

Infiltration with corticosteroids in temporomandibular joint: systematic review

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Abstract

Objective: Evaluate the effectiveness in the reduction of pain when infiltration with corticosteroids in TMJ disorders of joint and/or muscle type is performed.

Materials and methods: A comprehensive electronic search strategy was held in PubMed on July 2015; studies were selected independently by two reviewers according to the established protocol following the parameter in “a quality assessment (Guide CASPE)” and “risk of bias (Manual Cochrane systematic reviews)” for the included studies.

Results: Five hundred and twenty-six (526) items were found after applying the search strategy which identified 14 studies for review and analysis of the full-text. Five (5) items were selected of which most had high bias risk. Due to their heterogeneity it was not possible to perform a meta-analysis.

The included studies showed improvement in pain both intra-articular and muscular after infiltration with steroids, including patients with diseases such as Juvenile Idiopathic Arthritis; there were also a few cases with low incidence effects. Although it was not the objective of this review, it was noted that there was improvement in maximum incisal opening and radiological improvement in nuclear magnetic resonance imaging with infiltration with corticosteroids.

Conclusion: The systematic review shows that intra-articular and muscular corticosteroid infiltrations are an effective and safe treatment to improve pain and function in patients with any type of temporomandibular disorders, despite limitations. It is important to have more clinical trials to confirm these findings.

Keywords: corticosteroids, intra-articular injection, intramuscular injection, temporomandibular disorders, systematic review, Helkimo Index

Abbreviations: TMD: temporomandibular disorders, TMJ: temporomandibular joint, JIA: juvenile idiopathic arthritis, RCT: randomized clinical trials, CCT: controlled clinical trials, VAS: visual analogue scale, MMO: maximum mouth opening

Introduction

Temporomandibular disorders (TMD) are some of the most common causes of illnesses in the adult population. TMD comprised of the temporomandibular joint (TMJ), masticatory muscles and other related structures. Patients with TMD have referred pain, limitation in mouth opening, and articular clicking as the most common symptoms affecting the articular function according to disorder severity.¹

TMD prevalence varies from 5% to 60%. Women are the most commonly affected mostly between 20 to 40 years of age in a ratio of 9:1 compared to men. Less than 5% required surgical treatment.²

Bell proposed a classification of the stomatognathic system disorders, later, Okesson modified it.¹ In this classification the muscular, intra-articular, and related structure disorders are considered.³ TMD can be an isolated entity or can be accompanied by other illnesses such as Juvenile Idiopathic Arthritis (JIA) or any other illnesses that affect the joints.⁴

There are many kinds of treatments for TMD, from conservative to invasive, but the objective of each is the same, the control of symptoms and return to adequate function with no reduction in mouth opening and no pain when chewing.

There is no consensus or universally accepted guideline for TMD treatment, but there is a clear trend toward conservative management of TMD because of the risks and low predictability of surgical treatment.^{1,2,4} The necessity of treatment is based on pain and dysfunction level, and symptoms progression.¹ Intra-articular or muscular TMJ injections are considered an adequate treatment alternative,^{4,5} with different kinds of drugs being utilized such as botulinum toxin, hyaluronic acid, sodium chloride, and corticosteroids.⁷ Due to its high anti-inflammatory potency and its adequate safety profile, corticosteroids are considered the preferred drug for injection in joints.

The objective of this study is to evaluate the effectiveness of intra-articular or muscular corticosteroid TMJ injections for reducing pain according to the findings in selected studies.

Materials and methods

Selection criteria

These were the defined inclusion criteria: systematic reviews, randomized clinical trials (RCT), controlled clinical trials (CCT), observational studies, English language publications, treatment with intra-articular or muscular corticosteroids TMJ injections with or without control group, studies in humans with no range of age or gender, including patients with pathologies like JIA, osteoarthritis, or TMJ internal derangement. The considered variables were: outcomes, TMJ pain intensity (evaluated with visual analogue scale (VAS) or any other method), and adverse effects associated with injections.

Studies in animals, injections in combination with other treatment like surgery or arthrocentesis, opinion, reviews, case reports, and congress abstracts were excluded.

Two calibrated researchers made the selection of the studies by applying the risk of bias, the quality of the studies, assessment, and the data extraction. Disagreement between the authors was solved through discussion.

Search strategy and study inclusion

A comprehensive literature search was conducted in the PubMed database, in English language. The following MeSH terms were used crossed referenced: “Temporomandibular Joint Disorders”, “Temporomandibular Joint Dysfunction Syndrome”, “glucocorticoids”, “triamcinolone”, “prednisolone”, “betamethasone”, and “injection”.

Each researcher applied guides for critical lecture, quality assessment, and risk of bias of the fields.

Assessment of the risk of bias and quality

The bias was defined as any factor that had sufficient impact to have a notable effect on the results or conclusion of the study reviewed.

For clinical trials and observational studies we applied the Cochrane Handbook for Systematic Reviews 5.1.0⁸ that include the following domains: sequence generation, allocation concealment, blinding, incomplete outcome data, selective outcome reporting, and other bias.

Application to our own criteria was established using the PRISMA declaration⁹ and Cochrane Handbook for Systematic Reviews 5.1.0; the standards of these declarations were adapted.

The quality of the publications was assessed with Critical Appraisal Skills Program Spanish (CASPe) guides.¹⁰⁻¹² According to the methodological design of each of the selected fields the studies were included if they scored a minimum of 7 points using the CASPe guide.

Data extraction

The following variables were entered in a Microsoft Excel table: authors, year of publication, type of work, number of participants, objective of the written report, diagnostic method used, historic period, type of treatment, type of drug, follow up, outcomes, and adverse effects.

Results

The electronic search found 526 results, 24 duplicated references were taken out (Figure 1). Titles and abstracts applying inclusion criteria were evaluated and 14 studies were selected.^{4,13-25}

Nine studies were excluded: two used injections in combination with arthrocentesis in the same patient; six had no judgment of pain in the objectives with the VAS or any other method; one review of literature with no experimental design. Five studies achieved all the parameters of this systematic review: two systematic reviews, two series of cases, and one randomized clinical trial (Table 1).

STUDY	YEAR	TYPE OF STUDY	TYPE AND NUMBER OF PARTICIPANTS	OBJETIVE	DIAGNOSTIC METHOD	MEAN AGE	INTERVENTION	DRUG	FOLLOW UP	OUTCOMES	ADVERSE EFFECTS
Venancio et. Al	2008	Randomized clinical trial	Myofascial pain with headache activated by trigger point (45)	Compare lidocaine + corticosteroid with lidocaine alone and dry needle puncture, for trigger points headache	Criteria of the International Headache Society (IHS)	(18 - 65)	TPSI, TPSI+lidocaine, dry needle injection	Dexametasone, lidocaine	10 min later, 1 week, 1 month and 3 months	Improved: pain in all 3 groups. Used the Modified Sympton Severity Index, 3 sub-indexes clasified with VAS 0/28	No reports
Samiee et. Al	2011	Retrospective - series of cases	DDWOR (17)	Determine effectiveness of TMJ infiltrations in DDWOR without reduction	Clinical examination (AAOP criteria)	34.4 (16 - 70)	IACI	Triamcinolone + lidocaine	1 week	MMO, EVA improvement	Transient facial palsy
Arabshahi et. Al	2005	Retrospective - series of cases	IJA/TMJ (23)	Measuring effects of IACI of TMJ in children with JIA	Clinical exam and MRI	9 (4 - 16)	IACI	Triamcinolone	6 - 12 months, 23/23 MMO, 14/23 MRI	Improvement: pain (not quantified), MMO, MMR	Facial edema
Li et. Al	2012	Systematic review and meta-analysis (4 studies)	TMD internal dearegnt (349)	Compare effect and safety of drugs infiltration in lower or two spaces versus superior TMJ infiltration for TMD	Clinical examination (different indices) and radiologic exam	media 25.7 - 37.5	IACI, IAHA	Prednisolone, hyaluronic acid	1-6 months	MMO Improvement, decrease pain (VAS)	No reports
Stoustrup et. Al	2013	Systematic review (7 studies)	IJA/TMD (268)	Determine the current level of evidence for the use of IACI for TMJ arthritis in patients with JIA with a focus on clinical improvements and safety profile	Unspecified	(4- 18)	IACI	Triamcinolone	No reports	Improved, worsening or no changes in MRI/CT; improved: MMO, pain (not quantified), mandibular deviation	Lipoatrophy, swelling, heterotopic ossification of TMJ, pain, decreased oral opening

IACI: intra-articular corticosteroid injections; JIA: juvenile idiopathic arthritis; DDWOR: disc displacement without reduction; IAHA: intra articular hyaluronic acid infiltration; TPSI: trigger point steroid injection; MMO: maximal mouth opening; AAOP: American Academy of Orofacial Pain

Table 1: Studies.

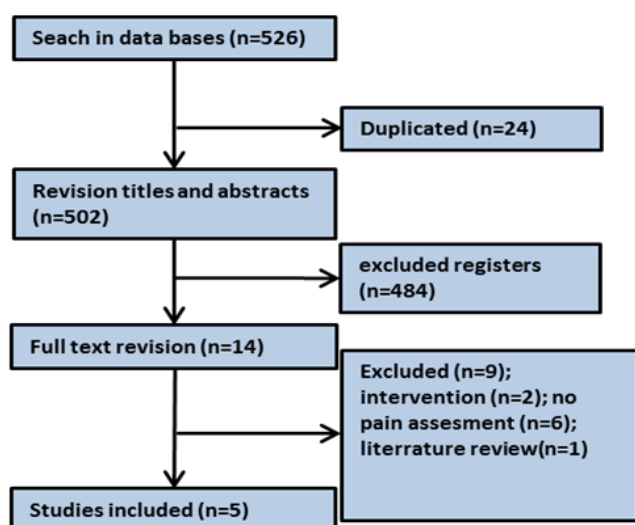


Figure 1: PRISMA flow chart describing the data selection process.

Risk of bias of the studies

The risk of bias assessment of the two series of cases and the one RCT was analyzed in Table 2.

The quality of the studies was classified into one of the following categories: 1) low risk of bias if the 6 domains were classified “adequate”; 2) mild risk of bias if one or more properties were classified “no clean”; and 3) high risk of bias if one or more lands were classified “inadequate”.

Table 2: Risk of bias assessment.

Type of bias	Venancio et al 2008	Samiee et al 2011	Arabshahi et al 2005
Selection	P	N	N
Performance	P	N	N
Detection	P	N	N
Attrition	P	N	N
Reporting	P	N	A
Other bias	P	P	P
Risk of bias	Mild	High	High

A = adequate; N= not adequate; P = not clear

TMJ muscular injection

Venancio et al.,¹⁹ an RCT study with three patient treatment groups (using a dry needle, lidocaine or lidocaine+corticosteroid). They evaluated the presence of pain, with the modified symptom severity index, and found pain improvement after 10 minutes from the injection of the trigger point. These results were stable until 12 weeks, including the dry needle group. The lidocaine + corticosteroid group had the best pain improvement.

The series of cases of Samiee et al.,¹⁵ used VAS for the evaluation of pain. They reported value of 4 to 10 (average 8) before injection and 2 to 7 (average 4) after injection. The difference was not statistically significant; no p value or confidence interval was reported.

Arabshahi et al.,¹⁴ reported a series of cases examining 13 of 23 patients with JIA referred pain symptoms in TMJ; 10 (77%) had complete improvement of pain after corticosteroids TMJ injections ($p < 0.05$).

Table 3: Systematic review bias.

	1. Possible selection bias by strict inclusion criteria
	2. Small sample
Li et al. ²⁴	3. No standardized protocol, type of medication, timing of application, dosage and frequency. Clinical heterogeneity
	4. Contact with authors to resolve doubts
	5. All studies in china, geographical limitations
	1. Retrospective studies, one prospective. Small samples in studies without pain assessment with vas
	2. No language limitations
Stoustrup et al. ⁴	3. Proper design, 2 reviewers in cases of doubt, multiple databases. Manual search and conference proceedings. Authors of studies contacted when doubts
	4. Appropriate inclusion and exclusion criteria

Li et al.,²⁴ conducted a systematic review and meta-analysis of infiltration in the lower space, the upper space or double space joints. They reported that short-term injection of the lower space and double space groups had a pain reduction of 9.01mm on average on VAS ($p = 0.001$). The long-term effect of the lower space infiltration group showed reduction of 22.02mm in VAS compared to the control group (95% CI [-29.27, -14.77], $p = 0.00001$).

Stoustrup et al.,⁴ in a systematic review reported pain relief but did not quantify with the VAS or any other method. Improvement of pain went from 67% to 100%. The characteristics of the analyzed studies were heterogeneous. They showed different sample sizes, no standardized protocols for drug administration, differences in follow up and outcome evaluation, and heterogeneity of inclusion criteria. Some reported one injection and others multiple injections.

Li et al.,²⁴ reported maximum mouth opening (MMO), in the short-term with superior space injection of hyaluronate has an improvement of 5.25mm and pain has a reduction of 5.1mm more than no injection group in VAS. An MMO with inferior space injection in the long-term could improve 6.43mm and 9.4mm of pain reduction in VAS. The conclusion was in short-term. The inferior and double space injection with hyaluronate could improve until 8.13mm of MMO and 16.81mm of pain reduction in VAS; with long-term could improve until 9.34mm of MMO and 31.42mm less in VAS, this has a clinical significance. The results are consistent with a Cochrane Systematic Review²⁶ which suggests that hyaluronate has the same effects in the short-term than corticosteroids, so this way the result can be compared in this meta-analysis.

Adverse effects

Three out of five evaluated studies reported minimal adverse effects and two^{19,24} did not mention any adverse effects.

In Arabshahi et al.,¹⁴ two of the 23 patients included in their study had facial edema; in one patient the swelling lasted two days, while in the other patient resolved in two weeks.

In Stoustrup et al.,⁴ five of the seven studies evaluated, they reported minor adverse effects such as facial edema in 2 of 23 patients; subcutaneous atrophy in 1 of 25 patients, and intra joint calcification in 2 of 25 patients, subcutaneous atrophy in one of 83 patients, pain and transient edema post infiltrations in 10 of 83 patients, TMJ discomfort when chewing (did not specify how many patients), facial swelling in 2 of 63 patients, fever in 1 of 63 patients, hiccups and skin pigmentation in 1 of 63 patients.

Samiee et al.,¹⁵ reports that only one patient developed temporal facial palsy, which persisted for 3 hours. The patient's facial nerve function was normal during the follow-up visit.

Other effects

Arabshahi et al.,¹⁴ reported that the incisal maximum aperture improved at least 0.5cm in 10 patients(43%) ($p=0.0017$); 6 patients were those who had a better response in the incisal maximum aperture ($p=0.2267$). Among 14 patients who had follow-up with magnetic resonance imaging 11 (48%) had resolution of the articular effusion.

Samiee et al.,¹⁵ established that the active mouth opening and manual mobilization after infiltration ranged from 25 to 50mm (average of 39mm; 6.54 SD); the average buccal opening increase was 10mm ($p=0.0004$).

Li et al.,²⁴ reported injection in the joint double space can increase MMO 2.54mm more than an upper space injection ($p=0.0005$), and the lower space injection group improved 3.07mm more than a superior space injection group ($p=0.03$); i.e. combining lower space and double space injection would show 2.88mm more in MMO ($p=0.0001$).

Regarding the Helkimo Index, the infiltration in the lower space group had a decline of 3, 78mm on average compared to an upper space group which dropped 2, to 32mm in the index without statistical difference (MD-0.93, 95% CI [-1.88, -0.02], $p=0.05$). There was also a long term effect on lower space group instead of the clinical variables synthesized, showing a decrease in the average of Helkimo Index in the lower space group of 5.41mm less compared to a decrease of 3.08 mm in the upper space group with a significant statistical difference (MD-1.80 (95% CI [-2.58, -1.02], $p=0.00001$).

Discussion

The present study is a summary of results of intra-joint or muscular corticosteroid injection for articular pain relief and management related to TMD of any type in any group of patients.

It was not possible to perform a meta-analysis because the five studies that dealt with the proposed topic are very heterogeneous. Four studies were rated with high risk of bias, and one with moderate risk of bias. Despite the risk of bias for different reasons such as lack of control group, retrospective design study, lack of standardized clinical protocol and lack of clarity about blinding, all of the studies tend to conclude that steroid injections are effective for the treatment of pain associated with TMD. This finding concurs what is found in literature.^{7, 13, 25, 27-29}

One of the main difficulties for an adequate analysis regarding improvement in pain is that only three of the studies used VAS for

quantifying pain pre and post-treatment. Of these studies only two reported 'p' or 'interval of confidence', the other just mentions that there is a statistically significant difference. Additionally, the method used for diagnosing TMD was different in each study, one used the Helkimo Index and the other four were diagnosed through clinical and radiographic examination.

Considering the heterogeneity in the studied groups, two studies had patients with JIA, while two other studies had patients with internal derangement and one study had trigger points; although all the studies had a favorable response to treatment, there may be factors influencing the course of symptomatology. For example, patients with JIA are treated with various immune modulators such as methotrexate or tumoral necrosis factor inhibitors, or according to the JIA type, if it is oligoarthritis or polyarthritis. Patients with internal disorders, the presence of occlusal splints, oral physiotherapy or any other conservative treatment can affect the outcome. These variables can modify the level of inflammation of the patient at the time during which it is studied, affecting the results of the intervention.

Different studies show a very wide range of follow up ranging from one week to 12 months. A one week follow up would have a high risk of bias, because there is no way to determine the stability and duration of results.

To assess the safety profile of interventions or possible adverse effects that may occur, it was found that in all the studies the prevalence is low or not reported. This is consistent with that found in the literature regarding the recommended use of small doses for a short time.^{13,30-32} The most commonly occurring complication was post injection edema, but they resolved by themselves in a short time. The adverse effects of further consideration are cutaneous hypopigmentation, and facial fat dystrophy. However, none of the studies reported the need for additional treatment or if there was improvement over the follow-up period.

It is not possible to give a recommendation on how TMJ injections should be implemented in actual clinical practice, because in the studies the treatment protocol was not standardized. The most widely used drug was triamcinolone, but dexamethasone and prednisolone were also used. There is no data suggesting that any of the above medications are more effective than the other in the treatment of pain.

A clinical outcome observed in the studies is the functional improvement expressed in the magnitude of the maximum incisal opening despite not being an objective of this systematic review, it is worth considering that studies evaluated it. There was a statistically significant improvement although none specified a protocol standard for this measure.

When a clinician decides to make infiltration in clinical practice, it is recommended to put in balance the cost/benefit considering the probability that intra-joint or muscular injections with corticosteroid may have a beneficial effect but also the possibility of an adverse reaction. The decision making depends on the clinical trial that includes a comprehensive and individual assessment for each case. Current evidence suggests beneficial effects when using this treatment in terms of pain improvement associated with TMD of any type and in different kind of patients.

The construction of intra-articular or muscular steroid TMJ injection treatment guidelines is required for future research practice. Clinical trials with an adequate methodological design, homogeneous samples, and diagnostic methods are needed to conduct clinical trials

and to have additional results with high standards of validity thus the conclusions have a scientific weight.

Limitations of this review include a possible bias by language (English); and the literature search carried out on PubMed as the only search engine. The included studies are heterogeneous, a clinical trial with a small sample, two series of cases (retrospective), one systematic review, and one systematic review with meta-analysis. Methods in the studies differ in the kind of drug, time, and form of administration. Method of measurement of pain was not standardized in all the studies which can be a confounding factor. The constraints described demonstrate the need for more stringent research involving larger samples, randomized clinical trials with an adequate methodological design, standardization in diagnostic methods (use of DC/TMD) and quantification of pain by EVA.

In conclusion, this systematic review suggests that despite the constraints, intra-joint and muscular corticosteroid injection appears to be an effective and safe treatment to improve pain and function in patients with any kind of TMD. More clinical trials are needed to confirm these conclusions.

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