Treatment of symptomatic lumbar spinal degenerative pathologies by means of combined conservative biochemical treatments.

Treatment of symptomatic lumbar spinal degenerative pathologies by means of combined conservative biochemical treatments.

University Experimental Protocol for the use in Public Health System.

Authors: Alexandre A, MD*

Corò L, MD*

Paradiso R, MD*

Dall'Aglio R.*

Alexandre AM., MD**

Fraschini F. ***

Spaggiari P.G:****

Address: * European Neurosurgical Institute (EU.N.I.)

Via Ghirada 2, 31100 Treviso, Italy

** Department of Bioimaging and Radiological Sciences, Catholic University Sacred

Heart. Policlinico "A.Gemelli". Rome, Italy.

*** Pharmacology Institute of Milan University School of Medicine, Milan, Italy

**** General Direction and Administration, Cremona Hospital, Italy

Keywords:

discoradicular conflict, spinal degenerative pathologies, oxygen-ozone injections, degenerative disc disease, FBSS, herniated lumbar disc, conservative biochemical treatments, Ozone, Discolysis, periduroscopy.

Summary:

Research in spine surgery has proposed new, soft and less invasive techniques. These are the results of our experience with oxygen-ozone therapy, which we could experiment inside the Italian National Health System through tree years. A total of 1920 patients were admitted on the basis of unselected enrolment because of lumbosciatic pain. Patients were divided in three groups: A) Patients with degenerative disc disease and arthropathy: 509 (26.5%), B) Patients with failed back surgery syndrome (FBSS): 1027 (53.489%), and C) Patients with pure herniated lumbar disc: 384 (20%). The rationale of the treatment for all these different pathologies which we have taken in consideration is the biochemical mechanism by which they can engender pain and dysfunction. Treatment for group A: paravertebral injection and phleboclysis (two cycles of 6 sessions, one each 3 days) + endoscopic neurolysis. Treatment for group B: paravertebral injection and phleboclysis (two cycles of 6 sessions, one each 3 days) + endoscopic neurolysis with intradiscal procedure. (named percutaneous peridurodiscolysis). Treatment for group C: paravertebral injection (two cycles of 6 sessions, one each 3 days) + percutaneous discolysis.

The perceived quality of result for this minimally invasive procedure, makes oxygen-ozone therapy an interesting weapon in the hand of the doctors. Furthermore if the technique loses its clinical effectiveness, it can be repeated without harm for the patient, and the cost for the health organization is notably very low, above all if compared to surgical procedures.

We underline the need that this treatment is performed in protected structures, in operative rooms, under anesthesiologic control, and in the hands of specialists.

INTRODUCTION

Problems connected with pain and dysfunction due to disco-radicular conflict in the lumbar or cervical area are nowadays well documented. Open surgery represents an option that is indispensable at times, but may cause a number of complications or adverse effects, which are not clearly defined because the case records are generally confined to short-term follow-up, while complete reviews and metanalysis are lacking. The fact that in

the long run a high percentage of patients will suffer recurrence and complications is evident. The frequency of the problem is so high as to be recognized and defined as a complete syndrome: the Failed Back Surgery Syndrome. Epidural scarring is a natural consequence of the bleeding caused by surgery, but it is not clear why at times this will provoke adhesion and compression on the nervous structures. Furthermore, instrumentation has contributed severely to an increase in this syndrome rather than helping to correct the problem (1, 2).

These are some of the reasons for the great increase of interest in mini-invasive techniques, which aim to act directly on the disc without entering the spinal canal.

Several substances have been injected into the disc in the last few decades and each substance has enjoyed a period of popularity, some adverse effects, criticism, rejection or reduced application.

Research in spine surgery has proposed new, soft and less invasive techniques. Some of them are readily available and have been practiced for years. Among these oxygen-ozone injections, which we could experiment inside the Italian National Health System through tree years.

The objective of the treatment is to avoid every possible negative aspect of conventional surgery: general anesthesia, days of hospitalization and long-lasting postoperative limitations, spinal instability as well as the consequences of epidural scarring.

Recently critical reviews of the etiopathogenetic mechanisms underlying these manifestations of pain (that is, not just the mechanical conflict between the degenerated disc and the nerve roots or other algogenic structures, but also chemical irritation) have on the one hand suggested decreasing the use of conventional surgery for disc pathologies and on the other pointed towards more conservative mini-invasive surgical techniques that respect the anatomy and obtain a good response to the clinical problem.

Such techniques do not replace conventional surgery which, in carefully selected cases, remains first choice. Mini-invasive surgical techniques represent a midway stage between simple physiotherapy and open surgery. An high percentage of patients are thus spared open surgery, which is instead used on those who have no other choice.

Nowadays the aim is to give the person the sensation of wellbeing and not of being “ill” due to these pathologies, which are not life threatening but spoil the quality of life dreadfully.

It has been fully understood that even if there is no hope of a “full recovery” in the sense of eliminating the problem, patients can be offered a good quality of life despite the structural alteration.

This is done using simple methods, whose target is mainly the biochemical correction of nerve disfunction and hyschemia. These techniques have no significant side effects and can be repeated over the years if it needed, can always be performed as one day procedures, and do not necessitate being confined to bed.

PATIENTS AND METHODS

Patients

In the period September 05–December 07, 1920 patients with lumbosciatic pain were treated by biochemical treatments, mostly based on oxygen-ozone therapy, according to the Experimental Protocol code 119 of the observational studies of the Lombardy Region, Italy, under the supervision of the Pharmacology Institute of Milan University School of Medicine (Prof.F.Fraschini)

Patients were admitted to evaluation on the basis of unselected enrolment because of lumbosciatic pain, in the Division of Neuropatic Pain Treatment at Sant’Angelo Hospital, Lodi (supervisor Prof. P.G. Spaggiari).

Upon enrolment all the patients underwent evaluation and score by the application of the Roland Morris international disability scale and of the International Pain Visual Analog Scale (VAS).

The same evaluation has been performed upon clinical controls during the follow-up.

Further to clinical diagnosis, patients were studied by neuroradiological and EMG investigations. On these basis they were divided in three groups:

A - Patients with degenerative disc disease and arthropathy: 509 (26.5% of the series)

B - Patients with FBSS 1027: (53.489 %)

C - Patients with pure herniated lumbar disc: 384 (20%)

Methods : Rationale for the treatment

All these different pathologies which we have taken in consideration have a biochemical mechanism by which they can engender pain and

dysfunction. This is the general basis to argue that a biochemical treatment might be useful for controlling symptoms and allowing a better quality of life, avoiding open surgery.

A - The process of disc degeneration is an aberrant, cell-mediated response to progressive structural failure. A degenerate disc is one with structural failure combined with accelerated or advanced signs of aging. The term “Degenerative Disc Disease” should be applied to a degenerated disc, which is also painful. Cell-mediated responses to structural failure can be regarded as the final common pathway of the disease process (3). Although mechanical loading precipitates degeneration, the most important cause of degeneration could be the various processes that weaken a disc before disruption, or that impair its healing response. The combined effects of an unfavorable inheritance, middle age, inadequate metabolite transport, and loading history appear to weaken some discs to such an extent that physical disruption follows some minor incident. An extensive review of nomenclature made clear distinctions between pathologic and age-related changes in discs, and included major structural changes such as radial fissures and disc narrowing in the former category (4). Physical and biologic mechanisms make structural failure progresses and, therefore, this is a suitable marker for a degenerative process. Damage to one part of a disc increases load-bearing by adjacent tissue, so the damage is likely to spread to adjacent articular and ligamentous structures. Referring to tendon degeneration, Riley et al (4) suggest an active, cell-mediated process that may result from a failure to regulate specific MMP activities in response to repeated injury or mechanical strain. There is a growing consensus that degeneration involves aberrant cell-mediated responses to progressively deteriorating circumstances in their surrounding matrix.

B- Failed Back Surgery Syndrome is a definition bespeaking the clinical effect of biochemical nerve structures dysfunction. This dysfunction may be provoked by peridural scarring, by local ischemia because of reduced blood flow and/or of reduced CSF perfusion on the nerve roots and ganglia. Several reports have shown that surgical reintervention and physical decompression may not be a solution.(6,7,8)

C- Pure herniated lumbar disc with no other concomitant factors. Herniated intervertebral disc tissue has been shown to produce a large number of proinflammatory mediators and cytokines (9). Several studies have identified inflammatory mediators (phospholipaseA2, prostaglandin Ez, leukotrienes, nitric oxide, immunoglobulins, proinflammatory cytokines such as interleukin [IL]-I~, IL-11~, IL-6, and tumor necrosis factor alpha (TNFM) and autoimmune reaction (macrophages expressing IL-11~, intercellular adhesion molecules) in disk herniation. An appealing hypothesis is that the leakage of these agents may produce an excitation of the nociceptors, a direct neural injury, a nerve inflammation, or an enhancement of sensitization to other pain-producing substances (such as bradykinin), leading to the nerve root pain. (7-13). With the exception of those cases in which the severity of the motor deficit or of intractable pain perfectly fitting with neuroradiological investigations made surgery the only correct indication, patients were offered the possibility of resolving their clinical problem without open surgery and with reduced amounts of drugs. In cases where dexamethasone was being administered, it was progressively stopped at the beginning of ozone treatment. Non-steroidal anti-inflammatory drugs were administered occasionally as needed.

Methods: Specific procedures

1) Intradiscal treatment, so-called discolysis entails a mixture of oxygen and ozone in concentrations of 35 micrograms per milliliter being injected directly into the disc.

The action of the ozone consists of dehydrating the amorphous matrix of the nucleus by breaking the mucopolysaccharide structure and thereby releasing water.

There is ample literature in various fields of medicine showing that in tissues with normal blood supply ozone activates antioxidant metabolism mechanisms, has an important anti-edema effect and a very powerful anti-inflammatory effect. It also helps oxygenation of the tissues and has a positive hemorheologic effect (14).

A mixture of oxygen and ozone has been used in medicine since the thirties for treating pain and dysfunction in patients with thrombotic and ischemic illnesses. Empirical observation of the long-lasting and potent effect of an injection of this mixture into the paravertebral muscles, to treat radicular dysfunction and pain caused by the disco-radicular conflict, has led to in-depth studies on the subject. Although working in different fields, researchers surprisingly noted that a short and calculated oxidative stress, obtained by administering ozone, can correct a persistent imbalance caused by an excessive or chronic oxidative trauma or stress. It is by now clear that repeated small injections of ozone increase superoxide dismutase, catalase and gluthatione-peroxidase activity, inducing a state of adaptation to the oxidative stress with consequent important therapeutic implications (14. In 1982 Jacobs (15) reported the absence of side effects in more than 5 million sessions of ozone therapy for various pathologies. Intramuscular treatment brings about pain relief in most patients together with decongestion, re-absorption of the edema and improved motility. All this led to the idea of injecting the oxygen-ozone mixture into the intervertebral disc and into the conjugate foramen in order to obtain a powerful effect directly on the pathogenetic mechanism. (16,17,18)

Many studies have been carried out on various aspects of disc pathology and possible solutions to the problem. Studies on pain originating from this pathology show that it can be the consequence of biochemical mechanisms of acid intoxication of the nerve, which to some extent may have nothing to do with the mechanical problem, but may depend on an autoimmune reaction that triggers a chronic inflammatory response, engendering an acid environment or ischemia (19, 20, 21). In the 90s attention was drawn to phospholipase A2 as the cause of radicular pain. Saal (13) showed that phospholipase A2 is the cause of radicular pain irrespective of the immunological response or a direct inflammatory process. Phospholipase A2 is responsible for freeing arachidonic acid and therefore prostaglandins. High levels of phospholipase A2 have been found in herniated discs. These problems can be resolved with a biochemical approach, thereby reducing the need for surgery (10, 11, 13, 22). Ozone injected into the disc and the epidural space of the conjugate foramen and along the posterior longitudinal ligament acts as a powerful stimulus in activating the antioxidant defence mechanism, helping normalize the oxidation-reduction balance with neutralization of acidosis, increase in ATP synthesis, uptake of calcium-ions and re-absorption of the edema (20, 21, 22, 23). On the other hand the mechanism of endplate sclerosis and the spontaneous elimination of herniated fragments have been meticulously studied over the years and it has been shown that an autoimmune response develops against "non-self" material with a chronic inflammatory reaction. (21) Experimental models suggest that the material of the nucleus pulposus subject to degeneration can act as a chemical or immunological irritant and that these mechanisms can produce an inflammatory response (7-9). Until now studies have presumed that the injection of such a powerful oxidant as ozone induces an excess production of antioxidant enzymes, which neutralize the chain formation of unstable reactive oxygen species (ROS)(22). Ozone seems to reactivate the immunity system response. After intradiscal injection ozone can accelerate

proteoglycan degradation in the nucleus pulposus that is degenerating, leading to its re-absorption and dehydration with consequent reduction of the hernia volume causing compression of the nerves (24-27).

The intradiscal injection follows the posterolateral, extra-articular route. A fully equipped aseptic operating theatre is required with the necessary anesthesiologic assistance. Fluoroscopic apparatus allows direct control of placement. The procedure includes discography.

After an anesthesiologic assessment and before entering the operating theatre the patient is sedated with Valium 25 gtt x os and with i.m. analgesic.

At the moment of disc puncture and immediately prior to the intradiscal injection, the anesthetist sedates the patient preferably with Diprivan, an i.v. hypnotic anesthetic.

The median line and the parallel line along the lateral margin of the paravertebral muscles on the side of the pathology are drawn on the skin of the back in preparation and then the edge of the iliac crest. The skin is then disinfected and the sterile field prepared.

A 22 G 8 Chiba type, TW, 72mm x 20.32cm needle is used in such a way as to compose the hypotenuse of a triangle in which the other two lines are: (a) the distance along the median line between the skin and the disc (approx. 9 cm), and (b) the distance between the median line and the marginal parallel line of the paravertebral muscles (approx. 9 cm). The puncture is then made along the paravertebral line with an inclination of approx. 45' towards the median plane in a craniocaudal direction so as to be as parallel as possible to the disc plates. A fluoroscopic check is made. Presuming a possible inter-reaction between the gas and the iodide ion we avoided the radiopaque contrast. We have instead exploited the possibility of seeing and photographing the same type of information regarding disc conditions through a minimal volume of oxigen injected.

The purpose of discography is:

a) to confirm correct needle placement;

b) to exclude communication with vascular or subarachnoid spaces;

c) to show the extent of disc degeneration;

d) to provide documentation of the procedure.

The mixture concentration is 35 micrograms ozone/ml, but higher dosages have been used in cases of smaller or intraforaminal herniation or in young patients.

The injected quantity varies according to disc conditions. A fissured and degenerated disc allows 20 to 30 ml of gas to be introduced, since it will also spreads into the surrounding tissues, thereby automatically creating an epidural and periradicular distribution. A solid taut disc on the contrary allows only 2 to 4 of ml of mixture at the most to be injected under great pressure.

After the procedure the patient should be made to rest in a supine position for at least two hours so that the gases are not immediately dislodged by the orthostatic load.

2) endoscopic epidurolysis is another technique which fits the carachteristics of minimal invasiveness. It aims at “freeing” the nerve roots from adhesions that could have formed as a consequence of the conventional microdiscectomy operation. Apart from the Failed Back Surgery Syndrome, endoscopic epidurolysis is indicated in stenosis of the vertebral canal due to arthrosis, which causes the classic neurogenic claudication.

The epidurolysis procedure consists of penetrating the spinal canal through the sacral jatus, with an endoscope containing an optic fiber 0.9 mm in diameter, a flushing and suction channel, and a metallic guidance sistem.

The endoscope goes up in the vertebral column as far as the first lumbar vertebra.

The procedure is carried out under local anesthesia with a very low iatrogenic risk. (28, 29)

3) outpatient treatment

In outpatients the purpose of the treatment was the nutrition of the nervous structure, against its actual situation of sub-ischemia, as well as the correction of the acid balance. This was done by a series of outpatient procedures, carried out in the pre- and post-operative phases.

Oxygen-ozone gas mixture has been administered locally to the site, in and through the paravertebral muscles (with a periganglionic or periradicular target), thereby greatly reducing the need for corticosteroids while having a fast, continual effect on the pain.The doses were 10 ml gas mixture, at 15 micrograms ozone concentration per ml, injected on each side paravertebral at the level of the pathology, through a 20 G needle 5 cm long. After the injection the patient is left 5 minutes resting lying down.

Patients often felt an instant benefit as if an anesthetic has been injected,thanks to the strong anti-edema and anti-inflammatory effect.

One of the Authors, a General Medicine Professional (R.d.A.) could add ozone into 300 ml venous blood drawn off into a transfusional bag, at the dose of 50 ml 0203 gas mixture at 30 micrograms per ml ozone concentration, performing the socalled Autohaemotherapy. (30–31)

All these procedures have greatly reduced the need for conventional anti-inflammatory drugs and cortisone, all to the benefit of suppressing the incidence of side effects.(32)

Based on these methods, this is the protocol of the treatment, for each pathological situation:

Treatment for group A: paravertebral injection and phleboclysis (two cycles of 6 sessions, one each 3 days) + endoscopic neurolysis

Treatment for group B: paravertebral injection and phleboclysis (two cycles of 6 sessions, one each 3 days) + endoscopic neurolysis with intradiscal procedure. (named percutaneous peridurodiscolysis)

Treatment for group C: paravertebral injection (two cycles of 6 sessions, one each 3 days) + percutaneous discolysis.

RESULTS

As mentioned we treated 1920 patients, 43.5 % of whom were men and 56.4 % women.

In the table , the age distribution.

age of patients	total	women	men
20 to 35	n.538 = 28.02 %	247 (45.9%)	291(54.09%)
36 to 45	n.774 = 40.31%	453 (58.52%)	321(41.47%)
46 to 88	n.608 = 31.66%	383 (62.9%)	225 (37%)

Patient Group A with degenerative disc arthropathy:

509 patients, the 26.5% of the entire series. These are persons suffering from problems involving multiple vertebral and disc levels with degenerative and arthrosic factors that make “conventional” surgery either impracticable or very invasive, probably involving stabilization with multi-level instrumentation, i.e. vertebral arthrodesis with metal implants.

Results come from the application of the Roland Morris international disability scale and from the International Pain Visual Analog Scale (VAS).

These patients underwent outpatient treatment with the prospect of passing on to the percutaneous operation of endoscopic neurolysis . In the outpatient phase

9 p. (1.76 %) showed no clinical result whatsoever during those applications, so treatment was suspended and they were removed from the classification.

225 p. (44.2 %) showed a moderate result and passed on to percutaenous endocopic neurolysis.

122 p. (23.9%) showed a good clinical result and passed on to the percutaneous endoscopic neurolysis

153p. (30.05%) showed an excellent result and the cure was considered sufficient and was ended.

We consequently assessed the results obtained after the percutaneous endoscopic neurolysis and compared to the situation scored at the end of outpatient therapy.

The 225 patients with moderate result changed as follows:

43 out of 225 (19.11%) passed to a situation of excellent result

57 out of 225 (25.33%) passed to a situation of good result

121 out of 225 (53.77%) remained with a situation of moderate result

4 out of 225 (1.77 %) passed to a situation of poorer result

the 122 patients with good result changed as follows:

65 out of 122 (53.27 %) passed to a situation of excellent result

55 out of 122 (45.08 %) remained with a situation of good result

2 out of 122 (1.63%) passed to a situation of moderate result

After outpatient treatment and the mini-invasive percutaneous endoscopic neurolysis, for patients with multi-level degenerative disc arthropathy of the lumbar column the result is:

Excellent in 153 + 65 + 43 = 261 cases out of 509 (51.27 %)

Good in 55 + 57 = 112 cases out of 509 (22 %)

Moderate in 121 + 2 = 123 cases out of 509 (24.16 %)

Poor in 4 = 4 cases out of 509 (0.78 %)

It was impossible to treat 9 cases out of 509 (1.76 %)

Adding together excellent + good gives 373 cases out of 509 = 73.28 %

Patient Group B: Failed Back Surgery Syndrome FBSS.

1027 people came to us because of persistent pain in the vertebral column having the characteristics of pain-dysfunctional suffering typical of the failed back surgery syndrome: lumbar pain, abnormal gait and fatigability, diffuse reduction in the strength of the lower limbs and frequently persistent pain also during the night.

As already mentioned, in this group the treatment was: paravertebral injection and phleboclysis (two cycles of 6 sessions, one each 3 days) + endoscopic neurolysis with intradiscal procedure (named percutaneous peridurodiscolysis)

With regard to outpatient treatment the results after two cycles of 6 sessions were:

2 p. (0.194%) treatment not tolerated and stopped immediately – eliminated from the study group

30p. (2.92%) no useful clinical result

256 p. (24.9%) moderate result

441 p. (42.94%) good result

298 p. (29.01%) excellent result

total 1027

Mini-invasive percutaneous peridurodiscolysis was then carried out with the following results:

out of the 30 p. with no result from the outpatient treatments: 10 poor result, insufficient

15 moderate improvement

5 good improvement

the 256 patients with moderate outcome changed as follows:

20 out of 256 (7.8 %) passed to a situation of excellent result

64 out of 256 (25 %) passed to a situation of good result

172 out of 256 (67.18 %) remained with a situation of moderate result

the 441 patients with good outcome changed as follows:

105 out of 441 (23.8 %) passed to a situation of excellent result

314 out of 441 (71.2 %) remained with a situation of good result

22 out of 441 (4.9 %) passed to a situation of moderate result

the 298 patients with excellent outcome changed as follows:

35 p. decided to suspend the cure, not feeling any need for further therapy (11.74% out of 298 patients).

263 underwent percutaneous epidural-discolysis:

258 out of 263 (98 %) remained with a situation of excellent result

5 out of 263 (1.9 %) had a reduction in the quality of the clinical result, which became moderate.

After outpatient treatment and the mini-invasive percutaneous peridurodiscolysis, for patients with failed back surgery syndrome, the result is:

Excellent in 20+ 105+ 35+ 258 = 418 cases out of 1027 (40.7 %)

Good in 5+64+314 = 383 cases out of 1027 (37.29 %)

Moderate in 172+ 22+5+15 = 214 cases out of 1027 (20.83 %)

Poor in 10 = 10 cases out of 1027 (0.97 %)

It was impossible to treat 2 cases out of 1027 (0.19 %)

tot 1027

Adding together excellent + good gives 801 cases out of 1027 = 77.99 %

Treatment Group C: patients with herniated lumbar disc and no other concomitant factors

The treatment for this group was: paravertebral injection (two cycles of 6 sessions, one each 3 days) + percutaneous discolysis. In some cases of very painful clinical situation, the intradiscal injection of 0203 (percutaneous discolysis) was performed simultaneously to the outpatient treatment, not after it.

Out of 384 patients, 78 (20.3 %) benefited greatly from the outpatient treatment to the extent that they did not wish to be admitted for the intradiscal injection of the 0203 mixture. They therefore finished the cure of just paravertebral therapy with a result considered

Good in 49 (12.76 %)

Excellent in 29 (7. 55 %)

Another 6 patients were not admitted for the intradiscal injection procedure of the 0203 mixture due to existing anti-coagulant therapy (4) or existing cardiologic problems. They therefore finished the cure of just paravertebral therapy with a result considered

Good in 4 (1.0 %)

Excellent in 2 (0.52%)

The remaining 300 patients were treated with an intradiscal injection of the 0203 mixture after the outpatient treatment: discolysis

In order to obtain a very careful evaluation, the result of the percutaneous treatment for these patients was compared with a similar series of 300 patients treated by the same group of professionals over the last 3 years, by the conventional open microsurgical removal procedure: microdiscectomy. The case record trend is as follows:

Level of lumbar hernia

	microdiscectomies	**percutaneous discolysis**
L1-L2	1 (0.33%)	3 (1%)
L2-L3	4 (1.33%)	3 (1%)
L3-L4	28 (9.33%)	36 (12%)
L4-L5	159 (53%)	165 (55%)
L5-S1	108 (36%)	93 (31%)

Type of lumbar hernia

	microdiscectomies	**percutaneous discolysis**
Contained	197 (65.6%)	200 (66.6%)
• Extruded	93 (31%)	82 (27.3%)
• Migrated	10 (3.3%)	18 (6%)

a) Regression of pain at check-ups (VAS Regression > 4 points)

Check-ups	**microdiscectomies**	**percutaneous discolysis**
• 4-6 months	292 / 300 (97.3%)	280 (93.3%)
• 1 year	275 (91.6%)	276 (92 %)
• 18 months	250 (83.3%)	262 (87.3%)

b) Regression of pain / level, after 1 year (VAS Regression > 4 points)

	microdiscectomies	**percutaneous discolysis**
• L1-L2	1 (100%)	3 (100%)
• L2-L3	3 (50%)	3 (100%)
• L3-L4	24 (82.1%)	33 (91.6%)
• L4-L5	143 / 159 (89.9%)	150 / 165 (90.90%)
• L5-S1	104 / 108 (96.2%)	88 / 93 (94.6%)

c) regression of pain / type of hernia (VAS Regression > 4 points)

• Hernia	**microdiscectomies**	**percutaneous discolysis**
• Contained	163/197 (82.74%)	172/200 (86%)
• Extruded	85 / 93 (91.39%)	76 / 82 (92.6%)

- Migrated 9 / 10 (90%) 15 / 18 (83.33%)

d) regression of pain / intraforaminal localization of the hernia (VAS Regression > 4 points)

microdiscectomies	**percutaneous discolysis**
22 (91.6%)	22 (84 6%)

e) regression of sensorial dysfunction at 18 months

	microdiscectomies	**percutaneous discolysis**
• complete	82.5 %	83.2 %
• partial	12.4 %	9.4 %
• insignificant	5.1%	2.4 %

f) regression of motor deficit at 18 months

	microdiscectomies	**percutaneous discolysis**
• complete	86.6%	85.7%
• partial	9.8%	8.3%
• insignificant	3.6%	6 %

g) regression of initial severe motor deficit at 18 months

	microdiscectomies	**percutaneous discolysis**
• complete	44.4%	40%
• partial	22.2%	20%
• insignificant	33.3%	40%

h) complications observed in the two series of case records related to the procedure:

microdiscectomies	**percutaneous discolysis**
4 fistulas of cerebrospinal fluid	2 chemical discitis
1 bacterial discitis	

Discussion and Conclusions

We have mentioned patients for whom the result was insignificant and who abandoned the cure, but we must call attention to the 2 patients who could not tolerate the treatment applied for FBSS (treatment group B), which was immediately stopped. They both showed reactions of intolerance to ozone with consequent sudden changes in systemic arterial pressure, hypertension and hypotension respectively, which were well controlled and managed and promptly resolved by the appropriated emergency care treatment. This made it impossible to re-propose the treatment to these patients. Such reactions were studied, and are explained to be very likely due to enzymatic changes in the hyperoxidation control mechanisms, which could in turn be due to existing latent clinical situations such as forms of favism in which certain anti-hyperoxidation control enzymatic chains are missing.

Patient Group A with degenerative disco arthropathy

At the end of paravertebral outpatient treatment, 122 patients (23.9% of the group) showed a good clinical result and 153 (30.05%) showed an excellent result. Summing together these two groups, we have a total positive effect of oxygen-oxone gas mixture administration in the paravertebral area of 53.95%. The remaining 225 (44.2 %) patients have shown a moderate result, which was anyway considered by them positive. The perceived quality of result, in consideration of the minimal invasiveness of the procedure, made several of these patients doubtfull on the need of the further peri- and intradiscal treatment which we had suggested in order to make the result more consistent and stable. After having performed peri and endoscopic neurolysis, 100 patients with moderate result passed to excellent or good result. Thereby the total result adding together excellent + good results gives 373 cases out of 509 , that is 73.28 % .

Patient Group B: Failed Back Surgery Syndrome FBSS

After outpatient treatment and the mini-invasive percutaneous peridurodiscolysis, for patients with failed back surgery syndrome, the result is positive in 801 cases out of 1027 = 77.99 %

This result should be compared with overall results averaging 40 % for open revision surgery and an average of 65–70 % for rigid vertebral stabilization techniques (arthrodesis) with metal implants.

Leaving aside the sizeable difference in clinical results and also considering that there is a natural tendency for the quality of the result to diminish after many months in both procedures (mini-invasive as described here and conventional open surgery), 3 essential reflections remain:

1 – the mini-invasive technique involves the patient in nothing more than outpatient treatment during days of life which remains normal. The single admission to hospital for 1 or 2 nights, is for a treatment without consequences that are disabling or limit the patient's active life either in the short or the medium term;

2 – when the mini-invasive techniques have lost their clinical effectiveness, they can be repeated without harm for the patient at a distance of 1 or 2 years .We are talking of patients currently considered either as untreatable or as needing an invasive major surgical procedure);

3- the cost for the health organization is notably very high for surgical revisions and even more for instrumented rigid stabilizations, while the costs for mini-invasive techniques are extremely limited.

Treatment Group C: patients with herniated lumbar discs

As observed in previous papers (19) there were no statistically significant differences in the outcome for microdiscectomy and oxygen-ozone injection at 18 months after treatment. There is, however, the absolute difference in invasiveness of approach, the percutaneous procedure being closed and without general anesthesia, using just pharmacological sedation under anesthesiologic control.

Microdiscectomy is indispensable in situations of particularly high pain levels and when there is acute and severe motor deficit. The morbility and mortality rates of the microdiscectomy procedure are well known, as is the possible consequence of FBSS.

Discolysis is a procedure that is practically free from short- and long-term complications and can be applied even when general health is poor. It should be noted that in the event of unsuccessful results with discolysis the situation is not worsened by difficulties for future treatment due to post-surgical scar or weakening of the bone structure, as is the case with open surgery.

General Comment

As a general consideration we must comment that the adverse effects which have been observed during oxygen-ozone treatment underline the need that this treatment should be performed in protected structures, in operative rooms, under anesthesiologic control, and in the hands of specialists. Anyway the incidence of these adverse effects is extremely low with respect with any other kind of medical treatment for these diseases.

The results which are given by this therapy are clinical results, and there is nowere the idea that this therapy will solve the problem. Pain and dysfunction coming from degenerative pathologies of the spine have no way a complete definitive solution: these are problems which can not be cured, since they represent the clinical expression of morphological alterations which are in the physiological range rather than "diseases". This should be clearly explained to all the patients, despite the kind of therapy which is undertaken.

Ozone therapy is useful in the terms in which it avoids major surgery and allows a better quality of life despite structural degeneration. Recurrence can be treated in the same manner,with irrelevant risk.

Ozone therapy

References:

1. Gibson A.J.N. G. Waddell (2007) surgical interventions for lumbar disc prolapse. Updated Cochrane review. Spine 32,16: 1735-1747

2. Weinstein J.N., Tosteson T:D:,Lurie J.D., et Al. (2006) Surgical versus nonoperative treatment for lumbqar disc herniation. The Spine Patient outcome research trial (SPORT): a randomized trial. JAMA 296: 2441 – 2450

3. Fardon DF. (2001) Nomenclature and classification of lumbar disc pathology. Spine; 26:461-2.

4. Roberts S; Evans H; Trivedi J; Menage J, (2006) Histology and pathology of the human intervertebral disc.J Bone Joint Surg Am. 88 Suppl

2:10-4.

5. Riley GP, Curry V, DeGroot J, et al. (2002) Matrix metalloproteinase activities and their relationship with collagen remodelling in tendon pathology. Matrix Biol; 21:185-95.

6. Fiume D, Sherkat S, Callovini GM, Parziale G, Gazzeri G. (1995) Treatment of the failed back surgery syndrome due to lumbosacral epidural fibrosis. Acta Neurochir Suppl; 64:116-118.

7. Ross JS, Robertson JT, Frederickson RC, et al. (1996) Association between peridural scar and recurrent radicular pain after lumb ar discectomy: Magnetic resonance evaluation. ADCON-L European Study Group. Neurosurgery; 38:855-61

8. Mannismaki P, Vanharanta H, Puranen J. (1993) Disability 20–30 years after disc surgery: A follow-up of 162 patients. Presented at the annual meeting of the International Society for the Study of the Lumbar Spine, Marseilles, France, June 15–19,

9. J. G. Burke, FRCS I (2002) R. W. G. Watson, PhD; D. McCormack; F. E. Dowling; M. G. Walsh; and J. M. Fitzpatrick.: Intervertebral discs which cause low back pain secrete high levels of proinflammatory mediators. J.Bone and Joint Surg. - British Volume, Vol 84-B, 2, 196-201.

10. Chang J, Gilman SC, Lewis AJ. (1986) Interleukin 1 activates phospholipase A2 in rabbit chondrocytes: a possible signal for ILI action. J Immunol;136:1283-7.

11. Kang JD, Georgescu HI, McIntyre-Larkin L, Stefanovic-Racic M, Donaldson WF, Evans CH. (1996) Herniated lumbar intervertebral discs spontaneously produce matrix metalloproteinases, nitric oxide, interleukin-6, and prostaglandin E2. Spine;21:71-7.

12. Olmarker K, Rydevik B, Nordborg C. (1993) Autologous nucleus pulposus induces neuro-physiologic and histologic changes in porcine canda equina nerve roots. Spine; 18:1425-32.

13. Saal JA, Saal JS, Herzog RJ. (1990) The natural history of lumbar intervertebral disc extrusions treated nonoperatively. Spine;15:683-6.

14. Bocci V. (1998) Ozonetherapy may act as a biological response modifier in cancer. Forsch Komplement; 5: 54-60.

15. Jacobs MT. (1982) Untersuchung uber Zwischenfalle und typische Komplikationen in der Ozon-Sauerstoff-Therapie. OzoNachrichten.1-5.

16. Alexandre A., Soattin G.B., Fumo G.: (1997) Intradiscal ozone injection: a new solution for herniated disc problems. Miami Cedars Course for Neurosurgery, Miami July 27.

17. Fabris G,Tommasini G, Lavaroni A et Al: (1997) Percutaneous treatment of lumbar herniated disk. Riv. Neuroradiol.10:523-532

18. Leonardi M, Barbara C, Agati R, Simonetti L, Giatti S. (2001) Percutaneous Treatment of Herniated Lumbar Disc by Intradiscal Injection Of Ozone Mixture. Riv.Neuroradiol.14:51-53.

19. Olmarker K, Larsson K. (1998) Tumor necrosis factor a and nucleus pulposus induced nerve root injury. Spine 23:2538-2544.

20. Paulescu L. (1991) Studies on the biological effects of ozone. Induction of tumor necrosis factor alfa on human leukocytes. Lymphocaine e Cytokaine Research. 10: 409-412.

21. Takebayashi T, Cavanaugh JM, Ozakatay AC, Kallakuri S, Chen C. (2001) Effect of nucleus pulposus on the neural activity of dorsal root ganglion. Spine 26:940-945.

22. Bocci V, Luzzi E. (1995) Studies on the biological effects of ozone. Biotherapy Biophys Acta, 1271: 64-67.

23. MacNab I. (1972) The mechanism of spondylogenic pain. In: Hirsch C, Zotterman Y, eds. Cervical Pain. Oxford: Pergamon Press,88-95.

24. Jucopilla N, Dall'Aglio R, Ferrarese C, Mazzo G, Robert A, Concione L, Dal Re MS. (2000) Effetti dell'0203 sul disco intervertebrale di suino. Presented on the 1° Congress of International Medical Ozone Society of Italy, Siena, November 2-4.

25. Leonardi M, Simonetti L, Barbara C. (2001)The effects of ozone on the nucelus pulposus: pathological data on one surgical specimen. Riv.Neuroradiol.14:57-59.

26. Paradiso R., Alexandre A. (2005) The different outcomes of patients with disc herniation treated either by microdiscectomy, or by intradiscal ozone injection, Acta Neurochir. Suppl; 92:139-42.

27. Postacchini F. Lumbar disc herniation. (2001) A new equilibrium is needed between nonoperative and operative treatment. Spine 26:601.

28. Alexandre A., Corò L., Azuelos A., Buric J.: (2001) Neurolisi endoscopica del canale lombare. 2 Corso di Aggiornamento di tecniche minimamente invasive della colonna vertebrale. Treviso 7-9 Novembre.

29. Raffaeli W., Righetti D. (2005) Surgical radio-frequency epiduroscopy technique (R-ResAblator) and FBSS treatment: preliminary evaluations. Acta Neurochir. Suppl; 92:121-125.

30. Bocci V. (1994) Autohaemotherapy after treatment of blood with ozone. A reappraisal. J Int Med Res,; 22: 131-144.

31. Bocci V. (1992) Ozonization of blood for the therapy of viral disease and immunodeficiencies. A hypothesis. Med Hypot; 39: 30-4.

32. T. Wainer DDM, Burton GW, Ingold KU, Locke S. (1985) Quantitative measurement of the total, peroxyl radical-trapping antioxidant capability of human blood plasma by controlled peroxidation. FEBS Lett; 187: 33-7.