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ORIGINAL ARTICLE

Evaluation of the Short-Term Efficacy of Transdermal Ozone Therapy in Turkish Patients with Internal Derangement of the Temporomandibular Joint

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Abstract

Objective: To investigate the efficacy of transdermal high-frequency ozone therapy in the management of pain and pain-related restricted jaw movements in patients with internal derangement of the temporomandibular joint (TMJ). **Material and Methods:** This retrospective study included 40 patients who had received transdermal high-frequency ozone therapy for the management of disc displacement with reduction of the TMJ. Subjects were treated 3 times for one week with a bio-oxidative high-frequency ozone generator with an intensity of 80% for ten minutes bilaterally. Pain scores and maximal interincisal opening (MIO) values of the patients were evaluated before and after the treatment. **Results:** An increase in the mean MIO value was achieved following the ozone therapy, however, the difference was not statistically significant (p=0.350). A statistically significant decrease in the mean pain score (48.13 ± 27.75) was observed following the ozone therapy. **Conclusion:** Transdermal application of high frequency ozone may be a good alternative for management of pain and pain-related restricted jaw movements in patients with internal derangement of the TMJ.

Keywords: Temporomandibular Joint Disorders; Facial Pain; Ozone; Administration, Cutaneous.

Introduction

Temporomandibular disorder (TMD) is defined as a collaboration of a number of signs and symptoms involving the temporomandibular joint (TMJ), muscles of mastication and related structures such as the synovium or ligaments [1]. The prevalence of TMD is about 12% and higher in women than men and in people between the ages of 20 and 40 years [2,3].

The etiology of TMD has been associated with various factors including occlusal abnormalities, parafunctional habits, orthodontic treatment, inflammatory conditions of the joint complex, trauma, poor systemic health and nutrition, and psychological problems [2,4]. Pain and decrease in the maximal interincisal opening (MIO) are the most frequent symptoms of TMD, while others include muscle or joint tenderness on palpation, limitation of mandibular movements, joint sounds and otologic complaints like tinnitus, vertigo or ear fullness [1,5,6] TMD is the second most common musculoskeletal disorder that causes pain and disability [7].

TMDs are basically classified into two categories: intra-articular disorders, which are pathological conditions within the joint and extra-articular disorders that involve the neighboring muscular, vascular and neurologic structures [5]. The intra-articular disorders include internal derangement (ID), congenital or developmental disorders, inflammatory and non-inflammatory degenerative joint disorders, infectious or neoplastic conditions of the joint, temporomandibular hyper- or hypomobility and trauma-related contusion, fracture or intracapsular haemorrhage [5,6,8].

Among these, internal derangement represents approximately 25% of the TMDs and is characterized by displacement of the intra-articular disc from its normal condyle-fossa relationship that hinder the function of the joint [9]. Internal derangements are described in five main stages with respect to clinical, radiological and anatomical findings (Table 1) [8]. Although pain may not be present in the early stage, as the condition progresses, pain and pain-related restricted jaw movements and dysfunction represent a significant part of the symptoms [8,10].

Table 1. Wilkes classification of internal derangement of TMJ.

Stage	Clinical	Radiological
I - Early Stage	Reciprocal clicking, no pain or limitation of motion	Slight forward displacement
II - Indermediate/Early Stage	Clicking, pain, joint tenderness, intermittent locking	Slight forward displacement, slight thickening of posterior edge
III - Indermediate Stage	Multiple episodes of pain, joint tenderness, limited mouth opening	Anterior displacement with significant anatomical deformity
IV - Indermediate/Late Stage	Chronic pain, limited opening	Severe displacement without reduction, degenerative osseous change
V - Late Stage	Variable joint pain, joint crepitus	Non-reduction of disk with perforation of disk attachment or disk degenerative osseous changes

The primary goal of treatment is to alleviate pain and/or mandibular dysfunction. Treatment modalities of internal derangement of TMJ include both non-surgical and surgical methods. In the initial stages, non-surgical methods such as modification of the diet, occlusal splints,

physical therapy or pharmacotherapy [6]. However the effectiveness of patient-reliant treatments is still questionable and depends significantly on the intensity of pain. Reduced levels of pain improve the patient compliance, which is also related to the efficacy of these treatments [11].

In cases with no response to conservative treatment invasive approaches may also be considered. Minimally invasive procedures include arthrocentesis for the management of internal derangements of the TMJ [6,12]. Surgical methods including arthroplasty, disc repositioning and reconstruction procedures, meniscectomy, eminectomy, lateral pterygoid myotomy, condylotomy or total TMJ reconstruction may also be performed [1,6,13]. In addition to above-mentioned methods, several newly emerging and non-surgical treatment options such as ultrasound, transcutaneous electrical nerve stimulation and low-level laser therapy (LLLT) have been proposed for the management of TMDs [6,14]. Recently, a small number of studies appeared in the literature, suggesting the ozone therapy as an alternative method for treatment of TMD [15-17].

Ozone is defined as a thermodynamically highly instable compound, which decomposes to pure oxygen with a short half-life. Ozone has several biologic effects including antimicrobial action, stimulation of oxygen metabolism, activation of the immune system, analgesic and anti-inflammatory effects and promotion of the hemostasis and microcirculation [18-20]. It was first used in medicine for the treatment of gangrenous wounds, suppurating bone fractures, inflammations and abscesses during the First World War [21]. Since then, ozone therapy has been extensively used for treatment of cancer, HIV, and rheumatoid arthritis, pain and scarring related to pressure ulcers, diabetic and leprosy-associated wounds and reducing muscle pain [22-24]. To date, various techniques have been developed for administration of ozone ranging from injection, inhalation, ingestion and more recently, to transdermal application, which possesses the advantages of being a non- invasive and well-tolerated method [15,17].

Given above-mentioned biologic effects of ozone and its promising outcomes in degenerative joint diseases, it is conceivable that ozone therapy may be a useful treatment option for patients with internal derangement of the TMJ. Nevertheless, there is only limited information in the current literature, which remains inadequate to draw conclusions. The specific purpose of this study is to investigate the efficacy of transdermal high-frequency ozone therapy in the management of pain and pain-related restricted jaw movements in patients with internal derangement of the TMJ.

Material and Methods

Study Design

This retrospective analysis evaluated data from medical records of patients who underwent ozone therapy with symptoms of TMDs at the Department of Oral and Maxillofacial Surgery, Faculty of Dentistry, Akdeniz University between January 2014 and December 2016.

Sample

Patients eligible for study inclusion had pain in the TMJ during mandibular movements and function, had Wilkes Stage II or III ID based on clinical and magnetic resonance imaging (MRI)

findings (Figure 1) and Diagnostic Criteria for Temporomandibular Disorders (DC/TMD) [3], and had received solely ozone therapy or had not receive any other conservative treatment (anti-inflammatory drugs etc.) at least 3 weeks prior to the ozone therapy.

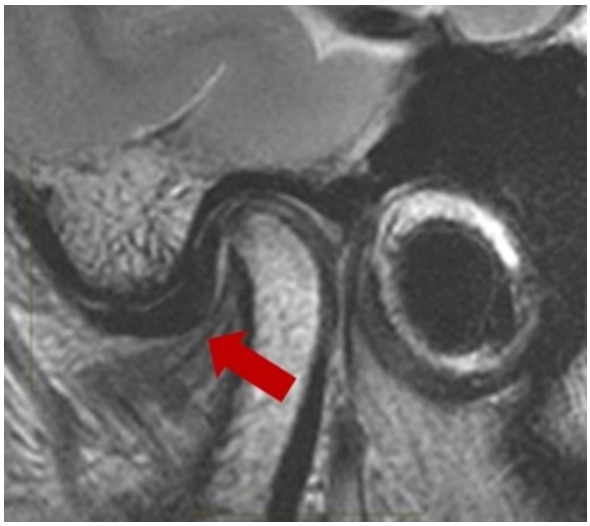

Figure 1. MRI section of one of the patients. Red arrow shows anterior displacement of the disc.

Patients were not enrolled to the study, if they had an uncontrolled systemic disease, missing medical records or a history of psychiatric therapy. Subjects with coexisting/history of degenerative joint diseases, history of trauma to the TMJ, head/neck radiation therapy, para-functional habits, malocclusion, dental caries, periapical or periodontal problems, and pain of muscular origin were also excluded from the study.

The data comprising demographics, pain characteristics and clinical examination notes were obtained for the remaining 40 patients. Pain level assessment was made subjectively, by asking the patient to rate the level of pain on a scale of 0 (no pain) to 100 (the worst possible pain) at initial presentation (t0), prior to the second session (t1) and during recall (tr), which was scheduled three days after the final session. Maximal interincisal opening (MIO) was also recorded at aforementioned intervals, in millimeters from the incisal edges of maxillary and mandibular central incisors. Additional clinical notes on the articular examination, which was performed by means of bilateral intra-auricular and pre-auricular palpations of the TMJ and pathological sounds of the TMJ, such as clicks or crepitation, were also recorded.

Ozone Therapy Protocol

Transdermal ozone therapy was performed via a bio-oxidative ozone generator (OzoneDTA; APOZA, Taiwan, Republic of China) using a high-frequency 7.5 cm deep tissue probe which was specifically designed for use over the skin. Ozone intensity of 80% was used. All patients received ten-minute long ozone application bilaterally on each TMJ while the probe was moved over and around the TMJ at the preauricular region away from the tissue enough to avoid contact. The patients were asked to open and close their mouths several times over the course of application.

Ozone therapy was applied three times for a week initially and the patients were recalled three days after the final application. Any medication (anti-inflammatory medicine or muscle relaxants) was not prescribed to the patients following the ozone application.

Statistical Analysis

Statistical analysis was performed using IBM SPSS Statistics version 22.0 (IBM Corp, Armonk, NY, USA). P values <0.05 were considered significant. Previously recorded data were analyzed using analysis of variables (ANOVA), McNemar's and Kruskal-Wallis tests. Analyses were proceeded with post-Hoc tests where applicable.

Ethical Aspects

The Declaration of Helsinki on medical protocol and ethics was followed and Clinical Researches Ethics Committee of the Akdeniz University approved the study (Approval number: 29/11.01.2017). All patients, who received ozone therapy, read and signed an informed consent before their treatment.

Results

During the study period, among 83 patients who underwent ozone application with various TMD diagnoses, 52 patients met the inclusion criteria. Of these, 12 patients were also excluded due to missing relevant information on clinical records. Forty patients (28 females and 12 males) with a mean age of 36.4 years (ranging from 17 to 74) were included in the study. Of these, 17 were classified as having Wilkes Stage II ID (intermediate/early) and 23 patients were classified as having Wilkes Stage III ID (intermediate).

Seventeen patients expressed more pain during function while 13 patients reported to have constant pain and the remaining ten patients experienced pain on non-specific occasions. In addition to joint pain, one patient mentioned accompanying pain in the ear, while two patients reported a headache, and seven patients reported to have both an ear and a headache. The duration of pain varied between two months and three years.

Twenty-three patients (sixteen unilateral and seven bilateral) reported to have joint sounds while 17 patients did not mention any joint sound. Following the treatment, three patients previously reported to have joint sounds stated that they no longer experienced joint sounds, however, this difference was not found to be statistically significant (p=0.250).

The mean pre-treatment MIO value was 38.35 ± 6.69 mm. An improvement in MIO was achieved both at t1 (40.73 ± 4.34 mm) and tr (39.65 ± 5.21 mm), however, these differences were failed to be statistically significant (p=0.350) (Table 2).

The mean pain score before treatment was found to be 71.00 ± 20.60, which decreased to 61.25 ± 24.90 at t1. The difference was not found to be statistically significant (p=0.202). The mean pain score at tr however, was found to be 48.13 ± 27.75 representing a statistically significant

difference between the initial and the final assessments (p= 0.000) (Table 3). Further analyses showed statistically higher scores in male patients at t0 and tr (p=0.001 and p=0.007, respectively).

Table 2. The difference between Maximal Interincisal Opening (MIO) values among sessions.

Session	N	Mean (mm)	SD (±mm)	p-value
t_0	40	38.35	6.69	0.35*
t_1	40	40.73	4.34	
t_r	40	39.65	5.21	

t_0: Initial Presentation; t_1: Prior to the Second Session; t_r: Recall; MIO: Maximum Interincisal Opening; SD: Standard Deviation. Kruskal-Wallis Test reveals the same distribution of MMO across categories of session (t_0, t_1, t_r). *The significance level is .05.

Table 3. The difference between pain scores among sessions.

Session	Test Statistic	Std. Error	Std. Test Statistic	Adj. Sig.
t_0-t_1	14.138	7.724	1.83	0.202
t_1-t_r	16.388	7.724	2.122	0.102
t_0-t_r	30.525	7.724	3.952	0.000*

Adj. Sig.: Adjusted Significance; t_0: İnitial Presentation; t_1: Prior to the Second Session; t_r: Recall. Each row tests the null hypothesis that the Sample 1 and Sample 2 distributions are the same. *The significance level is .05.

Discussion

Temporomandibular joint disorders are a group of conditions, which commonly present with joint pain, clicking or locking and cause disturbances of oral functions such as chewing, swallowing and speech [1,2]. Despite being common conditions, which have been previously reported to affect 5–12% of the population, the true etiology of TMDs remains a subject of debate, and is often reported to be associated with multiple factors such as malocclusion, trauma, emotional stress or parafunctional habits [7].

Unless there is an absolute indication for surgical treatment, TMDs are commonly treated in a conservative fashion. Analgesics, non-steroid anti-inflammatory drugs, corticosteroids, muscle relaxants, anti-depressants or combinations of these drugs may be prescribed as part of the pharmacological regimen, while physical treatment modalities with transcutaneous electrical stimulation, hot or cold applications, massage, ultrasound, laser, microwave or acupuncture may also offer some benefit [25,26]. Occlusal splints are generally recommended for patients with disc-condyle derangements or bruxism for whom trigger point injections or botulinum toxin applications may also provide symptomatic relief [27,28]. Minimally invasive procedures such as arthroscopy and arthrocentesis have been reported to be efficacious in the management of capsulitis or other capsular inflammatory conditions, degenerative arthritis or disc displacement without reduction [29].

Ozone was discovered in 1834 by the German chemist Christian Frederick Schönbein [30]. Although it was first used in medicine in 1870 by Landler, it was not until the 1930s, that ozone was widely used in medicine [18,30]. Direct exposure of the human blood to oxygen-ozone mixture was not considered until 1970s, when Wolff developed the first medically-purposed ozone generator and defined ozonated auto-hemotherapy [18]. In our day, ozone is widely used in medicine owing to its

additive effects on tissue-healing by increased oxygenation. In the field of dentistry, the use of ozone has also expanded rapidly because of its immunostimulating, analgesic, anti-hypoxic, detoxicating and anti-microbial properties [22]. Moreover, ozone is reported to have bioenergetic and biosynthetic properties that activate carbohydrate, protein and lipid metabolisms [19].

Utilization of ozone in the management of TMDs is a relatively new approach, of which the efficacy remains to be validated. Previously, it was compared to intra-articular ozone gas injection and drug therapy for treatment of internal derangement of the TMJ and concluded that the patients who were treated with ozone gas injections had a better clinical outcome than those who received nonsteroidal antiinflammatory drugs and muscle relaxants [16]. However, it should be noted that intra-articular administration of a substance is an invasive procedure, which carries associated risks of intraoperative and postoperative complications. The proposed method in our study is a non-invasive and complication-free procedure in which the ozone is administered to the region transdermally.

In another study, it was compared to compared outcomes of ozone therapy and medical treatment in the management of TMDs and reported significantly lower pain scores after ozone therapy, although both approaches have resulted in increased mouth opening and decreased pain scores postoperatively [17]. Similarly, some authors investigated the efficacy of bio-oxidative ozone application in the treatment of TMD of muscular origin and they reported that bio-oxidative ozone therapy showed positive effects in managing pain caused by TMD and improving mandibular function [15].

In the present study, an improvement in MIO scores was observed following the ozone application, however, the difference failed to reach statistically significant values. However, postoperative pain scores were found to be significantly lower, which is in line with previous studies [15,17]. Although ozone treatment was not found to be effective after the first application, significantly lower scores were achieved following final applications.

Initially, MIO scores were measured to be within the physiological range for all patients; therefore it was not expected to achieve significant differences in MIO after ozone therapy. New studies on ozone therapy with patients suffering from temporomandibular hypo- or hypermobility may be more beneficial to determine the true effect of ozone on MIO. Whereas the mechanism of action of bio-oxidative high-frequency ozone, through the decrease in the inflammatory processes at the application site, was considered to be the main reason for the significant reduction in pain scores.

Physiotherapeutical exercises are known to provide beneficial results in the management of TMDs as well as joint pain. These exercises are used either alone as the first line of treatment or following other pain-relieving treatment modalities [31]. However results from the physiotherapeutical exercises change depending on the level of pain. Tuncer et al. reported that patients with decreased pain levels tend to have an increased range of motion, signifying better and more effective outcomes with TMJ exercises due to better patient compliance [11,32-34].

Ozone generator functions through a glass probe that contains a mixture of noble gases that conducts and emits electromagnetic energy. The probe emits energy that splits diatomic oxygen in singular atomic oxygen and ozone. When the probe comes in contact over the skin of the TMJ, the same energy allows oxygen molecules and ozone to penetrate deep within the tissues [18]. When ozone contacts biological fluids, it promotes endothelial cells to normalize cellular redox and helps change the levels of inflammatory cytokine [35]. Ozone is documented to increase Transforming Growth Factor (TGF)-ß levels and promote tissue remodeling, while reducing Tumor Necrosis Factor (TNF)-α concentrations, a well-known pro-inflammatory cytokine, that perpetuates chronic inflammatory processes [20,24]. It also promotes the synthesis of biologically active substances (i.e. interleukins, leukotrienes and prostaglandins), which also help reduce the inflammatory processes [19]. When the inflammation is reduced, the pain often subsides along with other signs [36].

Repeated ozone applications activate certain enzymes, namely superoxide dismutases, catalases, dehydrogenases and glutatione peroxidases, which protect against the action of oxygen-free radicals. Inflamed tissues have been shown to normalize with ozone therapy, which enhances metabolism, increases oxygenation and reduces local inflammatory processes [37]. It was suggested that the effects of ozone are cumulative, which may be the reason why in this study, pain levels did not decrease after the first application significantly, but instead improved after the second session [21].

Besides this bioregulatory and pain-reducing effect of ozone, it also has an anti-hypoxic effect that increases pO2 in tissues and improves transportation of oxygen in blood. Local circulation is also improved as ozone promotes nitric oxide secretion, a well-documented vasodilator [19,38] Vasodilatation allows tissues to have a greater blood flow, which provides nutrients and improved immunological properties. Being oxygen – rich purifies the blood and prevents cellular wastes to build up [21].

Conclusion

Although there were no statistically significant improvements regarding maximum interincisal mouth opening, the decrease in pain levels after this treatment protocol might allow patients to apply unerring and more effective physiotherapeutical exercises. With the application of ozone treatment, lower pain levels may be achieved without the use of any medication such as non-steroidal anti-inflammatory drugs and their side effects; therefore provide improved results with TMJ exercises. In the light of this fact, transdermal application of high frequency ozone therapy may be a good alternative for the management of pain in patients with internal derangement of the TMJ. Further prospective, long-term, randomized clinical trials are required to validate outcomes of this study and secure the value of ozone therapy in the management of TMDs.

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Conflict of Interest: The authors declare no conflicts of interest.

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