

Ozone and Ozonated Growth Factors in the Treatment of Disc Herniation and Discartrosis Lumbar Spine

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Abstract

The management of the disc herniation and its complications through highly invasive surgical techniques has drawbacks including the high number of adverse effects. Discolysis with ozone has shown high therapeutic efficacy and the use of growth factors derived from platelets is increasingly used in tissue regeneration. The present study aims to demonstrate the efficacy and safety of ozone on the herniated disc and the healing and restorative effect of growth factors on the degenerated or damaged herniated disc. A prospective, single-center, nonrandomized study involving 60 patients in an age range of 35-82 years diagnosed with severe lumbo-sciatica, Visual Analog Scale (VAS) 7-8, and degenerative disc syndrome was carried out. The patients were intervened with discolysis with autologous plasma rich in growth factors derived from platelets and ozone. The evaluation of the patients was followed by monitoring clinical symptoms, EVA (visual analogue scale) assessment, and MRI (magnetic resonance imaging) methods. The results showed a 90% complete resolution with EVA at 4 and 6 months of 0-2, and MRI showed resolution of the hernia and rehydration of damaged discs. The remaining 10% showed a partial resolution. Five percent of the patients reported adverse reactions (2 patients with mild transient headache and one pneumocephalus patient). These results demonstrate the efficacy and safety of the procedure in this type of pathology.

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Introduction

Lumbar disc herniation sciatica surgery has been the invasive technique of choice for a long time and is still widely used, especially with the advent of new microsurgical techniques; however, its results are not entirely optimal.¹ Many complications and failures, especially by perineural fibrosis at the surgical site and infection, makes its use controversial. In addition, between 10% and 40% of these patients end up developing the dreaded failed back surgery syndrome (FBSS).² It is worth adding that until 10 years ago in U.S.A. between 150 000 to 200 000 back surgeries were performed annually, with a failure rate of 15% to 25% with 15% reinterventions.

Only in 2002 more than 1 million operations on the spine were performed in the U.S.A.. Recent observations about the weaknesses of these operations are reason for alarm and a need for reconsideration of these procedures (Dr. Charles V. Burton, medical director, Center for Restorative Spine Surgery, St. Paul, MN 55102, USA). Taking into account the above, it is not surprising that the current trend in the treatment of this pathology is toward minimally invasive percutaneous techniques which are characterized by high efficiency and are well tolerated.

The European Guidelines for the management of chronic lumbar pain , show how there is strong evidence that the complex and demanding surgery of the lumbar spine in which various forms of spinal instrumentation are used, is not more effective than a simple, safer and cheaper posterolateral fusion without instrumentation. Other recent studies show that there is a trend toward the use of minimally invasive techniques, and the abandonment of transpedicular fusions. This clearly indicates that we must properly apply the knowledge based on scientific evidence accumulated over at least two decades. All this allows us to recommend the abandonment of the instrumented pathway in many current indications, and find other ways in the field of conservative rehabilitation treatment properly applied. Thus we need to use all the interventionist resources currently offering the modern treatment of chronic pain intervention, before resorting to decompressive surgery and spinal fusion.

A recent study conducted by the Kovacs Foundation says than more 25 million Euros per year is spent in Spain in tests (MRI, X-Ray, CAT) for lumbar pain.

Treating discolysis and paravertebral facet with ozone and growth factors is a minimally invasive technique that avoids or diminishes considerably the complications of surgery with excellent results. It is a percutaneous technique, implemented under fluoroscopic guidance, on an outpatient basis, under sedation and local anesthesia. In recent years more and more randomized, controlled, large samples, with adequate scientific evidence (II) are published in journals with a high impact factor. Two recent studies in meta-analysis (with the maximum level of scientific evidence) prove that ozone therapy is as effective or better than surgery without adverse effects thereof. At the Gran Canaria University Hospital Dr. Negrín a controlled clinical trial comparing this technique with conventional surgery is being conducting, with public funding and no commercial interests. Moreover, the University of Sao Paulo in Brazil is conducting research on ozone implementation in the epidural area in patients where the surgical method has failed.

In 2002, Dr. A. Alexandre (Treviso, Italy) presented a multicenter study on a sample of 6 665 patients treated with percutaneous discolysis with ozone giving a result of 81% of abolition of pain and 12.5% of improvement. In 1999, Dr. Eduardo Anitua began to work in Spain with growth factors in collaboration with the orthopedist, Dr. Miquel Sánchez, demonstrating the regenerative nature of musculoskeletal tissues of these factors.

The purpose of this paper is to demonstrate the effectiveness and safety of ozone on the herniated disc and the healing and restorative effect of ozonated growth factors on degenerated or damaged spinal disc herniation,.

Materials and Methods

We conducted a clinical study performing a monocentric, prospective, nonrandomized intervention with ozone and ozonated Platelet Rich Plasma (PRPO3). Sixty patients at an age range of 35 to 82 years who attended the consultation of Fiorela Clinical Institute (San Pedro Sula, Honduras) from July 2012 to January 2013 were treated for severe lumbo-sciatica with an intensity of 7-8, according to the Visual Analogue Scale (VAS). Patients diagnosed with lumbar disc herniation and degenerative disc syndrome, according to recent magnetic resonance (not more than six months) were selected. In these 60 patients were performed 150 PRPO3 discolysis.

The research protocol was submitted for discussion by the participating researchers and review and approval by the Ethics Committee and Institutional Review (Fiorela Clinical Institute, San Pedro Sula, Honduras and Fiorela Clinic, Madrid, Spain). The protocol was implemented only after approval and it complied with the World Medical Association Declaration of Helsinki, Ethical Principles for Medical Research Involving Human Subjects. Patients received a detailed explanation about the research and they gave their consent verbally and in writing.

Clinical criteria for inclusion: Lumbosciatic with signs of nerve root involvement resistant to conservative treatment for at least three months.

Radiological criteria: Protrusion, contained and extruded disc herniation with less than 50% of the diameter of the dural sac with or without signs of disc degeneration, using MRI. Preserved disc. Interfacetaria osteoarthritis.

Exclusion criteria: Calcified herniated disc, herniated disc with free fragment, extrusion of more than 50% of the diameter of the dural sac and associated higher neurologic deficit.

Clinical protocol: Prior to discolysis patients underwent a session of lumbar paravertebral infiltration to 2 cm lateral from the line interapofisaria; the volume was 10 mL of O₂-O₃ to 10 µg/mL per point, plus 1 mL of procaine i.m. in different plane from the infiltration of ozone.

All discolysis were performed in the operating room, under full aseptic, fluoroscopic control, sedation and local anesthesia. Ceftriaxone was administered 1g. i.v. single dose during performance of surgery.

The Autologous Platelet Rich Plasma (PRP) was prepared in closed systems (PROTEAL®) in the operating room by a physician specialized in its preparation and acquisition. The ozone

generator used was Ozonobaric P® with CE0120 Certificate Class IIb (European Union certification) with direct and indirect concentration measuring, which makes it reliable.

The blood was heparinized, PRP was ozonolyzed to 40 and 80 mg / mL and was activated with 10% Calcium Chloride.

Discolysis: The patient was placed prone with abdomen upward to compensate for lumbar lordosis. Under fluoroscopic control with tunnel vision in anteroposterior projection and the help of a 22-gauge needle Chiva G, crossed the annulus fibrosus, placed the tip of the needle into the center of the disc and his lateral position was checked. After confirming the correct position of the needle intradiscal ozone administration proceeded, at a concentration of 30µg/mL and periradicular at 10 µg/mL concentration. Immediately infiltrating intradiscal PRPO3 and in the epidural space specially in diagnosed cases with advanced osteophytes interfascetaria osteoarthritic and narrow channel.

Post-discolysis: It proceeded with: 1) Six lumbar paravertebral facet sessions. 2) Two lumbar paravertebral facet PRPO3 sessions. 3) Ten sweeps magnet therapy. 4) Ten sweeps CO2 laser. 5) Reviews: At 15 days, 1 month, 4 and 6 months, with MRI control at 4 or 6 months.

The effectiveness of the method was based on the control of pain according to VAS scale from 0 to 10; on clinical examination according to Lasegue and Bragard maneuvers, at 15 days, 1 month, 4 and 6 months; and through MRI (magnetic resonance imaging) in 35 patients at 4 and 6 months. All patients were questioned about the possible side effects that may be related to the technique. The degree of patient satisfaction at the end of the study, according to the criteria: good, fair or poor was also recorded.

Results

The basic demographic data of patients studied are shown in Table 1.

150 percutaneous discolysis with ozonated growth factors were performed in 60 patients, of whom 41 were males (68.3%) and 19 women (31.6%) with an age range between 35 and 82 years, the L5-S1 and L4-L5 segments being the most frequent. The mean of segments touched per patient were 2-3.

	Variable	Ozone + PRPO ₃ (n=60)	
		n	%
Age (years)	35-45	12	20%
	46-55	21	35%
	56-65	15	25%
	66-75	7	11.6%
	76-85	5	8.3%
Gender	Female	19	31.6%
	Male	41	68.3%
Background	Hypertension ^a	11	18.3%
	Diabetes ^b	8	13.3%
	Ischemic Heart Disease	0	
Risk factors	Hypercholesterolemia ^c	21	35%
	Obesity ^d	48	80%
	Smoker	0	
	Alcoholic	0	
	Drug use	1	1.6%
Complementary teraphies (previous)	Medications	60	100%
	Supplements	31	51.6%
	Physical rehabilitation	15	25%
	Column surgery	3	5.0%
Location of lessions	L5-S1	58	96.6%
	L4-L5	55	91.6%
	L3-L4	22	36.6%
	L2-L3	15	25%
	Sacro iliac	32	53.3%

Table 1. Characterization of the patients studied.

a Hypertension was considered to be elevated systolic blood pressure > 140 mmHg and /or diastolic > 90 mmHg.

b Fasting Glucose > 3.58-5.6 mM.

c Cholesterol figures <200 mg/dl (5.18 mM).

d BMI figures > 27. BMI (Body Mass Index). PRPO₃, Platelet Rich in Ozonated Plasma.

At 15 days 58 patients reported 3-4 points VAS (Visual Analog Scale) responding primarily to local pain originating from the puncture site; negative Lasegue and Bragard; no pain at palpation over the spinous processes. Patients returned to their normal activities. One month after surgery 54 patients had 2-3 points VAS; negative Lasegue and Bragard; no pain at palpation over spinous processes. At 4 months 54 patients had a 0-1 point VAS. Negative lumbar

scanning and full functional recovery (Figure 1).

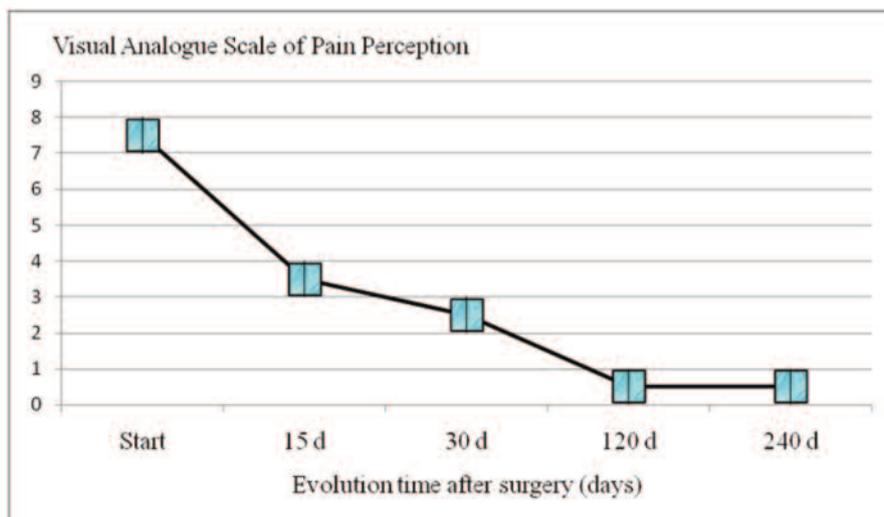


Figure 1.
Evolution of pain perception after treatment based on the visual analog scale (VAS). Ten represents excruciating pain and zero presence of non-pain.

At 6 months, only 6 patients had complaints of low back pain, qualified with a 5-6 VAS responsive to nonsteroidal anti-inflammatory drugs and physiotherapy, confronted with an initial VAS 7-8. Only one patient required a second discolysis within 15 days of the first operation because his response was partial. After the second operation the symptomatology was completely resolved. It should be noted that the patient was a regular user of cocaine and had not informed the researchers of the fact.

Two patients (female) had mild transient headaches, and one of them presented pneumocephalus with dizziness and vomiting disabled for 4 days, which forced her to rest in bed for a week and receive metaclopramida iv. Within a week the symptoms were completely resolved. MRI control was performed on 35 patients at 4 or 6 months (not all patients agreed to the implementation of MRI for lack of money; or not considering it necessary because of not presenting any symptoms), which showed a significant volume reduction of the hernia and rehydration of most treated discs (Figure 2).

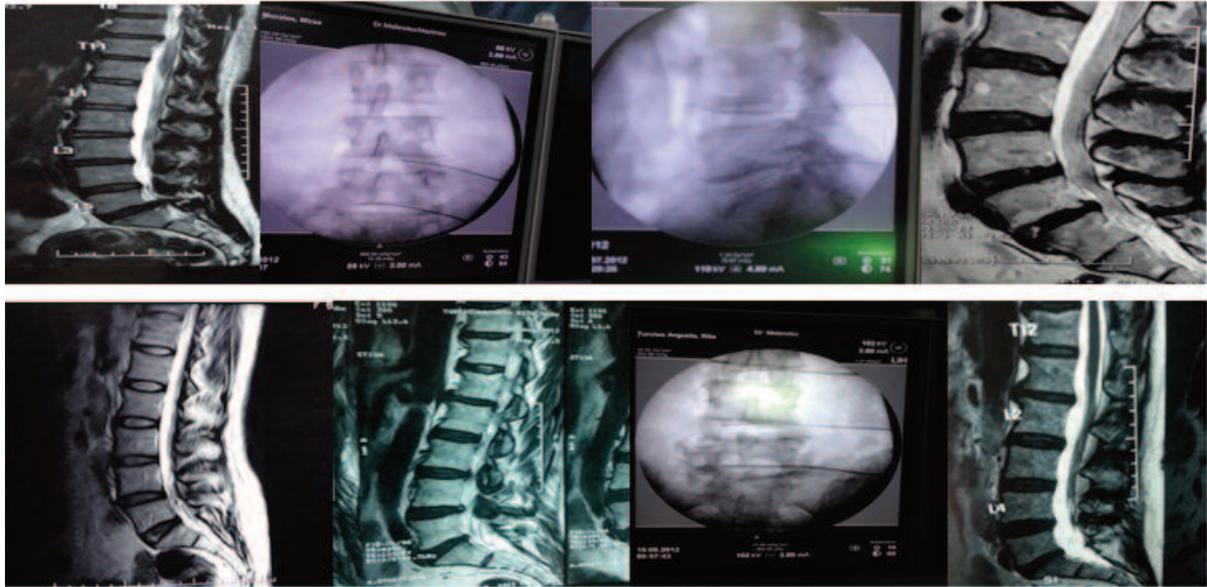


Figure 2.

Representative images of MRI of two patients before and 4 months after treatment. They clearly show the resolution of the root compression and the start of rehydration of disks L4-L5, L5-S1. The patients are asymptomatic.

According to the data provided in this paper, we can say that 90% of patients responded very satisfactorily to treatment. Only 10% of them had a partial result.

In terms of satisfaction expressed (Figure 3), 54 (90%) of the patients were good, 5 (8.3%) patients were fair with severe discartrosis, one patient (1.6%) was bad who expressed not getting any improvement (the patient did not follow postural hygiene and rest post-treatment directions).

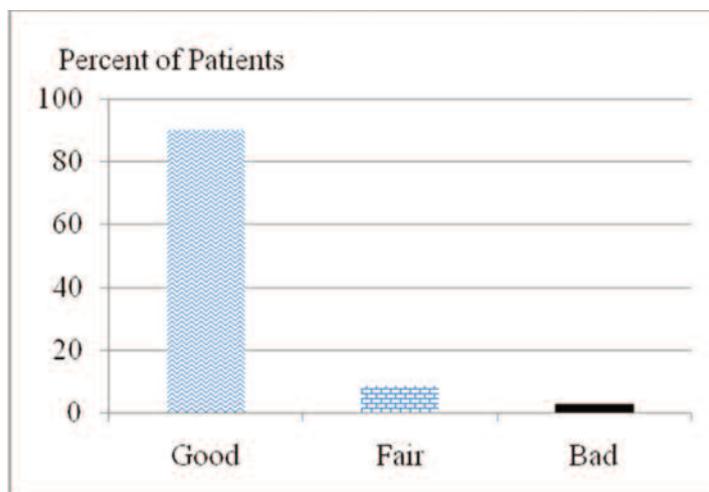


Figure 3.
Qualitative perception of the degree of satisfaction of patients 6 months after intervention.

Discussion

The use of platelet concentrated to accelerate the healing process was first described in 1997. Dr. Fernando Kirchner for the first time in 2012, applied Ozonated Growth Factors in the vertebral disc while performing the traditional discolysis with ozone. His results were more than good, 85% of resolution. This coincides with the high therapeutic success rate found in this study (90%).

The present paper is based on PRP regenerative properties which mimic the events occurring during the physiological process of healing due to the release of various growth factors. Being autologous the safety of the procedure is high and the required amount is obtained from the patient's own blood. The PRP is a concentrate which contains not only platelets but also consists of plasma, leukocytes, growth factors, protein secretion and all components of the coagulation cascade. It includes: Transforming growth factor beta 1 (TGF- β 1), vascular endothelial growth factor (VEGF) and the platelets derived growth factor (PDGF) among others.

The healing mechanism potentiation induced by supra-physiological concentrations of autologous platelets in damaged tissue or surgical site has been demonstrated both in basic and clinical studies. Due to the high concentration and release of these factors the PRP can potentially increase recruitment and proliferation of stem cells and endothelials. The ozone promotes platelet aggregation and the release of factors with mitogenic, angiogenic, cyto-protective and chemotactic properties, especially when using heparin as an anticoagulant; a significant increase of PDGF (platelet-derived growth factor), TGF - β 1 (Transforming Growth Factor β 1), eicosanoids and interleukin 8 (IL-8) is observed. Therefore, the choice of anticoagulant is crucial when we want to obtain a plasma rich in growth factors. For best results

it requires concentrated platelets between 3-5 times above the basal level. Considering that a normal individual has about 200 000 platelets/uL, a concentrated platelet with 1 million platelets/uL would be optimal for therapeutic purposes. It has been demonstrated that higher concentrations do not increase the effect in terms of wound healing .. Working under these conditions, this study shows that satisfactory results are achieved, maintained over time and evident both from the clinical point of view and from an objective manner as we have documented by magnetic resonance imaging.

To understand the mechanism of the action of ozone in spinal pain is essential to comprehend its pathophysiology. The isolated compression of the root gives deficit symptoms (paresthesia, dysesthesia, motor deficit), but no pain. To produce pain, there must be chemical irritation and inflammation of the root. The herniated disc nucleus pulposus contains high concentrations of phospholipase A2 ,which can initiate the inflammatory cascade and other inflammatory mediators such as prostaglandins, leukotrienes, bradykinin and histamine. When a crack occurs in the annular disk, which is the first phase of disc degeneration, these substances are released by the core and may produce radiculitis even if there is not root compression.

Thus, the application of Ozone and Intradiscal Growth Factors acts at different levels. It:

1. Produces inhibition of prostaglandin E2 and of phospholipase A2 (like steroids) and other citocinasproinflamatorias (IL 1, 2, 8, 12, 15, 17, interferon α).
2. Increases the release of immunosuppressive cytokines (IL10, factor B1), which comprises an analgesic and anti-inflammatory effect.
3. Increases local microcirculation, reduces stasis: analgesic effect, since the nerve root is very sensitive to hypoxia.
4. Presents direct effects on the mucopolysaccharides and proteoglycans in the nucleus pulposus, which is called ozonolysis, producing a chemical discolysis with water loss and dehydration.
5. Produces subsequently matrix degeneration, which is replaced by collagen fibers in about 5 weeks, and due to the formation of new blood cells, reduces the volume of disc.

In summary, there is a quadruple ozone action mechanism in the disc root complex: (1) Dehydration of the disc material that would diminish the compressive mechanical factors on the root. (2) Interruption of the inflammatory process with immediate installation of analgesic effect with a marked improvement of the immune system. (3) Healing of the damaged disc. (4) Revascularization of the area involved improving the blood supply with the disappearance of tisular hypoxia. These effects of ozone allowed the control of the pain syndrome in these patients and its association with PRPO3 increased the effectiveness of treatment to help the process of local tissue repair.

Conclusions

Addressing the disc herniation using minimally invasive techniques with ozone and PRPO3 is a safe and effective therapy, which is justified due to the high degree of complications posed by surgical methods. The practice of ozone therapy is based on solid scientific arguments.

When it is applied by trained personnel, following scientifically approved protocols (See Madrid Declaration on Ozone Therapy) and all regulations of this medical practice, its therapeutic success is very high and the degree of complication is minimal. This is demonstrated by the results of this study. The percutaneous discolysis with ozone and PRPO3 infiltration with its healing and restorative effect on the disc, makes this technique safe and effective therapy in the treatment of disc herniation and discartrosis.

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