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DIFFERENT ASPECTS OF OROFACIAL PAIN (PART II)
NON-STEROID ANTIINFLAMATORY DRUGS FOR CHRONIC TEMPOROMANDIBULAR PAIN TREATMENT

RAZLIČITI ASPEKTI OROFACIJALNOG BOLA (DRUGI DEO)
NESTEROIDNI ANTIINFLAMATORNI LEKOVI U LEČENJU TEMPOROMANDIBULARNOG BOLA

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Ključne reči
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Abstract

Nonsteroidal anti-inflammatory drugs, usually abbreviated to NSAIDs but also referred to as nonsteroidal anti-inflammatory agents/analgesics (NSAIAs) or nonsteroidal anti-inflammatory medicines (NSAIMs) — are a class of drugs that provide analgesic and antipyretic (fever-reducing) effects, and in higher doses, anti-inflammatory effects.. Although the use of analgesics for acute orofacial pain is well documented through hundreds of controlled clinical trials, the use of a broad spectrum of drugs for chronic orofacial pain is based on few studies. Toxicity associated with chronic administration of the drug can occur even in the absence of a therapeutic benefit. Recognition of the chronic adverse renal and gastrointestinal effects of NSAIDs indicates a need to examine critically their use for chronic pain conditions such as temporomandibular disorder (TMD).

INTRODUCTION

Temporomandibular disorders (TMDs) refer to a group of disorders affecting the jaw, temporomandibular joint (TMJ), masticatory muscles and the associated structures that control chewing and moving the jaw. These disorders share the symptoms of pain, limited mouth opening and joint noises (1, 2). Painful temporomandibular disorders (TMDs) are usually treated with physiotherapy, self-exercises, medication-based therapy and splint therapy

Epidemiology

Temporomandibular joint symptoms are relatively common, occurring in 10-25% of the population, although approximately only 5% of people with symptoms will ask for treatment. Temporomandibular disorders may occur at any age, but more frequently in women and persons in early adulthood [1, 3].

Aetiology

TMJ disorders are thought to have a multifactorial aetiology, but the pathophysiology is not explained completely jet. The causes can be classified into two groups: factors affecting the joint itself, and factors affecting both muscles and joint function [2].

A meta-analysis of the literature on TMD published from 1980. to 1992. identified more than 4000 references, but only 55 (1%) were randomized controlled trials [4, 6, 7]. Five of the controlled trials were drug studies, providing an extremely small amount of evidence on which they base generalizations regarding efficacy and toxicity. Many of the studies evaluating pharmacologic treatments are methodologically flawed with heterogeneous patient samples, lack of an adequate control group, and a fail to use standardized methods for measurement of pain and dysfunction. Knowledge of the clinical pharmacology of NSAIDs is

based mostly on studies performed on the oral surgery model. Ibuprofen, the prototype of the NSAID class, has demonstrated analgesic activity over a dose range from 200 mg to 800 mg with a duration of activity from 4 to 6 hours [8]. When given before pain onset, it suppresses the onset of pain and lessens the severity. Ibuprofen suppresses swelling over the initial 2- to 3-day postoperative course when oedema formation associated with the inflammatory process is most prominent. Interactions with the release of 3-day endorphin were demonstrated both intraoperatively during stress-causing surgical procedure and also during postoperative period, suggesting that NSAIDs can modify the neurohumoral response to pain (11,12). The plethora of data from clinical studies that use NSAIDs support these generalizations making them one of the most well-studied drug classes for ambulatory treatment of acute inflammatory pain.

A comprehensive review of the primary literature reveals little scientific support to the benefit of daily use of NSAIDs for chronic orofacial pain treatment; both in standard texts [1] and summaries [8] of expert opinions that provide recommendations or extrapolations from chronic inflammatory conditions such as arthritis. Yet the results of two placebo-controlled studies suggest that NSAIDs are ineffective for chronic orofacial pain. The analgesic effects of ibuprofen, 2400 md daily for 4 weeks, could not be distinguished from placebo in a group of patients with chronic orofacial pain with myogenic origin (9, 13). A similar comparison of piroxicam, 20 mg daily for 12 days, to placebo for TMD pain also failed to demonstrate any therapeutic advantage for the NSAIDs.

Both clinical and animal studies suggest that repeated administration of NSAIDs could develop tolerance. The mean reduction of chronic lower back pain intensity following an initial ibuprofen dose of 1200 mg was 23% [10,14]. Two weeks after administration of ibuprofen 2400 mg daily or placebo, the mean reduction of pain intensity for that dose was fourfold lower in the drug group. The initial low level of response (23%) suggests that lower back pain is not particularly sensitive to ibuprofen and may in part explain the poor response to chronic musculoskeletal pain in the orofacial area. The development of tolerance over 2 weeks suggests a similar process for TMD pain that could make the analgesic response negligible by the end of 4 weeks. Tolerance to diflunisal with repeated administration has been demonstrated in animals without a reduction in the amount of drug in the blood over time after administration of the first dose compared to a dose given after 3 days of diflunisal [9]. This suggests a functional change in the pharmacologic response rather than enhanced pharmacokinetic disposition such that the same amount of drug elicits less analgesia.

The lack of clinical studies to support the efficacy of ibuprofen for TMD contrasts with the growing body of evidence on the potential serious toxic effects of NSAIDs when given chronically at high doses. A short trial of an NSAJD may be considered patients with an apparent inflammatory component to their pain complaint. A lack of therapeutic effect: after a 7- to 10-day trial or the development of any gastrointestinal symptoms should prompt discontinuation of the NSAID (15).

RECOMMENDATIONS FOR USE OF NSAIDS IN DENTSTRY

One of the most widely used drug classes for dental pain are NSAIDs, along with aspirin, acetaminophen, and codeine. They are generally more efficious than other standard drugs in most studies, presumably due to the inflammatory cause of most dental pain and the NSAIDs' prominent antiinflammatory effects, A single dose of 400 mg to 600 mg of ibuprofen is usually more effective than combinations of aspirin or acetaminophen plus an opioid, usually codeine or oxycodone, with fewer side effects which makes it preferable for ambulatory patients who generally experience a higher incidence of side effects after using an opioid. Ibuprofen and flurbiprofen also exert a modest suppression of swelling after surgical procedures, providing additional therapeutic benefit but without the potential liabilities of administering a steroid. These considerations and the vast experience gained through 25 years clinical use make ibuprofen the drug of choice for dental pain in patients who do not have contraindications to its use. Limitations to orally administered NSAIDs for dental pain include delayed onset when compared to an injectable opioid, the inability to relieve severe pain consistently, and an apparent lack of effectiveness when given repeatedly for chronic orofacial pain. The best strategy for minimizing pain onset is administration of an NSAID before the induction of COX-2 (cyclooxygenase 2) postoperatively. For patients who do not receive satisfactory relief from a NSAID alone, combining it with an opioid may provide additive analgesia but also more frequent side effects. The optimal balance for an individual patient can be best achieved by supplying them with a NSAID taken by-the-clock and also codeine in a 30 mg dose if needed, titrated one or two tablets to achieve pain relief with minimal side effects. Oxycodone can be given in combination with ibuprofen in a similar manner, whereas a fixed dose combination of ibuprofen 200 mg and hydrocodone 7,5 mg is not sufficient, therefore ibuprofen dose has to be increased [16].

The use of repeated doses of NSAIDs for chronic orofacial pain treatment should be reevaluated considering its apparent lack of efficacy, and the potential for serious gastrointestinal and renal toxicity by repeated dosing. The lack of suitable alternatives predicts the continued use of ibuprofen and other NSAIDs for these patients; their consumption should be time limited and interrupted if serious gastrointestinal or renal toxicity is noted.

Sažetak

Nesteroidni antiinflamatorni lekovi, skraćeno NSAIL ili nesteroidni antiinflamatorni agensi/analgetici (NSAIA), odnosno nesteroidna antiinflamatorna sredstva (NSAIS) je grupa lekova koji imaju analgetičko i antipiretičko dejstvo (snižavaju temperaturu), dok veće doze imaju antiinflamatorno delovanje. Iako je upotreba analgetika za ublažavanje akutnog bola u orofacijalnoj regiji dokumentovana u stotinama kontrolisanih kliničkih studija, ispitivanje velikog broja lekova za ublažavanje hroničnog bola u ovoj regiji je rađeno u svega nekoliko studija. Toksičnost koju uzrokuje hronična primena ovih lekova se javlja i kada nema analgetičkog dejstva. Potrebno je kritički razmotriti upotrebu NSAIL u kontroli hroničnog bola, kao što je temporomandibularni sindrom (TMS), naročito hronične negativne efekte koje imaju na bubrege i gastrointestinalne organe.

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