The Efficacy of Pharmacologic Treatment of Temporomandibular Disorders

Gary M. Heir, DMD

KEYWORDS

• Pharmacotherapy • Temporomandibular disorders • Nociception • Peripheral sensitization
• Myofascial pain

KEY POINTS

- Successful pharmacologic management of temporomandibular disorders depends on an understanding of the pain mechanisms involved.
- Knowing why to prescribe is as important as knowing what to prescribe.
- The source of the pain determines the therapeutic choice.
- Improper diagnosis is a common cause of therapeutic failure.
- A common mistake is the use of peripherally acting analgesics for centrally mediated pain.

INTRODUCTION

Epidemiologic data indicates that 33% of the general population has at least one symptom of a temporomandibular disorder (TMD); 6% to 7% have TMDs severe enough to seek treatment. Pharmacologic therapy is commonly used as part of the management of these conditions. To accomplish this successfully requires an understanding of the pain mechanisms involved. Failure to understand these mechanisms leads to inaccurate diagnoses and ineffective, delayed, or harmful treatment.

Although it is the responsibility of the provider to accurately diagnose and treat the various TMDs, it is equally important to know when not to treat. Knowing why a treatment is provided is as important as knowing how it should be administered. Equally important is knowing what the medication does to the patient and what the patient does to the medication. This includes knowing the therapeutic target of any medication prescribed, its side effects, any drug interactions, and the medical history of the patient.

This article provides a brief review of pain mechanisms, identifies pharmacologic targets, and discusses the efficacy of pharmacotherapy routinely used for pain associated with TMDs and orofacial pain disorders.

NOCICEPTION

Nociceptors in the temporomandibular joint (TMJ) and masticatory muscles, when activated, transduce the stimulus into an electrical signal that is transmitted via an action potential to the trigeminal nuclei. As nociceptors synapse within the dorsal horn, they pass the signal on to second-order neurons via neurotransmitters released into the synaptic space. Activation of second-order neurons transmits noxious impulses to various sites within the central nervous system and brain, primarily through the medial and lateral thalamus, where

Disclosure: The author has nothing to disclose.
Department of Diagnostic Sciences, Center for Temporomandiublar Disorders and Orofacial Pain, Rutgers School of Dental Medicine, Room D880, 110 Bergen Street, Newark, NJ 07101, USA
E-mail address: heirgm@sdm.rutgers.edu

Oral Maxillofacial Surg Clin N Am 30 (2018) 279–285
https://doi.org/10.1016/j.coms.2018.05.001

they are then distributed for further processing. Medications that interrupt or reduce the release of neurotransmitters at the synapse between the first- and second-order neurons inhibit or modulate the pain and thus provide a target for its control.

The brain constructs a scenario from the information received via the nociceptors and determines if the stimulus is harmful, the degree of pain, and the action necessary to minimize the threat of potential injury. Contributions of memory of similar events, or emotional overlay, can result in a diminished ability to inhibit noxious input and pain facilitation by affecting the descending pain modulating system. This system regulates the release of excitatory and faciliatory neuropeptides, endogenous opioids, and has other functions that influence the perception of pain.

This simplistic description points to several targets for medications, such as peripheral receptors, primary afferent neurons, pain inhibition at the dorsal horn, the descending pain inhibitory system, and the brain.

PERIPHERAL AND CENTRAL SENSITIZATION

In a patient with a TMJ or myofascial pain there is a release of inflammatory mediators that sensitize the peripheral nociceptors. In this case, the administration of nonsteroidal anti-inflammatory drugs (NSAIDs), acting peripherally, reduces inflammation, decreases primary afferent sensitization, and results in pain reduction.

The process of peripheral sensitization typically ends when the source of pain is withdrawn, or the healing process is complete. However, in some cases, pain persists. In such instances, chronic noxious signals reach the central nervous system resulting in a phenomenon referred to as central sensitization, a process of strengthening synaptic connections and signal transmissions. Central sensitization results in a cascade of events, such as amplification of noxious signals, while at the same time reducing the efficiency of pain inhibition. This scenario points to additional pharmacologic targets. Treatment with anti-inflammatory drugs alone results in only partial success because the additional targets are more centrally located. The original injury may even have resolved, but central sensitization continues to drive chronic pain. Therefore, knowing the target of the treatment and classifying analgesics by the site of action, results in a better outcome (Box 1).

Box 1
Classification of analgesics by site of action

- Inhibits peripheral sensitization
  - NSAIDs
    - Cyclooxygenase 1 and 2 inhibitors
      - Blocks prostaglandin synthesis
      - Blocks or reduces afferent nerve transmission
  - Anticonvulsants
    - Gabanoids (neurontin, pregabalin)
      - Controls calcium influx
      - Reduces release of sympathetic excitatory amino acids
  - Antiepileptic drugs
    - Carbamazepine
      - Axonal membrane stabilizer
      - Sodium channel blocker
      - May stimulate release of serotonin and possibly act as a reuptake inhibitor facilitating pain inhibition
- Facilitates endogenous inhibitory mechanisms
  - Antidepressants
    - Serotonin reuptake inhibitors
    - Serotonin/noradrenaline reuptake inhibitors
  - Reduces signal transmission at the dorsal horn
- Presynaptic or post-synaptic inhibitory effect
  - Opioids

CHRONIC PAIN

If pain assumes a chronic nature, more centrally mediated mechanisms take effect, for which peripherally acting analgesics have less efficacy. The clinician must recognize the involved alterations in pain characteristics, such as quality, duration, and intensity, as peripheral pain becomes more continuous, diffuse, and difficult to localize. In such instances, the possibility of new targets for treatment emerges.

Chronic pain is not a symptom. It is a disease, often amplified by a sense of unpredictability of treatment. The lack of an understanding of the meaning of the symptoms, and negative expectations of recovery, lead to anxiety and depression, embellishing the pain response. Pain is perceived at the original site even though healing may be complete and no additional pathology has occurred. Stimuli are amplified, causing the perception of nonnoxious input as painful in this