POSICIONAMIENTO DE LA SOCIEDAD ESPAÑOLA DEL DOLOR FRENTE A LA OZONOTERAPIA EN EL TRATAMIENTO DEL DOLOR

La Sociedad Española del Dolor (SED) apoya y felicita al Ministerio de Salud por el **PLAN PARA LA PROTECCIÓN DE LA SALUD FRENTE A LAS PSEUDOTERAPIAS**. Sin embargo, quiere hacer unas puntualizaciones respecto a una de las terapias incluidas, la ozonoterapia en el tratamiento del dolor.

Esta Sociedad está a favor de que no se engañe a la población con falsas terapias. Muchas terapias sin evidencia clínica alguna y administradas incluso por personas sin cualificación médica, suponen un evidente riesgo para la salud. Compartiendo estos objetivos, esta Sociedad Científica expresa su interés en colaborar con aportaciones que clarifiquen algunos aspectos concretos.

Dado que se nombra a la ozonoterapia, y siendo ésta una técnica empleada en muchas Unidades del Dolor de España, Europa y América, expresamos a través de este documento el posicionamiento de la SED.

Introducción

La ozonoterapia consiste en la administración o aplicación de una mezcla de oxígeno (O2) y de ozono (O3) con finalidad terapéutica. El ozono es un gas inestable que no puede ni envasarse ni almacenarse, por tanto, la mezcla ha de ser producida in situ para cada aplicación, y en ella nunca habrá más de un 5% de ozono.

Al igual que el oxígeno, el ozono ha sido calificado como **sustancia autorizada por la Agencia Europea del Medicamento (EMA)** - "Ozone: EV Code: SUB33402, CAS No: 10028-15-6, Substancia autorizada"

Se han publicado en revistas médicas indexadas múltiples trabajos sobre mecanismos de acción, estudios clínicos de cohortes y ensayos clínicos aleatorizados en el tratamiento de diferentes patologías, muchas relacionadas con el dolor (de la columna vertebral, gonartrosis, síndrome fibromiálgico, tendinopatías, dolores neuropáticos como la neuralgia del trigémino o neuralgia postherpética), pero también en otro tipo de patologías (asma bronquial, caries dental, úlcera diabética, toxicidades de los tratamientos oncológicos). A día de hoy según PubMed se han publicado 3205 artículos sobre ozonoterapia en Revistas Científicas.
https://www.ncbi.nlm.nih.gov/pubmed/?term=ozone+AND+therapy.

Las formas de aplicación son básicamente tres: tópica, infiltrativa y sistémica.

En las últimas décadas han aparecido factores negativos, como el uso de ozonoterapia en contextos no facultativos, falta de estandarización, generadores de ozono sin fotómetro apropiado y sobre todo la falta de evidencia científica basada en ensayos clínicos robustos para muchas de sus indicaciones. La conjunción de todos estos factores explica el rechazo de esta técnica por parte de la medicina ortodoxa.

El número de publicaciones sobre la ozonoterapia es amplísimo pero, como hemos dicho, la calidad de éstas en muchos casos es pobre. Trataremos de dilucidar en este documento en qué patología causante de dolor existe suficiente evidencia científica de eficacia y seguridad en la administración como para recomendar su uso.

Analisis de la información:

Habiendo sido realizado por el Servicio de Evaluación del Servicio Canario de Salud un estudio titulado "Ozonoterapia: efectividad, seguridad, coste-efectividad e impacto presupuestario" de excelente calidad, nos remitimos a él y lo adjuntamos, así como asumimos las conclusiones aportadas por los autores y que reflejaremos a continuación https://www3.gobiernodecanarias.org/sanidad/scs/content/4c7be1f8-a10e-11e6-a33b-757951c5b2fa/Informe_Ozonoterapia_SESCS%202016.pdf
(accesible el 12-12-2018)

Posteriormente a la realización del informe previamente referido se han publicado estudios de elevada calidad sobre la eficacia de la ozonoterapia en el tratamiento de la gonalgia por gonartrosis (1 y 2) y para el tratamiento de proctitis por radioterapia (3), otorgándose en esta última patología un razonable grado de recomendación en algunas guías clínicas americanas.

Conclusiones:

- Existen evidencias sobre la efectividad de la ozonoterapia en el tratamiento del dolor por hernia discal, si bien se constatan conclusiones controvertidas entre las últimas Revisiones sistemáticas y Metaanálisis, siendo estos últimos de aceptable calidad científica. La ozonoterapia paravertebral aplicada para lumbalgias inespecíficas y lumbalgias o dorsalgias de causa predominante miofascial tiene un **nivel de recomendación fuerte** con evidencia de calidad moderada.

- Existen **evidencias** sobre la efectividad de la ozonoterapia intraarticular en la gonalgia secundaria a la gonartrosis.

- Aunque existen estudios sobre la eficacia de la ozonoterapia en muchos otros cuadros dolorosos, no se puede establecer su recomendación por la pobre calidad de estos estudios.

- En octubre de este año, la American Society of Colon and Rectum Surgeons, publicó una Guía Clínica en la que estableció un **grado de recomendación 1C** para la Ozonoterapia en el manejo de la proctitis crónica secundaria a radioterapia (Paquette, 2018).

- Las complicaciones o efectos adversos relacionados con la ozonoterapia suelen deberse al procedimiento médico en su administración, y no por el ozono en sí

mismo. Aparecen muy raramente y, generalmente, son de carácter leve y transitorio.

- Esta terapia es probablemente más económica que las posibles alternativas, aunque se precisan evaluaciones económicas de la ozonoterapia en comparación con el tratamiento habitual.

- La ozonoterapia lleva años utilizándose en muchos hospitales del Sistema Nacional de Salud español (Anexo 1), sin que se hayan comunicado reacciones adversas o complicaciones de relevancia.

- No existe una ficha técnica realizada por el Ministerio que establezca las indicaciones o la posología (dosis, concentración, intervalos, duración del tratamiento). La adecuada práctica clínica se viene realizando basándose en el conocimiento de la técnica, y en las indicaciones y recomendaciones realizadas por las respectivas sociedades científicas, amparadas en la experiencia clínica.

- Estas recomendaciones deben ser revisadas y confirmadas por nuevos ensayos clínicos con mayor tamaño muestral, correcta aleatorización y un seguimiento a largo plazo. Actualmente en el Hospital Universitario de Gran Canaria Dr. Negrín la Unidad de tratamiento del Dolor Crónico, en colaboración con el servicio de Neurocirugía, el servicio de Cirugía Cardíaca y el Servicio de Evaluación y Planificación del Servicio Canario de Salud, está realizando el **Ensayo clínico** titulado "Efectividad y coste-efectividad del Ozono en el manejo de pacientes con cardiopatía isquémica refractaria a tratamiento médico y quirúrgico: Ensayo clínico controlado, aleatorizado, triple ciego" (ClinicalTrials.gov Identifier: NCT03660657) y **el estudio postautorización**: "Impacto clínico y económico de la ozonoterapia intradiscal en el manejo de pacientes con hernia discal lumbar" (ClinicalTrials.gov Identifier: NCT03282695).

- Teniendo en cuenta lo previamente referido, creemos que la ozonoterapia es segura y eficaz en los cuadros descritos, ha de ser administrada por personal entrenado, tras obtener el ozono de generadores de última generación y homologados, y debe seguir incluida en la cartera de servicios de los servicios asistenciales públicos y privados que puedan garantizar su uso correcto.

&&: Como índice del reconocimiento otorgado a los tratamientos con ozono y su estudio, mencionar que el 23-11-2018 se entregaron las 12 becas/premios de investigación del Ilmo. Colegio Oficial de Médicos de Las Palmas, entre las que se concedieron 2 a proyectos del grupo de trabajo en ozonoterapia del Hospital Dr. Negrín de Las Palmas de Gran Canaria:

- I19/18 Investigador Principal Dra. Sara Bisshop: Impacto clínico y económico de la ozonoterapia intradiscal en el manejo de pacientes con hernia discal lumbar (dentro de un proyecto financiado por el ISCIII -FIS-).

- I24/18 Investigador Principal Dr. Bernardino Clavo: Citoquinas inflamatorias en cardiopatía isquémica "O3Cardio" (que además fue elegida como Beca Especial de Investigación "Dr. González Jaraba").

https://www.medicoslaspalmas.es/index.php?option=com_content&view=article&id=5122&Itemid=1816

En ambos proyectos participa el Servicio de Evaluación del Servicio Canario de Salud, que dirige el Dr. Pedro Serrano. Él, además, es Investigador Principal del Grupo 4 de REDISSEC (Red de Investigación en Servicios de Salud en Enfermedades Crónicas) que es una de las RETICS (Redes Temáticas de Investigación Cooperativa en Salud) del ISCIII (Instituto de Salud Carlos III).

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Anexo 1: Hospitales públicos en los que hay constancia del uso de la ozonoterapia.

1	HOSPITAL ARQUITECTO MERCIDE
2	HOSPITAL CRISTAL PIÑOR
3	HOSPITAL FUNDACION ALCORCON
4	HOSPITAL UNIVERSITARIO 12 DE OCTUBRE
5	HOSPITAL DE LA PRINCESA
6	HOSPITAL UNIVERSITARIO PRINCIPE DE ASTURIAS
7	HOSPITAL PUERTA DEL MAR
8	HOSPITAL REINA SOFIA
9	HOSPITAL UNIVERSITARIO TORREJON DE ARDOZ
10	HOSPITAL UNIVERSITARIO DE FUENLABRADA
11	HOSPITAL CENTRO CIUDAD REAL
12	HOSPITAL MORALES MESEGUER
13	HOSPITAL RAMON Y CAJAL
14	HOSPITAL COLLADO VILLALBA
15	HOSPITAL UNIVERSITARIO SANTA CRISTINA
16	HOSPITAL DR.NEGRIN DE GRAN CANARIA
17	CLÍNICO UNIVERSITARIO
18	LA FE DE VALENCIA
19	MANISES
20	HOSPITAL UNIVERSITARIO REINA SOFÍA

Anexo 2: Ensayos Clínicos y otros trabajos sobre eficacia y seguridad de la ozonoterapia en el tratamiento del dolor (recopilación por el Dr. Javier Hidalgo).

J Pain Res. 2018 Jul 31;11:1405-1410. doi: 10.2147/JPR.S164335. eCollection 2018.
Comparison of percutaneous intradiscal ozone injection with laser disc decompression in discogenic low back pain.
Rahimzadeh P(1), Imani F(1), Ghahremani M(1), Faiz SHR(2).
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Background: Intervertebral disc herniation with the pressure on the surrounding neural structures is one of the most important causes of chronic low back pain, which sometimes leads to open surgery. Reducing the pressure inside the disc with intradiscal intervention such as laser irradiation or ozone injection is a minimally invasive method and an alternative to surgery with satisfactory results. These two methods were compared with each other in this research.
Patients and methods: In this clinical trial, 40 patients with back pain radiating to lower limb due to lumbar intervertebral disc herniation were selected. These patients were randomly divided into two equal groups for percutaneous intradiscal intervention. The Laser Disc Decompression Group (LDG) (n=20) was exposed to 1500 J of laser irradiation into the disc center. In the Ozone Injection Group (OZG) patients (n=20), 6 mL of ozone 30 µg/mL was injected into the center of the disc. Considering the level of neural root involvement, both groups received 20 mg of triamcinolone injection via transforaminal epidural. Patients were followed up for 12 months regarding score on visual analogue scale and life performance improvement based on Oswestry Disability Index (ODI) and satisfaction level.
Results: According to the results, no difference was found between the two groups for ODI variable before intervention, whereas OZG showed better ODI scores in the measured time intervals. In LDG, only a significant difference in terms of ODI score was found between the times of before surgery and the first month.
Conclusion: Intradiscal ozone injection could be an effective and cost-effective method for treatment of patients with discogenic back pain.
KEYWORDS: Oswestry Disability Index; laser disc decompression; low back pain; ozone injection; visual analogue scale

Clin Rheumatol. 2018 Sep;37(9):2517-2527. doi: 10.1007/s10067-018-4147-6. Epub 2018 May 24.
The effects of ultrasound-guided corticosteroid injection compared to oxygen-ozone (O2-O3) injection in patients with knee osteoarthritis: a randomized controlled trial.
Babaei-Ghazani A(1), Najarzadeh S(2), Mansoori K(1), Forogh B(1), Madani SP(1), Ebadi S(1), Fadavi HR(3), Eftekharsadat B(4).
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Osteoarthritis (OA) is a chronic multifactorial disease characterized by progressive joint degeneration. The purpose of this study was to compare the effects of ultrasound-guided corticosteroid injection with oxygen-ozone injection in patients with knee OA. This double-blind randomized clinical trial was performed on 62 patients with knee OA. The patients were randomly divided into two groups. In the first group 40 mg triamcinolone (1 cc) and in the second group 10 cc (15 µg/ml) oxygen-ozone (O2-O3) were injected into the knee joint under ultrasound guidance. Outcome measures included the Western Ontario and McMaster Universities Osteoarthritis (WOMAC), knee flexion range of motion (ROM), effusion in ultrasound images of the suprapatellar recess, and visual analog scale (VAS), which were evaluated before injection, 1 week, 1 month, and 3 months after the treatment. Sixty-two patients (10 men and 52 women) were enrolled with mean age of 57.9 years. VAS improved in both groups (steroid P value = 0.001, oxygen-ozone P value > 0.001). The improvements seen in VAS and WOMAC scores 3 months after treatment were in favor of the oxygen-ozone group when compared to the steroid group (P = 0.041 vs P = 0.19). There was no significant difference between the two groups in ROM and joint effusion seen under ultrasound (ROM p = 0.880, effusion p = 0.362). However, in the oxygen-ozone-receiving group, joint effusion

was decreased significantly ($p < 0.001$). Both steroid and oxygen-ozone injections are effective in patients with knee osteoarthritis. Our study showed that the effects of oxygen-ozone injection last longer than those of steroid injection to the knee joint.
KEYWORDS: Corticosteroid; Knee; Osteoarthritis; Oxygen–ozone; Sonography

Pain Med. 2018 May 30. doi: 10.1093/pm/pny066. [Epub ahead of print]
Comparison of Ultrasound-Guided Local Ozone (O2-O3) Injection vs Corticosteroid Injection in the Treatment of Chronic Plantar Fasciitis: A Randomized Clinical Trial.
Babaei-Ghazani A(1), Karimi N(2), Forogh B(1), Madani SP(1), Ebadi S(1), Fadavi HR(3), Sobhani-Eraghi A(4), Emami Razavi SZ(5), Raeissadat SA(6), Eftekharsadat B(7).
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Objective: Plantar fasciitis (PF) is one of the most common causes of heel pain. The affected area is often close to the attachment of plantar fascia to calcaneus bone. The purpose of this study was to compare the effects of ozone (O2-O3) injection to corticosteroid injection under ultrasound guidance for the treatment of chronic PF.
Design: Randomized clinical trial.
Setting: Academic University and Neuromusculoskeletal Research Center.
Subjects: Thirty patients with chronic PF.
Methods: The patients were randomly divided into two groups receiving methylprednisolone (15 subjects) vs ozone (O2-O3; 15 subjects). The following outcome measures were assessed before injection and then two weeks and 12 weeks after the injection in each group; morning and daily pain via visual analog scale, daily life and exercise activities via the Foot and Ankle Ability Measure, and plantar fascia thickness at insertion and 1 cm distal to its insertion into the calcaneus via ultrasound imaging.
Results: Intragroup changes showed significant improvement in pain, functional parameters, and sonographic findings in both groups ($P < 0.05$). Pain reduction (both daily and morning) and daily activity improvement were better in the corticosteroid group two weeks after injection; however, at 12 weeks, the ozone (O2-O3) group had significantly more improvement ($P = 0.003$, $P = 0.001$, and $P = 0.017$, respectively).
Conclusions: Both methods were effective in the treatment of chronic PF. Steroid injection provided a more rapid and short-term therapeutic effect. However, ozone (O2-O3) injection led to a slow and longer-lasting treatment outcome. Ozone (O2-O3) injection can be an effective treatment, with slow onset and a longer durability in the treatment of chronic PF.

J Pain Res. 2018 Jan 4;11:111-117. doi: 10.2147/JPR.S142755. eCollection 2018.
Intra-articular ozone or hyaluronic acid injection: Which one is superior in patients with knee osteoarthritis? A 6-month randomized clinical trial.
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Purpose: Knee osteoarthritis (OA) is a common disease, imposing a great burden through pain and decreased function. There are many therapeutic modalities including non-pharmacologic choices and oral, topical, and intra-articular medications. New studies have shown promising results for ozone application in knee OA. Our aim was to compare the effects of ozone therapy versus hyaluronic acid (HA) intra-articular injection in knee OA patients.
Methods: In this randomized clinical trial, a total of 174 patients with more than 3 months of chronic pain or swelling in the knee joints along with consistent imaging findings were enrolled and randomly allocated into two groups of HA and ozone, which were planned to undergo 3 weekly injections of HA (Hyalgan®) and 10 mL of a 30 μg/mL ozone solution, respectively. Patients were evaluated at baseline and 6 months after the last injection for pain, stiffness, and function using the visual analog scale (VAS) and the Western Ontario and McMaster Universities Arthritis Index (WOMAC) questionnaire.
Results: No major adverse events were detected in this study. Total WOMAC score decreased from 40.8±9.8 to 20.4±4.9 ($p<0.01$) in the ozone group and from 38.5±7.9 to 17.1±4.2 ($p<0.01$) in the HA group. A similar trend was observed in pain improvement according to VAS. Pain, stiffness, and function significantly improved in both the groups, but no between-group difference was found.
Conclusion: Although both ozone and HA can be effectively used for improving function and reducing pain in selected knee OA patients, neither of the two showed any superiority at 6-month follow-up.
KEYWORDS: hyaluronic acid; knee osteoarthritis; ozone
Int J Surg. 2018 Oct;58:3-10. doi: 10.1016/j.ijsu.2018.08.007. Epub 2018 Aug 29.

Intra-articular oxygen-ozone versus hyaluronic acid in knee osteoarthritis: A meta-analysis of randomized controlled trials.
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OBJECTIVE: Knee osteoarthritis (OA) is a common disease, imposing a great burden through pain and decreased function. Numerous methods have been tested for pain management in knee OA and the optimal method is currently still under debate. We performed a meta-analysis from randomized controlled trials (RCTs) to compare the efficacy and safety of intra-articular hyaluronic acid (HA) and oxygen-ozone in the treatment of knee OA.
METHODS: Electronic databases included PubMed, Embase, web of science and the Cochrane Library. High quality RCTs comparing HA with oxygen-ozone in the treatment of knee OA were selected. We assessed statistical heterogeneity for each RCT with the use of a standard Chi2 test and the I2 statistic. Quality assessment was performed by using Cochrane Collaboration's tool. All data were carried out with Stata 14.0 software.
RESULTS: A total of four RCTs including 289 patients were included. The present meta-analysis indicated that there was a significant difference between groups regarding the visual analog scale (VAS) and WOMAC stiffness and function. The improvements in WOMAC pain were similar. No significant difference in adverse events occurrence was observed.
CONCLUSION: Intra-articular injection of HA was associated with a significantly reduction in VAS score at 1st month compared to oxygen-ozone. And there was significant differences in WAMAC stiffness, and function at 6-month follow-up between groups. Based on the current evidence available, more RCTs are needed for further investigation.
KEYWORDS: Hyaluronic acid; Knee osteoarthritis; Meta-analysis; Oxygen-ozone
J Pain Res. 2018 Aug 27;11:1637-1643. doi: 10.2147/JPR.S154154. eCollection 2018.
The effect and safety of ozone autohemotherapy combined with pharmacological therapy in postherpetic neuralgia.
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Introduction: We investigated the effect and safety of ozone autohemotherapy combined with pharmacological therapy in postherpetic neuralgia (PHN).
Methods: Ninety-eight patients with PHN were enrolled in this study and randomly divided into a pharmacological therapy group and ozone autohemotherapy group (49 patients in each group). The PHN patients in the pharmacological therapy group were administered pharmacological therapy for 2 weeks, whereas PHN patients in the ozone autohemotherapy group were given ozone autohemotherapy (200 mL blood from patients, the

concentration of medical ozone was set as 30 μg/mL using an ozone medical apparatus, 40 mL medical ozone was incubated in 200 mL autologous blood for 3-5 minutes) combined with pharmacological therapy for 2 weeks. The Visual Analog Scale (VAS), the 50% VAS reduction in the initial value, McGill Pain Questionnaire (MPQ), the Patients' Global Impression of Change (PGIC) scale, and the World Health Organization Quality of Life (WHOQOL-BREF) instrument were used to evaluate the outcomes of all PHN patients before therapy and at 1 week, 1 month, and 3 months after therapy.
Results: Forty-five patients in the pharmacological therapy group and 47 patients in the ozone autohemotherapy group completed the study. Compared with before therapy, the two groups showed significant improvements in VAS, MPQ, PGIC, and WHOQOL-BREF scores after therapy ($P<0.05$). Moreover, compared with the scores of the pharmacological therapy group, the ozone autohemotherapy group's scores were significantly improved in the VAS, MPQ, PGIC, and WHOQOL-BREF as well as the 50% VAS reduction of the initial value after therapy ($P<0.05$). Finally, there were no statistically significant differences in adverse effects between groups after therapy ($P>0.05$).
Conclusion: The results of this study demonstrated that ozone autohemotherapy combined with pharmacological therapy was superior to isolated pharmacological therapy in patients with PHN and was an effective and safe way to relieve PHN.
KEYWORDS:
clinical trial; ozone autohemotherapy; pharmacological therapy; postherpetic neuralgia

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Effectiveness of intra-articular ozone injections on outcomes of post-arthroscopic surgery for knee osteoarthritis.
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Abstract
The purpose of the present study was to evaluate intra-articular ozone injection following arthroscopic surgery for knee osteoarthritis (OA) with regard to its efficacy in pain reduction, joint function and quality of life improvement. The present study retrospectively evaluated 80 patients with symptomatic knee OA (Kellgren-Lawrence grade II or III), who either did or did not receive 20 ml of 20 μg/ml ozone as an intra-articular injection after arthroscopic surgery. The minimum follow-up period was 12 months. The outcomes evaluated for knee OA were pain on the Visual Analogue Scale (VAS), Lequesne Index, Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC) and Clinical Global Impression (CGI). The VAS score in the ozone group was significantly better than that in the control group at all post-operative follow-up time-points ($P<0.05$). The ozone group also exhibited a significantly greater improvement in Lequesne Index scores ($P<0.05$). In the ozone group, the score on the WOMAC-pain, WOMAC-stiffness and WOMAC-function subscales, as well as the total WOMAC score decreased significantly ($P<0.05$). Furthermore, in the ozone group a significantly higher number of patients ($P<0.05$) with better CGI grades was encountered compared with that in the control group at the 12-month follow-up assessment, despite comparable baseline values in all aforementioned clinical measures between the two groups of patients. The present study suggests that intra-articular ozone injections after arthroscopic surgery may effectively improve the outcomes of arthroscopic surgery in terms of pain relief, functional improvement and quality of life in patients with knee OA of Kellgren-Lawrence grade II or III.
KEYWORDS:arthroscopy; intra-articular; knee osteoarthritis; ozone

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Comparison of ozone and lidocaine injection efficacy vs dry needling in myofascial pain syndrome patients.
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Purpose: Myofascial pain syndrome (MPS) is a common musculoskeletal disorder among young adults associated with presence of myofascial trigger points. We aimed to evaluate efficacy of ozone injection (OI) in MPS patients, compared with two currently used methods including lidocaine injection (LI) and dry needling (DN).
Patients and methods: In this single-blinded study, a total of 72 eligible patients were included and then randomly divided into three equal groups: DN, OI, and LI. All patients received treatment in three weekly sessions. Visual analog scale (VAS) for pain, cervical lateral flexion, pain pressure threshold (PPT), and neck disability index (NDI) were the main outcome measures, which were evaluated at baseline and at 4 weeks after injections. Analytic results were demonstrated as both within- and between-groups mean difference (MD).
Results: Sixty two patients finished the study, 20 participants in both the DN and LI groups, and 22 persons in OI group. Distribution of all demographics and baseline clinical variables were relatively similar among groups. All three interventions were remarkably effective in improving patients' pain and PPT. Significant decrease in VAS (MD=-3.6±1.4) and increase in PPT (MD=7.2±5.1) within 4 weeks follow-up confirmed this finding. Also, NDI had similar significant improvement (MD=-9.9±8.7), but lateral flexion range did not show remarkable increase. There was also a statistically significant difference among three methods' efficacy on VAS, NDI, and PPT, favoring OI and LI.
Conclusion: In summary, this data showed that in short-term follow-up, all three methods were significantly effective in MPS treatment; however, OI and LI groups had slightly better results than the DN group, with no remarkable preference between them.
KEYWORDS: intra-muscular ozone injection; myofascial trigger points; wet needling

Zhong Nan Da Xue Xue Bao Yi Xue Ban. 2018 Feb 28;43(2):168-172. doi: 10.11817/j.issn.1672-7347.2018.02.011.
[Topical ozone therapy: An innovative solution to patients with herpes zoster].
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Abstract
To observe the clinical efficacy and safety of topical ozone therapy for patients with herpes zoster by reflectance confocal microscopy (RCM).
Methods: A total of 60 patients with herpes zoster were divided into a control group and an ozone treatment group (n=30). In the control group, patients took oral valacyclovir tablets or granules (0.3 g per day, three times a day) and they were subjected to local weak laser irradiation treatment plus topical 2% mupirocin ointment twice a day. In the ozone group, the treatment is same as the control group except mupirocin ointment was replaced with topical ozone treatment (hydrotherapy every day plus ozonated oil twice a day). The clinical symptoms, discoid cell and adverse reactions were observed and taken records at day 0, 3, 7 and 14. Statistical analysis was performed to compare the clinical efficacy between the 2 groups.
Results: On the seventh day of treatment, the discoid cells of the ozone group disappeared, and the difference between the control group and the ozone group was statistically significant ($P<0.05$). The difference of decreased percentage of pain scores at each time point between the 2 groups was statistically significant ($P<0.05$). The clinical efficacy was 100% in the ozone group and 86.7% in the control group, with significant difference between the 2 groups ($P<0.05$).
Conclusion: Topical ozone therapy in patients with herpes zoster is helpful in relieving pain, shortening the course as well as improving the clinical efficacy without obvious adverse reactions. It is worth to be popularized.

PLoS One. 2017 Jul 24;12(7):e0179185. doi: 10.1371/journal.pone.0179185. eCollection 2017.
Comparison between intra-articular ozone and placebo in the treatment of knee osteoarthritis: A randomized, double-blinded, placebo-controlled study.
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OBJECTIVE: The aim of the trial was to determine the effectiveness of oxygen-ozone injections on knee osteoarthritis concerning pain reduction, joint functional improvement, and quality of life.

METHODS: In this randomized, double-blinded, placebo controlled clinical trial, 98 patients with symptomatic knee osteoarthritis (OA) were randomized into two groups receiving intra-articular 20 μg/ml of ozone (OZ) or placebo (PBO) for 8 weeks. The efficacy outcomes for knee OA were the Visual Analogue Scale (VAS), Lequesne Index, Timed Up and Go Test (TUG Test), SF-36, Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC), and Geriatric Pain Measure (GPM).
RESULTS: After 8 weeks of treatment, ozone was more effective than the placebo: VAS [mean difference (MD) = 2.16, $p < 0.003$ (CI 95% 0.42-3.89)], GPM [MD = 18.94, $p < 0.004$ (CI 95% 3.43-34.44)], LEQ [MD = 4.05, $p < 0.001$ (CI 95% 1.10-7.00)], WOMAC (P) [median of diff = 9.999, $p = 0.019$ (CI 95% 0.000-15.000)], WOMAC (JS) [median of diff = 12.499, $p < 0.001$ (CI 95% 0.000-12.500)], WOMAC (PF) = [median of diff = 11.760, $p = 0.003$ (CI 95% 4.409-19.119)], TUG (no statistical difference) and SF-36 (FC) [(MD = -25.82, $p < 0.001$ (CI 95% 33.65-17.99)], SF-36 (PH) [MD = -40.82, $p < 0.001$ (CI 95% -54.48-27.17)], SF-36 (GSH) [MD = -3.38, $p < 0.001$ (CI 95% -4.83-1.93)], SF-36 (SA) [MD = 2.17, $p < 0.001$ (CI 95% -19.67-8.24), SF-36 (EA) [MD = -35.37, $p < 0.001$ (CI 95% -48.86-21.89)]. Adverse events occurred in 3 patients (2 in the placebo group and 1 in the ozone group) and included only puncture accidents.
CONCLUSIONS: The study confirms the efficacy of ozone concerning pain relief, functional improvement, and quality of life in patients with knee osteoarthritis.
TRIAL REGISTRATION: International Standard Randomized Controlled Trial Number Register ISRCTNR55861167.

Knee Surg Sports Traumatol Arthrosc. 2017 Feb;25(2):485-492. doi: 10.1007/s00167-016-4110-5. Epub 2016 Apr 7.
Choice of intra-articular injection in treatment of knee osteoarthritis: platelet-rich plasma, hyaluronic acid or ozone options.
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PURPOSE: This study was performed to compare the efficacy of treatment in three groups of patients with knee osteoarthritis (OA) given an intra-articular injection of platelet-rich plasma (PRP), hyaluronic acid (HA) or ozone gas.
METHODS: A total of 102 patients with mild-moderate and moderate knee OA who presented at the polyclinic with at least a 1-year history of knee pain and VAS score ≥4 were randomly separated into three groups. Group 1 (PRP group) received intra-articular injection of PRP × 2 doses, Group 2 (HA group) received a single dose of HA, and Group 3 (Ozone group) received ozone × four doses. Weight-bearing anteroposterior-lateral and Merchant's radiographs of both knees were evaluated. WOMAC and VAS scores were applied to all patients on first presentation and at 1, 3, 6 and 12 months.
RESULTS: At the end of the 1st month after injection, significant improvements were seen in all groups. In the 3rd month, the improvements in WOMAC and VAS scores were similar in Groups 1 and 2, while those in Group 3 were lower ($p < 0.001$). At the 6th month, while the clinical efficacies of PRP and HA were similar and continued, the clinical effect of ozone had disappeared ($p < 0.001$). At the end of the 12th month, PRP was determined to be both statistically and clinically superior to HA ($p < 0.001$).
CONCLUSION: In the treatment of mild-moderate knee OA, PRP was more successful than HA and ozone injections, as the application alone was sufficient to provide at least 12 months of pain-free daily living activities.
LEVEL OF EVIDENCE: Therapeutic study, Level I.

J Biol Regul Homeost Agents. 2016 Apr-Jun;30(2):621-5.

Comparison between intrarticular injection of hyaluronic acid, oxygen ozone, and the combination of both in the treatment of knee osteoarthrosis.

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This study aimed to compare short-term clinical outcomes between intra-articular injection of hyaluronic acid (HA), oxygen ozone (O2O3), and the combination of both, in patients affected by osteoarthrosis (OA) of the knee. Seventy patients (age 45-75 years) with knee OA were randomized to intra-articular injections of HA (n=23), or O2O3 (n=23) or combined (n=24) one per week for 5 consecutive weeks. KOOS questionnaire and visual analog scale (VAS), before treatment (pre) at the end (post), and at 2 months after treatment ended (follow-up) were used as outcome measures. Analysis showed a significant effect ($P < 0.05$) of the conditions (pre, post and follow-up) in all parameters of the KOOS score and a significant effect ($P < 0.05$) of groups (HA, O2O3 and combined) for pain, symptoms, activities of daily living and quality of life. The combined group scores were higher compared to the HA and O2O3 groups, especially at follow-up. The combination of O2O3 and HA treatment led to a significantly better outcome especially at 2-month follow-up compared to HA and O2O3 given separately to patients affected by OA of the knee.

Clin Radiol. 2014 Dec;69(12):1280-6. doi: 10.1016/j.crad.2014.08.008. Epub 2014 Sep 17.

Ozone-augmented percutaneous discectomy: a novel treatment option for refractory discogenic sciatica.

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AIM: To assess the short and medium-term efficacy and safety of a novel, minimally invasive therapeutic option combining automated percutaneous lumbar discectomy, intradiscal ozone injection, and caudal epidural: ozone-augmented percutaneous discectomy (OPLD).
MATERIALS AND METHODS: One hundred and forty-seven patients with a clinical and radiological diagnosis of discogenic sciatica who were refractory to initial therapy were included. Fifty patients underwent OPLD whilst 97 underwent a further caudal epidural. Outcomes were evaluated using McNab's score, improvement in visual analogue score (VAS) pain score, and requirement for further intervention. Follow-up occurred at 1 and 6 months, and comparison was made between groups.
RESULTS: OPLD achieved successful outcomes in almost three-quarters of patients in the short and medium term. OPLD achieved superior outcomes at 1 and 6 months compared to caudal epidural. There was a reduced requirement for further intervention in the OPLD group. No significant complications occurred in either group.
DISCUSSION: OPLD is a safe and effective treatment for patients with refractory discogenic sciatica in the short and medium term. OPLD has the potential to offer

an alternative second-line minimally invasive treatment option that could reduce the requirement for surgery in this patient cohort.

Funct Neurol. 2014 Jan-Mar;29(1):31-9.
An observational retrospective/horizontal study to compare oxygen-ozone therapy and/or global postural re-education in complicated chronic low back pain.
Apuzzo D, Giotti C, Pasqualetti P, Ferrazza P, Soldati P, Zucco GM.

Acute low back pain (LBP) is the fifth most common reason for physician visits and about nine out of ten adults experience back pain at some point in their life. In a large number of patients LBP is associated with disc herniation (DH). Recently, oxygen-ozone (O2O3) therapy has been used successfully in the treatment of LBP, reducing pain after the failure of other conservative treatments. The aim of this study was to assess the effects of O2O3 therapy in back pain rehabilitation, comparing three groups of patients suffering from chronic back pain associated with DH submitted to three different treatments: intramuscular O2O3 infiltrations, global postural An observational retrospective/horizontal study to compare oxygen-ozone therapy and/or global postural re-education in complicated chronic low back pain re-education (GPR), or a combination of the two (O2O3+GPR). The data show that pain severity before treatment was significantly lower in the patients treated with GPR alone (VAS score 7.4) than in the O2O3+GPR patients (VAS score 8.5) and the O2O3 patients (VAS score 8.6). At the end of treatment, pain severity was lower in the O2O3 patients than in the GPR-alone patients. After some years of follow-up only the difference between O2O3+GPR and GPR-alone remained significant.

Zhongguo Gu Shang. 2013 Oct;26(10):815-8.
[Treatment of lumbar intervertebral disc herniation with coblation combined with ozone nucleus pulposus ablation].
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OBJECTIVE: To compare the clinical effects between coblation combined with ozone nucleus pulposus ablation and single radiofrequency ablation of nucleus pulposus in treating a simple segment inclusive lumbar intervertebral disc herniation.
METHODS: From June 2009 to June 2011,33 patients with lumbar intervertebral disc herniation were treated with coblation combined with ozone nucleus pulposus ablation (group A),including 19 males and 14 females,ranging in age from 20 to 60 years old with an average of (40.4+/-8.8) years old,in the course of disease from 12 to 38 months with an average of (19.9+/-5.8) months;31 patients were treated with single radiofrequency ablation of nucleus pulposus(group B),ineluding 18 males and 13 females,ranging in age from 20 to 60 years old with an average of (39.8+/-7.3) years old,in the course of disease from 12 to 48 months with an average of (19.2+/-8.1) months. Visual analogue score(VAS) and JOA score system was respectively used to evaluate pain and function after operation.
RESULTS: All patients were followed up more than 1 year. No injuries of nerve root and cauda equina nerve,infection were found. There was no significant difference in VAS score between two groups at 1 month after operation ($P>0.05$),but at 12 months after operation,VAS score of group A was better than that of group B ($P<0.05$). There was no significant difference in JOA score between two groups at 12 months after operation ($P>0.05$). According to the functional improvement rate to evaluate the clinical effects,in group A,9 cases got excellent results, 21 good,3 fair;and in group B,6 excellent,18 good,7 fair. Clinical effects of group A was better than that of group B ($P<0.05$).
CONCLUSION: Clinical effects of coblation combined with ozone nucleus pulposus ablation is better in treating a simple segment inclusive lumbar intervertebral

disc herniation.

J Back Musculoskelet Rehabil. 2013;26(3):317-22. doi: 10.3233/BMR-130386.
Treatment of the lumbar disc herniation with intradiscal and intraforaminal injection of oxygen-ozone.
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BACKGROUND AND OBJECTIVE: Oxygen-ozone therapy is a minimally invasive treatment for lumbar disk herniation that exploits the biochemical properties of a gas mixture of oxygen and ozone. The purpose of our study was to prospectively evaluate the clinical effectiveness of oxygen-ozone therapy and compared the therapeutic outcome of injection of oxygen-ozone combined steroid with injection of ozone alone at different follow-up period.
MATERIAL AND METHODS: From Aug 2005 to Mar 2009, 172 consecutive adult patients (92 men, 80 women; age range: 23-59 years) with low back pain and radicular pain were included in this study and were randomly assigned to two groups. 90 patients (group A) underwent intradiscal and intraforaminal injection of oxygen-ozone and 82 patients (group B) received the same treatment with additional injection of 1ml of compound betamethasone. Visual analogue scale (VAS) and the Japanese Orthopedic Association's evaluation system for lower back pain syndrome (JOA score) were administered before treatment and at 3 weeks, 6 and 12-month follow-up period to evaluate the clinical results.
RESULTS: Satisfactory clinical outcomes were obtained in both groups. The reduction of VAS score from baseline to the end of the study was 7.68 to 2.17 and 7.49 to 2.23 in group A and group B respectively, and there were remarkable improvements of mean JOA score and recovery rate in every follow-up time in both groups. Furthermore, in 3 weeks follow-up the JOA recovery rate of group B is higher than that of group A, which there was significant different, but there were no significant differences between two groups in 6 and 12 months.
CONCLUSION: In our study, oxygen-ozone nucleolysis provides excellent pain relief in most herniated disc patients who failed to respond to conservative therapy. And there was no significant statistical difference between treatment of injection of oxygen-ozone combined with steroid and ozone only in the 6 and 12 months follow-up. Therefore, O2-O3 seems to play a role in pain relief, and we suggest the administration of the O2-O3 mixture as a first-choice treatment before recourse to surgery or when surgery is not possible and the addition of epidural steroid infiltration is not required.
LEVEL OF EVIDENCE: Level 1-1 (prospective study).

J Biol Regul Homeost Agents. 2012 Jul-Sep;26(3):467-74.
Treatment of radiculopathies: a study of efficacy and tollerability of paravertebral oxygen-ozone injections compared with pharmacological anti-inflammatory treatment.
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The study was performed to evaluate the effectiveness of lumbar paravertebral injections of a gas mixture of Oxygen and Ozone in patients with lumbar radiculopathies caused by L4-L5 or L5-S1 disk herniations compared to a pharmacological therapy based on non-steroidal anti-inflammatory drugs. Lumbar radiculopathy caused by disc herniation is widely spread. Many therapeutic options are available before steering patients to the surgery. Low back pain and sciatica represent some of the most frequent causes of antinflammatory-analgesic

drugs overuse. Recent findings have shown that medical Ozone can be used in the treatment of radicular syndrome caused by herniated intervertebral discs. Although widely spread, there are insufficient published data supporting the effectiveness of this approach in clinical practice. We studied 38 affected patients with acute L5 or S1 radicolopathy. The patients were randomly divided in two groups: A) 20 patients treated with lumbar paravertebral injections of Oxygen and Ozone; B) 18 patients treated pharmacologically with antinflammatory-analgesic drugs. All patients underwent a clinical and neurological examination at baseline (T1) and after 1 (T2), 2 (T3), 4 weeks (T4) and after 3 (T5) and 6 months (T6). An MRI and EMG examination were performed at baseline and after 6 months. The intensity of pain and the outcome of treatments were evaluated in all patients with the Visual Analogue Scale and with the Oswestry Disability Index. We found a reduction of pain and discomfort soon after one week with oxygen-ozone injections compared with pharmacological treatment, but this difference of response became statistically significant after two weeks (50 percent vs 16.6 percent) and is confirmed after 3 and 6 months, when 80 percent of patients treated with injections turned out pain free compared with half of the patients treated pharmacologically. No statistical difference were found in MRI and EMG examinations. No adverse effects were found in any patient of group A. We hypothesize that oxygen-ozone injections in paravertebral regions can induce a direct reduction of root inflammation with a corresponding reduction of pain. The paravertebral injections of oxygen-ozone represent a rapidly effective therapy, easily practicable and secure, in patients with lumbar radicolopathies secondary to disc herniation.