

Chronic Orofacial Pain Management: A Narrative Review of Pharmacological and Promising Therapy

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Abstract

Chronic orofacial pain is a multifactorial stressful condition. It devastates patients' lives and depletes medical and dental services. Assertion of a particular effective pharmacological treatment is difficult due to psychological involvement and variation of pain etiology. Proper diagnosis plays a crucial role in determining the proper therapeutic agent. Pharmacological therapy is the first-line treatment of chronic orofacial pain with multiple drug classes to consider. This review aimed to focus on temporomandibular joint-related chronic orofacial pain as a common dental practice type of chronic pain and trigeminal neuralgia. Highlighting their effective and available pharmacological treatment and promising therapies. For mild-to-moderate pain, nonsteroidal anti-inflammatory drugs are preferred; however, pain chronicity requires another class that tends to modulate neurology- and psychology-associated factors. Common in-practice drugs are antidepressants and anticonvulsants. In most instances, the combination of different pharmacological treatments with a diverse mechanism of action is required for better pain control and reduced monotherapy-related adverse reaction. Opioids should reserve to severe pain and as dual therapy. Palmitoylethanolamide is a promising nutritional therapy that needs further research to establish its effect and safety.

Keywords: Chronic pain, orofacial pain, palmitoylethanolamide, TMJ, trigeminal neuralgia

INTRODUCTION

Chronic orofacial pain is one of life's distressing problems. It is a long-standing pain with episodes of sharp acute flare up that rises patients' and health providers' concerns.^[1] It is a common problem with a prevalence of 7%.^[2] Patients' lives and their psychological status are highly affected by the long period of discomfort and unsatisfactory management. Chronicity of pain is the leading cause of disability and medication abuse with a management cost higher than that of cancer.^[3,4]

Although pain generally has sensory and psychological constituent, chronic pain has a significant psychological involvement that interferes with patients' perception of pain.^[5] This complexity of perception challenges diagnosis and impacts the treatment plan. The classification of chronic orofacial pain carries many facets, according to the etiology, orofacial pain could be odontogenic or nonodontogenic. Though, the nonodontogenic type is more difficult to diagnose and treat.^[6] On the basis of

anatomical structure, chronic orofacial pain could be of musculoskeletal, neuropathic, or neurovascular origin. Musculoskeletal pain involves temporomandibular joint (TMJ) and masticatory muscles, whereas the neuropathic type embraces cervical or peripheral nerve derangement such as trigeminal root disorders. Nevertheless, pain perception might be localized or it radiates to anatomically related sites.^[5,7] Pathologically, chronic orofacial pain is usually inflammatory, besides idiopathic pain.^[1,2]

Pharmacological treatments are still the first-line treatment strategy for chronic orofacial pain. A wide variety of analgesics is in use such as nonsteroidal anti-inflammatory drugs (NSAIDs), steroids, local anesthetics, and opioids.^[1,8] However, due to the chronicity of pain,

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Submission: 04-Dec-2022 **Accepted:** 21-Dec-2022 **Published:** 27-Apr-2023

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How to cite this article: Al-saadi MA. Chronic orofacial pain management: A narrative review of pharmacological and promising therapy. *Med J Babylon* 2023;20:24-7.

Access this article online

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DOI:
10.4103/MJBL.MJBL_312_22

its behavior, and drugs associated adverse reactions, these drugs are difficult to prescribe alone or for a long duration.^[9] Furthermore, another class of drugs appeared to the fore such as antidepressants, antiepileptics, and nutrients. These adjuvants prove their efficiency for chronic pain managements, particularly for old patients.^[10,11]

This review aims to focus on TMJ-related chronic orofacial pain as a common dental practice type of chronic pain and trigeminal neuralgia. Highlighting their effective and available pharmacological treatment and promising therapies.

TEMPOROMANDIBULAR JOINT CHRONIC PAIN

Chronic pain of temporomandibular area is a common orofacial pain. Pain might be related to joint disorders, masticatory muscles, or both. Psychological factors are highly implicated with this type of pain and have a great impact on pain chronicity. Other comorbidities like headaches and migraine are highly associated and interfere with proper diagnosis and treatment.^[4,12,13]

Joint disorders (arthralgia) owing to disc instability, rheumatoid arthritis, and other osteoarthritic diseases require accurate diagnosis as a result of multiple structure inclusion of pain. Instead, the pain of masticatory muscles could be diagnosed by muscle palpation.^[14,15]

Chronic pain of arthritic type is treated with NSAIDs, particularly drugs having long half-lives such as naproxen or meloxicam. Though, NSAIDs should not be prescribed for more than 2 weeks. Adverse reactions interfere with their long prescription, as they are highly associated with gastrointestinal, renal, and cardiovascular adverse effects when given for more than 2 weeks. These adverse effects confine NSAIDs use for acute mild-to-moderate TMJ pain without neurogenic involvement.^[16,17]

On the other hand, corticosteroids show great efficiency due to their effectiveness and possibility for local intra-articular administration. Indeed, corticosteroids are potent and efficient anti-inflammatory drugs but with a wide range of complex side effects that limit their prescription, especially for patients with a medical history of chronic systemic diseases.^[18,19] The principle mechanism of action of corticosteroids is anti-inflammatory effect by terminating synthesis of inflammatory mediators from the arachidonic acid step; allowing them to be more effective than NSAIDs. Platelet-rich plasma and hyaluronic acid are newer treatments for osteoarthritic TMJ conditions with promising effective results; however, more studies require to prove their effectiveness and safety.^[20]

Pain of muscular origin (myofascial pain) could be treated with muscle relaxants whether peripheral or central relaxant.^[17,21] Cyclobenzaprine, methocarbamol, orphenadrin, and other muscle relaxants prove their effectiveness in relieving skeletal muscle spasm associated

with TMJ problems. Cyclobenzaprine improves treatment outcome, range of jaw movement, and pattern of sleep in patients having TMJ chronic pain. However, central muscle relaxants are highly sedative and impair cognition, which requires lowering the prescribed dose and bedtime delivery.^[19,22]

Generally, monotherapy is seldom effective in chronic pain. Multiple drug prescriptions with physiotherapy were found to be effective noninvasive management of chronic TMJ pain.^[23,24] Antidepressants, anticonvulsants, and central muscle relaxant play an important role in pain modulation and reduce psychological impact through the potentiation of GABAergic pathway and reduction of excitatory neural pathways.^[25] Unspecified orofacial pain with TMJ correlation might be well managed with these drugs. However, it is difficult to specify a particular group.

To sum up, chronic TMJ pain challenges medical and dental services and requires a complete understanding of pain origin and behavior. Furthermore, a complete knowledge about safe and effective drugs is mandatory. Regarding prescribing analgesics with high margins of safety and tolerability, NSAIDs with gabapentin or pregabalin show more safety and effectiveness in chronic pain management compared with opioids or benzodiazepines and conceder as the first line in the management of pain except for trigeminal neuralgia.^[21,26] Unfortunately, limited evidence from well-organized clinical trials complicates the assertion.

TRIGEMINAL NEURALGIA

Pain of trigeminal nerve is an intense type of pain result from irritation of the fifth cranial nerve or its branches. Irritation could be due to tumor impingement, vascular pressure, or other neuropathies or idiopathic. Patients describe the pain as a shock and burning sensation of short duration. However, depending on the origin, pain can progress to chronic with parasthesia or auditory and corneal loss of reflexes up on clinical examination.^[27-29]

The available effective first-line treatment for trigeminal neuralgia is carbamazepine. Starting with low doses shows effectiveness in 80% of cases.^[30] On the other hand, oxcarbazepine is considered better tolerated.^[31] Whereas lamotrigine, gabapentin, and muscle relaxants can be considered the second-line pharmacological treatment for trigeminal neuralgia.^[32] Novel treatments include botulinum toxin A and local anesthesia injection to the site of pain. These treatments provide minimally invasive technique with lower adverse effects and a long duration of pain relief.^[33] However, it is difficult to point out an effective monotherapy due to a lack of sufficient evidences from well-controlled randomized trials and uncertain pain origin.^[31,34]

For severe chronic pain not responded to previous treatment options, opioids are considered a suitable choice.

Selection of the best one depends on multiple factors including the severity of pain, patients' age, availability of combination drugs, and patients medical history with opioids.

Tramadol was found to be effective for chronic neuropathic pain. It has a mild tendency to dependence, in addition to dual mechanism of pain modulation. Tramadol manages pain centrally by the classical opioid agonistic mechanism on opioid receptors as well as, and it inhibits the neuronal reuptake of noradrenaline and serotonin in a manner similar to that of antidepressants. Tramadol is actually a multimodal drug to consider in severe chronic pain management.^[32,35] However, tramadol should be prescribed with caution for patients having a history of dependence, taking antidepressants, antipsychotic drug, or another type of opioid due to risk of seizure.^[36] Chronic severe pain with neuropathic association requires a combination of treatment to manage the nociceptive and neuropathic involvement.

PROMISING TREATMENTS

The available pharmacological treatment for chronic orofacial pain is still perplexing. The safety of NSAIDs, opioids, and anticonvulsants is not asserted in addition to insufficient development of novel effective therapy. Accordingly, nutrients needed to investigate rigorously for their efficiency in pain management.^[37]

Among the investigated nutrients, palmitoylethanolamide was found effective in the treatment of neuropathic pain.^[38] Palmitoylethanolamide is an endogenous free fatty acid amide increased during inflammation. It has multimodes of action including cannabimimetic effect without direct stimulation of cannabinoid receptors, agonistic effect on peroxisome proliferator-activated receptor- α , and transient receptor potential vanilloid type 1 and inhibiting mast cell activity as well as reducing inflammatory mediators activities and proliferation.^[39,40] This drug show promising therapy for chronic pain of inflammatory origin without serious adverse reactions.^[41,42] It is available as a food supplement for medical purposes.

Several studies prove the efficiency of palmitoylethanolamide in managements of chronic pain as adjuvant or as monotherapy for the treatment of low back pain, chronic pain of critically ill older patients, and chronic prostatitis/chronic pelvic pain syndrome.^[43-45] Regarding chronic orofacial pain management, a triple-blinded randomized control trial including 24 patients was conducted to evaluate the efficiency of palmitoylethanolamide versus NSAIDs and found effective in inflammatory TMJ pain.^[46]

However, the available studies are not enough to estimate the beneficial and harmful effects of palmitoylethanolamide in orofacial pain management, which require well-designed randomized, placebo-controlled trials and much

more research to be done on it as a potential option for nonopioid pain treatment.

CONCLUSION

A combination of drugs is recommended to modulate pain and reduce monotherapy-associated adverse reactions. Mild-to-moderate TMJ's pain of inflammatory origin can be managed with long-acting NSAIDs in combination with safer anticonvulsants and muscle relaxants. Opioids should be set aside for severe pain, selecting the one with a mild tendency to dependence. The first-line treatment of trigeminal neuralgia is still carbamazepine or oxycarbamazepine. Palmitoylethanolamide is a promising alternative therapy for chronic orofacial pain with acceptable safety and efficiency. Further researches are mandatory to confirm.

Ethical consideration

Not applicable.

Financial support and sponsorship

Not applicable.

Conflicts of interest

There are no conflicts of interest.

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