Cardiopulmonary Arrest and Pneumoencephaly Developing after Epidural Oxygen-ozone Mixture Therapy

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Abstract

Pain treatment can comprise a combination of pharmacological, interventional, surgical, physical, psycholgical methods. Interventional procedures, particularly minimally invasive percutaneous therapies, have been widely used in recent years. Corticosteroid, hyperbaric saline or oxygen-ozone therapy is a safe procedure for patients in whom pain cannot be relieved by epidural adhesiolysis or other treatments. Complications related to oxygen-ozone therapy have been reported rarely in lumbar sciatalgia. Herein, we present a patient who developed cardiopulmonary arrest and pneumoencephaly as a rare but life-threatening complication of oxygen-ozone therapy, for epidural lysis, applied to the epidural space due to low back pain.

Keywords: Arrest, epidural, oxygen-ozone, pneumoencephaly, Racz catheter

Introduction

Low back pain is a common health problem that affects the majority of the population. Minimally invasive percutaneous therapies, including chemodiscolysis with Chymopapain, automatized percutaneous lumbar discectomy, percutaneous laser disc decompression, intradiscal electrothermal therapy, percutaneous coblation nucleoplasty, decompressor percutaneous discectomy, and intradiscal oxygen-ozone therapy, have been widely used in lumbar disc hernias.

Ozone (O₃) is a gas molecule composed of three oxygen atoms. Although the oxygen molecule is a stable molecule, O₃ is unstable. O₃ therapy involves the application of a certain amount of an oxygen/O₃ mixture to the body spaces or circulation. This mixture may be applied through the intravenous, intramuscular, intra-articular, intrapleural, intrathecal, or intradiscal route. Oxygen-O₃ chemonucleolysis is one of the most beneficial and cost-effective therapies, with a low complication rate (<0.1%). It is also considered to be among the epidural lysis therapies that could be performed endoscopically or nonendoscopically. Paresthesia, vitreoretinal hemorrhage, vertebrobasilar stroke, subcutaneous hematoma, syncope, air embolism, headache, visual disorders, and pneumoencephaly are the main complications reported in the literature for oxygen-O₃ therapy applied for lumbar disc herniation.

Here, we present a case of cardiopulmonary arrest and pneumoencephaly developing after oxygen-O₃ application to the epidural space due to low back pain.

Case Report

A 79-year-old female patient was admitted to our clinic due to pain radiating to her low back and heel for the past 2 years. She had hypertension, controlled diabetes mellitus, and asthma in her medical history, and her laboratory tests were within normal limits. The patient whose physical status American Society of Anesthesiologists Class III was taken to the operating table for O₃ epidurolysis. She underwent conscious sedation with 2 mg of midazolam and 50 µg of fentanyl following standard monitoring in the prone position. Skin and subcutaneous tissue was anesthetized with 2% lidocaine after the entrance point had been marked.

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been determined by C-arm fluoroscopy. The caudal space was accessed from the hiatus sacralis using an 18-gauge Tuohy-ended epidural needle. Epidurography was performed with injection of 10 mL\(^{-1}\) nonionic contrast medium. The radiopaque substance does not exceed the L5–S1 level, and full obstruction was determined by C-arm fluoroscopy. Next, the patient underwent insertion of a Racz neuroplasty catheter (Epimed International Inc., Gloversville, NY, USA), specially designed for adhesion lysis, and coated with a fine sheath, to the L5–S1 level under scope using a guidewire, and fixed to the skin with a suture at the obstruction level. O\(_3\) gas injection 8 mL\(^{-1}\) (20 µg/mL) was planned for 3 days. Epidural O\(_3\) injection performed for epidural lysis was completed easily on the 1st day. On postoperative day 2, 20 mL\(^{-1}\) (20 µg/mL) of the O\(_3\)-oxygen mixture was placed into a syringe. Although the mixture was planned to be administered at the dose 8 mL\(^{-1}\), it was inadvertently injected at a dose of 20 mL\(^{-1}\) (20 µg/mL). Cardiopulmonary arrest occurred following the abrupt loss of consciousness at the 2nd min after injection. Her pulse could not be palpated; thus, cardiopulmonary resuscitation was applied after she had been placed in the proper position. She was intubated and ventilated with 100% oxygen, 1 mg of adrenalin was administered, and a normal sinus rhythm was achieved at the 10 min of resuscitation. The patient was transferred to the intensive care unit and mechanical ventilation was started. After 2 h of intubation, her blood pressure was 106/54 mmHg, her heart rate was 88 bpm, her SpO\(_2\) was 97%, and her general condition was moderate, showing confusion. Cranial computed tomography (CT) was performed as her vital signs were normalized without the need for inotropic drugs. On CT, widespread air images were observed in the frontal region of the cingulate gyrus, adjacent to the right lateral ventricle in the left fronto-temporo-parietal region, at the convexity level in the right frontal lobe, in the left hemisphere, and in the left lateral section of the pons [Figure 1a-d]. She was followed up on mechanical ventilator with proper medication and extubated at the end of the 4th day; widespread air images were seen to be completely resorbed on control CT on the 7th day. She was discharged because her general condition was good.

**Discussion**

Cases of low back pain following lumbar laminectomy are gradually increasing. Surgical failure is seen in 20%–50% of cases, and additional treatment is often required.[9] Epidurolysis performed endoscopically or nonendoscopically is considered to be a minimally invasive procedure.[5] Corticosteroid, hypertonic saline, or O\(_3\) application was shown to be safe for patients in whom pain could not be relieved with epidural adhesiolysis or other treatments.[5] Bocci[3] suggested that O\(_3\) gas has two mechanisms of action. The first mechanism involves mechanical and chemical adhesiolysis and shrinkage of the disc region. O\(_3\) is dissolved in water when it contacts tissue and shows an effect by creating a reactive oxygen cascade that contains H\(_2\)O\(_2\) and more active hydroxyl radicals. These molecules react with proteoglycans, carbohydrates, and amino acids to form Type 1 and 2 collagen, resulting in dehydration due to the reabsorption of water and hydrolytic products. Progressive disappearance of herniated disc material and reduced mechanical irritation reduce the sensitivity of axon terminals of the nerves in the disc annulus.[6] The second mechanism of action of O\(_3\) is suggested to be a cytokine-mediated anti-inflammatory effect. There is evidence indicating that many cytokines, such as tumor necrosis factor and interleukin, play an important role in low back pain development.[7]

O\(_3\) therapy-related complications have been rarely reported in the literature.[1] Either little or no side effects were observed with the concentration used for treatment of lumbar disc hernias (10–40 µg/mL).[13] In one study, no severe side effects were reported using an intradiscal 4 mL\(^{-1}\) (27 µg/mL) and periganglion 8 mL\(^{-1}\) (27 µg/mL) oxygen-O\(_3\) mixture.[2] Side effects of oxygen-O\(_3\) mixture therapies include three clinical syndromes: vasovagal episode, syncope, and air embolism. Sweating, paresthesia, abdominal pain, headache, bradycardia, and dizziness are seen during the early period, whereas headache, dizziness, and visual disorders such as temporal scotoma are seen during the late period. Most of the symptoms were reported in the context of systemic application and there are few clinical data concerning the side effects of paravertebral oxygen-O\(_3\) application.[8]

In the screening data of a meta-analysis of studies conducted between 1996 and 2011, five different complications were observed.[1] Lo Giudice et al.[9] observed bilateral vitreoretinal hemorrhage following oxygen-O\(_3\) mixture therapy for lumbar disc hernia. In another study, pneumoencephaly-related severe headache was observed following intrathecal puncture.[10]

**Figure 1:** (a–d) Brain computed tomography revealed multiple air images.
Ginanneschi et al. observed paresthesia on the anterior and lateral sides of the leg a few minutes after intradiscal O₃ injection at the L4–L5 level, suggesting spinal nerve injury. In another study, carried out by Corea et al. in 2004, vertebrobasilar stroke was observed during the course of the oxygen-O₃ therapy procedure, whereas subcutaneous hematoma was seen in another report. 

Oxygen-O₃ therapy is accepted as a safe procedure for lumbar sciatic pain with very few reported complications. Head trauma and craniotomy are among the most common causes of pneumoencephaly. The oxygen-O₃ mixture was reported to be safe at up to 10–40 µg/kg in intradiscal applications; only one case of pneumoencephaly has been reported in the literature after oxygen-O₃. In that case reported by Devetag et al., sudden headache developed in the occipital region and left side of the face 2 min after intradiscal oxygen-O₃ injection at the L4–5 level due to lumbar disc hernia. CT was performed due to the presence of neurologic findings such as nausea, vomiting, and stiff neck. Pneumoencephaly occurred due to small air images in the pontomesencephalic region that were widespread in the frontal horn of the lateral ventricle. The reason for severe headache was stated to be the inadvertent transfer of oxygen-O₃ therapy to the intrathecal field. No alteration occurred in the vital signs of the patient. However, the vital signs of our patient changed after epidural oxygen-O₃ mixture application. The end of the Racz catheter was placed at the obstruction location such that the Racz catheter could have injured the dura inadvertently, for example, by tearing. We encountered no complications on the 1st day; however, damage could have developed following the migration of the catheter from the dura to the intrathecal field on the 2nd day. The occurrence of a clinical side effect immediately after the injection of an unplanned and high amount of oxygen-O₃ mixture and widespread air images in the cranium a few hours after the procedure suggest that the mixture directly reached the cranium through the intrathecal route.

The absence of cerebrospinal fluid or blood discharge on aspiration before injection does not guarantee that the Racz catheter is in the epidural field. The only way to ensure the correct positioning of the Racz catheter is by performing aspiration with a syringe. In this case report, pneumoencephaly, which is a rare but life-threatening complication, developed after oxygen-O₃ therapy for epidural lysis, applied to the epidural space due to low back pain.

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Conflicts of interest
There are no conflicts of interest.

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