Intradiscal Injection of O_2-O_3 to Treat Lumbar Disc Herniations

Results at Five Years

A. ALEXANDRE, J. BURIC, R. PARADISO, H. SALGADO*, M. MURGA*, L. CORÒ, A. ALBARREAL*, S. SCOPETTA, H. GIOCOLI**, F. MARIN***

EU.N.I. Treviso; Italy; and Italian Section of the International Medical Ozone Society (IMOS)
** Facultad de Medicina de Sevilla, Clinica de Fatima, Sevilla; Spain*
*** Universitad de Buenos Aires; Argentina *** Clinica del Rosario, Madrid; Spain*

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SUMMARY - *A method allowing shrinkage of a herniated disc, without an open surgical approach has long been sought. Studies on the spontaneous disappearance of disc fragments have demonstrated autoimmune responses with a chronic inflammatory reaction, and radicular pain has been shown to be mostly due to release of toxic acids [10].*

Researchers in different fields surprisingly noted that a short, calculated, oxidative stress by ozone administration may correct a persistent imbalance due to excessive chronic oxidative injury [4]. Oxygen-ozone gas injection in patients with pain has a dramatic effect on clinical symptoms. On these bases the intradiscal injection of oxygen-ozone gas was conceived [1,7,9]. We report the treatment of 6665 patients with disc pathology by intradiscal injection of an oxygen-ozone gas mixture. The effect on pain and radicular dysfunction was dramatic. The effect of the treatment has also been evaluated by pathological examination.

Il trattamento delle ernie discali lombari con iniezione intradiscale di O_2-O_3

Risultati a cinque anni

RIASSUNTO - Nella storia della chirurgia del rachide si è sempre ricercato un metodo che consentisse la correzione del problema ernia discale, senza ricorrere ad interventi a cielo aperto. Gli studi sulla scomparsa spontanea di frammenti discali estrusi hanno dimostrato la esistenza di risposte autoimmuni, con conseguente reazione infiammatoria cronica, e ricerche sul dolore radicolare hanno evidenziato che esso è per lo più dovuto al rilascio di sostanze acide tossiche [10].

Ricercatori in differenti campi hanno notato che un breve stress ossidativo calcolato, provocato dalla somministrazione di ozono, può correggere uno sbilanciamento persistente, causato da un trauma ossidativo cronico [4]. L'iniezione di questa miscela di gas nel disco patologico è stata concepita [1,7,9] partendo da osservazioni empiriche sul rilevante effetto della paravertebrale. Riportiamo qui il risultato del trattamento intradiscale in 6665 pazienti. Gli effetti sul dolore e sulla disfunzione radicolare sono drastici. L'effetto sulla morfologia dell'ernia è significativo. Quest'ultimo aspetto è stato valutato anche con studi istopatologici.

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Introduction

In cases of lumbar radicular dysfunction due to discal-radicular conflict, the classical surgical treatment by open surgery entails a high percentage of complications or failures. For fifty years neurosurgeons have been searching for a method which will allow shrinkage of herniated or protruded disc to solve the problem of severe pain and dysfunction of an enormous number of patients. A number of non invasive percutaneous techniques have been conceived, which aim to remove or provoke shrinkage of the discal tissue. The common principle of these techniques is that of acting directly on the discal structure, without access to the spinal canal. This will eliminate the possibility of scar tissue forming in the epidural space, which will make nervous tissues compressed and adherent to the moving bones. Disc puncture through a lateral approach has allowed injection of chondrolytic enzymes, hydrocortisone, papaine, collagenase, or aprotinin. Each of these substances has enjoyed a period of favour, but has given problems because of scanty results or major side-effects.

Much research has been done on the various aspects of disc pathology, and on the possible solutions to the problem. Studies on pain originating from this pathology show that it may be the consequence of biochemical mechanisms of acid intoxication of the nerve, which may somehow be independent from the mechanical problem, but depend on an autoimmune reaction, producing a chronic inflammatory response which engenders an acid environment, or a situation of ischaemia [10]. These problems may be solved by biochemical treatment, reducing the need for surgical aggression [1-3,7].

On the other hand, over the years the mechanisms of disc shrinkage and elimination of herniated fragments have been carefully studied and the development of an autoimmune response against a "non-self" material, leading to a chronic inflammatory reaction has been demonstrated [6].

A mixture of oxygen and ozone gases has been employed in medicine since the thirties to treat pain and dysfunction in patients with thrombotic and ischaemic diseases. The empirical observation of the powerful long-lasting effect of injection of this gas mixture into the paravertebral muscles to treat pain and radicular dysfunction because of discal-radicular conflict has led to detailed studies on the subject. Working in different fields, researchers have surprisingly noted that the short, calculated oxidative stress achieved by ozone administration may correct a permanent imbalance caused by excessive or chronic oxidative injury, and it is becoming clear that modest, repeated ozone treatment increases the activity of superoxide dismutase, catalase, and glutathione peroxidase, inducing a state of oxidative stress adaptation with major therapeutic implications [4]. The mixture is produced by an apparatus (ozone generator) which activates the molecules of biatomic oxygen in a voltaic arch. Ultraviolet spectrophotometry allows a precise quantification of ozone percentages in the mixture obtained. In 1982, Jacobs reported the absence of side effects in over five million ozone therapy sessions for different pathologies [8]. The paravertebral intramuscular treatment produces pain relief in the majority of patients, together with decongestion, reabsorption of oedema and increased mobility. This has led to the idea of injecting the oxygen-ozone mixture into the intervertebral disc and conjugation foramen to obtain a powerful effect directly on the pathological mechanism [1,7,9].

Patients and Methods

A total of 6665 patients with disc disease were treated by intradiscal oxygen-ozone (O_2-O_3) injection in the different centres participating in this study from 1994 to 2000. Each patient had undergone clinical, electrophysiological and neuroradiological investigation to establish a precise diagnosis. The presence of a disc herniation was demonstrated in each case. In 44.59% of cases herniation was observed at multiple levels. Enrolled patients had already received pharmacological and physical therapy without resolution of the clinical picture.

The prospect of solving the problem without drugs and without the conventional surgical treatment was offered to the patients, who accepted after detailed explanation. If pre-existing, dexamethasone administration was interrupted when starting O_2-O_3 administration, and it was never associated with O_2-O_3 treatment. Non steroidal drugs were allowed, if occasionally needed. The treatment consisted of an intradiscal injection of O_2-O_3, preceded and followed by five paravertebral injections.

- paravertebral injection consisted in the administration of 80 ml of O_2-O_3 at 10 micrograms/ml concentration, divided into four sites of injection in the paravertebral area around the metameric level of the pathology.

- intradiscal injection goes through the posterolateral extra-articular route. Its execution requires operative room equipment, allowing safe asepsis and anesthaesiological tools, a radiological apparatus for direct vision of the spine, and the source

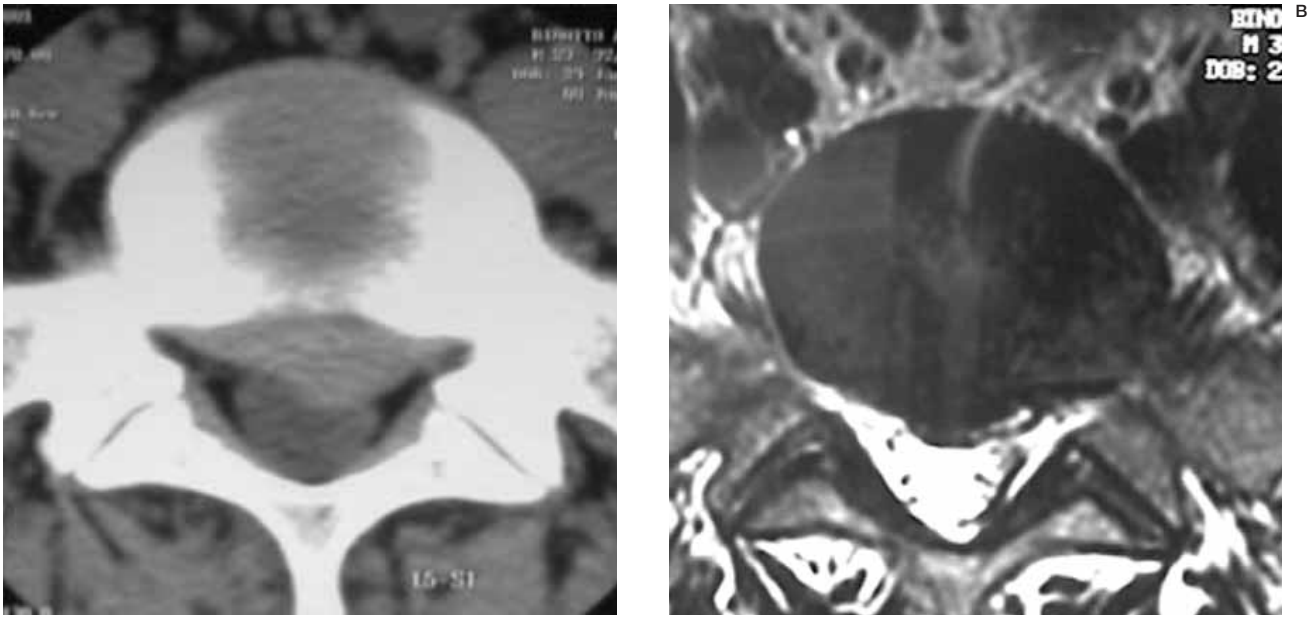

Figure 1 A) TC assiale, ernia discale L5-S1 mediana-paramediana sinistra (freccia). B) RM assiale, controllo dopo terapia. Netta riduzione volumetrica dell'ernia.
Figura 1 A) CT: L5-S1 discal hernia (A, arrow). B) Axial MRI T2 w SE, follow-up after therapy: reduction of the volume of the hernia.

of the oxygen-ozone mixture. After having positioned the needle in the disc, discography is performed to a) confirm the correct location of the needle, b) exclude a vascular or subarachnoid communication which are both contraindications to ozone injection c) show the degree of degeneration of the disc tissue, d) remain as documentation of the intradiscal procedure. The more or less positive effect of a single O_3 injection was not considered significant. The result was evaluated two months after the complete treatment.

Results

1 - Among the 6665 patients, pain symptomatology was completely abolished in 80.9% (5392 patients), amelioration was obtained in 12.4% (827 patients) and the result was poor in 6.7% (446 patients).

2 - Sensory dysfunction was abolished in 79.35% (5289 patients), improved in 15.8% (1053 patients), making a total of 95.15%. Dysfunction remained unchanged in 4.85% (323 patients).

3 - Various degrees of motor dysfunction were present in 69.6% of our 6665 patients, that is 4639 cases. Mostly it was a situation of slight strength defect, particularly evident when compared to the non-affected side. 297 of these 4639 patients presented a marked defect but either did not want to undergo surgery or agreed to the proposal of tentative conservative treatment because of general problems. 297 patients constituted 4.45% of the total group of 6665 and 6.4% of 4639 motor deficit group. The motor defect had pre-existed the treatment for six to 50 days, with a mean pre-existence of 10.2 days. Among the total group of 4639, we observed complete regression of motor deficit in 66% (3061 patients), partial in 20.7% (960 patients), and insufficient in 13.3% (617 patients). This makes a total of positive results in 86.7% of cases.

Among the patients with severe motor dysfunction (297 cases) we observed total recuperation in 18.18% (54 patients), partial improvement of strength in 32.65% (97 cases), not satisfactory or irrelevant improvement in 49.15% (146 patients). The latter patients underwent open surgery.

4 - Multiple level disc pathology was present in 2972 patients (44.59%). The treatment was performed simultaneously in all the pathological discs. The results obtained did not differ from those obtained for single level pathology.

5 - In 1199 patients, we have observed intraforaminal disc herniation. Improvement was excellent in 44.3% (2952 patients), good in 28.4% (1892 patients). Therefore, a positive result was obtained in 72.7%, limiting the need for surgery to 1821 cases (27.3%).

6 - In 933 patients (14%), an extruded and migrated herniation was demonstrated in the presence of a clinical situation which did not demand

surgery. The treatment gave complete resolution of the clinical picture in 234 cases and good results in 545 cases, making a total of positive outcomes in 83.5% (779 cases), and an insufficient result in 154 (16.5%).

7 - 3317 patients were randomly chosen by an external person to undergo CT/MRI control seven months after the treatment. In 41% (1360 cases), we observed a significant reduction in volume of the hernia (figure 1). In n 37% (1227 cases), the hernia had been completely eliminated, while in 730 cases morphology was unchanged.

Discussion

Experimental models suggest that material from the nucleus pulposus may act as a chemical or immunological irritant to the nerve, and that these mechanisms may produce an inflammatory response [10]. To date, studies have hypothesised that the injection of such a powerful oxidant as ozone induces over-expression of antioxidant enzymes, which neutralise the formation of excessive reactive oxygen species (ROS) [4]. Ozone seems to reactivate the immune system response. Several investigations have demonstrated that modest repeated ozone treatment increases the activity of superoxide dismutase, catalase, and other enzymes, for antioxidant defence.

After intradiscal injection, ozone can accelerate the degradation of proteoglycans in the degenerated nucleus pulposus, leading to its reabsorption and dehydration with the consequent reduction of herniated material responsible for nerve root compression [3,4].

On the other hand, studies on pain, which often is disproportionate to the morphological evidence of discal-radicular conflict, have demonstrated that it is provoked by the presence of acid metabolites coming from the degenerative processes inside the disc, and from ischaemia of the nerve root.

In the nineties, attention focused on A2 phospholipase. Saal demonstrated that phospholipase A2 is the cause of radicular pain, independently from the immunological response or a direct inflammatory process [10]. A2 phospholipase is responsible for arachidonic acid release, and hence prostaglandins. High levels of A2 phospholipase have been demonstrated in herniated discs. Ozone injected into the disc and the peridural space of the conjugation foramen and along the posterior longitudinal ligament will act as a powerful stimulus to the activation of antioxidant defence, favouring the normalisation of the redox balance with neutralisation of acidosis, increased synthesis of ATP, Ca2+ reuptake and reabsorbtion of oedema [4,6,10].

At the beginning of this experience, the indications we gave for the treatment were those which had been adopted for treatment by chymopapain [1]. We have changed our mind over the years. Since ozone is not harmful to the surrounding normal tissues, injection in cases of extruded and migrated fragments is possible, and it has demonstrated very good results.

This is probably due to the fact that the isolated fragment is totally separated from normal tissues, the tendency to dehydration is greater, with a faster degeneration process. On the contrary, contained disc bulging composed of a highly hydrated tissue under strong tension inside an intact anulus will offer little room for the gas: a minimal quantity of gas will be allowed to enter and the effect will be minimal. Recently, in cases of contained disc bulging we have preferred to perform disc radiofrequency coablation.

Discography was very helpful at the outset to understand the different situations. After two years of experience, we substituted the normal contrast media with ozone itself: immediately after injection it can be seen inside the disc, and at times around the dura in the spinal canal.

We performed histological examination of the disc tissue we removed in patients in whom O_2-O_3 treatment had not been sufficiently effective. Histology showed that ozone had provoked the breakdown and dehydration of the amorphous matrix, which otherwise is strongly hydrated, most of all around the islands of chondrocytes.

The consequence is the afflux of a large number of lymphocytes which assume macrophagic activity and progressively infiltrate the herniated tissue. Making a comparison with observations in cases of spontaneous elimination of the hernia [5,6], the effect of ozone can be considered an acceleration of the normal process. Much remains to be done, but the possibility of treating patients by an easy method which is rapidly effective for solving clinical problems is here.

This treatment is useful in patients who have not responded to physical therapy, and conventional pain therapy. Most of these patients have no FDA surgical indications (severe motor deficit or acute pain lasting more than four months) and benefit from this therapy.

Most of these patients after all will no no longer need surgery, since ozone may act directly on the cause. This technique is simple, has no risks, and offers the patient a solution without the discomfort of surgery and the possible risks of the variable skill of the surgeon.

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Dr A. Alexandre
EUNI srl
via Ghirada 2
31100 Treviso
e mail: alexandre@eunionline.com