CT-Guided Ozone Injection for the Treatment of Cervical Disc Herniation

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SUMMARY - We evaluated the therapeutic outcome of CT-guided ozone treatment for cervical disc herniation. All 86 patients with cervical spondylosis including myelopathy (37 cases), radiculopathy (30 cases), and sympathetic type (19 cases) were treated with ozone injection under CT guidance. The puncture route was anterolateral from the neck to the disk. A total of 2-7 ml of ozone at a concentration of 60 µg/ml were injected into the disk and 5 ml of ozone at a concentration of 40 µg/ml were injected into the paraspinal tissue. Therapeutic outcome was assessed three months after treatment by using a modified MacNab method. After injection of ozone, CT scan showed that ozone was distributed in the disk and extruded disk material in myelopathy and radiculopathy after injection, and distributed in the anterior peridural space and perivertebral body in sympathetic type. The excellent, good and poor clinical efficacy rates were 78%, 16% and 6% respectively three months after treatment. CT guided ozone injection is an accurate, safe and effective method in the treatment of cervical disc herniation.

Introduction

Non invasive procedures, minimally invasive percutaneous injection, and surgery represent the gamut of treatments available in the management of cervical disk herniation. Noninvasive treatments are usually the first choice in most cases, but when patients fail to respond, minimally invasive percutaneous injection or surgery is warranted. Minimally invasive treatments were developed to offer good clinical results combined with a well-tolerated low-cost procedure. In recent years, these procedures were further boosted due to the following drawbacks of traditional surgical therapy: significant soft-tissue injury, extensive hospitalization, and recovery time of six weeks or longer.

The most promising method to date in terms of simplicity and minimal invasiveness is ozone therapy. Ozone is used in medicine to treat different conditions based on its biologic effects: oxidization, bactericide, fungicide, and virustatic, immuno-modulating action, analgesic and anti-inflammatory effects. A vast bibliography on the topic can be found in a recent study on how ozone therapy works. As for herniated disk, a reduction in volume is one of the therapeutic aims of intradiscal administration of medical ozone, as disk shrinkage may reduce nerve root compression. Another reason for using medical ozone to treat disk herniation is its analgesic and anti-inflammatory effects.

This article assesses the results obtained in treating 86 patients with ozone injection under CT guidance, the guiding modality, puncture route, ozone concentration and dose, imaging changes in post-treatment and outcome of combination of various treatments.

Material and Methods

Patient Population

From January 2002 to December 2005, 86 patients (57 males, 29 females) aged 36-72 years (mean 52 years) received CT guided ozone injection. The levels of involvement were 11 at C3-4, 17 at C4-5, 32 at C5-6, 23 at C6-7, and 3 at C7-T1. The cases were classified into myelopathy type (37 cases), radiculopathy type (30 cases), and sympathetic type (19 cases); vertebral arterial type was not included in this study. The indications for injection were: (a) neck pain with radiation down the arm; (b) symptoms and signs of sensory loss, tingling, numbness, muscle weakness, and/or decreased deep tendon reflexes; (c) MRI or CT findings of no cervical spinal canal bony stenosis or lateral recess stenosis, no ossification of poste-
rior longitudinal ligament (OPLL) and ligament flavum and no malacia of spinal cord; (d) positive electromyography and/or nerve conduction studies; and (e) no improvement after 12 weeks of conservative therapy. According to the policies of our hospital review board, approval was not required for this retrospective analysis.

**Procedure**

**Puncture approach**

Before the procedure, all patients were fully informed about the anticipated benefits and potential risks of the procedure, including the possibility of recurrence of radicular symptoms during injection and/or transient exacerbation after treatment. The patients were placed comfortably in a supine position on the CT table with their arms at their sides and an anterolateral approach was used. Two-millimeter, axial, contiguous scans were obtained to locate and mark the puncture site. The distance from this point to the disc, puncture angle and puncture depth were subsequently measured. After the injection site was disinfected and local anesthesia applied using 0.1% lidocaine hydrochloride, a 22-gauge spinal needle was introduced by an anterolateral approach (with the vertebral artery located to avoid it) and gently pushed into the herniated vertebral disc under CT control. The puncture route differed at different levels of cervical disc, for cervical disc 3-4, the needle was introduced between the parapharyngeal space and the medial margin of the cervical arterial sheath; for cervical disc 4-5, the needle was introduced between the lateral margin of lamina of thyroid cartilage and the medial margin of the cervical arterial sheath; for cervical discs 5-6 and 6-7, the needle was introduced between the lateral margin of thyroid gland and the medial margin of the cervical arterial sheath. In addition, ozone injection into paraspinal muscles was performed on 11 patients with neck pain one week later after intradiscal injection.

**Dose and concentration of ozone**

After CT scanning to check correct needle placement, 2 mL 60 µg/mL ozone with 5 mL syringe from an ozone generator (CHY-11- ozone generator, YiDeKang medical Technology Co., Ltd., Shandong province, China and Hyper-Medozon Comfort ozone generator, Herrmann Apparatebau GmbH, Germany) were pumped and injected into the nucleus pulposus of the disc repeatedly until the correct distribution of the gas was checked by CT scanning. The needle was then pulled out, the puncture site was sterilized and dressed. The concentration of ozone injected into paraspinal muscles was 40 µg/ml and the total dose was not more than 10 mL. At the end of treatment, patients were discharged with collar securing and antibiotics administration for three to five days.

Clinical outcome was assessed three months after treatment by applying the modified MacNab method (table 1). Results were evaluated using a questionnaire and direct patient interviews.

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<th>Outcome</th>
<th>Description</th>
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<td>Excellent</td>
<td>Disappearance of symptoms complete recovery of working and sports activities</td>
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<tr>
<td>Good</td>
<td>Occasional episodes of low back pain or sciatica or no limitations of occupational activities</td>
</tr>
<tr>
<td>Poor</td>
<td>Insufficient improvement of symptoms or periodic administration of drugs or limitation of physical activities</td>
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**Results**

All patients were punctured successfully guided by CT with intradiscal injection dose of 3-7 ml ozone (mean 4 ml). CT scan showed that only a small amount of ozone accumulated in the disc and a great deal of ozone flowed out of the cranny of the annulus fibrosus and into the paraspinal space, perivertebral artery and peridural space. Hypoattenuation gas was shown in the extruded disc material on CT scan after injection in myelopathy type (figures 1-2), peri-extruded disc material and nerve root in radiculopathy type (figure 3), anterior peridural space and perivertebral body in sympathetic type (figure 4), and intramuscular space and posterior peridural space in cases receiving posterolateral paraspinal injection of ozone (figure 5). The excellent, good and poor clinical efficacy rates were 78%, 16% and 6% respectively three months after treatment.

**Discussion**

The initial pathologic change of spondylosis is disk degeneration, and then crack formation of annulus fibrosis. This results in displacement of the nucleus pulposus through a crack in the annulus
fibrosis, and then compression on the nerves or spinal cord causing radiculopathy and myelopathy. Repeated chronic trauma, injury and accumulation of local metabolic products and inflammatory factors may irritate the radicular and sympathetic nerves and cause clinical syndromes. With further degeneration, the uncinate process and facet joints hypertrophy and ossification of the posterior longitudinal ligament also occur, forming osteophytic bars, hypertrophy of ligaments and stenosis of the spinal canal. Clinically, cervical spondylosis may be classified as cervical type, myelopathic type, radic-
ulopathic type, sympathetic type and vertebral arterial type. These syndromes may be overlapping or distinct. Patients are often reluctant to receive traditional surgical therapy due to the following drawbacks: significant soft-tissue injury, extensive hospitalization, and recovery time of six weeks or longer. Ozone injection is commonly used for early and medial stages of cervical spondylosis. The proper concentration and dose of ozone injected into the disk can oxidize the nucleus pulposus and reduce pressure on the disk. This may lead to a return of protruded disk material or a reduction of nerve root compression. Ozone injected into perispinal tissue may exert its analgesic and anti-inflammatory effects, and improve local microcirculation, increasing the supply of oxygen due to reduced venous stasis caused by disk compression of vessels, at the same time, reducing hypoxia due to deoxidization of ozone into oxygen. Ozone injection, due to its minimal invasion, simple procedure,
efficacy and safety, is widely focused. The various imaging modality guidance techniques offer different advantages. C-armed X-rays fluorescence has a real-time visualization but cannot display the distribution of ozone. CT provides accurate guidance by measurement of software and experienced manipulation by the operator but has no real-time visualization. Cervical intradisk ozone injection through an anterolateral approach requires a two-degree cephalic tilt of the needle so as to puncture the disk precisely and requires manipulator skill and has a good spatial vision for fear of puncturing the endplate. A 5 to 15 degree cephalic tilt of the needle should be made according to the supine degree of the patient’s head, and the CT gantry should be tilted parallel to the axial position of the disk and the needle should penetrate the disk parallel to its level. Due to the needle insertion into the disk between the medial margin of the cervical arterial sheath and the midline, the angle of puncture is determined by distance between the medial margin of the cervical arterial sheath and the lateral margin of the vertebral body. A 45 degree cephalic tilt of the needle should be made for cervical disks 4-5 and 5-6; a greater degrees cephalic tilt should be made for cervical disk 6-7 due to greater distance between the medial margin of the cervical arterial sheath and the lateral margin of the vertebral body; a lesser degree from 35 to 40 cephalic tilt should be made for cervical disk 3-4 due to the shorter distance between the parapharyngeal space and the medial margin of the cervical arterial sheath, and the puncture should be more cautious for fear of piercing the pharyngeal mucous membrane and causing infection of the paraspinal space. The cervical arterial sheath should be manually displaced laterally with the middle finger and first finger (the apophysis of the bulging disc can be touched in thin patients), and then the needle is inserted dorsally to the middle finger and the first finger into the disk. When the needle reaches the annulus fibrosis, there is a resistance, and then the needle is gently pushed into the disk to a depth of 3 mm for fear of piercing the posterior part of the annulus fibrosis. CT scanning should be performed to determine and adjust the tip of the needle in the central part of the disk.

The ozone capacitance of the cervical disk is relatively small due to its smaller volume compared to the lumbar disk. Injection into the central part of the disk may help the dispersal of ozone to protruded disk material. After injection, there is hypoattenuating gas pervading into the protruded disk material, then the annulus fibrosis can be displayed clearly at CT. However, the injection pressure should be gentle for fear of the iatrogenic rupture of the annulus fibrosis. In this study, ozone pervading into the protruded disk material was clearly displayed at CT in the cervical disk herniation of myelopathic type and radiculopathic type. If the annulus fibrosis is ruptured, the injection pressure will be relatively lower and a small quantity (2 mL) and repeat injection should be made with intermittent CT scanning observing the distribution of ozone. A small deposit of ozone in the disk with a great deal of ozone dispersing out of the disk will occur in such cases, but it will not reduce the treatment efficacy because the intradisk nucleus pulposus has been oxidized in the process of dispersion of ozone. For the extruded nucleus pulposus, ozone should be pervaded into it in order to obtain a satisfactory efficacy. In this study, the needle tip was positioned adjacent to protruded disk material and post CT scanning showed that ozone diffused into it for patients with radiculopathic type. In the puncture process, the needle may frequently penetrate into the superior and inferior endplate due to narrow cervical disk, which has the same handle of penetration into the annulus fibrosus. This can be verified by difficult injection of ozone and CT scan. But C-armed fluoroscopy usually cannot differentiate it and display the distribution of ozone, so that the injection dose of ozone cannot be determined correctly. In this study, CT showed no ozone distribution into the disk after initial injection in 37 patients, and satisfactory distribution of ozone was shown at CT after adjusting the needle tip adjacent to the herniated disk material. Paraspinal injection of 40 µg/ml ozone for the sympathetic type obtained a satisfactory efficacy in 16 out of 19 patients in one week.
and three patients in one month after injection. It is very important for obtaining a satisfactory efficacy to strictly select the indications for injection. CT findings of osteophytes, ossification of posterior longitudinal ligament and ligament flavum and T2 weighted magnetic resonance imaging showing malacia of the spinal cord should be considered contraindications. Ozone injection should be used for early and medial stage cases with slight or medial symptoms and without bony spinal stenosis and spinal cord injury.

The concentration and dose of ozone is crucial for a satisfactory efficacy. Generally speaking, the degree of oxidation is positively related to the ozone concentration, too low a concentration lacking therapy efficacy and an exorbitant concentration causing injury to adjacent tissue. The dose of ozone administered must not exceed the capacity of antioxidant enzymes (superoxide dismutase and catalase) and glutathione to prevent accumulation of the superoxide anion (O2-) and hydrogen peroxide (H2O2), which can cause cell membrane degradation. Free radicals are mainly formed by ozone in a medium with a pH higher than 8, whereas at a pH below 7.5 the ozonolysis mechanism prevails, mainly leading to the formation of peroxides. In our study, the concentration of ozone injected into the disc was 60 µg/ml, and the concentration injected into peri-nerve roots was 40 µg/ml so as not to cause injury. The dose of ozone is determined by the degree of dispersion of ozone shown at CT.

This study had several limitations, including the fact that it was uncontrolled. Since it is well known that medical treatment may need time to be effective in cervical spondylosis, it would be important to design randomized controlled trials to compare the efficacy of medical treatment and injection. However, prospective studies comparing treatment regimens are bound to fail because a double-blind study design would be hard to apply. The small patient population did not permit us to evaluate the efficiency of a second injection in patients for whom the first procedure did not improve the symptoms.

Lastly, our follow-up period was only three months, which hindered long-term assessment of periradicular corticosteroid injections in cervical disk herniation.

Conclusion

CT-guided ozone injection is a minimally invasive, accurate, safe, and effective method in the treatment of cervical disc herniation of early and medial stages.

References


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The paper by Dr. Xiao and colleagues and their therapeutic results are interesting, but the article lends itself to some criticism in the light of the international literature.

Their study specifies that treatment was administered injecting ozone into the disc at a concentration of 60 µg/ml and into the paraspinal tissues at a concentration of 40 µg/ml.

Most authors deem these concentrations to be extremely high, especially with reference to experimental studies (Muto, Iliakis) in which administration of concentrations over 50 µg/ml to animals risked damaging the anulus fibrosus (Muto’s paper described anatomo-pathological preparations showing delamination of the anulus to necrosis in swine disc).

In the light of these findings, the quality of equipment is crucial.

Nowadays all ozone devices must be certified and fitted with photometric detectors of ozone concentration in the gas mixture.

We advise against administering very high ozone concentrations at more than one session to ensure full recovery of any microlesions caused during treatment.

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