Intradiscal Injection of O2O3 For The Treatment of Lumbar Disc Herniations. Results at 5 Years

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ABSTRACT

A method wich will allow shrinkage of herniated disc, without open surgical approach has been longly searched for. Studies on the spontaneous disappearance of disc fragments have demonstrated autoimmune responses, with a chronic inflammatory reaction, as well as radicular pain has been shown to be mostly due to release of toxic acids (10). Researchers in different fields surprisingly noticed that a brief, calculated, oxidative stress by ozone administration, may correct a persistent imbalance due to excessive, chronic oxidative injury(4). Oxigen-ozone gas injection in painful patients has a dramatic effect on clinical symptoms. On these bases the intradiscal injection of 0xigen-ozone gas has been conceived(1,7,9). We report the treatment of 6665 patients affected by disc pathology by intradiscal injection of Oxigen-Ozone gas mixture. The effect on pain and radicular dysfunction are dramatic. The effect of the treatment has been evaluated also by pathological examination.

INTRODUCTION

In cases of lumbar radicular dysfunction due to discal-radicular conflict, the classical surgical treatment by open surgery has shown to entail a relevant percentage of complications or of failures. Since 50 years neurosurgeons serch for a method wich will allow shrinkage of herniated or protruded disc, in order to solve the problem of severe pain and disfuncion of an enormous amount of patients. Thereby a number of percutaneous non invasive techniques have been conceived, which aim to remove or to 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 formation of scar tissue in the epidural space, which will make nervous tissues compressed, and adherent to the moving bones. Disc punction through a lateral approach has allowed injection of condrolytic enzymes, hydrocortisone, papaine, collagenase, or aprotine. Each of these substances has had a period of favour, but has given problems because of scanty results or relevant side-effects.

A large amount of research has been done on the various aspects of disk pathology, and on the possible solutions of 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 be somehow independent from the mechanical problem, but may dipend either from autoimmune reaction, producing a chronic inflammatory respons which engenders an acid environnement , or a situation of hyschemia (10). These problems may be solved by biochemical treatment, reducing the need of surgical aggression (1-3,7). On the other hand in the years the mechanism 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 is demonstrated (6).

A mixture of oxygen and ozone gases is employed in medicine since thirties for the treatment of pain and dysfunction in patients affected by trombotic and hischemic diseases. The empirical observation of the powerful and long lasting effect of the injection in paravertebral muscles of this gas mixture in the treatment of pain and radicular dysfunction because of discal-radicular conflict has brought to detailed studies on the subject. Working in different fields, researchers have surprisingly noticed that a brief, calculated, oxidative stress, achived 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 very important 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 obtained mixture. Jacobs in 1982 has reported (8) the absence of side effects in over five million ozone therapy sessions for different pathologies. The paravertebral intramuscular treatment produces pain relief in the majority of patients, together with decongestion, reabsorption of oedema and increased mobility. This has brought to the idea of injecting the oxygen-ozone mixture in the intervertebral disc and in the conjugation foramen in order to obtain a powerful effect directly on the pathological mechanism (1,7,9).

PATIENTS AND METHODS

From 1994 to 2000, in the different centres which have participated to this study, a total of 6665 patients has been treated because of disc disease, by intradiscal oxygen-ozone (0203) injection. Each patient had undergone clinical and electrophysiological and neuroradiological investigation in order to define a precise diagnosis. The presence of a disc herniation was demonstrated in each case. In 44.59% of cases it was observed at multiple levels. Enrolled patients had already received pharmacological and physical therapy without solution of the clinical picture.
The perspective of solving the problem without drugs and without the conventional surgical treatment has been offered to the patients, who have accepted after detailed explanation. If pre-existing, desamethasone administration was interrupted when starting 0203 administration, and it was never associated to 0203 treatment. Non steroideal drugs were allowed, if occasionally needed. The treatment consisted of an intradiscal injection of 0203, preceded and followed by 5 paravertebral injections.

- paravertebral injection consisted in the administration of 80 ml of 0203 at 10 micrograms/ml concentration, divided in 4 sites of injection, in the paravertebral area, around the methameric level of the pathology.

- intradiscal injection goes through the postero-lateral extra-articular route. Its execution requires the operative room equipment, allowing safe asepsis and anesthesiological tools, a radiological apparatus for direct vision of the spine, and the source of the oxygen-ozone mixture.

After having located the needle in the disc, discography is performed, which will
a) confirm the correct location of the needle,
b) exclude a vascular or a subaracnoideal communication which are both contraindication 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 03 injection was not considered significant. The result is 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). These make a total of 95.15% . Dysfunction remained unchanged in 4.85% (323 patients).

3- varius 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. In 297 of these 4639 on the contrary a marked defect was present, but the patient either didn't want to undergo surgery or agreed to the proposal of temptative conservative treatment because of general problems. 297 patients are 4.45% of the total group of 6665 and 6.4% of 4639 motor deficit group. The motor defect pre-existed since 6 to 50 days before the treatment, 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). These last patients underwent open surgery.

4- multiple level disc pathology was present in 2972 patients (44.59%). The treatment has been simultaneously performed in all the pathological discs. The results we have obtained do 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). Thereby the positive result has been obtained in 72.7%, limiting the need of surgery at 1821 cases (27.3%).

6- in 933 patients (14%) an extruded and migrated herniation was demonstrated in presence of a clinical situation which did not_demand surgery. The treatment gave complete resolution of the clinical picture in 234 cases , good result in 545 cases,that makes a total of positive outcomes in 83.5%(779 cases), insufficient result in 154 (16.5%).

7- 3317 patients have been randomly choosed by an external person for undergoing CT/MRI control 7 months after the treatment. In 41% (1360 cases) we have observed a significant reduction in volumen of the hernia. In in 37% (1227 cases) the hernia has been completely eliminated, while in 730 cases morphology was immodified.

DISCUSSION
Experimental models suggest that material from the nucleus pulposus may act as a chemical or immunologic irritant to the nerve, and that these mechanisms may produce inflammatory response (10). Up to now, studies have hypothesised that the injection of such a powerful oxidant as ozone induces over-expression of antioxidant enzymes, which neutralise excessive reactive oxygen species (ROS) formation (4).

Ozone seems to reactivate 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 hyschemia of the nerve root.
In the nineties attention has been brought on A2 phospholipase. Saal has demonstrated that phospholipase A2 is the cause of radicular pain, indipendently from immunological response or from a direct inflammatory process (10).
High levels of A2 phospholipase have been demonstrated in herniated discs. Ozone injected in the disc and in 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 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 the ones which had been used for treatment by chymopapain (1). We have changed our mind through the years. Since ozone is not harmfull 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 tendence to dehydration is higher, with a faster degeneration process. On the opposite, contained disk bulging composed by a highly hydrated tissue under strong tension inside an intact anulus will offer little room to the gas. A minimal quantity of gas will be allowed to enter, the effect will be minimal. Recently in cases of contained disc bulging we have preferred to perform disc radiofrequency coablation.

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

We have performed histological examination of the disc tissue that we have removed in patients in whom 0203 treatment had not been sufficiently effective. This exam has shown that ozone had povoked breakdown and dehydration of the amorphous matrix, which otherwise is strongly hydrated, most of all around the islands of condrocites.

The consequence is the afflux of a large number of lymphocytes which assume macrophagic activity and progressively infiltrate the herniated tissue. Making comparison with the observations in cases of spontaneous elimination of the hernia (5,6), the effect of ozone can be considered the 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 (heavy motor deficit or acute pain lasting more than 4 monts) and benefit from this therapy. Most of these patients after all will no more need surgery, since ozone may act directly on the cause. This technique is simple, has no risks, 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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