VAS of 4 or more points) at the end of the protocol of 10 paravertebral injections and 2 intradiscal injections.

Conclusions: We can conclude that ozone therapy is a first line treatment for the patient with CDD due to the positive results due to the modulation of the inflammation.

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OZONE OXIDATIVE POST-CONDITIONING REDUCES SLEEP DISORDERS AND OXIDATIVE PROTEIN DAMAGE IN PATIENTS WITH DISC HERNIA

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Introduction/Objectives: Sleep disorders is the medical disordes of the sleep, it can be caused by a chronic lumbar or cervical pain from disk herniation. Sleep disorders serious enough to interfere with normal physical, mental social and emotional functioning. In the other hand inflammation in disc hernia (DH) has been recognized and it is a well-known process mediated by loss of the cellular redox balance, only a few studies about the impact of chronic oxidative stress on this neurological disorder have been made. Ozone therapy has been widely used with clinical efficacy in DH. This work aimed at characterizing the insomnia degree and the systemic redox status of patients with low back pain and neck pain as well as studying if ozone oxidative post-conditioning modified the pathological oxidative stress and protected against oxidative protein damage and if there is any relationship between oxidative changes and pain in both DH.

Methods: Disorders sleep was evaluation in 160 patients with diagnosis of DH by Oviedo Scale, this type of evaluation is mainly subjective and includes quantitative aspects such as sleep duration, number of awakenings, latency time, and qualitative aspects such as rest sensation, mood and oneiric content. Patients Redox status of 53 patients with diagnosis of DH (from of 160 patients) by computerized axial tomography, nuclear magnetic resonance, and clinical evaluations was studied. Ozone was administered by paravertebral way and rectal inssuflation . After ozone treatment, plasmatic levels of antioxidant/ pro-oxidant markers, pain, and life quality disability parameters were evaluated. The Oviedo Scale was made before and after the Ozone therapy Treatment.

Results: One hundred percent of patients showed a severe oxidative stress. Major changes in superoxide dismutase activity, total hydroperoxides, advanced oxidation protein products, fructolysine content, and

malondialdehyde were observed. After ozone oxidative post-conditioning, there was a re-establishment of patients' cellular redox balance as well as a decrease in pain in both DH. A relationship between indicators of oxidative protein damage and pain was demonstrated. Respect to Oviedo Scale for the sleep disorders, Ozone treatment reduce the insomnia degree, increase the sleep duration and increase the state of mood of the patients.

Conclusions: Ozone therapy reduce the Sleep disorders in patients with chronic lumbar and cervical pain. Ozone therapy protected against oxidation of proteins and reduced the pain. Relationship between markers of oxidative protein damage, disability parameters, and pain suggests the role of oxidative stress in the pathological processes involved in DH.

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TREATMENT FOR RADICULAR COMPRESSION. EXPERIENCE OF 705 CASES IN BOLIVIA

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Keywords: Radicular compression, ozone therapy, nucleolysis, ozone

Introduction: This study reports the experience in Bolivia from August 2004 to August 2014. Were treated 705 patients with herniated discs in cervical, thoracic and lumbar level

Patients and Methods: Were treated 705 patients with radicular compression at cervical, thoracic and lumbar level 326 males and 236 females. Firstly, we performed intradiscal injections of ozone at 30 mcg/mL followed by 15 or 20 paravertebral injections at 20 mcg/mL.

Results: Among the 705 patients with radicular compression were observed that sensory and motor dysfunction were completely abolished in 465 patients (66%) improved in 149 patients (21%) and with poor results and the dysfunction remained unchanged in 91 patients 13% some of them underwent surgical treatment. As a whole 614 patients obtained excellent and good results 87%.

Conclusion: With the treatment of ozone therapy is possible to obtain excellent and good results in 87 % of the cases. Ozone is a useful alternative the effectiveness using this minimal invasive method can avoid complications like fail back syndrome

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INTRADISCAL VERSUS PERIDISCAL OZONE INJECTIONS

Alan Ayme
Cuba

We have compared our own results in lumbar disc herniation treated with ozone injections paravertebral, intradiscal and peridual (transforaminal, interlaminar). No differences were globally found comparing the three groups, neither in results nor in complications or relapses.

Due to the references that evaluate the possible negative effect of puncturing the disc and our results, we think that only massive hernia with severe radiculopathy should be considered for an intradiscal injection. The rest can be treated with peridural or paravertebral injections. The first method is quicker in achieving results.

Our results are supported by other publications.

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OZONETHERAPY IN FAIL BACK SURGERY SYNDROME

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Venezuela

We show in this presentation several examples of fail back surgery syndrome with posterior arthrodesis and internal fixation that improved after ostesynthesis removal and paravertebral ozone injections.

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OZONE THERAPY TO RESOLVE DISC SPACE INFECTION SPONDYLODISCITIS

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Keywords: Spondylodiscitis, lumbar puncture, ozone therapy

Summary: We describe twenty eight cases of disc space infection, spondylodiscitis treated by OZONE THERAPY. One case a spontaneous spondylodiscitis and the other two cases are caused as a postoperative complication. The predominant clinical feature was low back pain. The Ozone treatment produced very good results.

Introduction: In 1934, Mixter and Barr presented their classic paper on intervertebral disc herniation. Since then, laminectomies have been performed with increasing frequency for the treatment of this

condition. Inevitable complications of such surgical treatment have been recognized and they include disc space infection known as spondylodiscitis. However, the first description of intervertebral disc space infections did not come from surgical patients. Ghormley and colleagues in 1940 presented 20 cases of spontaneous disc space infection and differentiated this condition as a clinical separate entity, different from other pathologies, particularly vertebral osteomyelitis It was not until 1953, when Turbull presented a series of three patients in whom post operative disc space infection became a recognized clinical entity The infection of the intervertebral space is frequently caused by disc surgical interventions, but there are other causes like spinal puncture, spinal catheterism, alcoholism, drugs, HIV and others, which can cause the disease

Incidence: The true incidence of postoperative disc infection is difficult to determine because of several reasons. The condition can be mild and self limited and it resolves spontaneously; the patient may be misdiagnosed or labeled as functionally disabled or psychoneurotic; some patients operated on at one institution go to another for assessment and treatment of the disc space infection.

Pathophysiology: The disc annulus is composed of elastic fibrous layers, which surround the semi liquid gelatinous nucleus and they provide the disc with its inherent strength. The fluid properties of the nucleus pulpous provide incompressibility and shock-absorbing potential. The plate of hyaline cartilage at each end of the disc, from which the annulus arises, constitutes the interface between the bony vertebra and the rest of the disc, and acts as a barrier between one vertebra with the contiguous one This plate and the epiphyseal ring of the vertebra are in intimate association during embryological development, and are analogous to the epiphysis of a long bone. The disc itself, previous to its later avascular state, is the most distant element supplied by the intersegmental artery.

Initially, the disc material is vascularized by small arteries from the cartilaginous plate. Between childhood and the third decade these vessels gradually disappear, and the disc becomes totally avascular. These changes are the basis for the intervertebral disc space infections, whether they are haematogenous or post-operative.

Based on these premises, childhood disc infection is thought to be of haematogenous origin, with bacteria spreading directly to the intervertebral disc through the vessels from the epiphyseal ring and cartilaginous plate. Adult hematogenous infection, on the other hand, is a hematogenous infection, not of the disc substance itself, but of the epiphyseal vertebral ring plate region.

Postoperative disc space infections occur by direct inoculation of microorganisms into the disc space during a surgical procedure. The surgeon performs the operation on an avascular structure and leaves behind small pieces of degenerated disc, necrotic tissue, and hematomas of various sizes, all these elements strongly predispose to an eventual infection. In spite of the use of a scrupulous sterile technique, occasionally organisms might be introduced in most operations, in the “locus minoris resistentiae”, as Pilgaard names these structures. These types of infections have been reported after lumbar puncture myelography paravertebral injections, discography and recently, in several cases, after percutaneous discectomy.

Clinical Symptoms: The postoperative disc space infection has a characteristic clinical presentation.

The most common presenting symptom is severe back pain that can radiate towards the leg, buttock, groin or testis, mimicking a root compression syndrome; or into the perineum or abdomen. The pain can appear at any time from five days to three months after an uneventful operation; more than 85% patients suffer excruciating paravertebral muscle spasms which are relieved only by immobilization.

The appearance of the operative incision does not usually indicate an underlying infection. Although fever is not a uniform finding, it is present in 30% of patients.

Diagnosis: A post-operative disc space infection can be suspected on the basis of very few typical findings: severe low back pain with severe paravertebral muscle spam, elevated values of ESR; the findings in CT scan are very useful, they show early narrowing and destruction of the disc space and erosive changes in the vertebral end plates. CT scan also demonstrates any soft tissue involvement or paravertebral abscess.

The procedure of choice for diagnosing a disc space infection is MRI; it shows disc space changes consistent with an infection, as early as five days after operation. These changes include a reduction in signal intensity on T1-weighted images and an increase in signal intensity on T2-weighted images from the involved disc, plus a blurring of the disc margin on the T1-weighted.

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EVALUATION OF THE TREATMENT WITH OZONE THERAPY AND PLATELET RICH PLASMA IN THE CHRONIC LUMBAR DISC HERNIATIO

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Introduction: Chronic disc disease (CDD) is a common cause of pain and disability that is defined by typical anatomical, morphological and biochemical changes.

The use of ozone for lumbar back pain has been proved to be effective both in intradiscal or in paravertebral injections. Ozone therapy is a minimal invasive treatment for lumbar disc herniation based on the biochemical effect of ozone.

In last years, platelet rich plasma (PRP) has reached a high interest in regenerative medicine, as an effective treatment in joint, muscle and tendon pathologies.

It has been tested that ozone induces an increase in the release of PRP from the platelets that could enhance its effect.

This is the reason that lead us to combine both techniques in the treatment of CDD. We present here our experience from March 2012 to March 2015.

Material and methods: In our Institute, we have used this technique in patients from 20 to 61 years, any gender, and a MRI diagnose of CDD at L4-5 and/or L5-S1. All patients finished the protocol of 10 sessions of paravertebral ozone injections and 2 intradiscal injections of ozone and PRP. VAS and Owestry were assessed before the treatment and at the end.

Results: 76% of the patients showed a decrease of 4 or greater in the VAS meanwhile Owestry results were not significant.

Conclusion: The combination of ozone and PRP is an effective technique to reduce the pain in patients with CDD. However, to evaluate disability, maybe we should wait more time until using the Owestry scale.