31 USE OF OZONE IN PAIN DERIVING FROM SPINE

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Ozone originates from the Greek word "ozein" which implies "Breath of God" and this chemical compound is comprised of three oxygen atoms. Ozone occurs naturally in atmosphere and it is a colorless gas with a characteristic odor. One can smell the scent of ozone at high altitudes and in shoreline following stormy weather.

It is believed that ozone was discovered and named by Christian Freiderich Schonbein in 1840. Disputes on medical use of this had continued until a German Doctor Albert Wolf had written an article in 1915, stating that ozone therapy was successfully used in soldiers with gangrenous tissue during World War I. In addition, it had been used for treating tap water of metropolitan cities, such as Vienna and Los Angeles, during World War I.[3,4,12] Dr. Otto Warburg was granted Nobel Prize due to his works in the field of biochemistry and he evidenced in 1931 that deficient use of oxygen in the body facilitated development of cancer. He also demonstrated in blood samples treated with ozone that ozone is converted to oxygen and eliminated hydro peroxides and other free radicals. Dr. J. Hansler was granted patent of first medical ozone generator in 1957. Dr. Hans Wolf Frankfurt introduced the first major auto-hemotherapy in 1968. In 1975, Dr. Buckley evidenced that the high oxygenation resulting from peroxide formation during ozone therapy activates erythrocytes over glutathione enzyme.[3,4,12] Dr. H. Werkmeister published a letter in 1981, where the author stated that low-concentration ozone facilitates wound healing. In the same year, Dr. Zaid Fahmy started intra-articular ozone procedures.[3,4,12] Ozone therapy was first focused on spinal column by Dr. E. Riva Sanseverione in 1989.[9] Assessing effects of ozone on immune system, Dr. Bocci published scientific evidences on how ozone reinforces immune system and further, he demonstrated in 1990 how ozone activates antioxidant system against free radicals. [3]

Fields of Use of Medical Ozone

Medical ozone is a gas mixture comprising of pure oxygen (O2) and pure Ozone (O3). Concentration of medical ozone is below the toxic level (0,05% ~ 5% = 5μg ~80 μg). Some particular characteristics of medical ozone are as follows: the gas kills microorganisms such as virus, bacteria and fungus, and it activates immune system; it supports and reinforces healing process; regulation of hormone and enzyme production; enzymes eliminating "free radicals" and all enzymes guarding cells are triggered.[4,9,11,12] In this respect, medical ozone has a wide range of use ranging from wound care to anti-aging and recently, it has gradually increasing popularity. Medical ozone has pain-killer and anti-inflammatory effects and recently, ozone can be used in pain therapy with minimal invasive interventions due to advancement of injection techniques. Ozone is administered into disc, muscle, joints and transforaminal space for lumbar pain, neck pain, myalgia, arthralgia and pain deriving from spinal cord, respectively, and thus, it enables rapid improvement.[1,2,5] In addition, combined with auto-hemotherapy, which has

many other fields of use, medical zone can be intravenously administered and this modality is efficient in some rheumatoid pains such as fibromyalgia and tiredness syndrome. In addition to general contraindications of interventional techniques, medical ozone should not be used in hyperthyroidism and favism. Medical ozone has no extra severe side effect, which is added to usual side effects of interventional techniques. [1,2,5]

Medical ozone has many different effects on human metabolism depending on technique and concentration. It increases activity of enzymes, such as glutathione and catalase, resulting with inhibition of free radicals. It regulates erythrocyte metabolism via effects on peroxide generation in erythrocytes and glutathione system, and it prevents formation of erythrocyte clusters and increases capacity of carrying/delivering O2. Glycolysis is accelerated and more oxygen is released from hemoglobin to the tissue. It support production of acetyl coenzyme-A, which functions in metabolic detoxification,[4,9,10,11] Cell metabolism is accelerated due o influences on mitochondrial transport system and it induces protection of cell against mutagenic changes. Flexibility of erythrocyte is increased, resulting with regulation of blood viscosity and arterial pO2; it also decreases cluster formations, which impair normal metabolic functions of erythrocytes. Functions of leukocytes and phagocytosis are reinforced. Medical ozone enables induction of cytokines such as interferon, interleukin and growth factors.[4,9,10,11,12] Reticuloendothelial system is activated and tissue regeneration is accelerated. It is a potent antiseptic; Enteroviruses, Aeromonia Hidrofilia, Coliform bacteria and Staphylococcus Aureus can be inactivated. It destructs phospholipids, peptidoglycans and polysaccharies, which are found in cell membrane of many pathogen organisms**.** There are two significant studies investigating antimicrobial effects.[4,9,11,12] In an animal study, Schulz et al. demonstrated that the animals with septic peritonitis could survive if they were administered ozone before peritonitis was induced. In addition, lower dose of antibiotic agents can be used when antibiotherapy is indicated.[10,11]

Medical Ozone in Algology

Intra-discal procedres

Mechanical and inflammatory reasons are still disputed in pathogenesis of lumbar pain. In addition to direct effect of disc hernia on spinal ganglion, indirect stimulation of nociceptors, which are located on posterior roots of spinal nerve, by ligament and annulus deformation, and mechanical factors such as ischemia and venous stasis resulting from direct compression on arteries, lumbar spinal pain may occur secondary to inflammation, which is caused by biohumoral factors such as cellular mediators, Phospholipase A1, Prostoglandin E2 and matrix metalloproteins which are released in response to disc protrusion. Intra-discal medical ozone administration increases microvascularization at hernia site, resolves edema and reduces size of herniation due to molecular interactions. [6,7,8]

Patient is placed prone position on scopy table. Scopy is given 45-degree oblique position and an insertion site is determined which is on the mid-line between facet joints and lateral disc. 22G Chiba needle is used and nucleus pulposus of disc is reached. (Figure 1) In addition, CT-guided intervention technique

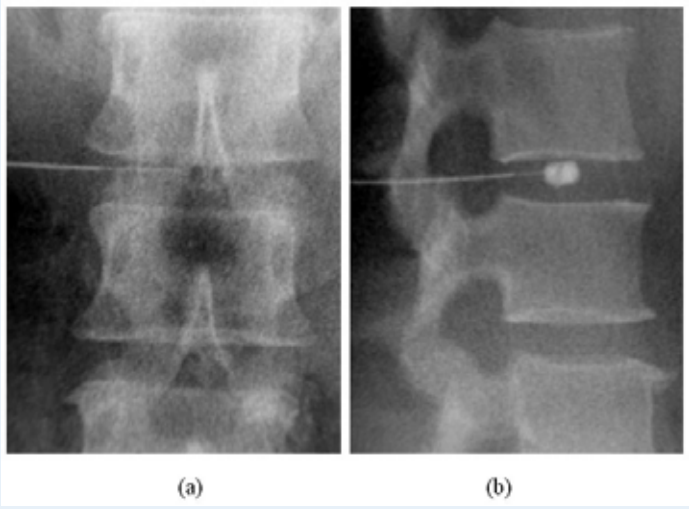

Figure 1: *Ozone injection under scopic control (a) AP, (b) lateral image.*

has been also published.[6-8] (Figure 2) Depth of needle is checked under lateral scopic imaging and O2/O3 mixture is administered at concentration of 27-30 microgram/ml at volume of 10 cc once a week for 4 weeks in the lumbar region or at concentration of 27-30 microgram/ml at volume of 5 cc once a week for 2 weeks in the cervical region. (Table 1)

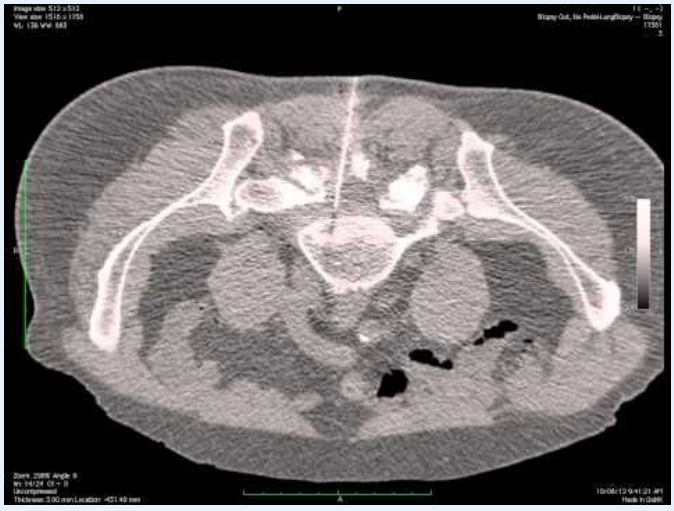

Figure 2: *CT-guided ozone injection: Localization of needle and distribution of ozone*

Intradiscal administration of O2/O3 mixture with needle was first introduced by Dr. Verga in '80s.[6] Histological assessments support direct effects of ozone (at specific concentrations) on proteoglycans of nucleus pulposus. Water molecules are released due to generation of matrix cells and intra-discal space is occupied by fibrous tissue within a period of 5 weeks. This process results with decreased disc volume. [1,2,5-7]

Most recent systematic meta-analysis include 8 observations, 4 randomized controlled (RCT) and 5 case studies, which also report complications and also suggests intradiscal ozon management.[7] Authors suggested that the result is deriving from scarcity of RCT publications and complete absence of placebo controlled studies and they added that it should be included in therapy algorithms due to infrequent side effects and present of beneficial effect.

Injection into facet joint

Facet joints are among most common reasons of lower back pain and leg pain. Arthrosis of facet join is not only associated with osteoarthrosis or degenerative joint disease, but it may also be secondary to disc degeneration or spondylosis. Facet joint syndrome is usually associated with discopathy; isolated cases account for only 20 percent of all cases.

Patient is placed prone position on the scopy table and a pillow is placed beneath abdomen in order to expand intra-articularspace of facet joints. Sterile conditions are ensured and C-arm scopy device is moved until facet joint is visualized at 45 degrees on oblique plane. The facet joint subject to the intervention is visualized with scopy device and 22G 3.5 inch needle is inserted at 3-cm lateral side of the mid-line. Scopic imaging is maintained and intra-articular space of facet joint is accessed; O2/O3 mixture is administered at concentration of 27-30 microgram/ml at volume of 1-4 cc once a week for 4 weeks in the lumbar region or at concentration of 27-30 microgram/ml at volume of 1-2 cc once a week for 2 weeks in the cervical region. There is no sufficient literature on this subject.

Table 1:
Disc hernia; intra-discal ozone administration protocol

Indication	Treatment	Concentration (Ug/ml)	Volume (ml)	Treatment Protocol
Hernia	Lumbar	27 - 30	10 - 20	Once a week for 4 weeks
	Cervical	27 - 30	5 - 7	Once a week for 4 weeks

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