

## Effectiveness of Ozone Injection Therapy in Temporomandibular Disorders

### Abstract

Temporomandibular disorder is a multifactorial disease that causes pain in the jaw and face area with nondental origin, which frequently limits talking, chewing, and other jaw activities. Various factors such as malocclusion, trauma, stress, parafunctional habits (clenching and bruxing), osteoarthritis, and synovitis play a role in its occurrence, although the etiology of these disorders is little understood. Several treatments are being used to treat these disorders. Ozone therapy has been recently introduced as one of these treatments. Considering that no extensive study has been found in this field so far, this study is aiming to report the studies that have been conducted to determine the efficacy of ozone injection therapy in temporomandibular joint disorders. This report addresses the studies which are conducted clinically, experimentally, and semi-experimentally over the past 10 years (2009–2019). The prepared articles are screened according to the inclusion criteria. In this study, total six related articles are addressed. One study was pre- and postintervention, and five studies were clinical trials. Studies show that although more studies are needed in contrast with occlusal splint, ozone therapy is generally more effective treatment for pain reduction compared to medication.

**Keywords:** *Ozone therapy, jaw, temporomandibular joint disorders*

### Introduction

The temporomandibular joint is a bilateral synovial joint formed by the mandibular condyle and mandibular cavity of the temporal bone, and the articular disc allows joint movements between them.<sup>[1]</sup> It is the most active joint in the body and needs to be opened and closed approximately 2000 times a day during chewing, speaking, breathing, swallowing, and yawning.<sup>[2]</sup>

In this joint, the articular surfaces are not composed of hyaline cartilage unlike most synovial joints of the body that are covered by the fibrous tissue. This joint is the only joint system that has a definite and hard closing end point that is the calcification occlusal surfaces of the teeth.<sup>[3]</sup> Since the right and left condyles are parts of a movable mandibular, the temporomandibular joint on the one side cannot have a function without the movement of the joint on the other side.<sup>[4]</sup>

Temporomandibular disorder (TMD) is a multifactorial disease that causes pain in the jaw and face area with nondental origin.

These disorders include muscle disorders, disc and condyle disorders, and inflammatory joint disorders. Any factor that can change the normal function of the masticatory muscles or their sensory input, joint fluid, ligaments, disc and condyle tissues, and disrupt the normal balance of the participating tissues in the temporomandibular joint, is considered as an etiological factor of joint disorders.<sup>[5]</sup>

Etiological factors in occurring this disorder include acquired factors such as infection, injury, iatrogenic (surgery, radiotherapy, habits, tumors, and finally, idiopathic), hereditary factors such as hemifacial microsomia, hemifacial atrophy, rheumatoid arthritis in young people and onycholysis, and other factors such as muscle spasms, inappropriate occlusal contact, stress, systemic diseases, and immunological factors.<sup>[6]</sup>

Tissue changes and psychological factors are the main predisposing factors in occurring TMDs. It is often associated with degenerative changes in its skeletal structures, such as flattening, erosion, osteophytes, subchondral sclerosis, and false cysts.<sup>[7]</sup>

**Sheila Haghghat,  
Samira Oshaghi**

*Department of Physical  
Medicine and Rehabilitation,  
Faculty of Medicine, Isfahan  
University of Medical Sciences,  
Isfahan, Iran*

**Address for correspondence:**  
*Dr. Samira Oshaghi,  
Department of Physical  
Medicine and Rehabilitation,  
Faculty of Medicine, Isfahan  
University of Medical Sciences,  
Isfahan, Iran.  
E-mail: [dr.samiraoshaghi@gmail.com](mailto:dr.samiraoshaghi@gmail.com)*

**Received:** 11 May 2020  
**Revised:** 31 May 2020  
**Accepted:** 28 June 2020  
**Published:** 28 November 2020

#### Access this article online

**Website:** [www.advbiores.net](http://www.advbiores.net)

**DOI:** 10.4103/abr.abr\_105\_20

#### Quick Response Code:



**How to cite this article:** Haghghat S, Oshaghi S. Effectiveness of ozone injection therapy in temporomandibular disorders. *Adv Biomed Res* 2020;9:73.

This is an open access journal, and articles are distributed under the terms of the Creative Commons Attribution-NonCommercial-ShareAlike 4.0 License, which allows others to remix, tweak, and build upon the work non-commercially, as long as appropriate credit is given and the new creations are licensed under the identical terms.

**For reprints contact:** [WKHLRPMedknow\\_reprints@wolterskluwer.com](mailto:WKHLRPMedknow_reprints@wolterskluwer.com)

These bone changes may be without symptom in the early stages but in the later advanced stages may be followed by clinical signs and symptoms such as pain and dysfunction.<sup>[8]</sup> Radiographic examining is part of the routine clinical evaluations of TMDs, and its main purpose is to confirm bone degenerative changes in joint components and to diagnose the disc displacement.<sup>[9]</sup>

The literature of the subject is rather rich. Some of the reports have addressed the epidemiology of the disorder.<sup>[10,11]</sup> Some others have indicated the symptoms that have to be observed in the diagnosis of the disorder.<sup>[12-14]</sup>

Today, various morphological parameters of TMDs can be more fully and accurately measured by the development of new techniques such as computer tomography and cone-beam computer tomography. The possibility of more complete analysis has been provided by the invention of three-dimensional technologies, especially cone-beam computer tomography.<sup>[15]</sup>

There are different ways to manage temporomandibular dysfunction. The mainstay of the therapy is the combination of the drug treatment with tricyclic antidepressant, physical modalities such as oral orthotic devices, physical therapy, and intra-articular injection of the joint with small amounts of local anesthetic and steroid.

After several years of research and development about a very innovative treatment method called ozone therapy, the medical community has recently concluded that it has many capabilities that can treat a variety of joint and bone problems.<sup>[16]</sup>

Ozone is a colorless gas that each of its molecules is made up of three oxygen atoms. These atoms are connected in a completely unstable way. This substance will have an oxidizing effect on organic compounds due to the positive charge in ozone. This ability is beneficial to neutralize foreign cells that have a negative charge such as bacteria, yeasts, viruses, and parasites, and it removes the active infections.<sup>[17]</sup>

The ozone which is used in medical science is made from pure oxygen with ozone generator, and it is prescribed in the precise treatment doses. The effect of ozone therapy on the body over the past few years has been proven by various scientific studies, which is highly compatible with the body, and it has the least side effects.<sup>[17]</sup>

In ozone therapy, ozone is converted into normal oxygen (O<sub>2</sub>) within 8 minutes after entering the body. During this conversion, some energy and gamma-rays are produced which accelerate the healing process of the damaged cells.

The authors couldn't find any coherent review in the literature about the effectiveness of ozone therapy in the treatment of TMDs. Considering that this disorder is observed in a relatively high percentage in all ages and according to the increasing trend and promising results

of using this treatment method, this study is conducted to determine the treatment effectiveness of ozone injection therapy in TMDs in the form of reviewing articles to provide an accurate report of this treatment method, its application, and effectiveness.

## Materials and Methods

Literature review was conducted in the Cochrane Library, MEDLINE, and EMBASE databases on the articles published over the past 10 years (2010–2019). The search method was based on the following keywords: ozone therapy, TMD, and musculoskeletal disorder. Abstracts of articles were extracted using the selected keywords. After deleting completely irrelevant articles, and some irrelevant articles were excluded again, the full text of other related articles was prepared. Then, the text of all the articles was examined and investigated according to the predetermined inclusion criteria. Inclusion criteria were as follows: the relevance, English language, comprehensive description of the figures and tables, validity and reliability of the used method, place of research, adequacy of the sample size, appropriate comparing of the findings with other studies, and availability of the suggestions for future study. Exclusion criterion was the inappropriate design of the survey method.

## Results

Six articles have investigated the ozone therapy of TMD out of the whole descriptive and intervention published articles about ozone therapy and TMDs over 10 years (2010–2019). One study was pre- and postintervention, and five studies were clinical trials.

Doğan *et al.*<sup>[18]</sup> studied 63 patients with TMDs in a clinical trial study. Thirty-three patients were treated with oxidative ozone and 30 patients were treated with thioglycoside capsules of ketoprofen tablets for 7 days. Patients assessed their pain using a Visual Analog Scale. The average opening of the mouth in the group under treatment with ozone in the preexperimental period was  $46.51 \pm 8.2$  mm, and after 1 week of the ozone therapy, this value immediately increased into  $48.78 \pm 7.5$  mm which was statistically significant ( $P = 0.04$ ). For those who received the drug, the average was 46.30 mm before treatment and 46.9 mm at the end of 1 week. Overall, the results of the treatment were promising.<sup>[18]</sup>

In a clinical trial study, Celakil *et al.*<sup>[19]</sup> in 2019 examined 40 patients who were randomly categorized into two groups of 20 patients (the group of ozone therapy) and 20 patients (the group of occlusal splint). The first group was treated with ozone three times a week for totally 6 sessions. Patients with occlusal splint were asked to use obstruction splints every night for a period of 4 weeks. The results showed that occlusal splint treatment was still

a gold treatment method for pain relief in patients with TMDs.<sup>[19]</sup>

Özalp *et al.*<sup>[20]</sup> in 2019 in an intervention study treated 40 patients with TMD with ozone therapy with high frequency of ozone. Patients were treated bilaterally three times a week with an ozone generator with high frequency of ozone with intensity of 80% for 10 min. The pain scores and maximal values of intermediate opening were assessed before and after the intervention. The increase of average intermediate opening was achieved after ozone therapy, although the difference was not statistically significant. However, the average pain score decrease in the patients treated with ozone therapy was statistically significant.<sup>[20]</sup>

In a clinical trial study, Reyes and Alghannam<sup>[21]</sup> in 2016 treated 57 patients with ozone. The volume of 3 ml, equivalent to 0.03 mg in a two-way section, was used ten times. The pain decreased before the fourth use of ozone (100%). Limitation of opening of the mouth was observed in (100%) less than the deviation and deviation of the mandible.<sup>[21]</sup>

In a clinical trial study, Dai<sup>f[22]</sup> in 2012 studied 60 patients (49 women and 11 men) with TMD. They were randomly divided into two equal groups. The first group was treated with direct injection of ozone gas into the joint space. Each joint received 2 ml of a mixture of ozone and oxygen (the concentration of ozone gas was 10µg/ml). Injections were repeated two times a week for 3 weeks. The second group received nonsteroidal anti-inflammatory drugs and muscle relaxants. Clinical signs and symptoms before and after treatment were assessed based on the clinical dysfunction index. The results showed that 87% of patients who received injection of ozone gas into the superior joint space (26 patients) were completely recovered.<sup>[22]</sup>

In another clinical study, Hammuda *et al.*<sup>[23]</sup> employed ozone in temporomandibular joint arthrocentesis. In their study, 30 patients were divided into two groups. The first group subjected to arthrocentesis using saline solution, while in the second group, arthrocentesis was carried out using ozonized water. They concluded that although a significant decrease in the pain level was observed in both the groups, a significant decrease in the second group was reported at postoperative, after the 1<sup>st</sup> month and 1 year. Furthermore, maximal mouth opening for all patients in both the groups was improved, and the significant increase was reported in Group II after the 1<sup>st</sup> month, 6 months, and 1 year postoperatively.<sup>[23]</sup>

A summary of the results obtained in the six presented studies is shown in Table 1.

## Discussion

TMD is used to express all disorders related to the function of the masticatory system, and its etiology is multifactorial. Treatments such as cognitive behavioral therapy,

physiotherapy (stimulation of the electrical nerve through the skin), and medication are considered to manage the first line of the disorder. Splint treatment is effective except the treatment methods that reduce pain and improve the range of motion of the mandible.<sup>[24,25]</sup>

One of the new treatments introduced is ozone therapy, about which no extensive study has been conducted so far. The use of ozone gas as a treatment method caused doubts due to its unstable molecular structure. However, extensive research has shown that ozone dynamic resonance structures have made some physiological interactions, which is beneficial in treatment.<sup>[26]</sup>

The dosage of the ozone in the presented articles is outlined in Table 2.

As it is observed in Table 2, different researchers have treated TMD with different dosages of the ozone. Since the method is new, there is no standard protocol for the dosage of ozone. In general, it can be concluded that ozone therapy with even low dosages of ozone can effectively reduce the pain in TMD patients.

In six studies, one study was pre- and postintervention and five studies were clinical trials.

An intervention study to measure the pain in patients before and after ozone therapy showed that after ozone therapy, not only the patients' pain decreases, but also the jaw range of movements in the patients increased.

Among the four clinical trials, two studies explicitly stated that the group under the ozone therapy was associated with a more pain reduction compared to the group under drug treatment. One study evaluated the results of ozone therapy positively but concluded that its extensive use depended on further studies. Another study compared ozone therapy and occlusal splint and found that both methods reduced pain in patients, but there was no significant difference between the two groups and ultimately evaluated that the occlusal splint treatment is more effective.

The results of some other studies have shown that ozone improves the joint faster than the traditional treatment. It could be due to the fact that ozone is a highly reactive molecule, and as a result, it has the ability to repair as well as reduce inflammation. It also produces cartilage while being injected into the joint capsule.<sup>[27-29]</sup>

## Conclusion

Overall results show that ozone therapy is an effective way to treat pain caused by TMD, and it is safe and effective than drug therapy. However, more extensive studies are necessary on different communities at different ages.

## Financial support and sponsorship

Nil.

**Table 1: Ozone injection therapy in temporomandibular disorders**

Final findings	Sample size	Study method	Title	Year	Author
Injecting intra-articular ozone gas is a promising treatment method for managing the internal contraction of the temporomandibular joint. However, more clinical and experimental studies are needed to provide direct evidence for mechanism of its performance and to prove the results	60 patients	Clinical trials	Role of intra-articular ozone gas injection in the management of internal derangement of the temporomandibular joint	2012	Daif <sup>[22]</sup>
29% of patients in the ozone therapy group and 24% of patients in the drug group experienced a gradual decrease in pain which the difference between the two groups was significant	63 patients	Clinical trials	Effects of high-frequency bio-oxidative ozone therapy in temporomandibular disorder-related pain	2014	Doğan <i>et al.</i> <sup>[18]</sup>
Patients of the ozone therapy group showed a significant decrease in the pain score compared to the control group	57 patients	Clinical trials	Ozone therapy as an alternative treatment to the pain in the temporomandibular disorder	2016	Reyes and Alghannam <sup>[21]</sup>
Clinical efficacy of arthrocentesis with ozone in the temporomandibular joint internal derangements. Efficacy of ozonized water as a clinically applicable form of ozone in ozone therapy for the temporomandibular joint	30 patients	Clinical trial	Use of Ozone in Temporomandibular Joint Arthrocentesis, Clinical Study	2013	Hammuda <i>et al.</i> <sup>[23]</sup>
Movements of mandible had a significant difference for the time factor in both ozone therapy and occlusal splint groups. Muscle pain and pressure threshold was significantly higher in the occlusal splint group. Both treatments statistically reduced Visual Analog Scale scores. However, statistically, there was no significant difference between the groups	40 patients	Clinical trials	Management of pain in TMD patients: Bio-oxidative ozone therapy versus occlusal splints	2019	Celakil <i>et al.</i> <sup>[19]</sup>
The use of high-frequency ozone therapy can be a good alternative for managing pain and jaw movements in patients with temporomandibular disorder	40 patients	Interventional	Evaluation of the Short-Term Efficacy of Transdermal Ozone Therapy in Turkish Patients with Internal Derangement of the Temporomandibular Joint	2019	Özalp <i>et al.</i> <sup>[20]</sup>

**Table 2: The dosage of the ozone for ozone therapy of the temporomandibular joint in different studies**

n	Dosage	Treatment period	Explanation
18	30% concentration	3 times per week for 10 min	
19	10-100 µg/ml, 60% ozone intensity	3 treatment sessions per week for 10 min, for 2 weeks; total 6 sessions	
20	80% ozone intensity	10 min bilaterally, three times for a week	
21	10 sections 3 mg/L for a volume of 3 ml equivalent to 0.03 mg in one bilateral section	10 sessions	Totally 3 mg
22	2 mL ozone-oxygen mixture (ozone gas concentration 10 µg/mL)	2 times per week for 3 weeks	Totally 120 µg
23	70 µg /ml	200 ml totally	Totally 14 mg

**Conflicts of interest**

There are no conflicts of interest.

**References**

- Singh V, Sudhakar KNV, Mallela KK, Mohanty R. A review of temporomandibular joint-related papers published between 2014 and 2015. *J Korean Assoc Oral Maxillofac Surg* 2017;43:368-72.
- Murphy MK, MacBarb RF, Wong ME, Athanasiou KA. Temporomandibular disorders: A review of etiology, clinical management, and tissue engineering strategies. *Int J Oral Maxillofac Implants* 2013;28:e393-414.
- Dellavia C, Rodella LF, Pellecchia R, Barzani G. Detailed anatomy of the temporomandibular joint. In: *Contemp Manage of Temporomandibular Disord*. Switzerland: Springer; 2019. p. 51-70.
- Tuijt M, Koolstra JH, Lobbezoo F, Naeije M. Differences in loading of the temporomandibular joint during opening and closing of the jaw. *J Biomech* 2010;43:1048-54.
- Alzarea BK. Temporomandibular disorders (TMD) in edentulous patients: A review and proposed classification (Dr. Bader's

- Classification). *J Clin Diagn Res* 2015;9:ZE06-9.
- Verma SK, Maheshwari S, Chaudhari PK. Etiological factors of temporomandibular joint disorders. *Natl J Maxillofac Surg* 2012;3:238-9.
  - Chisnoiu AM, Picos AM, Popa S, Chisnoiu PD, Lascu L, Picos A, *et al.* Factors involved in the etiology of temporomandibular disorders – A literature review. *Clujul Med* 2015;88:473-8.
  - Ferreira CL, Silva MA, Felício CM. Signs and symptoms of temporomandibular disorders in women and men. *Codas* 2016;28:17-21.
  - dos Anjos Pontual ML, Freire JS, Barbosa JM, Frazão MA, dos Anjos Pontual A. Evaluation of bone changes in the temporomandibular joint using cone beam CT. *Dentomaxillofac Radiol* 2012;41:24-9.
  - Tecco S, Crincoli V, Di Bisceglie B, Saccucci M, Macrí M, Polimeni A, *et al.* Signs and symptoms of temporomandibular joint disorders in Caucasian children and adolescents. *Cranio* 2011;29:71-9.
  - Sahebi M, Amlashi PB. Prevalence of temporomandibular disorders and its association with malocclusion in mixed dentition among patients referred to Tehran dental school. *JDM* 2010;23:153-60.
  - Rokaya D, Suttagul K, Joshi S, Bhattarai BP, Shah PK, Dixit S. An epidemiological study on the prevalence of temporomandibular disorder and associated history and problems in Nepalese subjects. *J Dent Anesth Pain Med* 2018;18:27-33.
  - Liu F, Steinkeler A. Epidemiology, diagnosis, and treatment of temporomandibular disorders. *Dent Clin North Am* 2013;57:465-79.
  - Kostrzewa-Janicka J, Mierzwinska-Nastalska E, Jurkowski P, Okonski P, Nedzi-Gora M. Assessment of temporomandibular joint disease. In: Pokorski M, editor. *Neurobiology of Respiration*. Vol. 788. Germany: Advances in Experimental Medicine and Biology; 2013. p. 207-11.
  - Larheim TA, Abrahamsson AK, Kristensen M, Arvidsson LZ. Temporomandibular joint diagnostics using CBCT. *Dentomaxillofac Radiol* 2015;44:20140235.
  - Wright EF, North SL. Management and treatment of temporomandibular disorders: a clinical perspective. *J Man Manip Ther* 2009;17:247-54.
  - Rowen RJ. Ozone therapy as a primary and sole treatment for acute bacterial infection: case report. *Med Gas Res* 2018;8:121-4.
  - Doğan M, Ozdemir Doğan D, Düğer C, Ozdemir Kol I, Akpınar A, Mutaf B, *et al.* Effects of high-frequency bio-oxidative ozone therapy in temporomandibular disorder-related pain. *Med Princ Pract* 2014;23:507-10.
  - Celakil T, Muric A, Gökçen Roehlig B, Evlioglu G. Management of pain in TMD patients: Bio-oxidative ozone therapy versus occlusal splints. *Cranio* 2019;37:85-93.
  - Özalp Ö, Yıldırım N, Sindel A, Ali AM, Şükrü KR. Evaluation of the short-term efficacy of transdermal ozone therapy in Turkish patients with internal derangement of the temporomandibular joint. *Pesqui Bras Odontopediatria Clín Integr* 2019;19:4442.
  - Reyes JM, Alghannam DJ. Ozone therapy as an alternative treatment to the pain in the temporomandibular disorder. *Int Conf Pain Res Manag* 2016;5 Suppl 5:61.
  - Daif ET. Role of intra-articular ozone gas injection in the management of internal derangement of the temporomandibular joint. *Oral Surg Oral Med Oral Pathol Oral Radiol* 2012;113:e10-4.
  - Hammuda A, Hamed MS, El-Sharawy EA, Elsholkamy MA, Iskandar A. Use of ozone in temporomandibular joint arthrocentesis, clinical study. *J Am Sci* 2013;9:508-13.
  - Kumar SR. Temporomandibular joint disorders. *Natl J Maxillofac Surg* 2016;7:1-2.
  - Srivastava R, Jyoti B, Devi P. Oral splint for temporomandibular joint disorders with revolutionary fluid system. *Dent Res J (Isfahan)* 2013;10:307-13.
  - Elvis AM, Ekta JS. Ozone therapy: A clinical review. *J Nat Sci Biol Med* 2011;2:66-70.
  - Wang X, Wang G, Liu C, Cai D. Effectiveness of intra-articular ozone injections on outcomes of post-arthroscopic surgery for knee osteoarthritis. *Exp Ther Med* 2018;15:5323-9.
  - Sagai M, Bocci V. Mechanisms of Action Involved in Ozone Therapy: Is healing induced via a mild oxidative stress? *Med Gas Res* 2011;1:29.
  - Saini R. Ozone therapy in dentistry: A strategic review. *J Nat Sci Biol Med* 2011;2:151-3.