

Painkilling effect of ozone-oxygen injection on spine and joint osteoarthritis

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ABSTRACT

الهدف: تم استخدام أوزون - الأكسجين في المجال الطبي في الثلاثينات من القرن العشرين، وقد استعمل كعلاج بديل متمم لمجموعة من الأمراض المختلفة. لتوضيح أثر حقن أوزون - الأكسجين في تسكين ألم التهابات المفاصل والعمود الفقري.

الطريقة: تمت هذه الدراسة المستقبلية في عيادة الأوزون بمستشفى راشد، في إمارة دبي، بدولة الإمارات العربية المتحدة وقد شملت الدراسة 220 مريضا أكثرهم من مواطني الدولة: (122 سيدة - ومتوسط العمر 47.05 عاما و 98 رجل - متوسط العمر 52.8 عاما). وقد وثقت إصابة المرضى بالتهابات العظام و المفاصل عن طريق الصور الإشعاعية. تم علاج المرضى على مدى ثلاث سنوات (أيلول / سبتمبر 2002م - آب / أغسطس 2005م) عن طريق حقن أوزون - الأكسجين لأثنتا عشرة جلسة مرتين أسبوعيا وقد استخدم معيار الألم السداسي الشدة كمرجع للألم لدى المرضى؛ وقد تم تسجيل مقدار الألم عند بداية العلاج و في الجلسات الرابعة والثامنة والثانية عشرة. وأعيد تقييم المرضى في نطاق 8.48 أشهر وتم تسجيل مقدار الإحساس بالألم في ذلك الوقت أيضا.

النتائج: مقارنة مدى الشعور بالألم في اليوم الأول إلى اليوم الرابع، والثامن، والثاني عشر أظهر مدى قياس الألم انخفاضا ملحوظا من (الجلسة الأولى إلى الجلسة الرابعة $p=0.005$ ، و من الجلسة الأولى إلى الجلسة الثامنة $p=0.005$ ، ومن الجلسة الأولى إلى الجلسة الثانية عشرة $p=0.0043$). و مع مقارنة مقياس درجة الألم في اليوم الأول مع مقياس درجة الألم النهائي والذي تفصل بينهما مدة عشرة أشهر أظهر انخفاضا ملحوظا في مقياس الألم ($p=0.0048$).

خاتمة: هذه الدراسة تظهر مدى فعالية حقن أوزون - الأكسجين على تسكين الآلام المصاحبة لالتهابات العمود الفقري و المفاصل على المدى الطويل، والتي تؤيد احتمالية وجود تغييرات نسيجية حسب آلية عملها.

Objective: To analyze the painkilling effect of ozone-oxygen injection on joint and spine osteoarthritis.

Method: This prospective study was completed at the Ozone Clinic, Rashid Hospital, Dubai, United Arab Emirates on 220 mainly local patients (122 women,

mean age 47.05 years; 98 men, mean age 52.8 years) with radiographic documented spine or extremities osteoarthritis. The patients were treated over 3 years (September 2002 to August 2005) by ozone-oxygen injection twice a week for at least 12 sessions. Using the 6 faces pain scale; the patients' pain was recorded at the beginning and at the 4th, 8th, and 12th sessions. They were followed for a mean of 8.48 months and their pain scale was recorded at that time too.

Results: Comparison of the patients' 1st day pains with their 4th, 8th, and 12th sessions' pains showed a significant decrease (1st day to 4th session $p=0.005$, 1st day to 8th week $p=0.005$, 1st day to 12th session $p=0.0043$). Comparison of the 1st day pain with the final follow-up pain, which was around 10 months from the first treatment, showed a meaningful decrease of pain ($p=0.0048$).

Conclusion: This study validates the painkilling effect of ozone-oxygen injection on osteoarthritis of the joints and spine. Its long term effect on pain advocates the likelihood of some histological changes as mechanism of its action.

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The medical application of ozone begins with Kleinmann¹ and was followed by Payr,² and Wolff.³ One of the first reliable models of medical ozone generators was developed by Hansler.⁴ In 1938, Aubourg⁵ published the results of 119 cases of coliform infection treated by ozone in Beaujon-Clichy. Then in 1956, the 2 times nobel prize winner Dr. Otto Warburg (who won this award for discovering and proving that cellular respiration, once damaged by a lack of oxygen,

caused cells to mutate uncontrollably and turn into cancer cells) addressed ozone medical applications in his paper "On the origin of cancer cells."⁶ In 1987, Rilling and Veibahn¹ collaborated on the publication of "The use of ozone in medicine," as the standard medical text on ozone application. Ozone has many medical applications. It removes viruses and bacteria from blood. It has been successfully used on acquired immune deficiency syndrome (AIDS), herpes, hepatitis, mononucleosis, influenza,⁷ cirrhosis of the liver, gangrene, cardiovascular diseases,⁸ arteriosclerosis, high cholesterol,^{9,10} osteoporosis,¹¹ cancerous tumors,^{12,13} lymphoma, and leukemia. It is effective on rheumatoid and other types of arthritis, and allergies of all types. Ozone improves multiple sclerosis, ameliorates, alzheimer's disease, senility, and parkinsonism. It is effective on proctitis, colitis, prostate diseases, candidiasis, trichomoniasis, and cystitis. Externally, it is effective in treating acne, burns, leg ulcers, open sores, wounds,¹⁴ eczema, viruses,¹⁵⁻¹⁸ bacteria,^{19,20} and fungi.²⁰⁻²² Many more indications are listed in the medical literature for ozone therapy.²³ The German Medical Society has published 384,775 patients who were treated with a minimum of 5,579,238 applications of ozone and the side effect rate observed was only 0.000005 per application. This is the lowest side effect rate existing. The report also stated; the majority of adverse effects were caused by ignorance on ozone therapy (operator error). The University of Innsbruck's Forensic Institute published Jacobs²⁴ dissertation quoting this in The Empirical Medical Acts of Germany. Sweet et al²⁵ studying the medical ozone effects on human cancer cells announced impairment of defense mechanisms of cancer cells against ozone damage in the human body. All of the cancer cells (lung, breast, uterine and others) showed marked dose-dependent growth inhibition in ozone at 3 and 5 parts per million while the normal cells were not affected. Evidently, cancer cells are less able to compensate for the oxidative burden of ozone than normal cells. They also stated that it inhibits cancer 40-60, and up to 90% in a dose-dependant manner. Wells et al²⁶ performed 15 replications of a study that interfaced ozone with human immunodeficiency virus (HIV) infected factor VIII of blood. It completely removed the HIV 97-100% of the time, yet was nontoxic to normal blood components. Listed contraindications to ozone treatment include acute alcohol intoxication, recent myocardial infarction, hemorrhage from any organ, pregnancy, hyperthyroidism, thrombocytopenia, and ozone allergy.¹ Although ozone-oxygen injection is used extensively for pain management for different parts of the body however, there is no publication analyzing its long term painkilling effect on osteoarthritis to the extent of our information. The objective of the present study was to analyze the painkilling effect of ozone-oxygen injection on joint and spine osteoarthritis.

Methods. Two hundred and twenty patients who had a history of spine or extremities osteoarthritis were studied at the Ozone Clinic, Rashid Hospital, Dubai, United Arab Emirates over 3 years starting from September 2002 to August 2005. This clinic, that is functioning under the Alternative Medicine Department, is taking care of patients with different diseases. Patients who had spine or joint osteoarthritis were received by the authors for ozone-oxygen treatment. After complete case record and x-ray examinations, the patients were explained the treatment in-detail. They signed a consent for the treatment and agreed to be included in the study group. The study proposal was approved by Medical Research Committee of Dubai Health Authority. All types of joint osteoarthritis were included in the study. Patients with hyperthyroidism, thrombocytopenia, recent myocardial infarction, bleeding tendencies, sensitivity to ozone therapy and pregnancy were excluded from the treatment and study. Due to the short half-life of ozone that is approximately 45 minutes at 20°C, it was generated freshly in the clinic, using Hyper-Medozon Comfort generator connected to pure oxygen source and used immediately for the patients. The ozone generators use oxygen through high voltage tubes with outputs ranging from 4,000-14,000 and produce ozone-oxygen mixture with concentration ranges extending to 5%. For intra-articular and paravertebral muscles injections, a concentration of 20 Mcg/ml was selected.²⁷ The authors and one more orthopedic surgeon treated osteoarthritic spines and joints using sterile injection technique. Each patient received ozone injections twice a week for a full course of at least 12 sessions. Treatment results were recorded by one ozone clinic nursing staff, using the 6 faces pain scale²⁸ at the beginning of treatment and at the end of 4th, 8th, and 12th sessions keeping the treating physicians unaware of the results. The same nursing staff traced the patients during the follow-up period to record their final pain scale. During the study course, the patients were instructed to continue their osteoarthritis medical treatment according to their physicians' treatment plan.

The data collected from the patients were analyzed to provide information on patients' demographics, the involved anatomical site, duration of the symptoms and the 1st, 2nd, 3rd, 4th, and final pain scales. The follow-up pain scale of the patients was also included in the analysis. The analysis efficacy included only those patients for whom all the above data were available. Subgroup analysis was performed by independent sample t-test and means analysis for patients' characteristics or paired sample t-test for pain scale determinations during follow-up. All such subgroup analysis was prospective. Statistical analysis was performed using SPSS software (version 11.5), and *p*-values below 0.05 were considered significant.

Results. Two hundred and twenty patients were studied from 1st September 2002 to 31st August 2005. There were 123 women (mean age 47.05 years, SD=7.545) and 97 men (mean age 52.8 years, SD=7.639) mostly United Arab Emirates nationals (191 cases). All the patients had radiographically proven osteoarthritis of spine or extremities (**Table 1**). The mean of ozone therapy sessions was 13.33 (women 13.18, SD=1.576; men 13.58, SD=1.936) and the patients were followed up for a mean of 8.48 months after finishing the last session of treatment (women 8.2, SD=1.733; men 8.98, SD=2.277). Comparison of the patients' 1st day pain with their pain after 4th, 8th, and 12th sessions (**Table 2**) showed a significant decrease, based on the 6 faces pain scale record (1st day to 4th session $p=0.005$, 1st day to 8th sessions $p=0.005$, 1st day to 12th sessions $p=0.0043$). Comparison of the patients' 1st day pain with the final follow-up pain, which was around 10 months from the first treatment also showed significant decrease of pain, ($p=0.0048$) although the mean of patients' pain scale was a little higher than the 12th week record. No case of any complication of infection, hypersensitivity, or other clinically detectable adverse effects were found with more than 2800 injections of ozone-oxygen mixture in the joints and spines during this study.

Table 1 - Osteoarthritic spines and joints treated by ozone injection in females and males.

Location	Female	Male	Total
	n (%)		
Neck	18 (8.2)	21 (9.5)	39 (17.7)
Back	33 (15)	28 (12.7)	61 (27.7)
Shoulder	12 (5.4)	9 (4.1)	21 (9.5)
Elbow	3 (1.4)	2 (0.9)	5 (2.3)
Wrist	2 (0.9)	2 (0.9)	4 (1.8)
Hip	11 (5)	5 (2.3)	16 (7.3)
Knee	40 (18.2)	27 (12.3)	67 (30.5)
Ankle	4 (1.8)	3 (1.4)	7 (3.2)

Table 2 - The mean of osteoarthritic patients' pain scale during the treatment sessions and follow-up in females and males.

Session	Pain Scale (mean)	Standard deviation	Standard error	Significance
1	8.02	0.762	0.057	0.005
4	6.92	1.221	0.091	0.005
8	5.76	1.151	0.086	0.005
12	4.59	1.549	0.115	0.0043
Follow-up	4.86	1.762	0.131	0.0048

Discussion. Intra-articular ozone-oxygen injections, particularly for the knee and shoulder joints, have shown themselves to be effective and relevant in acute and chronic painful diseases of the joints. This method of treatment represents a good alternative to anti-inflammatory medical treatment, providing rapid pain relief, subsidence of swellings, decongestion of hematomas/bruises, a reduction in temperature and improvement of joint mobility.²⁹ In fact, intra-articular ozone-oxygen applications are understood as a complementary medical treatment method of painful joint conditions (rheumatic, arthritic, or otherwise) with a low therapeutic risk.³⁰

The present study investigates long term pain relief of ozone therapy on joints and spine osteoarthritis. Nevertheless, other studies have proven the painkilling effect of ozone-oxygen injections on low back pain and spinal discopathies. Andreula et al³¹ studied the effects of ozone therapy for 600 lumbar disc herniations with intradiscal injection and found it had a cumulative effect, which enhanced the overall result of treatment for pain caused by disc herniation. Kazarin et al³² used ozone injection in combined therapy of 58 patients with glossalgia and validated its use for the treatment. A trial of ozone therapy on more than 1000 patients in Italy with lumbar sciatic pain has shown a pain relief and clinical improvement in 68%.³³

Bonetti et al³⁴ used oxygen-ozone treatment for 140 patients with non-disc vertebral disease and found it highly effective in relieving acute and chronic lower back pain and sciatica. Paradiso and Alexandre³⁵ investigated the different outcomes of 150 patients who received microdiscectomy and 150 patients who received intradiscal ozone injection. The results were in favor of discolysis for contained disc herniations. Even Buric and Molino³⁶ have shown the ozone chemonucleolysis as a possibly effective modality of treatment in patients affected by non-contained lumbar disc herniations that have overpassed conservative measures and have not yet fulfilled the indications for open surgical treatment. Other authors have found it effective for spondylolisthesis, spondylolysis, and different cervical and lumbar disc disorders.³⁷⁻³⁹ Measurement of tibialis anterior muscle oxygenation in 26 cases after ozone autohemotransfusion has shown a significant decrease in the percentage of low-oxygenated values that is the reason for pain relief in ischemic or hypoxic legs syndromes.⁴⁰

There is still a need for more clarifications on the mechanism of ozone treatment on pain relief and clinical improvement of joints osteoarthritis. Many probable mechanisms have been discussed in the literature on those effects, however, especially activation

of enzymes, which are involved in peroxidic reaction, and their protective function against degeneration sequel processes on an overproduction of peroxides and oxygen radicals has been postulated more.³⁰ Also, the biochemical events induced by medical ozone on tissues can make a chemical bond between ozone and water, giving rise to a 'fall' of oxidant compositions. These acting with various substrates (glucose, galactose, N-acetyl glucosamine, glucuronic acid and glycine) determine the breakdown of the glycosaminoglycans aggregates, leading to a collapse of their 3-dimensional structure.⁴¹ There is also a hypothesis of anti-inflammatory and local analgesic action, related likely to the ozone properties to modify the micro-circle and the hemoglobin reduction mechanism, with consequent release of oxygen to the tissues.⁴²

We followed the design of "same patients as control group and study group" to avoid the mismatch of different osteoarthritis stages. The same patients were selected as the study group and control group before and after intervention.⁴³ Our study results confirm the validation of safe painkilling effect of ozone-oxygen injection on osteoarthritic joints and spine. Due to its long-term effect on pain relief, it seems some histological changes are involved in its mechanism of action. The antioxidant mechanism, which becomes activated after ozone-oxygen injection possibly reverses the degeneration processes in the joints and their surrounding tissues.

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