Introduction

Backache, with or without sciatica nerve or femoral involvement, affects 90% of the population at least once in their lives and is one of the major causes of working days lost in the western world.

Until 15 years ago surgery was the treatment of choice. Nowadays the trend is to adopt conservative treatments given the many limitations of surgery in terms of short and long-term pain resolution. The different methods used to treat low back pain and sciatica include epidural injection of steroids and intramuscular paravertebral infiltration of an O₂O₃ mixture. Our study compared the short (three weeks) and long-term (six months) efficacy of the two treatments after failure to respond to conventional medical management (steroids and muscle relaxants). 351 patients were enrolled: 171 (Group A) were treated by epidural steroid injection, while 180 (Group B) underwent paravertebral administration of an O₂O₃ mixture. In the short-term 59% of patients treated by epidural injection and 88.2% (p<0.05) of patients treated with O₂O₃ had a total or near total remission of pain. Long-term outcome remained excellent or good in 47.3% of patients treated by epidural injection and 77.1% (p<0.05) of patients treated with O₂O₃. Given the relative simplicity of treatment administration, limited contraindications and the lack of side-effects, ozone therapy is the first choice treatment in patients refractory to conventional medical management.

Materials and Methods

Between January 2002 and January 2006 we treated 351 patients. All patients presented irradiating low back pain over the sciatic nerve lasting less than 180 days and failure to respond to medical management with steroids, NSAIDs, tramadol and muscle relaxants. After giving their informed consent, patients were randomly assigned to one of two groups.

Patients in the first group (A) were treated by epidural injection of steroid (80 mg, triamcinolone acetonide; Kenacort, Bristol-Myers Squibb, Italy), diluted in 20 ml saline solution, into the intervertebral space of the herniated disc or into the space immediately above it. A maximum of three injections were given at weekly intervals after no or only partial response to treatment.

Patients in the second group (B) were treated with a gas mixture of O₂O₃ (5 ml O₂O₃ at a concentration of 10-20 microg/ml injected bilaterally into...
the paravertebral muscle 2 cm from the spinous apophysis of the herniated disc and into the space immediately above and below. In case of failure to respond to the randomized treatment, a cross-over to the other group was planned after four weeks of treatment. In addition to personal details, the type of pain, irradiation, paraesthesias, presence of Lasegue’s sign, any sensory and/or motor deficits and osteotendon reflexes were recorded for each patient. The type of treatment each patient received (epidural steroid or paravertebral) was also recorded but the colleagues evaluating therapeutic response were blinded to this information.

Patients with clinical or electromyographic features of neurogenic or denervating pain were excluded from the study. Each patient enrolled was asked to produce CT or MR imaging documentation not more than six months old.

All infiltrations were carried out using a device (CE class 1B equipment, Alnitec, Cremosano, Italy) for the production of $O_2$-$O_3$ fitted with photometric detectors of $O_3$ concentration in the gas mixture (the machine automatically adjusts the change in concentration occurring when the syringe is filled) at a constant pressure during $O_3$ filling.

Injections in both groups were performed by a team of anaesthetists (A.Z., M.M.B., B.F.) belonging to three hospitals, whereas follow-up monitoring was undertaken by three doctors (R.P., G.T., L.M.) blinded to the type of treatment administered. Clinical outcome was assessed in the short (three weeks) and long-term (six months) using a modified version of the McNab method.

Clinical results were considered excellent with a complete resolution of pain and a return to previous activities; good with a 50-75% reduction of pain and a return to previous activities; satisfactory with a reduction of pain below 30-50% and partial return to previous activities; poor with no response to treatment or a response below 30%.

Statistical analysis was performed using Student’s t-test, the chi-squared test and Fisher’s test when necessary, and results processed using the SPSS 8.0 package for Windows.

## Results

Patient details are summarised in table 1.

### Table 1. Patient details

<table>
<thead>
<tr>
<th>No.</th>
<th>Sex *</th>
<th>Age (average ± sd)§</th>
<th>Response to conventional treatment °</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>M</td>
<td>F</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Poor</td>
</tr>
<tr>
<td>Group A</td>
<td>171</td>
<td>91</td>
<td>80</td>
</tr>
<tr>
<td>Group B</td>
<td>180</td>
<td>100</td>
<td>80</td>
</tr>
</tbody>
</table>

*, §, ° Differences not statistically significant (p >0.05)

### Table 2. Short-term outcome

<table>
<thead>
<tr>
<th>N° Patients</th>
<th>Excellent</th>
<th>Good</th>
<th>Excellent/Good</th>
<th>Satisfactory</th>
<th>Poor</th>
<th>Satisfactory/Poor</th>
<th>Cross-over</th>
</tr>
</thead>
<tbody>
<tr>
<td>Group A</td>
<td>171</td>
<td>77 (45.0%)</td>
<td>48 (28.0%)</td>
<td>125 (73.0%)</td>
<td>22 (12.8%)</td>
<td>24 (14.2%)</td>
<td>46 (27.0%)</td>
</tr>
<tr>
<td>Group B</td>
<td>180</td>
<td>131 (72.7%)</td>
<td>28 (15.5%)</td>
<td>159 (88.2%)</td>
<td>14 (7.9%)</td>
<td>7 (3.9%)</td>
<td>21 (11.8%)</td>
</tr>
<tr>
<td>p</td>
<td>&lt;0.05</td>
<td>&lt;0.05</td>
<td>&lt;0.05</td>
<td>&lt;0.05</td>
<td>&lt;0.05</td>
<td>&lt;0.05</td>
<td>&lt;0.05</td>
</tr>
</tbody>
</table>

Treatment outcome is summarised in tables 2 and 3.

In the short-term 59% of patients treated by epidural injection and 88.2% (p<0.05) of patients treated with $O_2$-$O_3$ had a total or near total remission of pain (33.3% in the epidural group, 72.7% in the $O_2$-$O_3$ group; p<0.05).

Long-term outcome remained excellent or good in 47.3% of patients treated by epidural injection and 77.1% (p<0.05) of patients treated with $O_2$-$O_3$. 61.1% of patients in the $O_2$-$O_3$ group reported excellent results (21.6% in the epidural group; p<0.05).

The patients in the $O_2$-$O_3$ group subjected to a
Table 3 Long-term outcome

<table>
<thead>
<tr>
<th>Control of pain</th>
<th>Group A</th>
<th>Group B</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patients N°</td>
<td>Excellent</td>
<td>Good</td>
</tr>
<tr>
<td>Group A</td>
<td>171</td>
<td>54 (%31.5%)</td>
</tr>
<tr>
<td>Group B</td>
<td>180</td>
<td>126 (%70.0%)</td>
</tr>
<tr>
<td>p</td>
<td>&lt;0.05</td>
<td>&lt;0.05</td>
</tr>
</tbody>
</table>

Table 4 Short-term outcome after cross-over treatment

<table>
<thead>
<tr>
<th>Control of pain</th>
<th>Epidural (post O₂O₃)</th>
<th>(post epid.)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patients N°</td>
<td>Excellent Good</td>
<td>Excellent/Good</td>
</tr>
<tr>
<td>Group A</td>
<td>11 (%9.1%)</td>
<td>4 (%)</td>
</tr>
<tr>
<td>Group B</td>
<td>38 (%35.4%)</td>
<td>17 (%)</td>
</tr>
<tr>
<td>p</td>
<td>&lt;0.05</td>
<td>&lt;0.05</td>
</tr>
</tbody>
</table>

ns = not significant

Table 5 Short-term outcome after cross-over treatment

<table>
<thead>
<tr>
<th>Control of pain</th>
<th>Epidural (post O₂O₃)</th>
<th>(post epid.)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patients N°</td>
<td>Excellent Good</td>
<td>Excellent/Good</td>
</tr>
<tr>
<td>Group A</td>
<td>11 (%18.2%)</td>
<td>2 (%)</td>
</tr>
<tr>
<td>Group B</td>
<td>48 (%50.0%)</td>
<td>24 (%)</td>
</tr>
<tr>
<td>p</td>
<td>&lt;0.05</td>
<td>&lt;0.05</td>
</tr>
</tbody>
</table>

ns = not significant

cross-over (tables 4 and 5) for epidural injection presented an excellent/good remission of pain in 36.4% of cases, whereas 70.8% (p<0.05) of patients in the epidural group submitted to cross-over for O₂O₃ reported an excellent/good outcome.

Long-term outcome remained excellent or good in 47.3% of patients treated by epidural injection and 77.1% (p<0.05) of patients treated with O₂O₃. 61.1% of patients in the O₂O₃ group reported excellent results (21.6% in the epidural group; p<0.05).

The patients in the O₂O₃ group subjected to a cross-over (tables 4 and 5) for epidural injection presented an excellent/good remission of pain in 36.4% of cases, whereas 70.8% (p<0.05) of patients in the epidural group submitted to cross-over for O₂O₃ reported an excellent/good outcome.

Fifteen patients in Group A (8.7%) and three patients in Group B (1.6%; p<0.05) opted for surgical treatment.

Discussion

The origin of sciatic or crural pain is only partly due to mechanical nerve root compression, while an aspecific inflammatory reaction plays a major role. Migration of the disc through its natural barrier of the anulus fibrosus exposes the autoantigen-reactive immune system of the muco-polysaccharide matrix on the disc surface. The inflammatory reaction is linked to the release of lytic enzymes like phospholipase A2 and prostaglandins E2. In fact the quantity of these enzymes in the peridiscal epidural space is a hundredfold higher in patients with herniated disc compared to those with only a bulging disc, thereby confirming the inflammatory origin of pain. The inflammatory reaction stimulates the macrophage activity favouring degeneration of disc fragments. The resulting process involves the root ganglion and mainly the nociceptive C fibres, enhancing their functions.
mechanical sensitivity and generating a painful stimulus. 

Indirect vessel-mediated mechanical factors are also involved. These may be ischaemic factors linked to compression of the feeding arteriole with impairment of perineural microcirculation and demyelination due to anoxia of nerve fibres, or venous factors causing oedema and partial or total blockage of venous reflux. These mechanisms explain the efficacy of both epidural anti-inflammatory treatment aimed at reducing inflammation and thereby favouring recovery of the ganglioneural myelin sheath and hence nerve function, and also paravertebral infiltration of a O2O3 gas mixture. The O2O3 mixture is claimed to favour the normalization of the level of cytokines and prostaglandins, increase levels of superoxide dismutase and improve the perineural and perianglionic microcirculation with a eutrophic effect on the nerve root, thereby combating the hypoxia linked to both arterial compression and above all to venous stasis. The mixture also seems to have a reflex therapy effect able to break the chain of chronic pain by stimulating antinociceptive antalgic mechanisms.

Epidural steroid injections have been widely used in the conservative treatment of symptomatic herniated lumbar disc. Some studies have reported an efficacy between 44% and 77%. Our study had significant short-term results (73.9% excellent/good outcome) with a worsening of symptoms in the follow-up assessment at six months (53.1%).

In recent years treatment by O2O3 infiltration has yielded significant results with a positive outcome in 65-75% of cases. Our findings are in agreement with literature reports with an excellent/good remission of pain in 88.2% (p<0.05 with respect to the epidural group) of patients.

Only a slight decrease was found at long-term follow-up (77.1%) (p<0.05 with respect to the epidural group). The comparison between the two therapeutic procedures showed that O2O3 infiltration was significantly more successful in terms of the number of patients with an excellent outcome with short (45.0% vs 72.7%; p<0.05) and long-term (31.5% vs 70.0%; p<0.05) remission of pain, vis-à-vis the number of patients reporting satisfactory/poor results in the short (26.9% in the epidural groups vs 11.6% in the O2O3 group; p<0.05) and long-term (22.2% vs 4.4%; p<0.05).

A similar but less successful treatment outcome was found in the cross-over patients. Patients treated by O2O3 obtained excellent/good short-term results in 70.8% of cases vs 30.4% in the epidural group (p<0.05), and a similar long-term outcome (72.9% vs 36.4%; p<0.05).

These findings fit the number of patients who subsequently underwent surgery: 15 patients in the epidural group (8.7%) and three in the O2O3 group (1.6%; p<0.05).

Conclusions

Most patients with low back pain with or without sciatic or femoral nerve involvement are treated with painkillers (NSAIDs or tramadol) and steroids, sometimes in association with muscle relaxants. Outcome is often satisfactory with complete clinical remission. Nonetheless a variable number of patients fail to respond to medical management, irrespective of whether the choice of associated treatment is appropriate. Until a few years ago, the only remedy available for these patients was surgery. Back surgery effectively attenuates symptoms but its effect over time is limited and tends to cease around four years after surgery. About thirty thousand operations a year are performed in Italy and most patients are between the ages of 30 and 50 years. The wide variability among different regions (the majority are performed in Lombardy) suggests that many of these operations are inappropriate. Bearing in mind the limitations of surgery and the fact that herniated disc will very often regress spontaneously, it is important for patients to be well informed and involved in the choice of treatment. Surgery is however indicated in patients presenting signs of neural injury which could give rise to permanent damage if all other treatments fail.

Peridural steroid injection is a valid treatment for patients refractory to medical management. However, this procedure carries the risk of potentially serious complications (post-dural puncture headache, subarachnoid haematoma, infection) although none occurred in our series or in the group receiving O2O3.

Paravertebral infiltration of an O2O3 gas mixture is a simpler alternative treatment in terms of administration and more limited side-effects and contraindications. Ozone therapy also has a higher success rate and is the first choice of treatment in patients refractory to conventional management. The possibility of a cross-over from one treatment to the other is a further means of reducing the number of patients referred to surgery.
References


Dr. Alessio Zambello
Servizio Anestesia e Rianimazione
Ospedale di Circolo e Fondazione Macchi - Azienda Ospedaliera
Via Luvini, 2
21033 Cittiglio (VA)
E-mail: a.zambello@libero.it