PHARMACOLOGIC THERAPY IN TEMPOROMANDIBULAR DISORDERS

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PHARMACOLOGIC THERAPY IN TEMPOROMANDIBULAR DISORDERS: A MINIREVIEW

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Abstract

The temporomandibular disorders (TMD) etiology is multifactorial and it affects the most important functions, such as eating, speaking, and facial expressions, and are usually accompanied by pain which results in distress for the patient. Despite the extensive studies in the management of TMD, which is commonly a multidisciplinary approach and the most commonly used steroidal or nonsteroidal anti-inflammatory, myorelaxant, tricyclic antidepressants, anticonvulsants and anxiolytics have been proven to be successful for related inflammatory, disc interference disorders only and neuropathic pain, but are still not an appropriate solution for definitive treatments and still carries risk due to their side effect profiles. Taking this into consideration there is still an emerging need to investigate the main pharmacological approaches for the appropriate management of the resulting acute and chronic pain. In this regard, many studies have been conducted so far to provide the role of pharmacotherapy on TMD. Therefore, in this review, we have summarized the current scientific evidence which supports the most common available safe, and effective drug treatments in the TMD.

Keywords: TMD, pharmacotherapy.

Introduction

The temporomandibular disorders (TMD) etiology is multifactorial and it affects the most important functions, such as eating, speaking, and facial expressions, and are usually accompanied by pain which results in distress for the patient (1). TMDs induces pain, joint sounds, mandibular movement problems or jaw function, malocclusion (2). TMD classification is shown in Table 1Patient with TMD experiences also headaches and sleep related problems, with a higher incidence in women's (3). Most common population, like 33% experience at least one TMD symptom, however 3.6-7.0 % have a need for management (4). However, despite the extensive studies in the management of TMD, it is usually considered as a multidisciplinary approach including non-pharmacologic and pharmacologic management. The most commonly used pharmacological agents for the management of TMD symptoms, especially inflammation and pain are, non-steroidal anti-inflammatory drugs (NSAIDs), corticosteroids, muscle relaxants, opioids and other central nervous agents such as anticonvulsants, antidepressant and anxiolytics (5). These agents have been proven to be successful for related inflammatory, disc interference disorders only and neuropathic pain, but are still not an appropriate solution for definitive treatments and still carries risk due to their side effect profiles and reduced or unknown efficacy. Therefore in this mini review, we have summarized their pharmacological actions and most common available treatments, their safety and efficacy in management of TMD.

Table 1. TMD classification based on the diagnostic criteria (Modified from Peck CC et al., 2014)[6]

1 Masticatory Muscle Disorders	1 Protective co-contraction
	2 Local muscle soreness
	3 Myofascial pain
	4 Myospasm
	5 Centrally mediated myalgia
2A Temporomandibular Joint Disorders	1 *Derangement of the condyle-disc complex*
	2. Disc displacements
	3 Disc dislocation with reduction
	Disc dislocation without reduction
2B Structural incompatibility of the articular surfaces	1 Deviation in form
	2 Disc
	3 Condyle
	4. Fossa
	5 Adhesions
	6 Disc to condyle
	7 Disc to fossa
	8 Subluxation (hypermobility)
	9 Spontaneous dislocation
2C Inflamatory Disorders of the TMJ	1 Synovitis/Capsulitis
	1 Retrodiscitis
	2 Arthritides
	3 Osteoarthritis
	4. Osteoarthrosis
	5 Polyarthritides
	6 Inflammatory disorders of associated structures
	7 Temporalis tendonitis
	8 Stylomandibular ligament inflammation
3. Chronic Mandibular hypomobility	1. *Ankylosis*
	2. Fibrous
	3 Bony
	4 *Muscle contracture*
	5 Myostatic
	6 Myofibrotic
	7 *Coronoid impedance*
4. Growth Disorders	1 *Congenital and developmental bone disorders*
	2 Agenesis
	3 Hypoplasia
	4 Hyperplasia
	5 Neoplasia
	6 *Congenital and developmental muscle disorders*
	Hypotrophy
	7 Hypertrophy
	8 Hypertrophy
	9. Neoplasia

2. Pharmacological Treatment of Temporomandibular Disorders

Pharmacologic therapy is needed for controlling inflammation, pain (acute or chronic), and muscle spasm as main symptoms of TMD. The most common pharmacological treatment is usually empirical and is divided into four different groups, including, anti-inflammatory drugs including nonsteroidal anti-inflammatory drugs (NSAIDs), corticosteroids, and systemic nervous system action drugs such as muscle relaxants, opioids, anticonvulsants, antidepressants, anxiolytics, and other target actions including hyaluronic acid and glucosamine and bioactive and traditional plants (7).

2.1 NSAIDs

Based on their anti-inflammatory and analgesic pharmacological properties, NSAIDs are the first-line medication for the treatment of pain and inflammation in TMD, with a focus on disc displacement, synovitis, arthritis, and capsulitis (8). These agents can be used also in the management of pain from masticatory myalgia and myofascial pain (9). The most common NSAIDs used are diclofenac, naproxen sodium, ibuprofen, celecoxib, piroxicam etc (10), and the period of use for such indication consists of a minimal 2 week period, suggesting long-term treatment to obtain the clinical effects (11). Despite their beneficial actions they possess gastrointestinal, renal, and cardiovascular side effects (12). The most common gastrointestinal and cardiovascular side effect is bleeding, ulceration, and risk for atherothrombosis, which alerts close monitoring during the period of their use (13). Even though the gastrointestinal effects are diminished with selective cyclooxygenase-2 inhibitors (COXIBs) they pave the road more for cardiovascular-related side effects, which faded their clinical use perspective due to safety concerns (14). They interfere with other drugs in increasing toxicity, including methotrexate, lithium, and reduction of antihypertensive drug effects (diuretics and ACE inhibitors) and increase anticoagulation effects (15). In addition to this NSAIDs are combined with derivates of p-aminophenol, such as acetaminophen or paracetamol to provide synergic effects in controlling acute TMD pain (16).

2.2 Corticosteroids

Corticosteroids are potent anti-inflammatory drugs in the management of moderate to severe TMD and are mainly administered as locally injected in the joints with intra-articular injections, topically or orally (17). Their use needs to be limited for no more than a sustained two-week period due to an increase of susceptibility for infections due to their immunosuppressive actions, hyperglycemia, osteoporosis, suppression of hypothalamic-pituitary-adrenal axis, etc (18). In order to minimize their side effects, they must be limited to a short period of use with a local intra-articular injection (19). Therefore, methylprednisolone, triamcinolone acetonide, betamethasone, dexamethasone alone or in combination with lidocaine, hyaluronic acid, and NSAIDs have been proven to improve symptoms of TMD (20). However, due to their poor side effect profile, with a focus on degenerative changes in joints, their use needs to be limited for every 3 to 4 months (21, 22).

2.3 Muscle Relaxants

Muscle relaxants reduce the skeletal muscle tone associated with higher masticatory and cervical muscle contraction and are used in a patient with TMD related to chronic orofacial pain or muscle-related symptoms (23). This includes central muscle relaxants cyclobenzaprine (similar structure to tricyclic antidepressants), carisoprodol, carisoprodolmetaxalone, methocarbamol, tizanidine, diazepam, and peripheral such as baclofen, botulinum toxin A, dantrolene (24). Central muscle relaxant use needs to be limited during the driving period and due to their sedative properties are in preferred in the lowest dosage before sleeping, and also their anticholinergic side effect profile need to be monitored (25). Their general use consists of a continuous 30 day period of use, followed by 2 weeks as a washout period, and return for additional 2-3 months if necessary (9). However, despite their meaningful clinical data, their long-term clinical use and efficacy are still not clear (16). For example, botulinum toxin alone or combined use is not supported by the currently available evidence in subacute and chronic pain (26).

2.4 Opioids

Opioids or narcotic analgesics are characterized and used for controlling more moderate to severe pain from TMD, where the other drugs are found ineffective (27). These agents are recommended to be limited to short-term and acute pain control, due to knowing the risk due to their side effect profile such as respiratory depression, sedation, constipation, and the most common pharmacological concerns regarding the tolerance and physical dependence caused by this agent (28). Despite that these agents are not considered as first-line therapy for managing TMD-associated pain, the most commonly prescribed opioids in TMD are oral use of hydrocodone, oxycodone, and codeine (4). However, fentanyl patches or intra-articular morphine injection can be also be considered when the oral route is not a reasonable option (29). The prescription of this agent should be carefully considered and limited due to special concerns of patients with substance use disorders, with a major focus in the chronic course of therapy since there are no final conclusions of long-term therapeutically benefits and due to tolerance and abusing tendency (30).

2.5 Central Nervous System Drug Agents

The central nervous drug agents used in TMD are anticonvulsants, antidepressants, and anxiolytics these agents are used to control pain, gabapentin, pregabalin as an anticonvulsant are used to treat pain and tenderness in masticatory muscles, with a focus in mainly neuropathic pain (31, 32). In addition, antidepressant drugs as alone or in combination with anticonvulsants, including mainly tricyclic antidepressants and serotonin-noradrenalin re-uptake inhibitors, serotonin selective re-uptake inhibitors are used to manage TMD-related bruxism, muscle pain-related sleep disorders, fibromyalgia, chronic pain in the orofacial region which might have depression or sleep as a comorbid disease. The common use of antidepressant drugs in TMD are amitriptyline, nortriptyline, desipramine, fluoxetine, paroxetine (33). These drugs need to be used with caution in a patient with cardiovascular diseases and concomitant use with monoamine oxidase Inhibitors (34). In the end, the anxiolytics include mainly benzodiazepines specifically: diazepam and clonazepam. Drugs in the central nervous system need to be prescribed with caution from the dental community and need to be in consultation with physicians to ensure their diagnosis, medical stability, and management of the side effects (35).

3. Other Complementary Alternatives

Despite the current presence of approved pharmacological treatments in the management of TMD, there are some complementary alternatives that are mainly empirical treatments without strong evidence to support their effectiveness and that are being used nowadays, including hyaluronic acid, glucosamine, and traditional agents (7, 36, 37). Hyaluronic acid is commonly used in combination with glucocorticoids via intra-articular injection for the treatment of TMD.This controls the myofascial pain within the masseter muscle, restores the viscoelasticity of synovial fluid in the inflamed joins, and creates lubrification (38). In addition to this, glucosamine has been considered an additional alternative due to its inhibition properties in cartilage decomposition and promotion of proteoglycan synthesis. This has been considered to be a safe option in higher dosage or in combination with hyaluronic acid (39). The most common plants which are being demonstrated efficacious in the different preclinical and clinical study investigations are Tephrosia toxic area, Euphorbia bicolor Latex Extract, Moringa oleifera, Grape Seed Extract, Purple Corn Extract, Resveratrol, Curcumin, Cocoa, Lectins, Terpenes, etc (7).

Conclusion

In this review, we summarized the knowledge regarding the pharmacological treatments of TMD, starting from the priority of treatment up to the recent developments and complementary alternatives. There are different pharmacological groups of treatments that are used alone or in combination with other modalities such as physical therapy or oral appliances. The current pharmacological agents help to control inflammation, pain and provide improvement of the symptoms but not a definitive cure. Despite the long history of their use, there are still difficult to prioritize them and specify their main indications. However, anti-inflammatory drugs, NSAIDs, and corticosteroids are frequently used followed by opioids, muscle relaxants, anticonvulsants, antidepressants, and anxiolytics. Careful consideration should be in their dosage and length of treatments, drug interactions due to their side effect profile of anti-inflammatory drugs, physical dependence, and tolerance in opioids, physician monitoring with other central nervous action drugs with other comorbidities.

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