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Medical Ozone in Herniated Disc: A Classical Review

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Abstract

Back pain associated with herniated disks has become an important and increasing general health problem across the world. After all methods of conservative treatment have been exhausted, nucleolysis may be a minimally invasive alternative to surgery. In nucleolysis, chondrolytic substances, or other substances which reduce the pressure within the disk by other means, are injected into the nucleus pulposus under CT scan or fluroscopic guidance. Among various substances, which have been employed for nucleolysis, an ozone-oxygen mixture appears to be very promising. The water-binding capacity of ozone results in a reduction of pain. Moreover, it has an anti-inflammatory effect and results in an increase of perfusion to the affected area. Ozone is converted into pure oxygen in the body and has a low allergic potential. Recent minimally invasive therapeutic methods such as percutaneous nucleotomy or laser treatment have not been shown to result in superior results compared with ozone nucleolysis.

Keywords: Ozone; Prolapsed disc; Pain management

Introduction

Low back pain (LBP) is one of the most common and important clinical, social, economic, and public health problems affecting the human population worldwide [1]. Around 70% of adults suffer from LBP at some point in their lifetime with various degrees of symptom severity. Additionally, 1.6% to 43% of these patients have LBP associated with sciatic symptoms [2]. In the United States, the incidence of chronic low back pain ranges from 15% to 45%, with a prevalence of 30% [1]. Most back pain has no recognizable cause on imaging studies and is usually attributed to muscle strain or ligament injuries (65%-70%). In 5% to 15% of cases, the source of LBP is related to degenerative joints and disc disease [2]. The natural history of disk herniation is favorable; improvement of symptoms is the norm, and most episodes resolve spontaneously or after conservative therapy. However, studies have shown that low back pain is sometimes still present after long periods of time (at least 12 months) in 37% to 54% of patients [1,3]. 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 [4,5]. Studies as early as 1934 drew attention to the role of herniated nucleus pulposus as an important cause of low back pain and leg pain [6]. Apart from conservative therapy, all other forms of treatment aim at decompressing the nerve roots, which are the cause of the patient's discomfort. These can be done by taking the disc out by surgery or by decompressing the foramen and disc by different interventions. Outcome studies of lumbar disc surgeries document an overall success rate between 49% to 95% [7]. 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/ or hypertrophic scarring with severe symptoms in 20% of patients [8,9]. 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-disckectomy 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 [9-11]. Besides oral pharmacological and rehabilitation treatments, ozone therapy has emerged as an alternative or additional treatment option for these patients. Ozone nucleolysis or ozone discectomy is a non-surgical intervention to treat hernia /disc prolapse and discogenic pain. This procedure proved via many studies and research to be very safe and associated with high sucess rate for improving the physiological condition as well as pain sensations. The success rates reported in different studies vary from 65 to 80% of excellent or good results with chemonucleolysis and aspiration. Epidural steroid injections under CT or fluoroscopic guidance are also

used to minimize radicular pain and to try to obtain complete pain relief [12-14].

Despite its widespread use to treat a variety of conditions, ozone therapy remains unknown to most physicians. Ozone (O_3) is an allotropic form of oxygen, primarily known for its ecological properties, industrial application and therapeutic effects. Questions persist concerning its potential toxicity as an oxidant agent versus its reported clinical efficacy. Percutaneous techniques minimize the invasive nature of surgery, rendering administration more straightforward and faster while sparing healthy tissue and avoiding or minimizing complications such as postsurgical infection. Those techniques have been applied as an adjunct treatment for LBP and used in association with ozone injections have yielded good results [12].

Traditional Open Back Surgery for Slip Disc

In traditional open back surgery, a five to six inches incision may be needed in order to see the affected nerve root. In creating such a sizeable incision, a large area of muscle also has to be cut to make an opening of three to five centimeters, leading to risks of substantial blood loss. Complications of back surgery also include the use of general anesthesia, which, depending on age and overall health, could be a significant risk factor. In addition to the invasiveness of the surgery, back surgery side effects that need to be considered are the length of the stay in the hospital, the painful weeks/months of recuperation time, the heavy use of pain medications afterwards, and the time a patient has to spend away from work. Another important complication after back surgery is the likelihood of scar tissue formation [9-12]. In many cases, the amount of back surgery scar tissue formation leads to additional spine conditions, which could eventually lead the patient to need another surgical procedure. Unfortunately, there is 60% success rate of full recovery of symptoms with open back surgery. This poor success rate appears to be due to complications from back surgery.

Scar tissue formation caused by back surgery can be extremely painful, limit mobility and flexibility, and greatly diminish quality of life. Extensive scar tissue build-up is typically associated with the long incisions and other tissue damage experienced during traditional open-back surgery. While scar tissue itself is typically not painful, excessive formation of scar tissue can trigger pain if it binds to or impinges on nerve roots [13,14]. Patients with failed back surgery often live in significant pain and disability. This is a loop in which patients are caught: good pain relief brings the illusion of improved physical ability. But for many patients with failed back surgery, after a brief honeymoon period, pain, spasm, and weakness reappear at a low activity level. Although the nerve roots were not damaged directly by the failed back surgeries, the nerves are now encased in a web of scar tissue, which causes pain and spasm every time there are movements of the spine and legs [12].

Reasons for Failure of Surgery

Causes of failed back surgery for herniated nucleus pulposus includes: dural fibrosis, arachnoidal adhesions, muscle and fascial fibrosis, mechanical instability resulting from the partial removal of bony and ligamentous structures required for surgical exposure and decompression leading to facet and sacro-iliac joint dysfunctions, radiculopathy and recurrent disc herniation [12-14].

Newer Ozone Disc Nucleolysis

Without the necessity of a surgical procedure, disc herniations can be treated with a minimally-invasive procedure using ozone. Muto suggested intradiscal injection of ozone for disc hernia in 1998 under CT guidance, and Leonardi popularized fluoroscopy guided ozone injection into the intervertebral disc [15]. Ozone modifies the core of the intervertebral disc in such a way that the disc herniation resolves. The treatment is carried out under local anaesthesia, and ozone is introduced through a fine needle into the intervertebral disc without the need to open the spinal canal. The micro-therapy is carried out under the precise guidance afforded by computed tomography or C arm. Under a skilled practitioner's hand, scar formation is minimal or non-existent. The procedure takes between 20 and 30 minutes. A Hospital stay and postoperative physiotherapy are not necessary.

Procedure

Ozone is administered in the form of an oxygen-ozone gas mixture at nontoxic concentrations ranging from 1 to 40 μg of ozone per mL of oxygen, using various percutaneous methods [16]. It is usually performed under local anaesthetic. Light May administered general anesthesia, patient's only fears. The patient will be used for the operation on the ground lying prone theatre. Very fine needle is in the diseased disc under fluoroscopic guidance. The position of the needle tip in May confirmed by some small amount of radio-opaque dye.

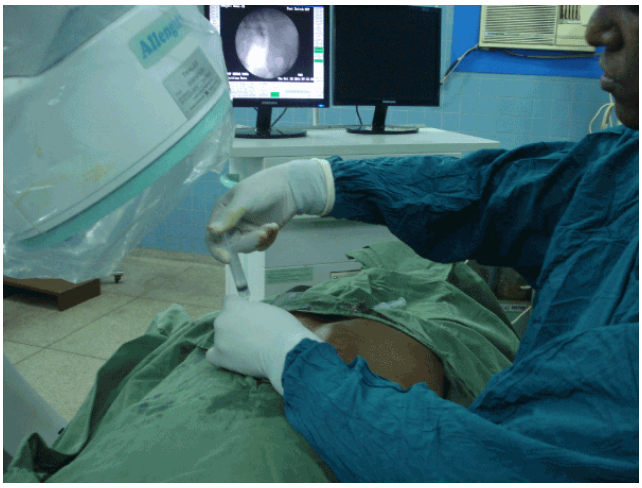

Figure 1: Ozone disc nucleolysis under fluoroscope guidance

Then some 3-5 cc of oxygen-ozone mixture (in a concentration of 29 micrograms /ml) If, in the disc. In the ozone concentration is not harmful to the surrounding tissue. So, when ozone spreads to the surrounding tissue, including spinal cord caused no damage. Ozone molecule is not stable. It has a half-life of only about 20 minutes. Also, within 20 minutes only half of the original ozone remains, the rest is oxygen. Increasing the temperature drops his half-time. For the injection, it is always freshly prepared on the spot (by an ozone generator) for the immediate application. Only ozone resistant syringes can be used for the injection. While the needle of the syringe is some amount of ozone-oxygen mixture is injected into the paraspinal muscles and para-radicular soft tissue to reduce nerve root inflammation, and increases the oxygen supply to the para-spinal cord

muscles. About 15 to 30 minutes to make the whole process as a function of the experience of interventionist [1,3,13,14,17] (Figure 1).

How does Ozone Nucleolysis Work?

Several mechanisms of action have been proposed to explain the efficacy of ozone therapy including analgesic, anti-inflammatory and oxidant action on proteoglycans (e.g., in the nucleus pulposus). The effects of ozone therapy are due to the action of active, free radical oxygen atoms being liberated during the breakdown of ozone molecules, a process which occurs within the nucleus pulposus. In the disc, this oxygen free radical (also called the singlet oxygen) attaches to the proteo-glycan bridges in the jelly-like material of the nucleus pulposus [13]. This results in the destruction of these proteoglycan bridges. Water is released from the breakdown of this matrix, which casues the disc to solidify and shrink back into the annulus fibrosis [18]. As a result disc shrinks and mummified. The intradiscal volume and intradiscal pressure is reduced. It is almost equivalent to surgical discectomy, and so the procedure is called ozone discectomy. It is also known as ozone nucleolysis or ozonucleolysis. The result is the decompression of nerve roots, and the elimination of radicular pain. Other positive effects have been attributed to ozone nucleolysis. It has an anti-inflammatory action by inhibitions of the educational materials produced by inflammation and tissue oxygenation increased due to increased 2.3 diphosphoglycerate level in the red blood cells. All of these factors lead to decompression of nerve roots, decreased inflammation of the nerve roots and increased oxygen supply for the diseased tissue to repair work. In a recent study LeonFernandez et al. showed ozone oxidative post-conditioning reduces oxidative protein damage in patients with disc hernia. In his study, One hundred percent of patients showed a severe oxidative stress. Major changes in superoxide dismutase activity, total hydroperoxides, advanced oxidation protein products, fructolysine content, and malondialdehyde were observed. After ozone oxidative post-conditioning, there was a re-establishment of patients' cellular redox balance as well as a decrease in pain in both DH. A relationship between indicators of oxidative protein damage and pain was demonstrated [19].

Indications of Ozone Nucleolysis

Ozone nucleolysis may be done in most disc-related pain. The following are possible situations in which this therapy may be efficacious. It can be done in degenerated disc without any prolapse or nerve root irritation. This category is called discogenic back pain, or back pain due to internal disc disruption. Axial dull ache in the low back which increases with the flexion of the spine is the main clinical feature. Leg pain is not a feature, and there should not be any dermatomal pattern of radiation. Provocative discogram should be performed for diagnosis. Positive discogram (provocation of similar pain more than 7/10 at a pressure below 15 psi) proves the presence of sensitized nociceptors and suggests that ozone therapy may be efficacious. It can be done in contained disc prolapse or disc bulge with root irritation. It may be done in non-contained disc (extruded or sequestrated disc) [2,4,5,20,21].

Contraindications of Ozone Nucleolysis

There are few conditions when ozone therapy should not be performed. These are active bleeding from any site, pregnancy, G6PD deficiency, active hyperthyroidism, loss of control of urination and defecation, and progressive sensory and motor loss, calcified disc herniation, intraforaminal herniation [5,20,21].

Complications

Complications of ozone therapy are very rare. They include post-procedural muscle spasm, burning pain (which is transient), and discitis (very rare due to the bactericidal effect of ozone). Other complications are similar to a discographic procedure. On the other hand, surgical discectomy has much higher side effects compared to remarkably few side effects of ozone discectomy. Ozone therapy is usually a day procedure and general anesthesia is not usually required. Ozone therapy is gaining popularity in different countries, including India, due to low cost, shorter hospital stays, less post-procedural discomfort, and good side effect profile [22-24]. Fort et al. reported a unique case of L5-S1 Achromobacter xylosoxidans infection secondary to oxygen-ozone therapy for the treatment of lumbosacral disc herniation. Histopathological evaluation of the disc material confirmed the diagnosis of chronic osteomyelitis and septic discitis at L5-S1. Intraoperative cultures grew A. xylosoxidans and Propionibacterium acnes. She had prompt improvement in her level of pain and was discharged on a 6-week course of piperacillin-tazobactam without complication [25].

Comparative Studies

There has been surge of interest in search of safer alternative methods of decompressing the nerve roots while maintaining the structural stability. Epidural steroid injection, transforaminal epidural procedures has a high success rate (up to 84%) but chances of recurrences are also high [25,26]. Chemonucleolysis using chymopapain has moderate success rate (approximately 66% at one year) [27-29]. It has also the chances of anaphylaxis following intradiscal chymopapain injection.

Injection of ozone for discogenic radiculopathy (low back pain with radiation to legs) has developed as an alternative to chemonucleolysis and disc surgery. Bonetti et al. also reported excellent results in 74.4% patients after six months [30]. Andruela et al. had similar results (70.3% at 6 months). Lu et al. showed “excellent” or “good” results of over 90%. However, ozone disc nucleolysis is a fairly new technology, and there are few (if any) randomized, controlled trials concerning this procedure. Further clinical research will be required to elucidate its efficacy. On an anecdotal level, however, ozone disc nucleolysis (performed by the first author on this article) has led to significantly improved pain and function in a number of patients in Bangladesh, and improved results have been tracked over many months. In addition, the relatively low cost of the technology means that it can be purchased and used in areas of poor financial resources, such as hospitals in the developing world. Owing to its fairly high success rate, less invasiveness, and remarkably fewer side effects, ozone therapy for slip disc is becoming very popular in different areas of world [18-20].

Oder et al. studied 621 patients to determine associations among the morphology of the disc disease, patient-specific data, and treatment outcomes. Six hundred twenty-one consecutive patients were subjected to CT-guided ozonucleolysis in combination with periradicular infiltration by steroids under local anesthesia. Patients younger than 50 years had significantly better values on the VAS and in ODI scores, 6 months after treatment [31]. Andreula et al. reported a 78.3% success rate in patients treated with ozone therapy and periganglionic steroid injection compared with a 70.3% rate in those

treated with ozone therapy alone; complications occurred in 2 of 235 patients and consisted of episodes of impaired sensitivity in the lower limb on the treated side, which resolved spontaneously within 2 hours [20]. In a series of 45 patients, Buric et al. studied the differences in outcome between intradiscal ozone chemonucleolysis and microdiscectomy in patients with noncontained lumbar disc herniations; they documented that 27 patients (90%) in the chemonucleolysis group showed a statistically significant improvement in pain and function; the same was true in 14 (93.3%) patients in the microdiscectomy group [17] Das et al. in an Indian population cohort study, evaluated 53 consecutive patients with lumbar disc herniation. All presented with clinical signs of lumbar nerve root compression supported by CT and MRI findings. They were treated with a single session of intradiscal ozone therapy. Therapeutic outcome was assessed after 2 years. Pain intensity was significantly reduced following treatment (VAS baseline was 7.58; after 2 years, 2.64). Similar ODI results were seen ($P < 0.05$). No major complication was observed in this case series [18]. Xu et al. included 187 patients with sciatica and low back pain with positive Lasègue sign and diagnostic verification by CT and MRI exhibited disc protrusion with nerve root or thecal sac compression. They compared the effectiveness rates after one week (103 cases), 2 weeks (61 cases), and 4 weeks (23 cases) treatment sessions of intradiscal ozone therapy. They were evaluated by Macnab criteria at 48 months. The effective rate was 82.02% in all groups [32].

Magalhaes et al. did a systematic review and meta-analysis of randomized controlled trials on ozone therapy as a treatment for low back pain secondary to herniated disc. He concluded as ozone therapy appears to yield positive results and low morbidity rates when applied percutaneously for the treatment of chronic low back pain [33].

Apuzzo et al. did an observational retrospective/horizontal study to compare oxygen-ozone therapy and/or global postural re-education in complicated chronic low back pain. The aim of this study was to assess the effects of O_2O_3 therapy in back pain rehabilitation, comparing three groups of patients suffering from chronic back pain associated with DH submitted to three different treatments: intramuscular O_2O_3 infiltrations, global postur re-education (GPR), or a combination of the two (O_2O_3+GPR). The data show that pain severity before treatment was significantly lower in the patients treated with GPR alone (VAS score 7.4) than in the O_2O_3+GPR patients (VAS score 8.5) and the O_2O_3 patients (VAS score 8.6). At the end of treatment, pain severity was lower in the O_2O_3 patients than in the GPR-alone patients. After some years of follow-up only the difference between O_2O_3+GPR and GPR-alone remained significant [34].

Conclusion

To conclude, ozone nucleolysis is a new procedure which offers the promise of excellent pain relief and the avoidance for surgery in patients with prolapsed nucleus pulposus. In addition, it has the benefits of being a safe, cheap procedure which does not require highly expensive equipment. For these reasons, it appears to be an excellent option.

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