Pharmacologic treatments for temporomandibular disorders

Raymond A. Dionne, DDS, PhD,[a] Bethesda, Md.
NEUROBIOLOGY AND ANESTHESIOLOGY BRANCH, NATIONAL INSTITUTE OF DENTAL RESEARCH, NATIONAL INSTITUTES OF HEALTH

Drugs are widely used in the management of acute and chronic orofacial pain. Whereas 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 pain is based on very few studies. In the absence of data supporting a therapeutic benefit for a drug used chronically for pain, toxicity associated with the drug can still occur. It is critical, therefore, to assess the balance between therapeutic benefit and safety. This article reviews current evidence supporting the use of several drug classes for temporomandibular disorders (TMD) and identifies therapeutic controversies in need of further research. **(Oral Surg Oral Med Oral Pathol Oral Radiol Endod 1997;83:134-42)**

Pharmacologic intervention in the management of chronic orofacial pain is usually considered adjunctive to definitive treatment on the assumption that more definitive treatments will eventually correct the underlying pathophysiologic process. It is now recognized that many putative dental and surgical therapies for TMDs have not withstood scientific scrutiny, which has led to the use of drugs as the primary intervention for some forms of chronic orofacial pain. Palliative management of intractable pain may also be considered as an indication for pharmacologic management when pain is poorly controlled showing failed treatments such as surgical interventions or when no other treatment is available.

The current literature on the use of drugs for TMDs was reviewed as part of a meta-analysis of the literature published from 1980 to 1992.[1] Although more than 4000 references were identified, only 15% were clinical studies and only approximately 1% (N = 55) were randomized controlled trials, which provide the type of evidence usually considered essential for evaluating the efficacy of a therapeutic modality. Five of the randomized controlled trials identified in this literature search were drug studies that provided an extremely small body of evidence upon which to base generalizations regarding efficacy and toxicity. The author of the meta-analysis concluded that, on the basis of these data, it is not clear whether the therapies currently in use for TMDs provide any benefit over placebo alone.[1]

Many studies evaluating pharmacologic treatments are methodologically flawed. The population of patients with TMDs is heterogeneous; patients with myogenous pain, for example, are often not distinguished in clinical trials from those who have TMJ disorders such as degenerative arthritis or displacement of the meniscus.[2, 3] Observations by clinicians and case series often fail to use standardized methods for measurement of pain and dysfunction. The main evidence of a positive treatment outcome is too often the clinician's impression of improvement or the patients' failure to seek further treatment.[4, 5] Another major weakness in previous studies has been the lack of an adequate control group receiving either a placebo, a drug with known efficacy as a positive control, or no treatment. These deficiencies in study design are particularly significant given the high rate of success reported for manipulations such as placebo splints, placebo drug, sham occlusal equilibration, a positive doctor-patient relationship, and enthusiastically presented treatment.[6-8]

Another factor that may affect the evaluation of treatment outcome to drug therapy is the fluctuating nature of orofacial pain, which may undergo remissions and exacerbations independent of treatment.[9] The high incidence of concurrent psychological problems described in this population may also influence the onset of symptoms, reporting of pain levels, and treatment response.[10-12] Many patients eventually improve even if an initial course of therapy is not successful[13] or if they receive no treatment at all,[9] which suggests that the natural history of this condition may be one of exacerbations and remissions. Such responses may explain the high rate of success reported in loosely controlled studies for many of the therapeutic modalities used for TMDs.

The natural history of therapeutic interventions for the management of pain is illustrated in Figure 1. Novel treatments first described on the basis of initial case reports, case series, or poorly controlled

[a]Chief, Clinical Pharmacology Unit, Neurobiology and Anesthesiology Branch, Division of Intramural Research, National Institute of Dental Research, National Institutes of Health.

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Table I. Pharmacologic modalities described in the literature for the treatment of TMD

Analgesics
NSAIDs
Opioids
Corticosteroids
Iontophoresis
Intracapsular Injections
Antidepressants
Muscle Relaxants
Sedative-Hypnotics
Anxiolytics
Hypnotics

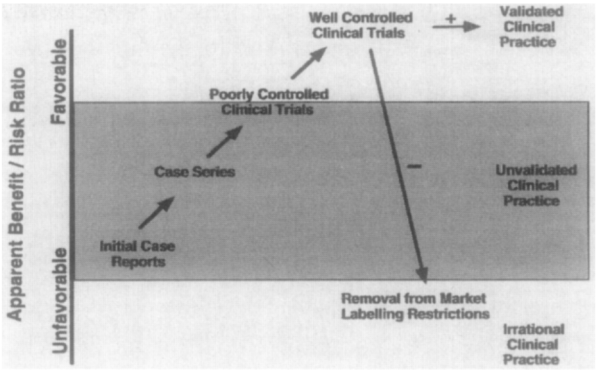

Fig. 1. Natural history of therapeutic modalities for TMD: increasingly favorable reports based on uncontrolled or poorly controlled trials superceded by well-controlled trials that demonstrate whether a treatment is a validated clinical practice or an irrational clinical practice. Most pharmacologic modalities for TMD should be considered as unvalidated clinical practices that have not been subjected to scientific validation in the form of well-controlled clinical trials.

clinical trials usually appear to have a favorable benefit-to-risk relationship, that is, the benefit to a group of patients exceeds the adverse effects that can occur in any individual patient. Following several well-controlled clinical trials, a number of alternative interpretations are possible. If several well-controlled clinical trials indicate that the treatment is effective and has minimal toxicity, it is then considered to be a validated therapeutic practice. An example of this outcome is the use of nonsteroidal antiinflammatory drugs (NSAIDs) for the control of acute orofacial pain. It the treatment is found not to be effective or toxicity becomes evident, then the drug is removed from the market (which occurred with zomepirac in the 1970s) or labeling restrictions are imposed (as was done for ketorolac more recently). Unfortunately, most drugs that are used for TMDs fall into the category of unvalidated clinical practices. This does not mean that they don't have some therapeutic value; rather, they have not been subjected to the well-controlled clinical trials that would allow the biomedical community to make the determination either that use of these drugs is a validated clinical practice with a therapeutic value that exceeds their potential for toxicity or, possibly, that their use represents an irrational clinical practice that should not be continued.

A wide variety of drug classes have been described for chronic orofacial pain, ranging from short-term treatment with NSAIDs and muscle relaxants for pain of muscular origin to chronic administration of antidepressants for less well-characterized pain (Table I). In general, enthusiastic claims of efficacy on the basis of clinical observations have been superceded by equivocal findings of efficacy and belated recognition of adverse effects or toxicity associated with long-term administration (e.g., elevated incidence of kidney failure with chronic NSAID use). The pharmalogic management of TMDs rests on the same principles that apply to all other drugs: demonstrated efficacy for the indication (chronic orofacial pain), an acceptable side effect liability, and safety when given for prolonged periods.

NONOPIOID ANALGESICS

Nonopioid analgesics comprise a heterogeneous class of drugs including the salicyclates (aspirin and diflunisal), para-aminophenol derivatives (primarily acetaminophen), and the NSAIDs (ibuprofen and many others). Despite their diverse structures, nonopioid analgesics have similar therapeutic effects, oral efficacy, and similar side effect profiles. Nonopioid analgesics are better tolerated than opioids by ambulatory patients, have less sedative effects, and are much less likely to produce tolerance or dependence. Conversely, the hazards of long-term administration of these drugs are belatedly being recognized as increased incidences of serious toxicity to the gastrointestinal tract and kidneys occur.

A review of the primary literature reveals few well-controlled studies, which suggests that daily use of nonopioid analgesics offers benefit for chronic orofacial pain.[14] Standard texts[15] and summaries of expert opinion[16] often provide recommendations for specific drugs and doses but either do not provide support for these recommendations or extrapolate 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 mg per day for 4 weeks, could not be separated from placebo in a group of patients with chronic orofacial pain characterized as myogenic in origin.[17] The com-

parison of piroxicam, 20 mg daily, to placebo for TMD pain (N = 28) also failed to demonstrate any therapeutic advantage for the NSAID.[18]

The lack of clinical studies to support the efficacy of NSAIDs for TMD becomes important when contrasted with the growing body of data on the serious toxic effects of NSAIDs when they are given chronically. Suppression of prostaglandins by aspirin and NSAIDs is not limited to the site of injury and also results in alteration of normal function in the gastrointestinal mucosa and kidney blood flow. The resultant changes in the gastrointestinal tract can manifest as localized irritation, ulceration, occult blood loss, or even frank hemorrhage. Retrospective studies have established an association between increased risk of upper gastrointestinal bleeding and ingestion of aspirin or NSAIDs.[19-21] A meta-analysis of 16 controlled studies suggests that users of NSAIDs have a threefold greater risk of developing serious adverse gastrointestinal events than nonusers and that this risk is greater for those over 60 years of age.[22]

NSAIDs alter kidney blood flow by interfering with the synthesis of prostaglandins in the kidney involved in the autoregulation of blood flow and glomerular filtration.[23] It is estimated that detectable kidney function abnormalities will develop in approximately 1% (500,000) of the persons exposed to NSAIDs yearly (approximately 50 million Americans).[24] The inhibitory effects of NSAIDs on kidney prostaglandin production leads to acute, reversible kidney failure in 0.5% to 1% of patients who take NSAIDs on a chronic basis.[24] The most significant kidney-related side effect of NSAIDs is hemodynamically mediated acute kidney failure, which occurs in persons with pre-existing reduced kidney blood perfusion. A retrospective analysis of patients with end-stage kidney disease requiring hemodialysis demonstrated an association between chronic NSAID use (more than 5000 pills over a lifetime) and a ninefold increased risk of end-stage kidney disease.[25] Aspirin was not associated with increased risk, but heavy acetaminophen use (also defined as more than 5000 pills over a lifetime) was associated with an approximately 2.5-fold increase in kidney failure requiring hemodialysis.

Therapeutic recommendations

The lack of clinical evidence demonstrating a therapeutic effect for nonopioid analgesics in the symptomatic treatment of chronic orofacial pain must be weighed against the potential for serious toxicity with chronic use. A short trial of an NSAID may be considered in patients with an apparent inflammatory component to their pain complaint. A lack of therapeutic effect after a 7- 10-day trial or the development of any gastrointestinal symptoms should prompt discontinuation of the NSAID. Patients with risk factors for gastrointestinal or kidney disease should be managed cautiously with NSAIDs or acetaminophen and should not take these drugs for prolonged periods of time.

OPIOIDS

The long-term administration of opioids for nonmalignant pain is controversial. As recently as 5 years ago it was suggested that there is no place for opioids in the treatment of chronic benign pain.[26] Several reports published since then, however, support the long-term administration of opioids for chronic nonmalignant pain. An open label study in 100 patients with chronic pain for whom all other possible treatments had failed demonstrated good (51%) or partial (28%) pain relief from sustained-release opioids with no signs of respiratory depression.[27] A more controlled trial evaluated sustained-release oral codeine in 46 patients enrolled in a 7-day double-blind trial. Patients receiving the opioid reported significant analgesia and improvement on a pain disability index but a higher incidence of nausea in comparison with placebo.[28] A recent study evaluated the use of oral morphine (up to 60 mg twice a day) in a randomized, double-blind crossover study of 6 weeks' duration in patients nonresponsive to codeine, NSAIDs, and antidepressants. The opioid produced significant pain relief with little effect on cognitive function or memory.[29] Although patients with head and neck pain were included in these studies, no direct evaluation was made for long-term administration of opioids for patients with TMD.

The long-term use of opioids in clinical practice was assessed in a survey of randomly selected physicians (N = 1912).[30] The results of this survey indicate that prescription of opioids for long-term administration is widespread for the treatment of nonmalignant chronic pain in medical practice. Surprisingly, physicians in states that require multiple copies of prescription forms indicated a greater frequency of opioid prescriptions, which suggests that drug regulations are not a barrier to the use of opioids in clinical practice.

Most concern over the chronic use of opioids centers on the potential for "addiction." The term "addiction" implies the development of physical dependence and tolerance requiring continued opioid use with increasing doses. Physical dependence or the development of tolerance in a therapeutic context do not necessarily equate with addiction, because the maladaptive behavior associated with addiction is not

expected. Drug seeking is not necessary if the drug is medically available. Similarly, cycles of intoxication and withdrawal symptoms should not occur with sustained release formulations.

Therapeutic recommendations

Considering the possible serious adverse effects associated with NSAIDs when they are given chronically and the absence of effective therapies for some forms of TMDs, the use of opioids should be further evaluated. Initial studies should focus on patient populations with intractable pain, such as patients for whom TMJ implants have failed, with a parallel control group and, ideally, an active placebo to better blind the subjects to the treatments. Sustained release formulations would minimize cyclic fluctuations in pain associated with standard formulations. The chronic use of opioids for patients with TMDs before scientific and professional consensus is reached on their use requires careful patient selection to rule out drug-seeking behavior or other personality disorders; careful monitoring to individualize dose, thereby minimizing side effects and dose escalation; and careful attention to regulatory procedures.

CORTICOSTEROIDS

Corticosteroids have been injected directly into the TMJ and applied topically in an attempt to reduce the pain and dysfunction associated with TMDs. In a 4-week study of three treatment groups totaling 41 patients with TMD, a corticosteroid, hyaluronic acid, or placebo was injected directly into the TMJ. All groups showed reduced clinical signs of dysfunction, but the corticosteroid and hyaluronic acid groups showed a greater decrease in the number of painful muscles and a marked increase in the ability to open.[31] In another study of 16 patients who were treated with intra-articular injections of corticosteroid and then followed up for 8 years, the authors reported an improvement in clinical signs of TMD. In addition, they reported radiographic findings suggesting remineralization of areas of condylar erosion.[32] The long-term effect (2 years) of occlusal treatments or intra-articular injections consisting of corticosteroids and local anesthetic were compared in two groups of 15 patients. Both treatments were reported to have a prolonged palliative effect on pain and TMJ dysfunction. Conversely, other clinicians have reported adverse effects on the TMJ as a result of chronic corticosteroid administration.[33, 34]

The iontophoretic administration of steroids has been recommended by some experts and clinicians (see Murphy's article in this issue). It is hypothesized that iontophoresis will result in higher drug levels at the site of injury or pain, such as the TMJ, by applying an electric current to ionized drug solutions. Reid et al.[35] compared iontophoresis with dexamethasone in a lidocaine vehicle with placebo for TMD following three sessions of drug administration over 5 days with 7 and 14 days follow-up. Both groups of subjects showed improvement over the course of therapy and continued to report less pain and improved range of motion at the 7- and 14-day follow-up in comparison with placebo (Fig. 2). These data illustrate the dichotomy of opinion that often exists between clinical observations and the results of a controlled clinical trial. If one compared the pain and dysfunction reported by all patients before treatment and at the follow-up appointments, it would appear logical to conclude that the improvement was the result of the treatment being evaluated, in this case the iontophoretic application of a steroid to the TMJ. Evaluation of the drug therapy in the context of a controlled trial, as illustrated by the dexamethasone and placebo groups, leads to the opposite conclusion, that the drug had no detectable therapeutic effect. Alternative interpretations include cyclic fluctuations in symptomology over time and patient expectations of improvement from receiving medications applied by a novel method in a therapeutic environment. These data also illustrate that reliance on expert opinion, textbook citations, poorly controlled clinical trials, or extrapolation from other indications for a drug or route of administration are inadequate substitutes for reliable evidence from a controlled clinical trial in a sample selected from the relevant patient population.

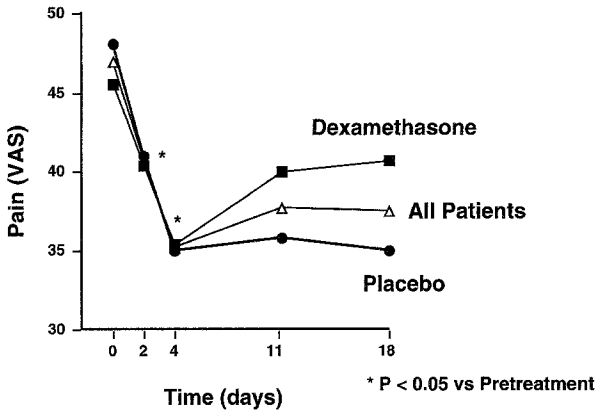

Fig. 2. Comparison of dexamethasone applied by iontophoresis to placebo. Evaluation of all patients combined over time (similar to clinical observations) would suggest that patients improved from baseline to observations during and following therapy. Comparison of the dexamethasone group with the placebo group indicates that the corticosteroid was without effect.

ANTIDEPRESSANTS

Antidepressant drugs have been used for more than 30 years[36] for the management of pain from a wide variety of conditions, including chronic orofacial pain.[16] Three independent reviews of controlled studies of the use of antidepressants for pain management indicate that their analgesic effects are largely independent of antidepressant activity.[36-38] The analgesic effects can be differentiated from placebo, are seen at doses lower than those usually effective in depression, and can occur in patients who are not depressed. Studies in patients with nondental chronic pain, primarily diabetic and postherpetic neuropathy, indicate that drugs that inhibit reuptake of both serotonin and norepinephrine, such as amitriptyline, are more efficacious than drugs that are selective for either neurotransmitter.[38, 39]

Indirect evidence that antidepressants produce analgesia independent of the alleviation of depression comes from studies with low doses of amitriptyline in patients with chronic pain. Sharav et al.[40] demonstrated that a low dose of amitriptyline (mean dose = 23.6 mg) was as effective for chronic orofacial pain as a higher dose (mean = 129 mg); the usual daily antidepressant dose is 75 to 150 mg. A daily dose of 25 mg amitriptyline for 3 weeks was also demonstrated to be superior to placebo in a variety of patients with chronic nonmalignant pain.[41] A dose-response comparison of 25, 50, and 75 mg amitriptyline demonstrated increased analgesia with increasing dose, improved sleep with the 75 mg dose, but significantly higher incidence of adverse effects at the 75 mg dose.[42] Zitman et al.[43] also reported analgesia with 75 mg amitriptyline and improved sleep over 6 weeks but considered the magnitude of the effect modest. If antidepressants produced therapeutic effects through alleviation of depression, the doses used in these studies would be similar to those needed for depression.

Therapeutic recommendations

The biomedical literature supports the clinical use of antidepressants for chronic nonmalignant pain when other treatments have failed or if depression accompanies the pain. Tricyclic antidepressants with both serotinergic and noradrenergic effects (e.g., amitriptyline or doxepin) appear to be most effective. Lower dosages (25 to 75 mg) should be used initially for nondepressive patients with antidepressant doses reserved for patients who are depressed, possibly prescribed in collaboration with a clinician experienced in the diagnosis and treatment of psychiatric illness. Sedative antidepressants may be useful when patients have sleeping problems and may help to reduce the use of hypnotics. The dose of antidepressants will usually be limited by anticholinergic side effects (dry mouth, constipation, blurred vision, and urinary retention) and should be adjusted in response to individual variation in analgesic response and side effects. Cardiovascular effects can occur, ranging from postural hypotension to serious ventricular arrhythmias, especially in patients with pre-existing heart disease; medical consultation or parallel management should be considered in patients at risk.

Whereas approximately 40 placebo-controlled studies have been identified in the literature regarding the use of antidepressants for chronic pain, only three of these studies evaluated their use for orofacial pain, and one of these three studies was published nearly 30 years ago.[44] The two most recent studies[40, 45] evaluated amitriptyline in a total of only 121 patients. More clinical research is needed to determine prognostic factors in this patient population predictive of analgesic responsiveness to antidepressants and to determine which drugs have the most favorable balance of analgesia and side-effect liability.

BENZODIAZEPINES

Drugs of the benzodiazepine class are frequently administered to patients with chronic pain, often for prolonged periods, despite long-standing professional concern about their ability to produce dependence. A survey of 114 consecutive new patients at an academic pain center found that 38% were taking one or more benzodiazepines and that the majority were chronic users of 1 to 2 years' duration.[46] While the most common indication (86%) for the use of the benzodiazepine was to improve sleep, the authors concluded that these patients reported as many sleep problems as new patients who were not taking benzodiazepines. Whereas the efficacy of benzodiazepines for chronic pain is not generally recognized, their long-term administration is controversial because of adverse effects, their potential for abuse and dependence, and the possibility of initiating or exacerbating depression in patients with chronic pain. Conversely, several studies have demonstrated therapeutic effects for musculoskeletal pain, which suggests that the use of benzodiazepines for chronic orofacial pain be re-examined.

Administration of clonazepam to patients with chronic TMD-associated myofascial pain was demonstrated to be superior to placebo in a double-blind 30-day trial.[47] Subjects reported a reduction in pain at all sites tested, with several areas reaching significance despite the small sample size (N = 10 per group). No instances of dependence or withdrawal symptoms were noted upon discontinuation of the

drug after 30 to 60 days; however, the small sample size limits generalization. A larger study (N = 78) of patients with fibromyalgia who met the published criteria for primary fibrositis/fibromyalgia syndrome received alprazolam, ibuprofen, or a combination of the two in comparison with placebo.[48] Clinical improvement in patient ratings of disease severity and tenderness on palpation were significant in the alprazolam plus ibuprofen group after 6 weeks. It was not clear whether alprazolam or ibuprofen was primarily responsible for the improvement seen. Four patients withdrew because of side effects in the placebo group in comparison with a total of only two withdrawals among the three active drug groups, which suggests that the doses of ibuprofen (2400 mg daily) and alprazolam (0.5 to 3.0 mg per day) were well tolerated. A total of 52 patients completed 24 weeks of open label with the combination; the authors report that many patients tapered their alprazolam dosage by one or more tablets (0.5 mg) per day below the level offered, contrary to a pattern of drug abuse.

A similar study in patients with chronic orofacial pain of myogenic origin (N = 39) evaluated ibuprofen (mean dose = 2400 mg/day), diazepam (mean dose = 17 mg/day), and the combination of the two in comparison with placebo in a 4-week double-blind trial.[17] Pain, as measured by a visual analog scale, was significantly decreased in the diazepam and diazepam plus ibuprofen groups but not for the ibuprofen or placebo groups. Analysis of variance showed a significant drug effect for diazepam but not for ibuprofen, indicating that the pain relief was attributable to diazepam. Depression showed a tendency toward improvement on both the depression adjective checklist and the Zung depression scale in the groups receiving diazepam; there was also a trend for less anxiety in the benzodiazepine groups. The small sample size in this study (N = 9 to 11 per group) limits its generalization of the findings, but these data are supportive of benzodiazepine-mediated relief of symptoms in chronic orofacial pain of myogenic origin.

A recent review[49] addressed several commonly held beliefs regarding the long-term use of benzodiazepines for chronic pain. The authors concluded that there is evidence that chronic use of benzodiazepines is effective for some pains of presumed musculoskeletal origin, based in part on the studies previously reviewed. They suggest, however, that the antidepressant effects attributed to triazolo-benzodiazepines, such as alprazolam, may be artifactual because of overlaps in diagnostic criteria used for depression and anxiety disorders and the impact of the sedative effects on rating scales used to assess depression. These authors also conclude that benzodiazepines used in high doses produce reversible side effects that are mistakingly interpreted as depression and that they do not actually initiate endogenous depression. The literature reviewed indicates that a high proportion of patients with chronic pain have some type of depressive syndrome that may develop concomittantly with the chronic pain state rather than be drug induced.

Therapeutic recommendations

The scientific literature does not provide unequivocal support for either the use of benzodiazepines or their condemnation on the basis of lack of efficacy or potential toxicity. Like all drugs, they should only be used in patients whose symptoms are suggestive of potential efficacy and should not be prescribed in large amounts that would permit dose escalation without professional supervision or the development of dependence with long-term therapy. Patients whose pain appears to be of musculoskeletal origin may benefit from a 2- to 4-week course of a benzodiazepine, possibly in combination with an NSAID. A lack of efficacy or the onset of sedative side effects or depressive symptoms should be an indication to reduce the dose or discontinue the benzodiazepine. If difficulties in sleep onset or duration are the primary complaint, consideration should be given to the use of a benzodiazepine indicated for hypnosis (triazolam) to minimize drug effects during the day. Patients who appear to have depressive symptoms before therapy should be referred to a psychiatrist for consultation and possible antidepressant therapy rather than being prescribed a benzodiazepine with putative antidepressant properties. In any event, therapy with a benzodiazepine should not be extended beyond a few weeks, because the natural course of myofascial pain combined with conservative therapy will likely result in a lowering of symptomology to acceptable levels, which would not justify the risks of pharmacologic intervention. Patients for whom such a therapeutic course fails should be reevaluated rather than "managed" with long-term benzodiazepine treatment.

MUSCLE RELAXANTS

Drugs that are thought to reduce skeletal muscle tone are often administered to patients with chronic orofacial pain to help prevent or alleviate the increased muscle activity attributed to some forms of TMD.[16] Although the use of benzodiazepines is sometimes rationalized on the basis of putative muscle relaxing properties, drugs of this class decrease muscle tone at doses that produce unacceptable lev-

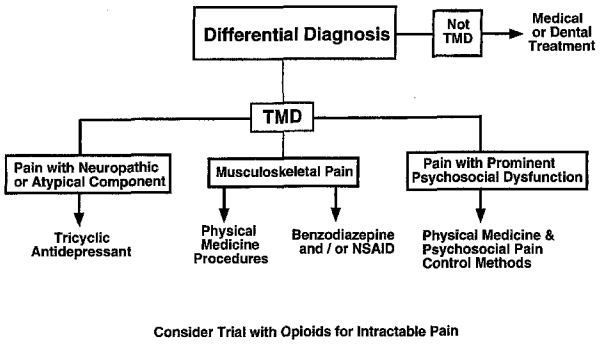

Fig. 3. Therapeutic recommendations for the use of pharmacologic modalities in the treatment of TMD based on the few controlled studies reviewed. Opioids may be considered for intractable pain but have not been validated for use in chronic orofacial pain.

els of central nervous system depression. Muscle relaxants are thought to decrease muscle tone without impairment in motor function by acting centrally to depress polysynaptic reflexes. Other drugs with sedative properties, such as barbiturates, also depress polysynaptic reflexes, making it difficult to assess if centrally acting skeletal muscle relaxants actually are muscle relaxants as opposed to nonspecific sedatives.[50]

Carisoprodol, one of the oldest drugs of this class, was first evaluated for chronic orofacial pain in a study published in 1960. Despite initially favorable clinical observations, a double-blind placebo-controlled evaluation found that carisoprodol was equally efficacious with placebo and with a similar incidence of side effects.[51] Similarly, carisoprodol could not be differentiated from placebo in a double-blind comparison to placebo in 60 patients.[52] A critical review of centrally acting skeletal muscle relaxants concluded that carisoprodol and related propanediols were better than placebo for acute musculoskeletal disorders but less effective for chronic conditions.[50]

A possible exception is cyclobenzaprine (Flexeril), which has been demonstrated to be effective in some chronic musculoskeletal disorders.[50] Cyclobenzaprine is superior to placebo for pain in the cervical and lumbar regions associated with skeletal muscle spasms[53, 54] and reduces electromyographic signs of muscle spasm.[55] Although it has not been directly assessed for TMD, these findings are suggestive of efficacy for muscle relaxation in the orofacial region.

Therapeutic recommendations

There appears to be a discrepancy between the common clinical use of skeletal muscle relaxants and the results of controlled clinical trials evaluating their efficacy in comparison with placebo. It is also not clear whether they are specific for muscle relaxation or produce nonspecific central nervous system depression, thereby reducing muscle tone. Little supporting evidence exists for their efficacy in chronic orofacial pain of myogenic origin, nor is it clear if they provide an additive effect with exercises or splint therapy aimed at muscle relaxation. Given this modest scientific support, clinicians should probably limit the use of skeletal muscle relaxants to a brief trial in conjunction with physical therapy regimens. Further studies are needed to document efficacy for chronic orofacial pain in comparison with an active placebo with sedative properties to help differentiate nonspecific sedative properties from muscle relaxation.

THERAPEUTIC SUGGESTIONS FOR PHARMACOLOGIC MANAGEMENT OF TMDs

Review of the drug classes most commonly used for TMD does not reveal a wealth of data upon which to base therapy. The wide variety of other drug modalities currently in clinical use for chronic orofacial pain has even less scientific support. Given the potential for serious toxicity that can accompany long-term administration of drugs that are safe enough to be marketed without a prescription (i.e., the NSAIDs), a lack of demonstrated efficacy for drugs with even greater potential toxicity may be indicative of risk to the patient without therapeutic benefit. A need exists for well-controlled studies of drugs used for chronic orofacial pain in the relevant patient population, for periods of administration that approximate their use clinically, with appropriate indices of therapeutic efficacy and toxicity, and in comparison with a group receiving placebo medication to control for cyclic fluctuations in symptomology. In the interim, dentists who treat patients with TMD should consider the use of many drug classes as nonvalidated clinical practice that carries the burden of proof for efficacy and liability for adverse outcomes.

On the basis of these considerations, a conservative scheme for the use of drug therapy for the management of temporomandibular disorders is described in Fig. 3. Assuming that a reliable differential diagnosis can be performed, pain with a neuropathic or atypical component would recommend a trial with a tricyclic antidepressant. Pain of musculoskeletal origin is probably best managed by physical medicine procedures, possibly supplemented with a short trial of a benzodiazepine or an NSAID. Patients with manifestations of psychosocial dysfunction may not benefit from drug therapy aimed at pain and should be considered as canditates for physical medicine mo-

dalities and behavioral methods. For patients for whom other therapeutic modalities have failed or for whom a specific treatment is not readily apparent, such as patients for whom TMJ implants have failed, a trial with opioids should be considered, especially as an alternative to iatrogenic injury from experimentation with unvalidated or irrational clinical procedures.

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Reprint requests:
Raymond A. Dionne, DDS, PhD
10 Center Drive
Building 10, Room 1N-103
Bethesda, MD 20892