INTRADISCAL INJECTION OF OXIGEN-OZONE GAS MIXTURE FOR THE TREATMENT OF CERVICAL DISC HERNIATIONS

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ABSTRACT
In cases of disc herniations the use of open surgical approaches is reduced, since new percutaneous methods which will allow shrinkage of the disc, and improvement of radicular function are preferred.
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 oxigen-ozone gas has been conceived (1,7,9).
We report the treatment of a series of patients affected by cervical disc pathology, by intradiscal injection of Oxigen-Ozone gas mixture.
The effects both on pain and on radicular dysfunction are impressive.
The morphological effect of the treatment has been evaluated also by pathological examination.

INTRODUCTION
In cases of radicular dysfunction due to discal-radicular conflict, the classical surgical treatment by open surgery has shown to entail a percentage of complications or of partial results.
Since 50 years neurosurgeons search for a method which will allow shrinkage of herniated or protruded disc, in order to solve the problem of severe pain and dysfunction 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 drastically reduce the epidural formation of scar tissue, which might make nervous tissues compressed, and adherent to the moving bones.
Percutaneous techniques, applied on the lumbar area through the years, are part of a large amount of research that 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 depend either from autoimmune reaction, producing a chronic inflammatory response 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).
The 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.
After decades of experience on those fields, 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 had surprisingly noticed that a brief, 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 very important therapeutic implications (4).
The mixture is produced by an apparatus (ozone generator) which activates the molecules of diatomic 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).
Recently the application of these gases has been utilized also in cervical disc pathology.

PATIENTS AND METHODS
From 1997 to 2003, in the different centres which have participated to this study, a total of 252 patients has been treated because of cervical disc disease, by intradiscal oxygen-ozone (0203) injection. Mean patient's age 38 years, 47% males.
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 67 (39.8% of cases) it was observed at multiple levels.
Patients affected by cervical spinal canal stenosis, discarthrosic processes, osteophytes or concomitant CSN pathologies where not included in the series.
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. Desamethasone administration, when pre-exiting, was interrupted when starting 0203 administration, and it was never associated to 0203 treatment.
Non steroidal 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 20 ml of 0203 at 10 micrograms/ml concentration, divided in 2 sites of injection, in the paravertebral muscles, around the methameric level of the pathology.
- intradiscal injection goes through the classical anterior approach. 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.

RESULTS
1- among the 252 patients pain symptomatology was completely abolished in 79.3% (200 patients), amelioration was obtained in 9.9 % (25 patients) and the result was poor in 10.7 % (27 patients).

2- sensory dysfunction was abolished in 78,1 % (197 patients) improved in 16.6 % (42 patients). These make a total of 94.7 % . Dysfunction remained unchanged in 5.1 % (13 patients).

3- various degrees of motor dysfunction were present in 78.9 % of our 252 patients, that is 199 cases. In the great majority of cases it was a situation of mild strength defect, of which the patient was aware and complained, and, particularly evident when compared to the non-affected side. The motor defect pre-existed with a mean pre-existence of 14 days. Among the total group of 252 we observed complete regression of motor deficit in 61.9% (156 patients), partial in 21.4 % (54 patients), and insufficient in 13.4 % (34 patients). This makes a total of positive results in 83.3 % of cases.

4- multiple level disc pathology was present in 114. 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- patients underwent CT/MRI control 7 months after the treatment. In 39.6 % (100 cases) we have observed a significant reduction in volume of the hernia, but the correlation with clinical signs was not strict.

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).
In our opinion anyway the most important aspect is the byochemical modification of the medium in the extradural space. 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).
A2 phospholipase is responsible of the arachidonic acid liberation, and hence prostaglandines.
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 of oedema (4,6,10).
The complete biochemical mechanism is not yet understood, but there is strong clinical evidence that the effect is dramatic, and long lasting.
Benefit is rapidly obtained on pain, and on nerve dysfunction, with progressive reduction of tingling.
EMG controls have confirmed the recuperation of nerve function. We presume that this is given by the amelioration of nerve hyschemia.
Injection even in cases of extruded cervical disc pathology, has been performed and it has given good results.
This is probably due to the fact that the isolated fragment is separated from normal tissues, has higher tendency to dehydration, and a degeneration process is engendered in the time.
Although this outcome analysis may receive criticism sine it is neither randomized to a placebo-controlled group nor double-blinded, the data is nevertheless compelling.
We must remark that several reports indicate that the results of non-randomized or observational studies are not necessarily inferior to the results of randomized, controlled trials (12,13).
The typical double-blinded pharmacological trials involve a drug versus placebo.
Designing a similar blinded trial for an invasive procedure versus a control or placebo arm presents logistic difficulties, since not doing the procedure in the control arm in itself would un-blind the study. While a sham procedure arm could be incorporated as a control arm, it would pose further ethical and medico-legal dilemmas.
The large sample size in our analysis is very significant from a statistical standpoint.
The theme has to be followed through the years without scepticism.
Several fields of research can be added and paralleled to this, since these percutaneous techniques which will softly reduce the water presence in the amorphous matrix without putting out of function condrocytes, deserve careful analysis in the sense of tissue healing promotion.
Studies have shown the possibility of enhancing intradiscal cellular metabolism by increasing oxygenation (13), implanting of healthy disc cells to replenish disc eight and stability (20,17), and applying growth factors to repair the annular tissue (14).
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 after all will no more need surgery, since ozone may act directly on the cause eliminating clinical symptoms. The target of a doctor must be to solve clinical problems, not to correct a morphological aspect of a radiological image.
This technique is simple, has no risks, offers the patient a solution without the discomfort of surgery and the possible risks it entails.

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