TREATMENT OF HERNIATED LUMBAR DISC BY INTRADISCAL AND INTRAFORAMINAL OXYGEN-OZONE ($O_2$-$O_3$) INJECTION

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SUMMARY

Material: We report our experience between May 1996 and May 2003 with 2200 patients affected by low back pain or sciatica due to herniated disk treated by intradiscal and intraforaminal oxygen-ozone injection.

The patients received medical and physical therapy before treatment for at least 2 months; the patients with conus-cauda syndrome and hyperalgesic sciatica were excluded. We never performed discography before the treatment that was performed under CT guidance or fluoroscopy. CT provided monitoring of gas distribution in the disk and epidural space.

Results: No side effects were recorded at short and long-term follow-up. Clinical results were evaluated with the modified McNab method showing an 80% success rate and 20% failure rate in 1750 patients followed up to 6 months while the success rate dropped down at 75% and failure increased at 25% in 1400 followed up to 18 months. CT showed reduction in the size of the herniated disk in only 63% of the followed patients (420 patients).

The failure has been mostly related to: calcified herniated disk; spinal canal stenosis; recurrent herniated disk with epidural fibrosis; small descending herniated disk at the level of the lateral recess.

Key words: oxygen-ozone therapy, CT, Low back pain, sciatica.

INTRODUCTION

Nerve root pain and low back pain are one of the commonest conditions affecting the lumbar spine. Around 80% of the population in western countries will experience at least one episode of low back pain in their lifetime and 55% suffer from low back pain associated with radicular syndromes [14]. Back pain is often caused by disc disease even though other factors are responsible for nerve root syndromes and should be entertained when clinical symptoms fail to correlate with CT and/or MR findings [17].

In this paper, we report our experience between May 1996 and May 2003 with 2200 patients affected by low back pain or sciatica due to herniated disk treated by intradiscal and intraforaminal oxygen-ozone injection.

MATERIAL AND METHODS

Material

In the five-year period from January 1997 to May 2003, 2200 patients aged between 13 and 89 years underwent percutaneous chemonucleolysis with periradicular and pariganglionic injection of oxygen-ozone mixture.

The following selection criteria were adopted for inclusion:

1) clinical: low back and/or nerve root pain resistant to previous medical treatment, physiotherapy and other therapies (manipulation, acupuncture, etc.) for a period of not less than two months;

2) psychological: a firm resolve on the part of the patient to recover with a commitment to cooperate and undergo subsequent physiotherapy with postural and motor rehabilitation;

3) neurological: paresthesia or hypoesthesia over the dermatome involved, mild muscle weakness and signs of root-ganglion irritation;
4) neuroradiological (CT and/or MR): a) evidence of small and medium-sized herniated discs correlating with the patient’s symptoms with or without degenerative disc-vertebra disease complicated by intervertebral disc changes (protrusion, herniation); b) residue of surgical (micro)-discectomy with herniation recurrence and/or hypertrophic fibrous scarring.

The exclusion criteria were:
1) CT/MR evidence of a herniated disc fragment with symptoms of motor and/or sphincter disturbance;
2) CT/MR evidence of disc herniation corresponding to clinically severe motor deficit and/or sphincter disturbance.

The indications for O₂-O₃ treatment were extended to FBSS patients when it was understood that the ozone mechanisms of action could be exploited to treat the chronic inflammation and venous stasis present in FBSS. Technical approach to the disc is the same as that used for both discography and other percutaneous intervertebral disc procedures. We used an 18-20G Chiba needle inserted from a posterior paravertebral oblique approach under CT or fluoroscopic guidance. The L5-S1 space is not always an easy target to reach and may require additional 30° craniocaudal inclination of the needle. Once the needle has been positioned in the centre of the disc, the gas mixture is injected into the disc (3-4ml) and into the epidural and intraforaminal spaces (10ml) at the concentrations of 30 micrograms/ml (figures 1 and 2).

We no longer perform discography before percutaneous treatment as the procedure adds no further diagnostic information needed for treatment. A CT scan is done before therapy to rule out the presence of a retro-psoas bowel loop.

CT guidance was adopted instead of the well-tested radiological monitoring by isocentric angio suite with double arm due to the need for meticulous positioning of the needle within the nucleus pulposus. In addition, CT avoids the use of intradiscal contrast administration which even in low doses
reduces the discal absorption of ozone and the space available and hinders the search for the site of intraforaminal injection of the O₂-O₃ mixture.

A CT scan was always performed to confirm the intradiscal injection, and the epidural and intraforaminal diffusion of the O₂-O₃ mixture.

Methods

There are many and different protocols to analyze in an objective way the clinical results in patients with low back pain and HNP (16-18). We evaluated our results according to a modified Mac Nab method (table I) in the following situations: degenerative disease complicated by herniated disk, L4-L5 or L5-S1 herniated discs, multiple disc herniations, FBSS, calcified disc herniations and disc herniations associated with spinal stenosis.

The first three situations represented 78% of all treated patients. Evaluation at 6 months was performed clinically in all 2200 patients with CT or MR Follow-up obtained in 420 patients while clinical follow-up evaluation at 18 months was available for 1400 patients (table I).

Fig. 2. – CT axial scan (a-c) and coronal and sagittal MPR (d-e). Left paramedian herniated disk (a) with evidence of intradiscal needle positioning at the L4-L5 level (b) Intradiscal (c) (4ml) and epidural (d-e) (15ml) injection of oxygen-ozone mixture at CT control after the procedure.
RESULTS

The results at 6 and 18 months are summarized in tables II and III. Clinical follow-up for up to 18 months in 1400 patients confirmed persistent good outcome in 75% of cases. CT or MR follow-up was done in 420 patients, documenting a reduction in herniated disc size only in 63% of cases (figure 3). We analyzed the failures reported herein, focusing on possible technical errors to establish whether indications for treatment had been too broad or whether correlations exist between certain types of herniated disc, site of herniation, type of intervention and treatment failure.

Retrospective analysis of our failures disclosed that a successful outcome was much more unlikely in the presence of calcified herniated discs, herniations associated with stenosis of the spinal canal and large extruded herniations.

DISCUSSION

We know from the natural history of herniated disc that clinical symptoms tend to disappear in up to 50% of patients and the disc herniation can shrink at CT or MR scans within eight to nine months after the onset of back pain, but not all patients can wait so long before improve symptoms [5-14]. The short-term success rate after surgery for lumbosacral disc herniation is around 95-98% with a 2-6% incidence of true recurrence of herniation. This percentage decreases to around 80% in the long-term due to the onset of symptoms linked to Failed Back Surgery Syndrome (FBSS) characterised by recurrence and/

<table>
<thead>
<tr>
<th>Success</th>
<th>Failure</th>
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| **Excellent** | — disappearance of symptoms  
| | — complete recovery in working and sport activities |
| **Good** | — occasional episodes of low back pain or sciatica |
| **Fair** | — improvement of symptoms  
| | — limitation of heavy physical activity |
| **Mediocre** | — insufficient improvement of symptoms  
| | — periodic administration of drugs  
| | — limitations of physical activity |
| **No results** | — no improvement  
| | — surgery required |
| **Bad** | — worsening of clinical situation  
| | — surgery required |

| TABLE II. – Results at 6 month follow-up.  
| TABLEAU II. – Résultats à six mois. |
| In patients with degenerative disease complicated by herniation:  
| — excellent in 40%  
| — good or fair in 38%  
| — mediocre or bad in 20% |
| In patients with L4 L5 or L5-S1 herniated discs:  
| — excellent in 64%  
| — good or fair in 13%  
| — mediocre or bad in 23% |
| In patients with multiple disc herniations:  
| — excellent in 58%  
| — good or fair in 11%  
| — mediocre or bad in 31% |
| In FBSS patients:  
| — excellent in 45%  
| — good or fair in 20%  
| — mediocre or bad in 35% |
| In patients with calcified disc herniations:  
| — excellent in 25%  
| — good or fair in 20%  
| — mediocre or bad in 50% |
| In patients with herniated disc associated with stenosis:  
| — excellent in 25%  
| — good or fair in 25%  
| — mediocre or bad in 50% |

| TABLE III. – Results at 18 month follow-up.  
| TABLEAU III. – Résultats à 18 mois. |
| In patients with degenerative disease complicated by herniation:  
| — excellent in 40%  
| — good or fair in 38%  
| — mediocre or bad in 22% |
| In patients with L4 L5 or L5-S1 herniated discs:  
| — excellent in 62%  
| — good or fair in 14%  
| — mediocre or bad in 24% |
| In patients with multiple disc herniations:  
| — excellent in 56%  
| — good or fair in 12%  
| — mediocre or bad in 32% |
| In FBSS patients:  
| — excellent in 43%  
| — good or fair in 19%  
| — mediocre or bad in 39 |
| In patients with calcified disc herniations:  
| — excellent in 25%  
| — good or fair in 25%  
| — mediocre or bad in 50% |
| In patients with herniated disc associated with stenosis:  
| — excellent in 25%  
| — good or fair in 25%  
| — mediocre or bad in 50% |
or hypertrophic scarring with severe symptoms in 20% of patients and FBSS proper in 15% [9, 10]. These figures have stimulated research into newer minimally-invasive techniques to improve clinical results. At the same time, advances in percutaneous techniques by interventional procedures (chemonucleolysis with chemopapain, nucleo-discectomy introduced by Onik, IDET, discectomy LASER, and recently nucleoplasty) have minimized the invasive nature of surgical techniques and avoid or decreased complications such as postsurgical infection.

Reducing intervertebral disc size by mechanical aspiration of disc fragments or partially dissolving the herniation by drying reduces the conic pressure on the torn annulus and creates the space necessary for retropulsion whenever the circular fibres of the annulus regain a minimum capacity to contain the disc under tension.

All percutaneous procedures are mildly invasive entailing only a short hospital stay. By avoiding the spinal canal, these techniques also eliminate the risks of post-operative scarring linked to surgery which is often responsible for recurrence of pain. Percutaneous techniques can also be repeated in the same patient without precluding recourse to traditional surgery if they should fail. The success rates reported in different studies vary from 65 to 80% of excellent or good results with chemonucleolysis and aspiration [10]. Epidural steroid injections under CT or fluoroscopic guidance are also used to minimize radicular pain and to try to obtain complete pain relief [2, 4, 8, 15, 20, 21]. Discography is often used to decide regarding the possibility to perform percutaneous discectomy and chemonucleolysis but is useless in case of O₂-O₃ therapy.

Chemonucleolysis with “nucleoptesis” combined with drying the nucleus with an oxygen-ozone mixture (O₂-O₃) uses a colorless irritant gas with a pungent odour which is unstable and has a strong oxidizing power with good antiseptic, disinfectant and antiviral properties. Ozone is prepared and administered as required by transforming a small percentage of oxygen into ozone using special generators. The O₂-O₃ gas mixture produced can be injected into the intervertebral disc and root foraminal, 3-4 ml into the disc and 15-20 ml into the neural foramen and root canal. The concentration of the mixture is adjusted by the equipment. The dose mainly administered to treat disc disease is 30 micrograms/ml, a concentration calculated from experimental studies as the amount best suited to dry out the nucleus and minimize inflammation. A number of studies have been published in the literature on the O₂-O₃ treatment of disc herniation with satisfactory results in selected cases [1, 3, 6, 7, 13, 18]. The causes of backache are the topic of scientific investigation. Mechanical and/or inflammatory irritation of the nerve endings is responsible for low back pain [11, 19, 20, 23, 24]. The natural response of any structure to injury is to trigger a repair process by means of an inflammatory response. The number of direct or immune-mediated inflammatory events accounts for decompressive FBSS in some patients.

**Mechanism of action of the O₂-O₃ mixture**

The nucleus pulposus can set off an immune-mediated inflammatory process as the proteoglycan component of its nucleus is segregated from the immune system after birth. Herniation of the nucleus pulposus would therefore trigger an autoimmune reaction, generating an inflammatory process whose cell component is mainly supported by macrophages. On the other hand, the nucleus pulposus can also give rise to an inflammatory process through a non-immune-mediated mechanism supported by the many inflammatory agents identified in its nucleus.

The reactive tissue surrounding the disc contains histiocytes, fibroblasts in the herniations, and chondrocytes in the disc protrusions able to produce cytokines (Interleukin-1 alpha, Interleukin 6 and TNF-alpha) with an increase in phospholipase A2 leading to the release of prostaglandin E2, leukotrienes and thromboxanes found in larger quantities in non-contained discs hernia-
tions and patients presenting more severe symp-
toms.

Prostaglandins cause pain. In small amounts, they
enhance sensitivity of the nerve roots and other
pain-producing substances like Bradykinin. Exper-
imental studies have shown that an oxygen-ozone gas
mixture at the concentrations used for intradiscal
treatment have the same effect as steroids on inhib-
itng cytokine production and hence the pain
induced by the same [12].

The oxygen-ozone mechanisms of action are cur-
rently being investigated and include:
1) enhanced oxygenation and reduced inflamma-
tion in the disease site due to the oxidizing effect on
pain-producing mediators;
2) direct effect of ozone on the mucopolysaccha-
drides making up the nucleus pulposus of the inter-
vertebral disc with rupture of water molecules and
shrinkage of the disc exerting compression on the
nerve roots;
3) improved microcirculation due to resolution of
venous stasis and lack of oxygenated blood supply
following mechanical compression of the herniated
disc and disc protrusion on the vessel components.

Tissue structure alterations

In vivo experimental studies on swine interverte-
bral discs and in vitro tests on human discs with
intradiscal administration of an O₂-O₃ mixture at a
concentration of 27mcg/ml demonstrated dehydra-
tion of the fibrillary matrix of the nucleus pulposus
disloosing the collagen mesh/network and regressive
events (fragmentation and vacuole formation). Neo-
angiogenesis was sometimes present with mild
hyperplasia of the chondrocytes in the matrix
periphery. Such changes are thought to be due to the
decomposition of ozone with release of free radicals
which act directly on the disc matrix or indirectly via
proteolytic enzymes.

Complications and risks

No early or late neurological or infectious compli-
cations have been reported following O₂-O₃ injec-
tion. The results are virtually the same as those of
other percutaneous techniques (75-80% success
rate), injections can be repeated if necessary, and
there are no side effects. However, the low costs of
this O₂-O₃ therapy make this the method of choice
in the percutaneous treatment of herniated lumbar
disc.

CONCLUSION

In our experience, intradiscal O₂-O₃ treatment of
herniated lumbar disc has revolutionized the percu-
taneous approach to nerve root disease making it
safer, cheaper and easier to repeat than treatments
currently in use. In addition, O₂-O₃ therapy does not
preclude later recourse to surgery should patients
fail to benefit. The technique is also reliable and
compatible with other percutaneous procedures.
O₂-O₃ treatment also has the advantage of being
feasible in virtually all patients with root syndromes
without the contraindications of chemonucleolysis or
nucleoaspiration which must be ruled out by disco-
graphy.

In our experience the failure has been mostly
related to patients with spinal canal stenosis, recur-
rent herniated disk, calcified herniated disk and
small descending herniated disk of the lateral recess
with significant compression of the nerve sheath.

On the basis of our results and the assessment of
our failures, we recommend careful selection
patients to avoid broadening the indications for
treatment, thereby ensuring a high success rate.

Accurate diagnosis of the lesion and the spinal
level to be treated, accurate technique under CT or
fluoroscopic guidance in expert hands and patient
follow-up by the neuroradiologist after treatment
are key factors in ensuring the successful outcome of
percutaneous treatment for this common condition.

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**Analyse de livre**
