

The Effectiveness of Pharmacology in Disorders of the Manducatory System

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ABSTRACT

Summary: The wide variety of disorders and abnormalities affecting the manducatory apparatus has led to a multitude of therapies of various kinds including orthopedic, kinesiological as well as pharmacological treatments.

Several studies have highlighted the effectiveness of orthopedic therapies using occlusal splints as well as kinesiological treatments. However, pharmacological treatments, by their multitude and their diversity remain little documented regarding clinical efficiency, with the absence of a global conclusive study.

The aim of this work is to conduct a systematic review evaluating the clinical efficacy of the drugs used in the treatment of temporomandibular dysfunction

Materials and Methods: This is a systematic review questioning the Pubmed database.

The research was conducted using the following key words: "Craniomandibular disorders"; "Drug therapy"; "Relaxing Muscle, Central". Articles published between January 2012 and end of August 2017 and meeting the eligibility criteria were identified after reading their titles then summarized by 2 readers. The critical analysis of the methodology was conducted based on the PICO criteria and the JADAD scoring analysis (strengths and weaknesses of each study). The effectiveness of drugs was evaluated based on their action on the following three parameters: Dyskinesia, pain and noise.

Results: Of the 420 references originally found on Pubmed, 23 articles were selected.

After full reading of the 24 articles selected and application of the JADAD score:

- 3 articles treated botulinum toxin including 1 high rank and 2 low ranks for a conclusion in favor of the toxin.
- 7 articles discussed hyaluronic acid, 5 of which ranked high and 2 of low rank all agreeing on the efficacy of this therapy.

5 articles on corticosteroids, including 1 high and 4 low, however, no consensus has been reached on its effectiveness.

Only 1 item of high rank proved the beneficial effect of anesthetics on muscle pain.

1 high-ranked study and 1 low-ranked trial for nonsteroidal anti-inflammatory drugs that have not been conclusive about its effectiveness.

- 3 low-grade items treating PRP were able to demonstrate efficacy as an adjunct to arthrocentesis.

1 low ranking article on painkillers has proven its value as an adjunct to arthrocentesis.

1 high-ranked and 1 low-ranked article dealing with central muscle relaxants have both agreed on their side effects, but their effectiveness has not been proven.

Only 1 item of high rank for bee venom has been proven effective.

Discussion: *Through this systematic review, we can draw the following conclusions:*

Data from the literature on the therapeutic effects of injected corticosteroids are mixed. Their effects are mainly pain-related and short-term. Other symptoms are not sensitive to this therapy.

Work on botulinum toxin fluctuates between studies confirming its efficacy and the other reversing it. However, are short-term effectiveness on joint pain seems to be proven.

Hyaluronic acid is generally effective in treating AMD and is more effective than long-term corticosteroids.

TMJ arthrocentesis is a simple, minimally invasive procedure that significantly improves the symptoms of AMD. It is even more effective when combined with an active ingredient such as PRP, HA, Steroids etc.

NSAIDs, analgesics, anesthetics and central muscle relaxants are adjuvant therapies rather than independent and self-sufficient therapeutic techniques. Their use often makes it possible to accelerate the healing mainly conveyed by an orthopedic device of gutter type.

Bee venom does not benefit from enough studies but seems to have positive effects, especially on muscular pathologies.

Further studies are needed in order to make a better analysis of the effectiveness of certain active ingredients and to distinguish between the different studies and the contradictory results.

Keywords

Craniomandibular Disorders, Muscle Relaxants, Central, Craniomandibular Disorders, Drug Therapy.

Introduction

Temporomandibular disorders (TMD) is a term grouping the dysfunctions of the masticatory muscles as well as those of the joints.

In order to treat these dysfunctions, a panoply of treatments has been developed including: orthopedic treatments (Occlusal splint, antero-position, decompression, releases, etc.), physical treatments such as laser, infrared, electrotherapy, physiotherapy, post urology, acupuncture... and the pharmacological means that we have chosen as the subject of our study.

Several active elements are used as temporomandibular treatments, we will cite:

Botulinum toxin, Hyaluronic acid, Corticosteroids, Anesthetics, Nonsteroidal anti-inflammatory drugs, Plasma rich-fibrin (PRF), Glutamic acid, Analgesics, Analgesics, Central muscle relaxants; Bee Venom

In this study, we will try to clarify the real effectiveness of each active ingredient.

Material and Methods

Documentary Sources

The search, electronic and manual, was carried out on the Data-base Medline.

Articles meeting the following criteria were included: Clinical trials and randomized controlled clinical trials, conducted on human beings, Published between 01/01/2012 and 31/08/2017

- Written in English.

- Relating to pharmacotherapy during craniomandibular dysfunctions

The articles excluded from our research were the following:

- Case series, Studies carried out on animals or corpses, Retrospective studies, Studies financed by manufacturers or containing a conflict of interest, Studies dealing with the effect of pharmacological agents combined with laser, Studies proposing as treatment autologous blood injection or ozone gas.

Data Collection and Searched Data

The PICO criteria were used in order to best structure our systematic review:

♣ P: Participants => Patients suffering from temporomandibular dysfunctions

♣ I: Intervention => Use of active principles at the joint or muscle level for the treatment of these patients

♣ C: Comparison => Comparison of the effectiveness of these active ingredients

♣ O: Results => Result on pain, noise, dyskinesia, efficiency and masticatory motor skills.

This allowed us to classify the data of the articles in a reading grid comprising different categories:

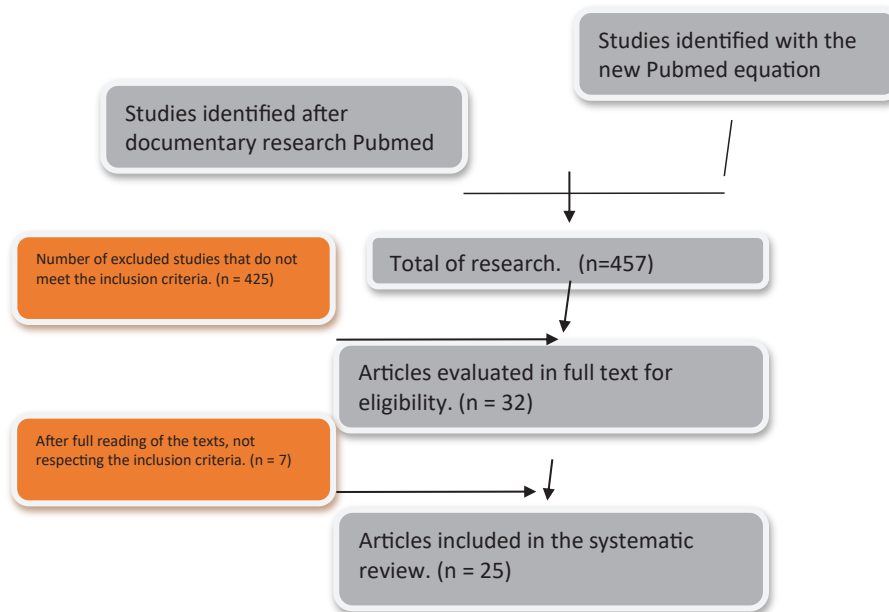
- Author and year of publication, Type of study, Population / Pathology, Type of drug, Intervention, Measuring tools, Noise, Pain, Dyskinesia, Other

The results of our research are presented in the form of a flow diagram showing the selection of selected articles.

Results

Selection of Articles

The selection of articles followed the flow diagram below:



Descriptive Results

In this part, the selected articles will generally be described according to the PICO criterion (patients, intervention, comparison, outcomes) for each active ingredient.

Botulinum Toxin

-No significant difference between the 2 groups for pain relief.
 - The botulinum toxin group shows a significant improvement in the left laterotrusion.14
 Group A has significant efficacy of botulinum toxin in the short term (1 month) in pain and loses its efficacy at 4 months [1].
 Group 2 (botulinum toxin) shows better results with a reduction in the loads on the joint disc.

Hyaluronic Acid

There is a significant improvement in pain in terms of the parameters of opening and masticatory efficiency.

There was a significant improvement in pain in the parameters of opening and chewing in the 2 groups.
 Corticosteroid drug therapy presents a significant improvement in aperture 8.

There was a significant improvement in pain at rest and chewing in the 5 groups with 5 weekly sessions including improvement in pain, aperture and chewing efficiency.
 - Hyaluronic acid is the most effective against pain compared to corticosteroids and NSAIDs [2].
 Arthrocentesis and arthrocentesis + hyaluronic acid reduce pain; increase aperture and chewing efficiency [3].
 - Arthrocentesis alone and with hyaluronic acid have shown good results for pain; aperture and masticatory efficiency [2].

Corticoides [2,4-6]

- Significant improvement in pain in the short term and relative in

the long term.

- Significant increase in aperture and long-term function for the 2 groups.
 - Significant improvement in pain; aperture and function in the 2 groups.
 - Corticoids do not add any effects to arthrocentesis. (-)
 - Arthrocentesis is effective in improving pain and aperture with or without corticosteroids.
 - Arthrocentesis is effective in improving function; aperture and pain with or without corticosteroids.
- Hyaluronic acid is the most effective at pain compared to corticosteroids and NSAIDs.

The Anesthetic [7]

-Decrease in spontaneous pain; pressure and pain caused by 4 kg pressure [7].

Non-Steroidal Inflammatory Anti (NSAID) [8-10]

Hyaluronic acid is the most effective at pain compared to corticosteroids and NSAIDs.
 - The NSAID used as an adjuvant to the occlusal splints promotes rapid analgesia (3 days)
 - At 10 days, all the therapies are effective against pain.

Plasma Rich Fibrin (PRF)

- The use of PRP in addition considerably reduces pain.
 PRP and arthrocentesis reduce pain; improve aperture and reduce snapping [11].
 - The arthrocentesis + PRP treatment is more effective than that of the arthrocentesis alone [12].
 - Increased opening, chewing efficiency and function [12].

Glutamic Acid [13,14]

- No significant difference between the maximum intensity and the total duration of pain between injections (Muscle and ATM).

- The overall MPQ pain index for muscle pain is significantly lower than for Temporomandibular joint (TMJ) pain.

Analgesics

Tramadol and morphine more effective in pain and aperture than placebo group compared to arthrocentesis alone [15].

Central Myorelaxants [16,17]

- Significant reduction in pain at rest and when chewing; increased aperture and movement; of the functionality of ATM in the 2 groups but better results for the DDN Group.
- Secondary effects of pharmacotherapy in muscle relaxants

Analgesics [18]

- Better efficacy of Tramadol and morphine on pain and aperture than the placebo group = arthrocentesis alone.

Bee Venom [19]

- Significant effect of Bee Venom in decreased muscle tone and muscle contraction [19].

The last decade has seen a growing interest in the use of certain active ingredients as a treatment for dysfunctions of the temporomandibular joints.

The clinical value of their use is controversial: some advocated their use without reservation, while others preferred a reluctant and hesitant approach [19].

In this section, we will try to assess the real effectiveness of these pharmaceutical agents.

Discussion

Botulinum Toxin

The results of studies by Amit A. Patel et al. [1] and Malgorzata E. Pihut et al. [20] both concluded that the botulinum toxin was significantly effective in short-term pain and in reducing joint loads.

As for the 3rd trial conducted by Luca Guarda-Nardini et al. [21], the comparison was made between Botulinum toxin injection and facial manipulation. There was no significant difference between these two pain treatments.

While the systematic review by Chen. YW et al. [22] included Five studies and a total of 117 participants could not reach a consensus on the therapeutic benefit of botulinum toxin on TMD.

The conclusions of this review are in favor of the toxin. However, other trials should be carried out with a larger population, the use of electromyography (EMG) as a guide and several injections of botulinum toxin instead of just one in order to have more conclusive results.

Hyaluronic Acid

A total of 7 randomized trials have discussed the efficacy of hyaluronic acid.

Studies by Zeliha Kapusuz Gencer et al. [14], Luca Guarda Nardini et al. [23,24] and S. Serap Moroglu Ozdamar et al. [25], all four demonstrated the effectiveness of adding hyaluronic acid to arthrocentesis in significantly improving pain scores, aperture and masticatory efficiency.

As for the second study by S. Serat Moroglu Ozdamar et al. [25], it also demonstrated a reduction in the level of Myeloperoxidase when adding Hyaluronic acid to arthrocentesis.

Increasing the number of arthrocentesis sessions gives better results.

The systematic review by Eduardo Machado et al. [3] was able to demonstrate the efficacy of hyaluronic acid compared to corticosteroids in the long term.

All the studies included in our research have concluded that hyaluronic acid is effective in treating temporomandibular joints.

Corticoids

Studies by Songul Comert Kilic et al. [2], Reza Tabrizi et al. [4] and H. Olsen-Bergem et al. [5] comparing the action of arthrocentesis alone to that of arthrocentesis combined with corticosteroids found a significant improvement in pain, aperture and function with or without corticosteroids.

As for the essay by Peter Stoustrup et al. [6] comparing the bilateral injection with the unilateral injection, he reported a significant improvement in short-term and relative pain in the long term as well as a significant increase in opening and long-term function for both groups.

While a literature review by Peter Stroustrup et al., [6] found no scientific evidence confirming the effect of corticosteroid injection in terms of significant improvement in the maximum opening capacity of the mouth, reduction in the progression of radiological disease, mandibular growth and increasing efficiency after repeated injections for the treatment of juvenile idiopathic arthritis.

Even if the results of the articles confirm the effect of corticosteroids for some in the short term only, this is invalidated by the systematic review. More studies are required for better results.

Non-Steroid Anti-Inflammatory

The trial of Fernando Kurita Varoli et al. [9] concluded that the non-steroidal anti-inflammatory drug used as an adjuvant to the occlusal splints promotes rapid analgesia (3 days) but at 10 days, this therapy and the placebo are both effective against pain.

While the systematic review by Mireya Senye et al. [10] noted a decrease in the pain index in the placebo groups treated with NSAIDs but with no significant difference. Hence the need for further studies to judge the real action of NSAIDs.

PRP

M.Pihut et al. [26], Mustafa Hanci et al. [11] and Songul Comertkilik et al. [2] concluded during their studies that treatment with arthrocentesis + PRP is more effective than that with the arthrocentesis alone, which reduces pain and clicks, increases opening, chewing efficiency and function. Therefore, PRP can be considered as an effective adjuvant to arthrocentesis in the treatment of TMJ dysfunctions.

Analgesics

A. Sipahi et al. [18] deduced that Tramadol and Morphine are more effective in pain and aperture than arthrocentesis alone. However, a single study remains insufficient to judge the real action of painkillers.

Anesthetics

Monica Firmani et al. [7] found a reduction in spontaneous pain, on pressure and caused by a pressure of 4 kg following the injection of lidocaine. Although this study proves the effectiveness of anesthetics in reducing muscle pain, it will need to be supported by other trials for more conclusive results.

Central Myorelaxants

The research of Luis-Miguel Gonzalez-Perez et al. [16] resulted in a significant reduction in spontaneous pain, pain in chewing, increased opening and movement, functionality of TMJ in patients treated with muscle relaxant and dry injection, but better results for the latter, with side effects to pharmacotherapy in patients treated with muscle relaxants.

While the second research by Francisco Guedes Pereira from Alencar Junior et al. [17] on Tizanidine (TZA) and Cyclobenzaprine (CYC) concluded that these muscle relaxants do not reduce pain and its symptoms nor the quality of sleep and produce side effects.

If the action of muscle relaxants is still to be proven, their side effects seem to be effective.

Bee Venom

Aleksandra Nitecka Buchta et al. [19] noted a considerable effect in the reduction of pain, tone and muscle contraction following the injection of bee venom. However, only one study seems insufficient to judge the real effectiveness of bee venom.

Conclusion

The therapeutic management of any TMJ disorder necessarily responds to a careful diagnostic process, the objective of which is to define beforehand the best therapeutic approach adapted to the patient.

The use of drug treatments often comes as a complement to initial cognitive behavioral therapy or orthopedic therapy with occlusal splints. In certain situations of mild TMD, the administration of anti-inflammatory drugs or muscle relaxants can resolve the problem and quickly improve the symptoms. However, the

stage and nature of the pathology, such as grade 3 and 4 disunity associated with acute symptoms, require different management. Since pain is predominant and incapacitating, the combination of active ingredients becomes necessary.

In other situations where orthopedic therapy has failed, the use of drug therapies such as arthrocentesis or intra-articular injections is inevitable. This situation is often encountered in advanced degenerative disorders, accompanied by an overall deterioration of the manducatory function and intense pain. The effectiveness of certain active ingredients such as hyaluronic acid or corticosteroids offers the patient a final alleviation of the symptoms, sometimes enabling him to recover noticeably from masticatory functions.

Through this systematic review, we can draw the following conclusions:

- The data in the literature on the therapeutic effects of injected corticosteroids are mixed. Their effects are mainly focused on pain and in the short term. Other symptoms are not sensitive to this therapy
- Work on botulinum toxin fluctuates between studies confirming its effectiveness and others confirming it. However, its short-term effectiveness on joint pain seems to be proven.
- Hyaluronic acid is generally effective in the treatment of TMD and is more effective than long-term corticosteroids.
- TMJ arthrocentesis is a simple, minimally invasive procedure that significantly improves symptoms of TMD. It proves to be even more effective when it is combined with an active ingredient such as PRP, HA, steroids etc.
- TMJ arthrocentesis is a simple, minimally invasive procedure that significantly improves symptoms of TMD. It proves to be even more effective when it is combined with an active ingredient such as PRP, HA, steroids etc.
- NSAIDs, analgesics, anesthetics and central muscle relaxants are more adjuvant therapies than independent and self-sufficient therapeutic techniques. Their use often makes it possible to accelerate the healing mainly conveyed by an orthopedic device of the occlusal splint type.
- Bee venom does not benefit from enough studies but seems to provide positive effects especially on muscular pathologies.

Drug therapies allow practitioners to optimize the results of their occlusodontic therapies. Through this systematic review, the practitioner is now warned as to the different uses and therapeutic effects of each active ingredient. It is up to him to decide whether to use them either as a first line, as an adjuvant or as a last resort before incapacitating and morbid symptoms.

Further studies are required in order to draw up a better analysis of the effectiveness of certain active ingredients and to make a distinction between the various studies with contradictory results.

Ethical Approval and Consent to Participate

The Author guarantees that the Contribution to the Work has not been previously published elsewhere or that if it has been published

in whole or in part, any permission necessary to publish it in the Work has been obtained and provided.

The Author declares that any person named as co-author of the contribution is aware of the fact and has agreed to being so named.

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