

Efficacy of Photo biomodulation Therapy Compared with Hyaluronic Acid Injections in Temporomandibular Disorder Treatment: A Systematic Review

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ABSTRACT

BACKGROUND

Temporomandibular Disorder (TMD) has been postulated as a condition of multifactorial aetiology, usually resulting from muscle hyperfunction or parafunction, traumatic sources, hormonal impact, and alterations in the structure of the joint. Treatment modalities for management are numerous and include the invasive and non-invasive modalities. Photo biomodulation therapy is a non-pharmacologic and non-invasive treatment which has been found to have positive impacts in the treatment while intra articular injections with or without arthrocentesis is a minimally invasive procedure but is very potent in alleviating pain and inflammatory signs.

METHODS

The current review was carried out in the context of PRISMA guidelines. A systematic search in PubMed, Google Scholar, Wiley library, Cochrane library databases, Scopus and grey literature was done for the published studies between 1st January 2003 and 1st October 2023. For randomized controlled trials, quality assessment was done with the help of Cochrane risk of bias tool (ROB-2) using Review Manager 5.4.1

RESULTS

Through search strategy 76 articles were yielded. After screening through titles and abstracts, 55 articles were excluded and finally 21 articles were included in this review.

CONCLUSION

In conclusion Photo biomodulation is found to be effective in reducing pain, mean mouth opening in the treatment of temporomandibular disorder when compared to hyaluronic acid, however this systematic review acts as a scoping review to conduct more comparative studies to obtain an evidence-based analysis.

Keywords

Photo Biomodulation, Hyaluronic Acid, TMJ

INTRODUCTION

Temporomandibular Disorder (TMD) is a multifaceted condition, often arising from factors such as muscle hyperfunction or parafunction, traumatic injuries, hormonal influences, and changes within the joint structure. It encompasses a wide range of clinical issues that affect the muscles involved in mastication, the temporomandibular joint, as well as the surrounding bones and soft tissues, either individually or in various combinations.

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Researchers have identified connections between occlusion and TMJ symptoms, with studies like Mohlin and Kopp's indicating associations between occlusal interferences and myofascial pain and dysfunction. Additionally, they found correlations between conditions like posterior crossbite and muscular discomfort. Deep biters, class II malocclusion, and anterior open bites also have a potential higher predisposition to myofascial pain.

Symptoms of TMD include reduced range of jaw motion, muscle pain during mastication, discomfort in the temporomandibular joint (TMJ), audible joint sounds during movement, widespread myofascial pain, and limitations or deviations in the functional opening of the jaw.

TMD has high prevalence, with notable effects on physical and psychosocial aspects. Its prevalence has been found to range from 3.7% to 12%, and is three to five times more prevalent in females. TMD also accounts for a high percentage of socioeconomic burden, which is typically linked with comorbidities, like depression and other psychological factors.

Usual management methods used are conservative in nature such as pain relief medication, physiotherapy to facilitate jaw movement, and the use of occlusal splints. Furthermore, patients are also provided with self-management skills to deal with day-to-day symptoms. Cognitive-behavioural skills are crucial in the management of psychological aspects of TMJ disorders. Surgical interventions can be implemented in serious cases or where conservative methods are ineffective. Effectively manage temporomandibular joint conditions needs an individualized approach considering the unique nature and severity of the patient's symptoms.

The foundation of TMD management is a multidisciplinary management comprising physical therapy modalities like manual therapy, electrotherapy, ultrasound, transcutaneous electrical nerve stimulation (TENS), or laser treatment.

With respect to physical therapy modalities, Photo biomodulation therapy has become increasingly popular in recent years due to its simple applicability, minimal treatment time, and lesser contraindications. Numerous prospective clinical trials have been conducted to assess the effectiveness of LLLT.⁴

Pharmacological strategies for TMJ disorders closely align with those used for the symptomatic treatment of

osteoarthritis. This includes the use of non-steroidal anti-inflammatory drugs (NSAIDs) and the administration of either steroids or hyaluronic acid through intra-articular injections into the superior joint space.⁵

Use of intra articular hyaluronic acid is regarded as a secure, straightforward, and minimally invasive method for addressing temporomandibular disorders (TMD) characterized by pain that does not respond to conventional conservative treatments.⁶

Literature reports indicate that hyaluronic acid (HA) injections, with or without arthrocentesis, have been found to be effective in reducing pain associated with symptomatic joints. Hyaluronic acid is a natural glycosaminoglycan produced by synovial cells, naturally present in the synovial fluid.⁶

Through our systematic review we aim to compare efficacy of photo biomodulation therapy and intra-articular hyaluronic acid injection in managing Temporomandibular Disorders (TMD), we aim to uncover meaningful insights that will enrich evidence-based practices. Our endeavour is geared towards expanding the current understanding of these interventions, providing guidance for clinicians and researchers to adopt more informed and effective strategies in addressing symptoms associated with TMD.

OBJECTIVE OF THE STUDY

Focused Question

Is Photo biomodulation therapy better than Hyaluronic acid in the treatment of Temporomandibular Disorder?

TABLE 1: PICO PATTERN

Population	Patients who presented with symptoms of temporomandibular disorders
Intervention	Photo biomodulation therapy and / or hyaluronic acid
Comparison	Control/ Placebo laser OR saline/ With each other
Outcome Primary outcome	Post operative pain score using a standardized VAS scale and mean mouth opening (distance between maxillary and mandibular incisor tooth)
Secondary outcomes	Assessment of joint clicking sounds

METHODOLOGY AND DATA EXTRACTION

Eligibility Criteria

Inclusion Criteria

Below are the inclusion criteria used for this systematic review:

- Studies done in human population
- Studies done in patients with Temporomandibular disorders
- English studies from January 2003 to October 2023.
- Randomized controlled trials, non-randomized controlled trials comparing the effectiveness of photo biomodulation and intra-articular hyaluronic acid in TMD.
- Studies that report outcomes like pain improvement, functional recovery, and joint clicking evaluation.
- Only original articles are included.

EXCLUSION CRITERIA

- Those studies not in the English language are excluded
- Single-arm trials, case reports, case series, and non-comparative observational studies are excluded
- Any animal study or study with inadequate or irrelevant outcomes are excluded.
- Any study outside the inclusion criteria is excluded.

Data Extraction

An aggressive electronic search was conducted using Cochrane Library, PubMed Central, Scopus, Google Scholar, Science Direct, and grey literature to look for articles within the period of January 2003 to October 2023 following the inclusion criteria. Data extraction was simultaneously performed by two investigators using a manual approach. Initial screening was conducted through reading the abstract, followed by cross-checking full-text articles to remove duplicates and irrelevant articles that did not fit the criteria.

The search strategy used an extensive method, combining a mix of Medical Subject Headings (MeSH) terms and keywords for Temporomandibular Disorders (TMD), photo biomodulation, and hyaluronic acid. Using a mix of controlled vocabulary and free-text terms, the plan set out to cover a wide range of literature without compromising on relevance to the research question. Boolean operators “AND” and “OR” enabled

the systematic combination and filtering of search terms for a more subtle probing of the databases. This strategy made it possible to catch articles that fulfilled the criteria for TMD, photobiomodulation, and hyaluronic acid.

- (“Temporomandibular Disorders”[Mesh] OR “Temporomandibular Joint Disorders”[Mesh] OR “TMJ Disorders”[Title/Abstract]) AND
- (“Photobiomodulation”[Mesh] OR “Low-Level Laser Therapy”[Mesh] OR “Hyaluronic Acid”[Mesh]) AND
- (“Intra-Articular”[Title/Abstract] OR “Intra-Articular Injections”[Mesh])

Filters that were added were:

- Time frame placed between 2003–2023
- Type of study restricted to randomized controlled clinical trials
- Language limited to English

A comprehensive search was performed with MeSH terms and their combinations, and two independent investigators chose a list of articles. The preliminary screening was performed upon reading the abstracts, and comprehensive reading of full-text articles was done to verify whether they satisfied the inclusion criteria. Duplicates and irrelevant articles that failed to match the outcome were excluded. In situations of conflicts, resolution was achieved through mutual agreement among the investigators. This transparent and methodical procedure ensured that only studies eligible according to the predetermined criteria were selected for the final analysis, giving rise to 21 articles being included in this study.

DATA ITEMS:

TABLE 2: List of Data Items Included for Extracting the Data

1.	Authors name	Name of the author
2.	Year of publication	Year in which study was published
3.	Study Design	Randomized controlled clinical Trial
4.	Sample size and groups	Age and number of participants in each group
5.	Intervention	photo biomodulation therapy and / or hyaluronic acid

6.	Comparison	Control/ Placebo laser OR saline/ With each other
7.	Primary Outcome	Pain assessment using VAS scale, measurement of mean mouth opening
8.	Secondary Outcome	Assessment of joint clicking
9.	Follow up period	Duration of follow up period
10.	Conclusion	Result of each study

STUDY OF RISK OF BIAS ASSESSMENT

The methodological quality of the 21 clinical trials was assessed with the risk of bias tool of the Cochrane Collaboration. Two independent reviewers classified each study as having a low, unclear, or high risk of bias, and disagreement was resolved by discussion between a third reviewer.

Outcomes measured included randomization, allocation concealment, attrition bias, detection bias, reporting bias, blinding of the outcome assessors, incomplete outcome data, selective reporting, and other biases. Each study was also appraised for its objectives, population, setting, eligibility criteria, sampling strategy, outcome data, and generalizability.

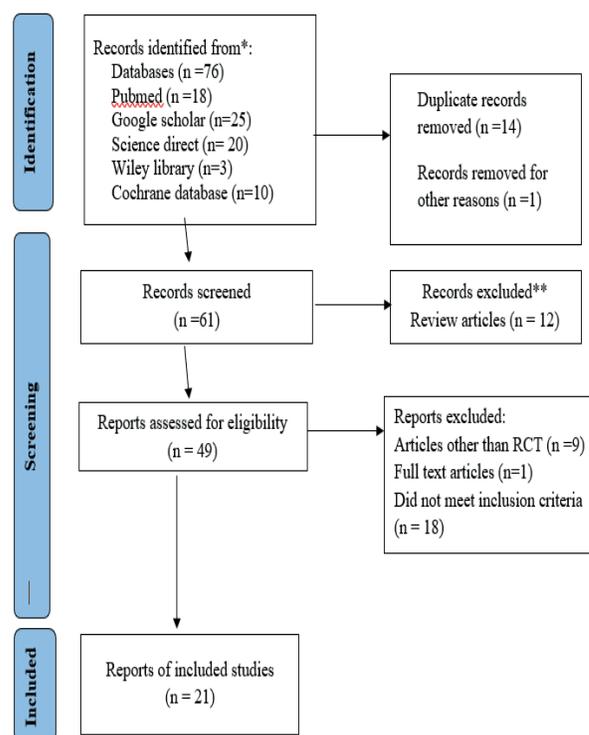
The overall risk was graded as low, moderate, or high. A study was graded as low risk if all domains were graded low, high risk if one or more domains were graded high, and moderate risk if uncertain domains were paired with some low-risk ratings.

RESULT

STUDY SELECTION

Screening of all the articles was performed by utilizing the combinations of keywords and Mesh terms with appropriate filters. Initial database turned out to be 76 articles that were searched from PubMed central, google scholar, science direct, Cochrane library. Among these 15 articles were excluded because they were duplicate, 12 were review articles, full text of 1 article could not be obtained, 10 articles were not Randomized controlled trial and 18 articles were not inclusion criteria. At last, 21 articles which were available as full text in English language and were conforming the inclusion criteria was included in the study as shown in Figure 1 below.

FIGURE 1: PRISMA FLOW DIAGRAM



STUDY CHARACTERISTICS

A total of 4,905 patients were included in all the studies that were studied for the management of temporomandibular disorder using either Low level laser therapy or intra-articular hyaluronic acid injection. All the studies were Randomized controlled trial and were compared either with a placebo group or with each other. A complete data extraction was done from all the studies depicted in the Table 3.

21 eligible studies that were included are:

Ida Marini 2010, Alessandro Del Vecchio 2019, Bakry Saleh Ahmed 2021, Camila Haddad Leal de Godoy 2015, Esshagh Lassemi 2008, Lia Alves da Cunha 2008, Lui's Monteiro 2020, Marco Antônio Moreira Rodrigues da Silva 2012, Mayela Bustamante Ortiz 2012, Onur Yilmaz 2019, Poornima Patel 2016, R. DE ABREU VENANCIO 2005, Rosana Mengue Maggi Borges 2018, Rüdiger Emshoff 2008, S S Moroglu Ozdamar 2016, SEDAT ÇETINER 2006, Sevinc Kulekcioglu 2003, Shobha R 2017, Smaranda Buduru 2018, Ya-ling Tang 2010, Yavuz Tolga Korkmaz 2016

SUMMARY OF FINDINGS

Intervention	No. of RCTs (n=21)	Sample Size (Range)	Main Outcomes	Follow-Up	General Outcome
Low-Level Laser Therapy (LLLT / PBM)	15	20-99 patients	Pain reduction (VAS), MMO, mandibular movements, joint function	Immediate 12 months	Effective in 10 studies vs placebo; 5 showed no difference. Diode/GaAlAs lasers (635–980 nm) showed better results.
Hyaluronic Acid (HA)	6	24–90 patients	Pain reduction (VAS), MMO	1–12 months	Consistently effective vs saline in 5 studies; 1 study (Serap et al.) found no significant difference.
Laser vs HA	1 (Bakry et al.)	40 patients	Pain (VAS), MMO	3 months	Laser was more effective than HA at later follow-up.
Laser vs Anti-inflammatory Drugs	2 (Alessandro et al., Ida Marini et al.)	86–99 patients	Pain (VAS), MMO	Immediate 1 month	Laser performed better than drugs for pain reduction and mouth opening improvement.
Different Laser Dosages	2 (Marco Antonio, Rosana Borges)	40–44 patients	Pain, MMO	5 weeks – immediate	Dose-dependent improvements observed; lower dosages were often effective.

RESULT OF INCLUDED STUDIES

21 randomized controlled trials were analyzed. Bakry Saleh Ahmed compared hyaluronic acid (HA) and low-level laser therapy (LLLT) in 40 patients and observed increased pain reduction and mean mouth opening (MMO) in the laser group at 3 months. Lia Alves da Cunha had a placebo-controlled trial in Brazil with 40 patients and showed less VAS score in the experimental group. In a similar study, Rudiger Emshoff reported no significant difference from placebo at 8 weeks with LLLT. Ya-ling Tang compared intra-articular sodium hyaluronate with saline in TMJ osteoarthritis in patients from China and had similar results. Alessandro Del Vecchio tested a home LLLT regimen in 86 patients and noted substantial pain improvement in the study and drug arms versus placebo. Sedat Çetiner in Turkey noted reduced pain scores and increased MMO in the LLLT group at 1 month. Luís Monteiro found significant improvement in pain and MMO in a 635 nm diode laser compared to placebo. Marco Antônio Rodrigues da Silva had dose-dependent LLLT effectiveness at several sites around the TMJ. Esshagh Lassemia found that LLLT was superior to placebo in short and long

follow-up. Sevinc Kulekcioglu noted increased MMO but no difference in pain among groups. Rosana Borges measured various photobiomodulation dosimetries in 44 patients, with decreased pain scores in active groups. Shobha R showed improved pain and MMO at 1 month in the laser group, albeit joint clicking remained. R. de Abreu Venancio found no significant difference between active and placebo laser at 60 days. Camila Hadad treated adolescents and detected no considerable enhancement with LLLT.

Yavuz Tolga Korkmaz reported HA injections and stabilization splints both had an effect, best with double HA injections. Serap Moroglu detected arthrocentesis with or without HA likewise lowered pain and enhanced MMO. Mayela Ortiz showed LLLT alleviated TMJ pain versus placebo for 12 days. Smaranda Buduru verified LLLT was more effective than placebo for 14 days. Ida Marini contrasted laser, drugs, and controls in 99 patients, with laser providing the most significant pain and MMO gain.

Onur Yilmaz contrasted HA, arthrocentesis, and combination treatment in 90 patients and found HA plus arthrocentesis to be superior. Poornima Patel concluded

that combining sodium hyaluronate with arthrocentesis produced more pain relief and MMO than arthrocentesis alone.

RISK OF BIAS IN THE STUDIES

Quality of included studies were independently evaluated by two reviewers through the application of a Cochrane risk of bias tool to 21 clinical studies that are presented in figure 2, 3. Quality assessment was conducted according to risk of bias. Allocation concealment was unclear in 6 articles, low risk in 12 articles and high in 3 articles, selection bias was unclear in 5 articles, high in 3 articles and low risk in 13 articles, performance bias was unclear in 5 articles, low in 8 articles and high in 8 articles, detection bias was high in 11 articles, unclear in 5 articles and low risk in 4 articles, attrition bias was low in 18 articles and unclear in 3 articles and reporting bias was unclear in 2 articles and low in 19 articles. Overall, there is a moderate to high risk of bias found in all the studies.

DATA SYNTHESSES

Among the 21 studies that were included in the systematic review 5 studies^{20,19,17,8,14} was conducted in Brazil, 5 studies^{12,16,21,22,26} was conducted in Turkey. 2 studies^{27,18} was conducted in India. Rest other studies was conducted in different parts of world. We categorized the follow up in 4 categories of follow up. There were 5 studies^{8,10,11,17,20} that had immediate post operative follow up. 7 studies^{7,12,13,16,18,19,22} had a minimum follow up period of 1 month, 4 studies^{15,21,27,26} had a minimum follow up period of 6 months and 5 studies^{9,14,23,24,25} had various follow up based on number of applications, number of days or weeks.

All the article that was included are randomized controlled clinical trial that had studied the effect of laser, hyaluronic acid, or both in the treatment of temporomandibular disorder. All the studies have measured the pain outcome using a VAS scale. Mean mouth opening was measured in 12 studies^{7,12,13,14,16,18,19,21,22,25,27} whereas joint clicking was measured only in study conducted by Shobha et al¹⁸. 5 studies^{13,14,16,19,25} assessed the mean protrusive and lateral movements of mandible.

Only one study in the literature was found that had compared the effectiveness of laser and hyaluronic acid conducted by Bakry et al⁷ that concluded that laser is more effective in comparison to hyaluronic acid. All the other studies used either laser or hyaluronic acid alone, out of which Diode laser with different wavelength was used in 5 studies^{7,13,15,18}, GA-AL-Arsenide laser with different wavelength was used in 6 studies,^{8,12,17,14,20,25} and 6 studies^{10,21,22,27,26,7} had included hyaluronic acid.

In studies conducted by Rossana et al¹⁷, Marco Antonio¹⁴, authors compared different dosage of laser categorized under different groups. In studies conducted by Alessandro et al¹¹ and Ida Marini et al²⁵



Risk of bias summary: review authors' judgements about each risk of bias item for each included study.

FIGURE 2: Risk of bias summary: author's judgements about each risk of bias item for each included studies

, authors compared lasers with inflammatory drugs and concluded its efficacy to be better than drugs. Low level laser when compared to placebo was found to be effective in 10 studies^{11,12,13,14,15,16,17,23,24,25} and not effective in 5 studies^{8,9,18,19,20}. Hyaluronic acid when compared to saline injections was found to be effective in all the studies except one study conducted by Serap et al²² stated that there was no statistical significant difference between arthrocentesis and arthrocentesis with hyaluronic acid groups. Due to presence of heterogeneity among the studies that was included in this review, a meta-analysis could not be performed.

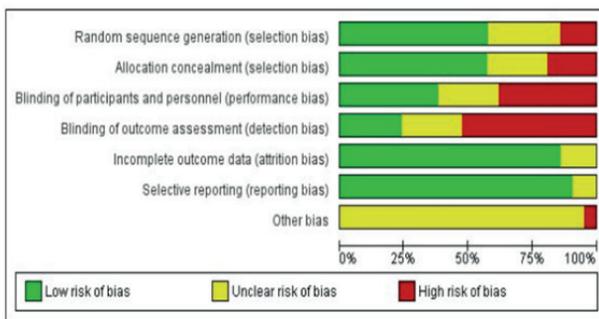


FIGURE 3: RISK OF BIAS GRAPH: Author's judgement about each risk of bias item presented as percentages across all included studies

DISCUSSION

A significant portion of the population experiences temporomandibular disorders, a pathological condition frequently marked by severe pain that can restrict jaw movements and negatively impact the individual's quality of life.⁷

A broad range of treatments are available for temporomandibular disorders (TMD), encompassing both non-surgical and surgical approaches. Non-surgical treatments comprise pharmacological, occlusal, and physical therapy. Pharmacological therapy involves the use of non-steroidal anti-inflammatory drugs (NSAIDs), antidepressants, and muscle relaxants. Occlusal and physical therapy encompass techniques such as moist heat application, ultrasound therapy, laser therapy, exercises, transcutaneous electrical nerve stimulation (TENS), microwave therapy, and manual therapy.⁷

A comprehensive approach to TMD management is advisable, often incorporating physical therapy, cognitive-behavioral therapy, and pharmacological

interventions. The overarching aim of treatment is to alleviate pain, enhance joint function, and minimize the necessity for invasive procedures.²⁸

Managing TMD is intricate and demands a thorough evaluation of the patient's symptoms and underlying factors. While LLLT and HA injections may offer benefits in certain cases, a multidisciplinary strategy involving diverse nonsurgical methods is typically recommended for optimal TMD management.^{28,29}

LLLT operates via photo biomodulation, a process that involves metabolic activation through stimulation of the cellular respiratory chain in chondrocytes and synoviocytes. This mechanism leads to a reduction in pain and stiffness while enhancing joint function. Conversely, hyaluronic acid (HA) serves as a natural component of synovial fluid, functioning as a viscous lubricant during slow movements and exerting anti-inflammatory properties. Intra-articular injections of HA are currently showing promising results in clinical practice.^{28,29}

In a study by Bakry S et al 2021 when comparing the evaluation of low-level laser therapy and sodium hyaluronate, among the two groups no statistically significant differences were found between group A and group B concerning changes in pain measured on the visual analogue scale (VAS) and maximum painless opening from pre-operative to post-operative at one month. However, statistically significant differences were observed between the two groups from pre-operative to post-operative at the three-month follow-up periods.⁷

In a study reported by Khairna et al. in 2019²⁴, who conducted a comparison between low-level laser therapy (LLLT) and ultrasound therapy for reducing TMD pain. Their study revealed a statistically significant difference in VAS pain scores before and after treatment for both groups individually. However, when comparing post-therapeutic pain VAS scores between the two groups, there was a statistically significant difference favouring the Laser group.⁷

Furthermore, a randomized controlled trial discovered that both LED light and LASER therapies demonstrated effectiveness in alleviating pain linked to myogenic TMD, with no notable discrepancies observed between the two modalities.³⁰

LLLT emits no heat, sound, vibration, or light for a wavelength in the infrared spectrum. It is therefore

possible to apply a placebo therapy indistinguishable from the active laser therapy.³¹

In a systematic review and meta-analysis conducted by Clijisen R et al evaluating the effect of low-level laser therapy in musculoskeletal disorders LLLT emerges as an effective treatment approach for attaining pain relief in adult patients with musculoskeletal disorders. Therapists employing LLLT should adhere to the dosage recommendations outlined by the World Association for Laser Therapy (WALT) to achieve clinically significant improvements in pain relief when managing patients with musculoskeletal conditions.³¹

While both LLLT and HA injections show promise in treating TMD, it is crucial to acknowledge that their effectiveness can vary based on the severity and root cause of the disorder. Additionally, the use of LLLT home devices requires further assessment to ensure both efficacy and safety.

Although HA exhibits potential in TMD treatment, it is crucial to emphasize the necessity for additional research and comparative studies to comprehensively assess its efficacy compared to other treatment modalities. The utilization of HA in TMD therapy remains an evolving area, prompting ongoing efforts to gather updated evidence-based data on its effectiveness.³²

In the present systematic review it was found that in the article where low level laser was compared to the hyaluronic acid, laser was found to be effective and among the comparison of laser with placebo, maximum number of studies found low level laser to be statistically significant than placebo and hyaluronic acid was found to be statistically significant than the arthrocentesis or plain placebo injections except for one study where there was no statistical significant difference between arthrocentesis alone and hyaluronic adjunct with arthrocentesis. Due to presence of heterogeneity among the studies, a meta-analysis could not be performed in this study.

In summary, both LLLT and HA injections demonstrate potential in TMD treatment. Nonetheless, thorough research is warranted to comprehensively assess the efficacy of these interventions. Furthermore, a multidisciplinary approach integrating diverse nonsurgical strategies is advisable for effective TMD management.

LIMITATIONS

Less articles comparing photo biomodulation and

hyaluronic acid were found. The follow up periods were not uniform in the included studies. The outcomes that were measured were uniform but at different time intervals. Meta analysis cannot be done due to heterogeneity of the studies.

FUTURE IMPLICATIONS

1. This study contributes in the development of clinical guidelines for the management of temporomandibular disorders (TMDs).
2. By identifying the outcomes of comparison of photo biomodulation and hyaluronic acid, modification of the approach for patient treatment can be done improving quality of care.
3. This systematic review highlights gaps in the existing literature that may require further investigation.
4. This study opens a scope for future studies comparing the hyaluronic acid and photo biomodulation.

CONCLUSION AND FUTURE PERSPECTIVES

Based on the literature available, laser therapy appears to be an effective modality for reducing pain and increasing mean mouth opening compared to hyaluronic acid treatment. However, it is important to note that a quantitative data analysis can only be performed when there are sufficient comparative studies available. This systematic review serves as a scoping review, highlighting the need for further studies to be conducted to obtain evidence-based results. Additional research in this area will contribute to a more comprehensive understanding of the efficacy of laser therapy compared to hyaluronic acid, ultimately informing clinical practice and treatment decisions.

In conclusion, according to the literature available laser acts as an effective modality to reduce pain, mean mouth opening when compared to hyaluronic acid, however a quantitative data analysis can only be done when sufficient comparative studies are done. Photo biomodulation was found to be statistically significant than placebo and hyaluronic acid was found to be statistically significant than the arthrocentesis or plain placebo injections. This systematic review acts a scoping review to conduct further studies and obtain an evidence-based results.

OTHER INFORMATION

PROTOCOL AND REGISTRATION

This systematic review has been officially registered with PROSPERO, the international prospective register of systematic reviews (Registration Number: [\[CRD420251144488](https://www.crd.york.ac.uk/CRD420251144488)

]). PROSPERO is supported by the National Institute of Health Research and managed by the Centre for Reviews and Dissemination (CRD) at the University of York.

This study abides by the preferred Reporting Items for Systematic review and Meta-analysis (PRISMA) guidelines in the 2020 checklist.

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