# A Controlled Evaluation of Ibuprofen and Diazepam for Chronic Orofacial Muscle Pain

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*The clinical efficacy, side effect liability, and hormonal effects of two prototypic pharmacologic agents were evaluated for the management of chronic myogenous facial pain in a double-blind, randomized, controlled clinical trial. Thirty-nine subjects (35 women, 4 men) with daily or near-daily orofacial pain of at least 3 months' duration and tenderness to palpation of masticatory muscles participated. Patients were randomly allocated to one of four treatments: placebo, diazepam, ibuprofen, or the combination of diazepam and ibuprofen. Pain, mood, muscle tenderness, maximal interincisal opening, and plasma levels of β-endorphin were measured following 2-week baseline and 4-week treatment periods. 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 pain relief was attributable to diazepam. No significant changes were noted in muscle tenderness, interincisal opening, or plasma β-endorphin level. This study supports the efficacy of diazepam in the short-term management of chronic orofacial muscle pain. The lack of effect following administration of an anti-inflammatory analgesic suggests that inflammation is not the basis for chronic muscle pain in the orofacial region, and that the analgesic effect of such medications is not sufficient for pain relief in this condition.*

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Many different therapeutic modalities have been proposed for the management of chronic orofacial muscle pain, each based on a different perceived etiology of pain and dysfunction. These modalities include dental therapy (occlusal equilibration, intraoral appliances), myotherapy (trigger point injections, physical therapy), pharmacotherapy, and behavioral therapy.[1–7] However, no clear consensus exists within the dental or medical community on what constitutes the treatment of choice for this condition.

Despite the large body of literature on therapeutic modalities, few studies have evaluated pharmacologic treatment of temporomandibular disorders (TMD) in a well-controlled fashion. A meta-analysis[8] of more than 4,000 references to TMD published from 1980 to 1992 found that approximately 1% (n = 55) were randomized controlled studies, with only five of these evaluating pharmacologic agents. Studies of TMD are often confounded by the

heterogeneous nature of the study population; patients with muscle pain may not be distinguished from those who have temporomandibular joint disorders such as degenerative arthritis or displacement of the meniscus.[9,10] Investigators often fail to use standardized methods for measurement of pain and dysfunction. The main evidence of a positive treatment outcome is often the clinician's impression of improvement or the patients' failure to seek further treatment.[4,11] Another major weakness in previous studies has been the lack of an adequate control group.[6,11] These deficiencies in study design are particularly significant, given the high rate of success reported for manipulations such as placebo splints,[12] placebo drug,[13] sham occlusal equilibration,[14] a positive doctor-patient relationship,[13] and enthusiastically presented treatment.[13]

Other factors that may affect the evaluation of treatment outcome include the fluctuating nature of orofacial pain, which may undergo remissions and exacerbations independent of treatment.[15,16] The high prevalence of concurrent psychologic problems described in this population may also influence the onset of symptoms, reporting of pain levels, and treatment response.[17–22] Many patients eventually do well, even if they fail an initial course of therapy[23,24] or receive no treatment at all,[16] suggesting 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 TMD.

The present study sought to control for responses to nonspecific factors and cyclic fluctuations in pain through the use of standardized clinical trial methodology. The efficacy of two prototypic drugs, ibuprofen and diazepam, in the short-term management of TMD was evaluated in a double-blind, randomized, factorial study. These drugs are widely prescribed for this indication, but there are relatively few controlled studies justifying their use. Ibuprofen is a prototype of the nonsteroidal anti-inflammatory drug (NSAID) class, and diazepam is representative of the benzodiazopine anxiolytics and has also been used to treat muscle spasms. The clinical trial tested the hypotheses that active drug treatment can be differentiated from placebo in this patient population and that the effects of ibuprofen and diazepam are independent and additive.

Plasma β-endorphin is elevated during acute pain and surgical stress; its release is suppressed by the administration of analgesics and anxiolytic drugs such as diazepam.[25–27] Conversely, ibuprofen administration prior to oral surgery results in significantly elevated β-endorphin release in comparison to placebo pretreatment during the stress of surgery.[28] A secondary objective of this study was to examine the relationship between the drug treatments, clinical outcome, and circulating levels of β-endorphin.

## Materials and Methods

### Patient Population

The study sample consisted of patients referred to the National Institute of Dental Research Pain Research Clinic by local dentists and physicians. Informed consent was obtained with an institutionally approved document. All patients had an initial evaluation consisting of a general physical, neurologic, and dental examination. Laboratory evaluation included a complete blood count, blood chemistry profile, cyanocobalamin and folate levels, thyroid panel, sedimentation rate, and serology for rheumatologic disease. Open- and closed-mouth radiographs of the temporomandibular joint (TMJ) were also obtained. The Minnesota Multiphasic Personality Inventory[29] and Beck Depression Inventory[30] were administered as part of a general psychologic screening program. On the basis of the results of these tests, psychiatric evaluation was done to exclude patients with suicidal ideation or severe mood disorders, or who were substance abusers.

Inclusion criteria were as follows: *(1)* daily or near-daily pain in the orofacial region as assessed by baseline pain diaries; *(2)* pain of at least 3 months' duration; and *(3)* muscle tenderness to palpation in the muscles of mastication. Limited opening and the presence of clicking were not necessary for inclusion if these three criteria were met. Exclusion criteria included *(1)* clinical or radiographic evidence of primary TMJ pathology (ie, crepitus, tenderness on palpation through the external auditory meatus, erosion of the condyle); *(2)* pain attributable to recent facial trauma, dental surgery, or placement of a dental appliance; *(3)* other local causes of pain (trigeminal neuralgia, dental abscess, or migraine); *(4)* muscle pain associated with a systemic illness (rheumatoid arthritis, myalgia secondary to hypothyroidism); *(5)* the presence of another disorder that required ongoing treatment with analgesics, muscle relaxants, or mood-altering drugs, which would confound the evaluation of orofacial pain; or *(6)* allergy or other contraindications to the study drugs.

### Treatments

Patients were instructed to discontinue all drugs and intraoral prosthetic devices for pain and to keep a 2-week baseline diary of pain. They were assigned in a randomized, double-blind fashion to one of four treatment groups. Each patient was treated for 4 weeks with either placebo, diazepam, ibuprofen, or ibuprofen plus diazepam. The dosage of ibuprofen was 600 mg four times daily (total daily dose 2,400 mg); 2.5 mg of diazepam was administered four times daily for 1 week and then 5 mg four times daily for the remaining 3 weeks if not limited by side effects (total daily dose up to 20 mg). Ibuprofen and its placebo were identically appearing tablets supplied by the manufacturer (UpJohn, Kalamazoo, MI). Diazepam and its placebo were administered as identically appearing capsules prepared by the National Institutes of Health Pharmaceutical Development Service. One investigator monitored medication dosage and side effects; another independently assessed the patients' pretreatment and posttreatment.

### Dependent Measures

Patients completed a diary twice daily for pain using a visual analog scale.[31] Pretreatment and posttreatment measures of pain included category scales for pain and pain relief, visual analog scale (VAS) for pain and pain relief, and the McGill Pain Questionnaire.[32] Mood was measured via the Spielberger State-Trait Anxiety Inventory,[33] Profile of Mood States,[34] the Depression Adjective Checklist Form A,[35,36] and the Zung Depression Scale.[37] Maximal interincisal opening was measured with a Boley gauge; patients were instructed to open as wide as they could. Muscle tenderness of head and neck muscles was rated by the patients in response to manual palpation as no pain (0) (same as pressure on a nonpainful site on forehead), slight pain (1), moderate pain (2), or severe pain (3).

Plasma levels of immunoreactive β-endorphin before and after treatment were determined using a previously described radioimmunoassay.[27] In brief, 21 mL of blood was collected into tubes containing 10.5 mg of ethylenediamine tetraacetic acid (EDTA) per 7-mL tube (Vacutainer No. 6454, Becton-Dickenson, Rutherford, NJ), chilled in ice, and centrifuged at 4°C for 10 minutes at 2,000 rpm. The plasma was decanted and frozen in dry ice. Two 6-mL plasma aliquots were extracted in parallel and assayed in duplicate to yield four determinations for each sample. Each 6-mL aliquot was layered over commercially prepared separation columns (Sep-Pak C-18 Cartridges, Waters Associates, Milford, MA), and fractions were sequentially eluted with 3-mL washes of 0%, 50%, and 100% $CH_3CN$ in 0.1% trifluoroacetic acid. These fractions were concentrated by rotary evaporation for 1 hour at 40°C, followed by lyophilization. Each fraction was resuspended in 0.5 mL of buffer at the time of assay, resulting in a 12-fold concentration from the original 6-mL plasma aliquot. The resuspended samples were incubated for 72 hours at 4°C in glass tubes with phosphate buffer, β-endorphin antibody, and radiolabeled trace. Additional tubes containing known amounts of β-endorphin standard were analyzed in parallel. This assay has been demonstrated to detect changes in plasma levels of β-endorphin because of the effects of surgical stress,[25] catecholamines,[26] hormones,[27] and a variety of drugs, including ibuprofen.[25,28]

### Statistical Analyses

Data analysis was accomplished with the BMDP Statistical Software Package (BMDP Statistical Software, Los Angeles, CA). Pain measured by VAS was compared across groups by two-way analysis of variance with two grouping factors: diazepam and ibuprofen. Other continuous variables, such as opening and plasma β-endorphin levels, were compared by one-way analysis of variance followed by Duncan's multiple range test. Categorical data were tested with the Kruskal-Wallis test. The pain diaries were assessed by analysis of variance for repeated measures (ie, pain ratings each week for 4 weeks). Values are reported throughout the present article as the mean ± one standard deviation. Statistical significance was accepted as $P < .05$.

## Results

Of the original 49 patients, 10 did not complete the study for a variety of reasons: failure to return for appointments (5); insufficient pain relief at three days (1); spontaneous remission (1); delayed menses (1); rash (1); and intercurrent illness (1). The final sample consisted of 35 women and 4 men with a mean age of 36.1 years and a mean duration of pain of 7.0 years. Subjects reported a mean of 2.7 previous medications (most commonly an analgesic) and a mean of 1.6 previous treatments (most commonly an intraoral appliance). The duration of pain was similar across

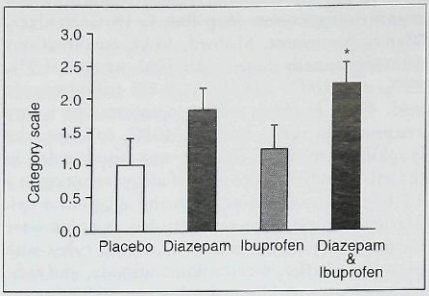


Fig 1 Pain relief (mean and SEM) after 4 weeks, as measured by a category scale. *P < .05 versus placebo.

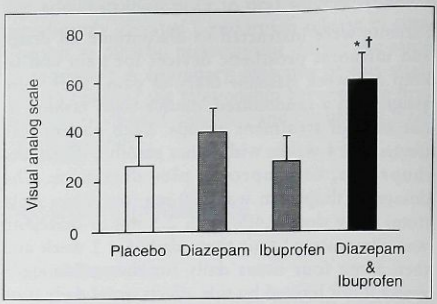


Fig 2 Pain relief (mean and SEM) after 4 weeks, as measured by a 100-mm visual analog scale. *P < .05 versus placebo; †P < .05 versus ibuprofen.

Table 1 Pain Intensity Over Time (Mean ± Standard Deviation)

| | Visual analog scale | | Category relief scale | | McGill Pain Questionnaire | |
|---|---|---|---|---|---|---|
| | Baseline | Four weeks | Baseline | Four weeks | Baseline | Four weeks |
| Placebo | 38.7 ± 36.9 | 23.2 ± 22.4 | 1.7 ± 0.9 | 1.4 ± 0.5 | 20.1 ± 15.1 | 19.0 ± 17.9 |
| Diazepam | 50.9 ± 21.6 | 39.5 ± 29.3 | 1.8 ± 0.4 | 1.5 ± 0.7 | 21.2 ± 9.1 | 14.8 ± 7.8 |
| Ibuprofen | 37.7 ± 27.0 | 25.9 ± 24.4 | 1.7 ± 0.5 | 1.3 ± 0.7 | 14.0 ± 7.1 | 9.8 ± 5.3 |
| Diazepam and ibuprofen | 28.5 ± 17.2 | 13.4 ± 6.2 | 1.5 ± 0.5 | 0.8 ± 0.6 | 22.7 ± 12.8 | 16.0 ± 13.6 |
| Total sample | 39.3 ± 26.5 | 25.9 ± 25.4 | 1.7 ± 0.6 | 1.3 ± 0.7 | 19.7 ± 11.4 | 14.9 ± 12.0 |

groups. The mean daily dose of ibuprofen was 2,400 mg; the mean daily dose of diazepam was 17 mg (five patients had their dose reduced because of drowsiness and/or irritability). Pain at the end of the 2-week baseline period, prior to drug administration, was very similar between groups on the category scale and the McGill Pain Questionnaire (Table 1). The mean level of pain on the VAS ranged from 28.5 for the group that received diazepam plus ibuprofen to 50.9 for the diazepam group, but it did not differ significantly between groups ($F = 1.30$, $P < .30$).

Pain relief after 4 weeks of treatment demonstrated a statistically significant difference among groups for both the category relief scale (Fig 1) and pain relief (VAS) (Fig 2). Two-way analysis of variance for the VAS relief data revealed a significant drug effect for diazepam ($F[1,35] = 4.56$, $P < .05$), but not for ibuprofen ($F[1,35] = 1.02$). The diazepam plus ibuprofen group had significantly greater pain relief ($P < .05$) than either the placebo or ibuprofen alone, suggesting that the pain relief associated with the diazepam-ibuprofen combination was attributable to the diazepam component. Pain relief, as measured by category scale, was also significantly greater for the diazepam-ibuprofen group ($P < .05$) than for the placebo group.

Pain intensity, as measured by the VAS, decreased in all groups from the end of the 2-week baseline to the end of the 4-week treatment period; no statistically significant differences existed between groups (Table 1). Similar nonsignificant decreases were demonstrated for pain as measured by the category relief scale and the McGill Pain Questionnaire (Table 1). Depression, as measured by the Depression Adjective Checklist, showed a trend for improvement (decrease in score) in the three nonplacebo groups (Table 2). No statistically significant difference was seen between treatments on the Zung Depression Scale (Table 2). There was a nonsignificant decrease in anxiety on the State-Trait Anxiety Inventory in the two groups receiving diazepam (Table 2).

Table 2 Mood Changes (Mean ± Standard Deviation)

| | Zung Depression Scale | | Depression Adjective Checklist | | Anxiety state | |
|---|---|---|---|---|---|---|
| | Baseline | Four weeks | Baseline | Four weeks | Baseline | Four weeks |
| Placebo | 40.2 ± 8.3 | 37.6 ± 10.6 | 9.9 ± 6.1 | 10.7 ± 8.2 | 42.0 ± 9.2 | 40.3 ± 12.8 |
| Diazepam | 34.0 ± 9.1 | 31.9 ± 4.1 | 8.7 ± 6.6 | 5.4 ± 4.3 | 41.3 ± 9.9 | 36.3 ± 8.4 |
| Ibuprofen | 35.7 ± 7.6 | 36.2 ± 9.3 | 8.1 ± 3.6 | 6.4 ± 3.6 | 38.6 ± 10.1 | 37.6 ± 8.6 |
| Diazepam and ibuprofen | 37.2 ± 9.8 | 37.6 ± 7.7 | 9.6 ± 4.8 | 7.4 ± 5.1 | 43.4 ± 10.5 | 37.1 ± 9.2 |
| Total sample | 36.7 ± 8.7 | 35.7 ± 8.1 | 9.1 ± 5.3 | 7.4 ± 5.7 | 41.4 ± 9.7 | 37.7 ± 9.5 |

Table 3 Clinical and Hormonal-Dependent Measures (Mean ± Standard Deviation)

| | Muscle tenderness | | Interincisal opening (mm) | | Endorphin (μg) | |
|---|---|---|---|---|---|---|
| | Baseline | Four weeks | Baseline | Four weeks | Baseline | Four weeks |
| Placebo | 14.8 ± 5.2 | 14.7 ± 7.96 | 43.3 ± 8.1 | 43.8 ± 8.0 | 1.0 ± 0.1 | 1.1 ± 0.1 |
| Diazepam | 13.0 ± 5.9 | 11.0 ± 6.5 | 42.1 ± 4.0 | 42.2 ± 6.6 | 0.9 ± 0.1 | 0.9 ± 0.1 |
| Ibuprofen | 15.4 ± 8.1 | 13.2 ± 6.0 | 43.4 ± 6.4 | 45.1 ± 6.0 | 1.0 ± 0.3 | 1.0 ± 0.3 |
| Diazepam and ibuprofen | 12.8 ± 6.0 | 10.7 ± 6.2 | 41.6 ± 9.2 | 40.9 ± 8.6 | 0.7 ± 0.1 | 0.7 ± 0.1 |
| Total sample | 13.9 ± 6.1 | 12.3 ± 6.7 | 42.6 ± 6.9 | 42.9 ± 7.3 | 0.9 ± 0.4 | 0.9 ± 0.4 |

Muscle tenderness to palpation (calculated as the sum of all muscles measured) and interincisal opening did not change significantly over the 4-week observation period (Table 3). Plasma levels of β-endorphin remained stable from the baseline sample to the 4-week posttreatment sample in all four groups (Table 3).

## Discussion

The results of this study suggest that the combination of diazepam and ibuprofen, and diazepam alone, are more efficacious than either ibuprofen or placebo in the management of chronic orofacial muscle pain. Analysis of variance indicates that the diazepam was predominantly responsible for the clinical effect of the drug combination. This finding is consistent with an earlier study[3] that reported pain relief with diazepam for myofascial pain.

Ibuprofen alone appeared to be ineffective in producing pain relief in the study sample. It is possible that the sample was skewed, with patients who responded to NSAID having been eliminated from the referral pool because of relief of symptoms. Alternatively, the etiology of chronic muscle pain may not be inflammatory in nature. This is supported by a biopsy series of "tender points" from muscles of patients with fibrositis (a condition similar to TMD in its predominance in women, localized muscle tenderness, and in stiffness); this series showed no evidence of inflammatory changes.[38–40]

Review of the primary literature reveals few well-controlled studies suggesting that daily use of NSAIDs offers benefit for chronic orofacial pain.[41] Standard texts[42] and summaries of expert opinion[43] often provide recommendations for drugs and doses, but either they do not provide support for these recommendations or they extrapolate from chronic inflammatory conditions such as arthritis. The lack of clinical studies to support the efficacy of NSAIDs for masticatory pain becomes more important when contrasted with the growing body of data on the serious toxic effects of NSAIDs when given long term. Retrospective studies[44–46] have established an association between ingestion of aspirin or NSAIDs and increased risk of upper gastrointestinal tract bleeding. Users of

NSAIDs have a threefold greater risk of developing serious adverse gastrointestinal tract problems than nonusers, and this risk is greater in persons older than age 60 years.[47]

The inhibitory effects of NSAIDs on renal prostaglandin production leads to acute, reversible renal failure in 0.5% to 1.0% of patients who take NSAIDs on a long-term basis.[48] Retrospective analysis of patients with end-stage renal disease requiring hemodialysis demonstrated an association between chronic NSAID use and a ninefold increased risk of end-stage renal disease.[49] A possible lack of clinical efficacy for ibuprofen in the treatment of chronic orofacial muscle pain, as suggested by the results of the present study, must be weighed against the potential for serious toxicity with chronic use. In the absence of positive results from controlled clinical trials, patients with risk factors for gastrointestinal tract problems or renal disease should be prescribed NSAIDs cautiously and not for prolonged periods of time.

Diazepam, which significantly reduced pain symptomology in the present study, has both antispasmodic and anxiolytic properties. Muscle hyperactivity, caused by tension-associated habits of bruxism and clenching, and muscle spasm have been proposed as possible etiologies for chronic TMD pain,[15,50] perhaps acting by inducing local muscle ischemia and/or the accumulation of algesic substances that sensitize muscle nociceptors. However, ischemia alone is unlikely to be the cause of chronic myofascial pain; experimental evidence suggests that skeletal muscle blood flow actually increases during experimental bruxism[51] and also during muscle tension-type headache.[52] Bruxism and clenching were common (according to self-reports) in the study sample, but we did not measure whether diazepam reduced these habits. Mood was not worsened by 4 weeks of diazepam administration on either the Depression Adjective Checklist or the Zung Depression Scale. Diazepam produced only a minor decrease in anxiety as measured by the Spielberger State-Trait Anxiety Inventory. These small, equivocal changes in mood and anxiety do not support the hypothesis that pain relief associated with diazepam is a result of the anxiolytic properties of the drug.

No significant improvement was seen for either interincisal opening or muscle tenderness to palpation. Several factors may explain the discrepancy between self-report of pain relief following diazepam administration and a lack of change on these somatic indexes of muscle dysfunction. The mean opening was within normal range in all groups (although some individual patients were below this range); thus, little potential improvement was possible with treatment. Some subjects who were evaluated for muscle tenderness appeared to be poor reporters of pain; for example, some patients had no visible response to pressure but reported severe pain. Manual palpation might be less reliable in assessing changes in muscle tenderness than the use of a mechanical algometer. Many patients had markedly nonuniform tenderness, with some very painful and some nonpainful muscles. Our index summed all muscles together, which may have diluted changes in the most symptomatic muscles. We may have had more significant results if we evaluated each muscle separately.

The present study demonstrated that patients with chronic muscular pain in the temporomandibular region may respond to some active drug treatments when compared with placebo medication. Improvements in diazepam-treated patients and the lack of response to ibuprofen suggests that inflammation does not play a prominent role in the etiology of chronic muscular pain in this region. This outcome also suggests that the analgesic properties of ibuprofen are not adequate for pain relief in these conditions. These data, however, do not differentiate whether improvement with diazepam was the result of its muscle relaxant properties, its anxiolytic properties, or nonspecific central nervous system depression.

The hazards of chronic benzodiazepine use are well documented. Physicians and dentists have been warned about the potential hazards of increased depression and habituation in the chronic pain population.[53,54] A recent review, however, of commonly held beliefs regarding the long-term use of benzodiazepines for chronic pain concluded that drugs of this class produce reversible side effects mistakenly interpreted as depression, rather than initiating or unmasking endogenous depression.[55] Like all drugs, benzodiazepines should be used only in patients whose symptoms suggest potential efficacy, and they should not be prescribed in large amounts, permitting dose escalation without professional supervision, or the development of dependence with long-term therapy.

The results of the present study reinforce the necessity of evaluating putative therapies for TMD in carefully controlled studies. Such studies are needed to provide scientific validation for the use of a drug or other therapeutic modality for TMD. Controlled studies in a sample of patients with TMD disorder also help to differentiate treatments with efficacy in other clinical conditions, ie,

ibuprofen for rheumatoid arthritis, from those with documented efficacy in a sample selected from the relevant patient population. Conversely, the small sample size in the present study requires replication of these findings in a larger sample of patients, possibly using a crossover design to minimize the effects of confounding factors and to maximize assay sensitivity for detecting a difference between treatments.

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## Resumen

### Evaluación controlada del ibuprofén y el diazepam para el dolor muscular orofacial crónico

Se evaluó la eficacia clínica, los posibles efectos colaterales y los efectos hormonales de dos agentes farmacológicos prototípicos utilizados en el control del dolor facial miógeno crónico, en un estudio clínico controlado, con pacientes distribuidos al azar, y al doblecíego. Participaron 39 personas (35 mujeres, 4 hombres) que sufrían de dolor orofacial diariamente o casi-diariamente, con una duración de por lo menos 3 meses. Además, los músculos masticatorios de los pacientes eran sensibles a la palpación. Los pacientes fueron distribuidos al azar a uno de los siguientes tratamientos: placebo, diazepam, ibuprofén, o a la combinación de diazepam e ibuprofén. Se determinó el dolor, el ánimo, la sensibilidad muscular, la apertura interincisal máxima y los niveles plasmáticos de la endorfina B luego de realizar medidas basales de 2 semanas, y 4 semanas de tratamiento. El dolor disminuyó significativamente tanto en el grupo que tomaba diazepam solo como en el que tomaba diazepam mas ibuprofén, pero no en el grupo que tomaba ibuprofén, ni en el grupo de placebo; de acuerdo a las medidas tomadas con la escala análoga visual. El análisis de varianza demostró que el diazepam tenía un efecto significativo, pero esto no sucedió con el ibuprofén, lo que indicaba que el alivio del dolor se debía al diazepam. No se notaron cambios significativos en cuanto a la sensibilidad muscular, apertura interincisal, o los niveles plasmáticos de la endorfina B. Este estudio indica que el diazepam es eficaz para el tratamiento a corto plazo del dolor muscular orofacial crónico. La falta de efectos luego de la administración de un analgésico anti-inflamatorio indica que la inflamación no es la base para el dolor muscular crónico en la región orofacial, y que el efecto analgésico de tales drogas no es suficiente para es alivio del dolor de este problema.

## Zusammenfassung

### Eine kontrollierte Auswertung von Ibuprofen und Diazepam bei chronischem orofazialen Schmerz

Es wurden die klinische Wirksamkeit, die Neigung zu Nebenwirkungen sowie die hormonalen Wirkungen von zwei prototypischen pharmakologischen Substanzen für die Behandlung von chronischem myogenen Gesichtsschmerz in einem doppelblinden, zufälligen, kontrollierten klinischen Versuch ausgewertet. Neununddreissig Personen (35 Frauen, 4 Männer) mit täglichem oder nahezu täglichem orofazialen Schmerz mit einer Dauer von mindestens 3 Monaten und Palpationsempfindlichkeit der Kaumuskulatur nahmen teil. Die Patienten wurden zufällig zu einer der vier Behandlungen zugeteilt: Placebo, Diazepam, Ibuprofen oder einer Kombination von Diazepam und Ibuprofen. Es wurden Schmerz, Stimmung, Muskelempfindlichkeit, maximale interinzisale Oeffnung und b-Endorphin Plasmaspiegel nach 2 Wochen Basis und 4 Wochen Behandlung gemessen. Die Schmerzen, gemessen mittels visual-analog Skala, waren signifikant vermindert in den Diazepam- und Diazepam plus Ibuprofen-Gruppen, jedoch nicht in den Ibuprofen- und Placebo-Gruppen. Die Varianzanalyse zeigte einen signifikanten medikamentösen Effekt für Diazepam, aber nicht für Ibuprofen, dies deutet darauf hin, dass die Schmerzverminderung dem Diazepam zuzuschreiben war. Keine signifikanten Veränderungen wurden in Bezug auf die Muskelempfindlichkeit, die interinzisale Oeffnung oder den Plasma-b-Endorphin-Spiegel festgestellt. Diese Studie unterstreicht die Wirksamkeit von Diazepam in der kurzzeitigen Behandlung von chronischen orofazialen Muskelschmerzen. Das Ausbleiben einer Wirkung nach Verabreichung eines anti-inflammatorischen Analgetikas lässt vermuten, dass keine Entzündung die Basis für chronischen Muskelschmerz in der orofazialen Region darstellt, und dass die analgesierende Wirkung solcher medizinischer Behandlungen unter dieser Bedingung ungenügend ist für die Schmerzabnahme.