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Case report

Management of a patient with Trigeminal Neuralgia associated with failed endodontic therapy using Ozone Therapy: A Case Report

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Keywords

oxygen ozone therapy, trigeminal neuralgia, endodontic therapy

Abstract

Trigeminal Neuralgia (TN) is a painful disorder that can affect one or more branches of the fifth cranial nerve. Pain may be triggered by normal mechanical or sensory stimuli or may be spontaneous. This case report describes the management of a patient that presented with a 10 year history of constant dull pain with mechanical and sensory stimuli of acute, sharp pain along the distribution of the third division of the right trigeminal nerve. The onset of pain was associated with root canal therapy on tooth # 30 (IS-46). The patient had received pharmacological and surgical interventions some of which had provided temporary relief, but the pain had always returned and steadily increased over time. Radiographically, the tooth presented with evidence of apical lesions because of root canal failure. Based on clinical and animal studies, it is known that areas of chronic osseous infection or mechanical compression produce elevated levels of reactive oxygen species, and other tissue degradation products that could be responsible for pathological changes in the nerve fibers, resulting in chronic pain.
Medical oxygen/ozone (MOZO) is a medical modality that has been demonstrated to have multiple local and systemic effects, including analgesia and reduction of inflammation. Major autohemotherapy is one of the method of systemic delivery of MOZO that can applied to treat conditions that are a result of chronic oxidative stress. This case report describes how major autohemotherapy was used to facilitate the resolution of TN that was the result of a chronic dental infection.

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Introduction

Trigeminal Neuralgia (TN) is defined by the International Headache Society [IHS] (2018) as is a painful disorder that can affect one or more of the three fifth cranial nerve branches and may be triggered by stimuli or spontaneous. The pain is characterized as paroxysmal, repetitive, unilateral, severe, electric shock-like or stabbing, sharp and it can last from a few seconds to a couple of minutes. TN can be classified into three categories, Classic (Purely paroxysmal, continues pain), Secondary (Associated to multiple sclerosis, a space occupying lesion or other cause), and Idiopathic (Kes & Matovina, 2017; IHS, 2018). This condition affects approximately 4.3 persons per 100,000/year, with a slight predilection for women over men (Overman, 2010). Melek, Devine, and Renton (2018) in their systematic review found that TN is a debilitating condition that has a significant psychosocial impact contributing to co-morbidities such as depression and anxiety. They also found that the pain management for these patients not only include a pharmacological approach, but that they may also require surgical and/or psychosocial interventions. Pharmacologically, the first-choice for medical treatment are anti-epileptic drugs (Cruccu, 2017) but other approaches include neuroleptic drugs, and muscle relaxants (Obermann, 2010). These drugs have a wide range of side effects including memory loss, dizziness, insomnia, somnolence, renal dysfunction and cardiac arrhythmias (Tentolouris-Piperas et al., 2017; Oomens & Forouzanfar, 2015).

Ozone (O3) is an allotropic modification of the oxygen molecule into a chain of three atoms of oxygen that has a high oxidative potential. It is produced by natural events like ultraviolet radiation or electrical discharges. The gas is unstable and is easily degrades to oxygen or by oxidation. Because of its high oxidative potential, it has a high affinity for carbon double bonds and can interact with many organic and inorganic compounds. (Schwartz, 2017; Bocci, 2011). Stoker (1916) reported the first use of ozone in medicine as a germicidal agent in the treatment of German soldier affected by gaseous gangrene. Since them, the understanding of complexity of the mechanism of action that medical oxygen/ozone (MOZO) can have on the human body go beyond the bactericidal effect. Metabolically, the principal effects are (1) an increase usage of glucose use at the cellular level, (2) an increase in protein metabolism and (3) oxidation of unsaturated lipids that produce oxides that can signal the upregulation of the tissue repair mechanisms. In the realm of pain control, MOZO has a dual effect acting as an analgesic and an anti-inflammatory (Schwartz & Martinez-Sanchez, 2012). Studies have demonstrated that MOZO is able to decrease the production of inflammatory mediators, as well as inactivate the metabolic mediators of pain.

At the same time, locally injected MOZO can improve the blood microcirculation by facilitating oxygen delivery to the affected tissues (Re et al., 2011; Iliakis et al., 2001). However, there are limited number of studies that have examined the utility of systemically applied ozone for neurological pain (Clavo, 2013). The aim of this case report is to present the management of a patient with trigeminal neuralgia utilizing major autohemotherapy in conjunction with surgical debridement of an osteonecrotic lesion of the mandible.

Case Presentation

The patient was a 49 years old Caucasian female who presented with constant dull pain along the distribution of the third division of the right trigeminal nerve for the past ten years. The patient associated the onset of pain with the completion of endodontic treatment on tooth #30 (46 International System (IS)) in 2008. In 2010 she was diagnosed with idiopathic trigeminal neuralgia. The patient had experienced short episodes of relief with various pharmacological interventions but, in the long-term, the pain had always returned and steadily increased over time. In 2012 she had undergone decompression surgery of the 7th cranial nerve along the mastoid segment with no relief of her symptoms. At one point, approximately 8 years after the initial endodontic treatment, the patient was taking both oxycodone and oxycontin to control the pain. The patient became concerned by the effects the drugs had on her ability to focus, concentrate on a task and to drive a car. She had weaned herself off of the opioids but had shortly thereafter starting taking Lyrica® (Pregabalin) in an effort to control the pain. While the Lyrica® had fewer side effects, it did not control the pain as effectively and she was concerned by her increase in suicidal thoughts. In 2017 she had sought medical advice from an osteopathic physician. After reviewing her history, he recognized that the pain might have a dental origin and referred her to our office. At the initial appointment, the patient was unable to smile without causing pain. Even though there was no damage to the seventh cranial nerve, she spoke with the corners of the mouth turned down in an effort to prevent causing any pain. Even the retraction of the patient's lips for the photographs caused sharp pain. Her medical diagnoses at the initial appointment were idiopathic trigeminal neuralgia and deep vein thrombosis. The deep vein thrombosis had been a consequence of a motor vehicle accident in 1994 for which she took 5 mg Warfarin (Coumadin®) daily. Her other medication was twice daily 150 mg of Lyrica®. Supplements included a daily dose of a multivitamin, supplemental calcium and 1000 mg of vitamin C.

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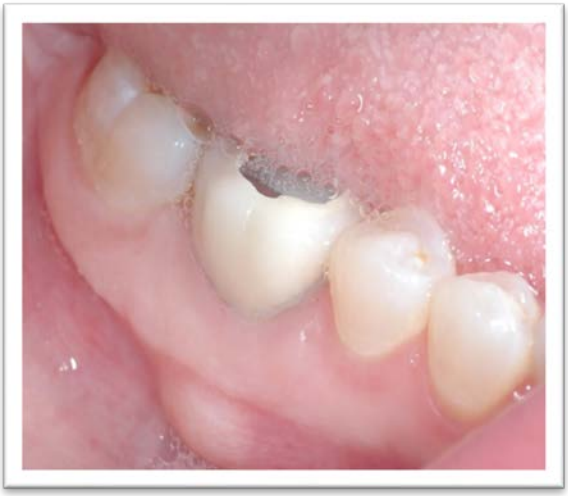
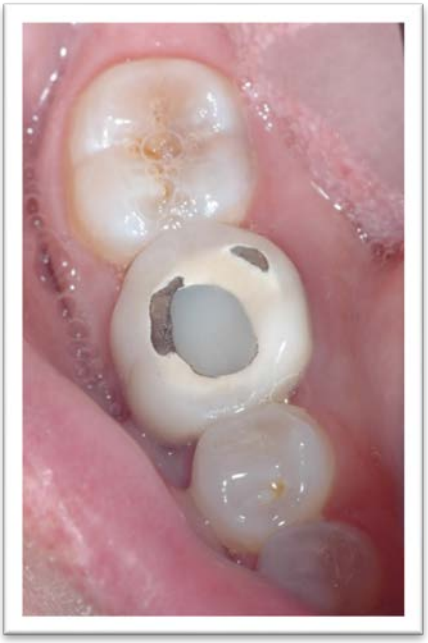
Fig. 1 and 2:
Intraoral photos of the lower right





Additional dental findings included no signs of facial erythema, swelling nor any intra- or extra-oral pathologies. Intraorally, tooth # 32 (48 IS) was missing, tooth # 30 (46 IS) presented with a porcelain fused to metal crown (PFMC) with an occlusal restoration closing the access for the endodontic treatment of the tooth and some signs of wear. The rest of the teeth in the quadrant appeared free of caries lesions, restorations or periodontal involvement. Buccal exostosis and large lingual tori were noted in the right mandible (Fig. 1). The baseline pain would vary anywhere from 3 to 7 out of 10 without stimulus. Upon stimulation, the pain was 9 out of 10. The patient did not smile because it was a pain stimulus.

Radiographically, in a panoramic view of the patient (Fig. 2), it was found that tooth # 30 (46 IS) presented with a root canal and a crown. A standard panoramic view of the data did not reveal any evidence of bone pathology. A cone beam computed tomography was performed to determine if there was any evidence of bone pathology along the inferior alveolar nerve bundle.

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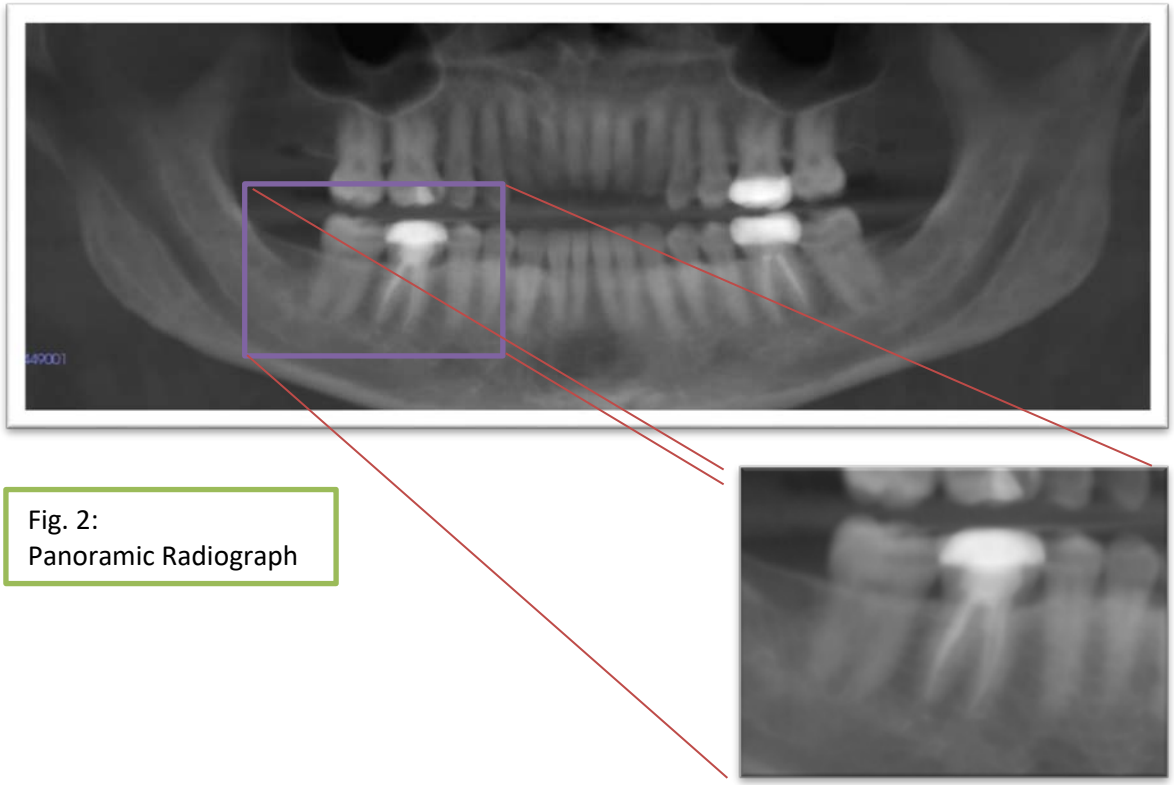

Fig. 2:
Panoramic Radiograph

The CBCT slice along the long axis of tooth #30(46 IS) (Fig. 3) demonstrated areas of radiolucency associated with both the mesial and distal root apices. The inferior alveolar nerve canal is radiographically located approximately 7 mm from the apex of the distal root of #30.

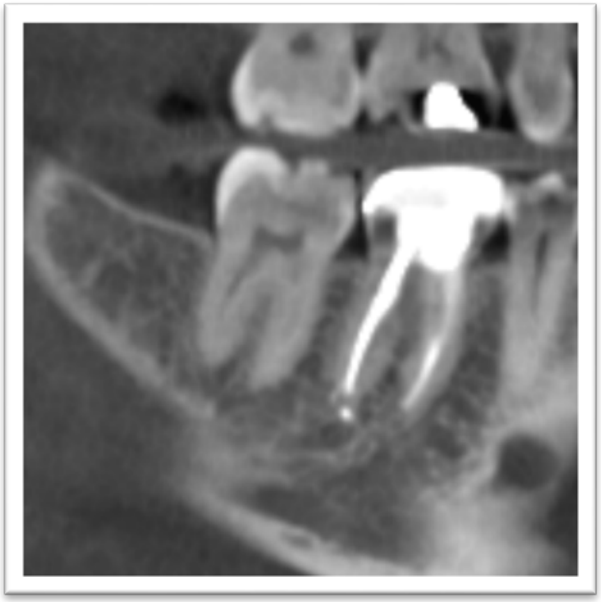

Fig. 3: CBCT slice along the long axis of tooth #30 (46 IS) prior to treatment.

Tangential slices through tooth #30 (46 IS) demonstrate multiple radiolucent areas (as indicated by the arrows on each slice) (Fig. 4) However, even the largest area indicated on figure 4D is approximately three millimeters from the inferior alveolar nerve canal.

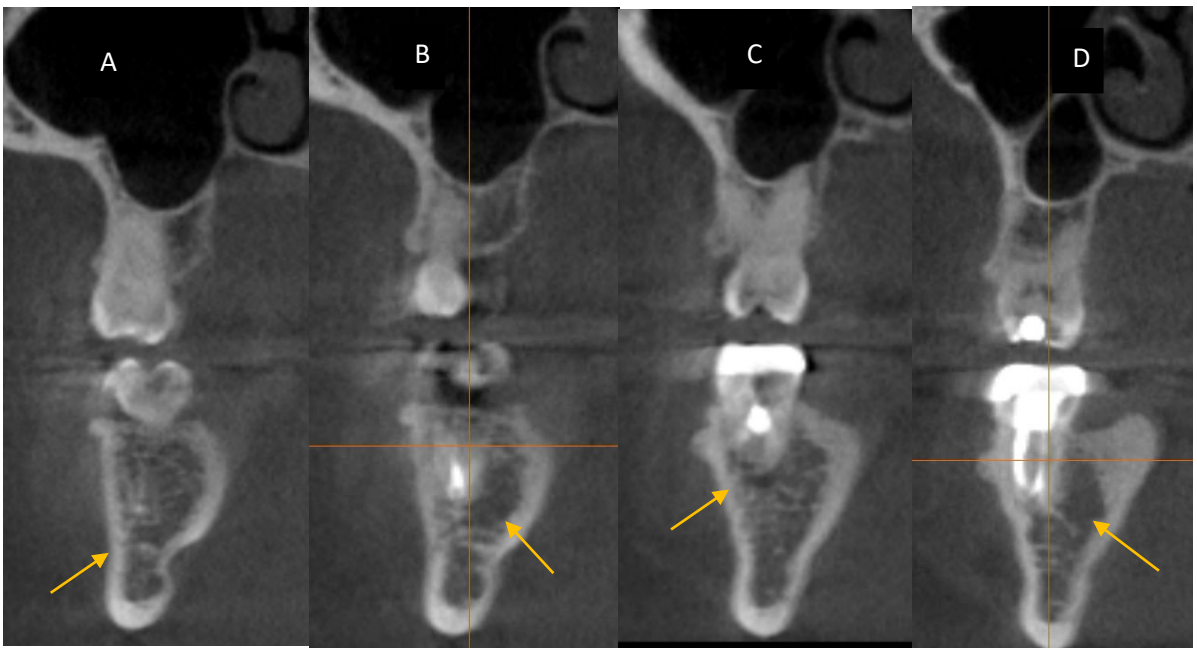

Fig. 4A: Slice through the distal root tip #30 (47 IS) 4B: Distal root #30 (46 IS) 4C: Slice through the furcation of #30 (46 IS) 4D: Mesial root #30 (46 IS)

Treatment

The patient had already undergone endodontic retreatment and did not wish to consider endodontic surgery as a treatment option. The prior chronic use of opioids and the current daily use of Lyrica® had upregulated the patient's cytochrome p450 liver enzymes. As a consequence, she had a very low pain threshold and thus reduced therapeutic range for local anesthetics, pain medications and sedatives. Following a review of the CBCT images, the patient decided she would prefer to have tooth #30 (46 IS) removed. Following consultations with both a dental anesthesiologist and the patient's physician, it was decided to:

1) Provide the patient with three sessions of major autohemotherapy during a two week period prior to the surgical removal of the tooth.
2) Remove the tooth under general anesthesia
3) Perform an aggressive debridement of the lamina dura and surrounding cancellous bone with piezosurgery if there was a lack of bleeding from the extraction socket
4) Not place any bone graft materials nor growth factors into the extraction sites to prevent any possible inflammation due to a foreign body reaction.

Three sessions of major autohemotherapy were provided by a physician with over 5 years of experience in this therapy. Each session consisted of drawing 60 mL of blood into a 60 mL syringe containing 250 units of heparin. This was then discharged into 250 mL container with an additional 250 units of heparin, 1 mL of B-100 complex and 2 mL of calcium gluconate. An equal volume of ozone (60 mL) at a concentration of 45 µg/mL was then injected into the container and gently mixed for at least one minute. The blood was then exposed to UV light and infused back into the patient over a period of (35 to 45) min. Each session was at least 5 days apart over the two weeks prior to surgery with the last session occurring approximately 3 days prior to surgery. No complications were experienced during the major autohemotherapy.

The dental surgery was done in an outpatient surgery clinic for general dental anesthesia. A presurgical interview with the patient revealed:

1) That the patient could smile without causing pain,
2) That her baseline pain had decreased to a range of 2 to 4 out of 10,
3) That even though she had a marked decrease in pain, she still wished to have tooth #30 (46 IS) extracted.

The patient was provided general anesthesia and local anesthesia for removal of the tooth and for debridement of the necrotic alveolar bone. The patient had a nasal-tracheal intubation line and an oral obturator placed during surgery. Local anesthesia was provided via an inferior alveolar block and local infiltration of 3.4 mL of 2 % lidocaine with 1:100,000 epinephrine to the right mandible. The crown was removed, the tooth sectioned through the furcation in a buccal-lingual direction and the mesial and distal tooth segments elevated separately. Minimal bleeding of the extraction socket was noted. Hence, an aggressive debridement of the trabecular bone was done until no granulation tissue could be tactilely noted with a small Miller curette and it was noted that the blood would fill the socket in the course of approximately one minute. An effort was made to avoid any flap reflection so that postoperative pain would be reduced. Surgery was less than one hour without complications. The patient was appointed for a follow up evaluation two weeks following surgery.

At the initial follow up appointment two weeks following surgery, it was noted that the patient's pain level had reduced to a baseline level of 1 to 2 with occasional episodes of acute pain (5 out of 10) but with a marked decrease in frequency. A fibrin clot was noted in the extraction site with no swelling and no erythema. (Fig. 5) The patient reported that she had started to cut back on the dosage and frequency of her Lyrica without consulting her neurologist but with no adverse side effects. The patient agreed to return to clinic in 4 months for a re-evaluation.

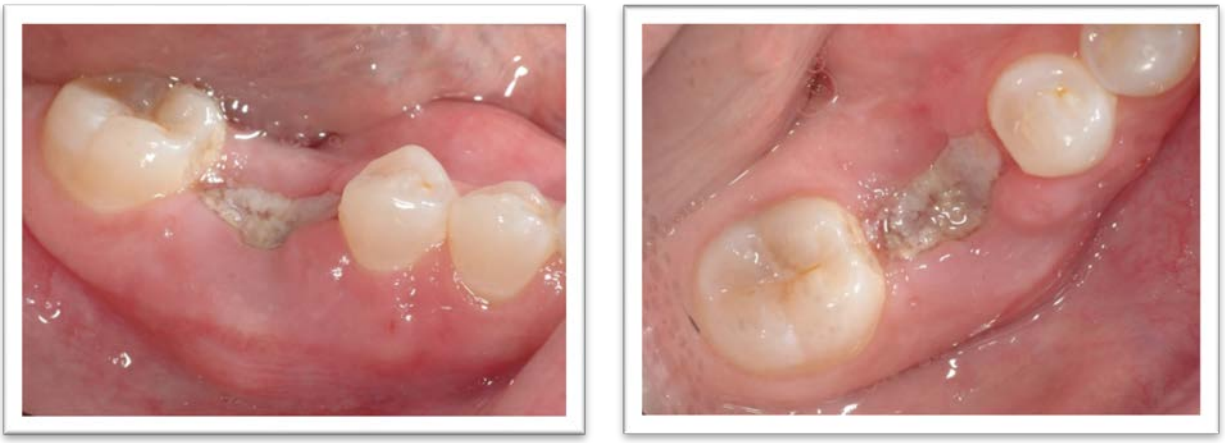

Fig. 5. First follow up appointment after extraction of tooth # 30 (46 IS)

At the re-evaluation appointment the gingival mucosa presented normal soft tissue healing and no signs of inflammation or other pathologies.

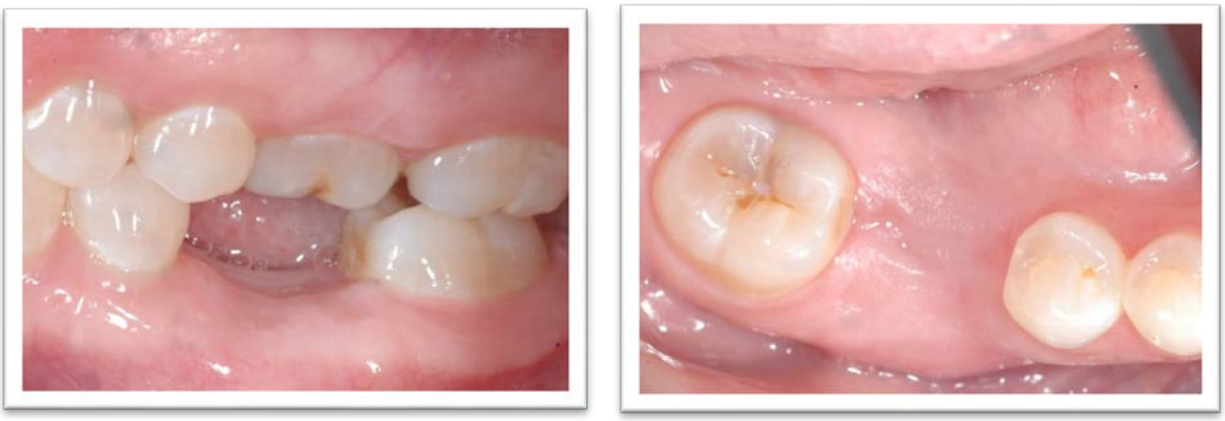

Fig. 6. First follow up appointment after extraction of tooth # 30 (46 IS)

Fig. 7: CBCT tangential slices of tooth # 30 (46 (IS)) after extraction

At the four-month evaluation, the patient stated that she had discontinued all pain medications including Lyrica. The patient stated she had experienced intermittent masticatory pain in tooth #31 in the week prior to the examination but otherwise no pain in the right mandible in the two months prior to the appointment. A new CBCT was done of the mandible to discern if there was sufficient bone regeneration for placement of an endosseous implant in the site. While there was evidence of bone fill, it was incomplete. The examination of the radiograph, also revealed a carious lesion in the occlusal aspect of tooth #31. The patient was asked to schedule for restoration of the lesion.

Discussion

Trigeminal neuralgia is a well-defined medical condition whose etiology can be challenging since it can arise from a variety of causes. In this case study, the diagnosis was made by a neurologist after the onset of chronic right jaw pain shortly following endodontic therapy on tooth # 30 (46 IS). Trigeminal neuralgia associated with dental treatment was reported by Rothen, et al. (1974), when they evaluated the incidence of facial pain in 283 patients; 192 of them were diagnosed with trigeminal neuralgia, and the rest had some other atypical facial neuralgia. Of those patients, 33 indicated that their pain started as a consequence of the dental treatment. While TN associated with endodontically treated teeth is not common, it has been previously reported in the literature (Francica, et al., 1988). The most common reason for pain after endodontic treatment is damage to the inferior alveolar nerve because of over-instrumentation of the canals in the molar teeth, pressure from the gutta-percha, the sealant material or the effect of the intraoperative medications. (Kes & Motivina, 2017; Escoda-Fancoli, et al., 2007; Pogrel, 2007).

Besides trauma, there are other local factors that can also cause TN. Among them, the most accepted etiology is a neurovascular conflicts, where an artery or vein can produce compression of the trigeminal nerve (TR N) (Thomas & Vilensky, 2014). Anatomical factors such as focal arachneoid thickening, or other local changes associated with the nerve or surrounding structures (Yadav, et al., 2017) can also cause compression of the TR N. Ultrastructural and immunohistochemical examinations of the affected TR N in patients with TN had found pathological changes in the nerve fibers principally showing segmental demyelination and degradation of the myelin, and that those changes were more significant in patients that had long-lasting neuralgias (Marinković, et al., 2009).

Pulpal necrosis or the failure of endodontic treatment can produce apical periodontitis (AP) also referred to in general terms as an apical lesion (AL). This is a chronic osseous infection that is a result of the body's attempt to rid itself of a biofilm that sources its nutrition from the necrotic tissues within a non-vital tooth. Under normal circumstances in a healthy host, a biofilm infection within the mandible is eliminated by the host through a localized inflammatory reaction that produces a transient oxidative burst through the release of reactive oxygen species (ROS) such as superoxide (O2-) or hydroxyl radical (●OH) from polymorphonucleocytes and macrophages. Because a necrotic tooth acts as a continual "injector of infection" to a central bone space, the continual production of ROS, matrix metalloproteinases (MMPs) plus the inhibition of tissue inhibitors of metalloproteinases (TIMPs) produce a dysregulation of normal bone homeostasis through their inhibition of both osteoclasts and osteoblasts (Hernandez-Rios, et al., 2017).

This type of lytic lesion can also degrade the myelin sheath of major and minor nerve bundles that wind their way through the jaws (Lin, L., & Langeland, K., 1981). A rat model with mechanically induced TN demonstrated symptoms of hyperalgesia, non-evoked nociceptive behavior, mechanical allodynia and cold hypersensivity due to increased oxidative stress of the first division of the TR N. These TN symptoms were reversed by reducing the oxidative stress (Treveisan et al., 2016).

The use of MOZO via major autohemotherapy has been shown in numerous clinical studies to be beneficial in the treatment of chronic diseases that have oxidative stress as a central etiological feature (Srivastava, K. K., Kumar, R., 2015; Martinez-Sanchez, G., et al., 2012; Bitkina, et al., 2010) Direct application of MOZO gas to treat ischemic biofilm infections is a well-established methodology (Schwartz, 2017). TN secondary to a dental infection possesses both these qualities. When a patient's blood is exposed to a hormetic dose of MOZO, direct oxidation byproducts of plasma and cellular membranes of red blood cells produces ozonides, aldehydes, peroxides and hydrogen peroxide (H2O2). These act as signaling messengers to induce upregulation of the cellular antioxidant systems such as Nrf2 (Laboda, 2016) that serve to counteract the oxidative stress component. It is reasonable to assume that the increased hydrogen peroxide may also serve to decrease the chronic dental infection component but has not been conclusively demonstrated in vivo. Achieving a direct effect on the biofilm produced by an infected tooth via a direct injection of MOZO into the bone is possible but, carries the risk of pain and possible damage to an already demyelinated nerve bundle. In this instance, the use of major autohemotherapy was chosen as a safer and less invasive alternative to direct injection of MOZO.

Conclusions

TN is a painful condition that can be a consequence of a necrotic tooth or failed endodontic therapy. The alveolar bone surrounding an endodontically treated tooth can become infected producing a localized inflammatory response of the periradicular tissues. A chronic infection of the bone will cause a dysregulation of the normal bone homeostasis, increased oxidative stress and localized enzymatic tissue degradation. Single or multiple lytic lesions within the bone can occur. If a lesion encroaches on a myelinated nerve bundle, such as the inferior alveolar nerve, demyelination can occur, and chronic pain can ensue.

The use of systemically administered MOZO via major autohemotherapy is a new approach for the treatment of chronic neuropathic pain secondary to a chronic dental infection. The rationale for its use stems from the ability of MOZO to decrease oxidative stress without the inherent risks associated with the direct injection of MOZO into a bone compartment. While a positive clinical outcome was achieved in this case, controlled clinical studies are needed to establish the viability of this treatment for patients with TN resulting from apical periodontitis or other chronic osseous infections of the jaws.

References

Bitkina, O. A., Kopytova, T.V., Kontorshchikova, K.N. & Bavrina, A.P. (2010). Oxidative stress level in patients with rosacea and rationale for the therapeutic use of an ozone-oxygen mixture. Klin Lab Diagn, 4, 13-16.

Bocci, V. (2011). Ozone. A new medical drug. (2nd ed.). New York: Springer.

Clavo, B., Santana-Rodriguez, N., Gutierrez, D., Lopez, J.C., Suarez, G., Lopez, L., et al. (2013) Long-term improvement in refractory headache following ozone therapy. J Altern Complement Med, 19(5), 453–458.

Cruccu G., (2017). Trigeminal Neuralgia. Continuum, 23(2), 396-420.

Escoda-Fancoli, J., Canalda-Sahli, C., Soler, A., Figueiredo, R., & Gay-Escoda, C. (2007). Inferior alveolar nerve damage because of overextended endodontic material? A problem of sealer cement biocompatibility?. J. Endod, 33 (12), 1484-1489.

Francica, F., Brickman, J., LoMonaco, C.J. & Lin L.M. (1988). Trigeminal neuralgia and endodontically treated teeth. J. Endod, 14 (7), 360-362.

Hernandez-Rios, P., Pussinen, P.J., Vernal, R. & Hernandez, M. (2017) Oxidative stress in the local and systemic events of apical periodontitis. Front. Physiol., 8, 1-8.

Iliakis, E., Valadakis, V., Vynios, D.H., Tisiganos, C.P., & Agapitos, E. (2001) Rationalization of the activity of medical ozone on intervertebral disc: a histological and biochemical study. Riv Neuroradiol, 14 (suppl 1), 23–30.

International Headache Society (2018). The International Classification of Headache Disorders, 3rd Edition. Cephalgia, 38(1), 1-211.

Kes, V. B. & Matovina, L. Z. (2017) Accommodation to diagnosis of trigeminal neuralgia. Acta Clin Croat, 56, 157-161

Srivastava, K. K., Kumar, R. (2015). Stress, oxidative injury and disease. Ind J Clin Biochem, 30(1), 3-10.

Kes, V. B. & Matovina, L. Z. (2017) Accommodation to diagnosis of trigeminal neuralgia. Acta Clin Croat, 56, 157-161.

Lin, L. & Langeland, K. (1981). Innervation of the inflammatory periapical lesions. Oral Surg. Oral Med. Oral Pathol., 51 (5), 535-543.

Loboda, A., Damulewicz, M. Pyza, E., Jozkowicz, A., & Dulak, J. (2016). Role of Nrf2/HO-1 system in development, oxidative stress response and diseases: an evolutionarily conserved mechanism. Cell. Mol. Life Sci., 73, 3221-3247.

Marinković, S., Gibo, H., Todorović, V., Antić, B., Kovačević, D., Milisavljević, M., et al. (2009). Ultrastructure and immunohistochemistry of the trigeminal peripheral myelinated axons in patients with neuralgia. Clin Neurology and Neurosurgery, 111, 795-800.

Martinez-Sanchez, G., Delegado-Roche, L., Diaz-Batista, A., Perez-Davison, G. & Re, L. (2012). Effects of ozone therapy on haemostatic and oxidative stress index in coronary artery disease. Eur J Pharmacol, 691 (1-3), 156-162.

Melek, L.N., Devine, M., & Renton, T. (2018). The psychosocial impact of orofacial pain in trigeminal neuralgia patients: a systematic review. Int.J. Oral Maxillofac. Surg., Accepted for publication 15 February 2018.

Obermann, M. (2010). Treatment options in trigeminal neuralgia. Ther Adv Neurol Disord, 3(2), 107-115.

Oomens, MAE-M. & Forouzanfar, T. (2015). Pharmaceutical management of trigeminal neuralgia in the elderly. Drugs Aging, 32, 717-726.

Pogrel, M.A., (2007). Damage to the inferior alveolar nerve as the result of root canal therapy. JADA, 138 (1), 65-69.

Re, L., Sanchez, G.M., & Mawsouf, N. (2011). Clinical evidence of ozone interaction with pain mediators. Saudi Med J, 32(12), 1363-1367.

Rothen, F., Dolfi, G., Mumenthaler, M., & Neuner, O. (1974). Dental aspects of facial pain, particularly trigeminal neuralgia. Z. Neurol, 208, 39-51.

Schwartz, A. & Martinez-Sanchez, G. (2012). The ozone therapy and its scientific foundations. Revista Española de Ozonoterapia, 2(1), 199-232.

Schwartz, A. (2017). Manual de ozonoterapia clínica. Spain: Medizeus.

Stoker, G. (1916). The surgical uses of ozone. The Lancet, 188, 712.

Tentolouris-Piperas, V., Lee, G., Reading, J., O'keeffe A.G., Zakrzewska J.M., & Cregg R., (2017). Adverse effect of anti-epileptics in trigeminal neuralgiform pain. Acta Neural Scan, 1-9.
Thomas K. L. & Vilensky, J. A. (2014). The anatomy of vascular compression in trigeminal neuralgia. Clinical Anatomy, 27, 89-93.

Trevisan, G., Benemei, S., Materazzi, S., De Logu, F., De Siena, G., Fusi, C., et al. (2016). TRPA1 mediates trigeminal neuropathic pain in mice downstream of monocytes/macrophages and oxidative stress. Brain, 139, 1361-1377.

Yadav, Y.R., Nishtha, Y., Sonjjay, P., Shailendra, R., Yatin, K. (2017) Trigeminal Neuralgia. Asian J Neurosurg, 12, 585-587.