A Possible Therapeutic Solution for Stomatodynia (Burning Mouth Syndrome)

Alain Woda, DCD, D es S
Professor
Université d'Auvergne, Faculté de Chirurgie Dentaire
Clermont-Ferrand, France

Marie-Louise Navez, DM, Anesthésiologiste
Consultant
Centre Anti-Douleur
Centre Hospitals-Universitaire
St Etienne, France

Pascale Picard, DM, Anesthésiologiste
Consultant
Centre Anti-Douleur
Centre Hospitals-Universitaire
Clermont-Ferrand, France

Christèle Gremeau, DCD
Resident
Service Odontologie
Centre Hospitals-Universitaire
Clermont-Ferrand, France

Evelyne Pichard-Leandri, DM, Anesthésiologiste
Consultant
Centre Anti-Douleur
Institut Gustave Roussy
Villejuif, France

Correspondence to:
Dr Alain Woda
Laboratoire de Physiologie Oro-faciale
11 Boulevard Charles de Gaulle
63000 Clermont-Ferrand, France

Stomatodynia is a difficult disease for both patients and clinicians. When facing true stomatodynia, ie, idiopathic burning mouth, patients are offered poorly effective treatment. This open study reports the results of local application of clonazepam (0.5 or 1 mg) two or three times daily in 25 subjects who suffered from idiopathic stomatodynia. At the first evaluation, 4 weeks after the beginning of treatment, a visual analogue scale (VAS) that represented the intensity of pain decreased significantly from 6.2 ± 0.3 to 3.0 ± 0.5. At the second evaluation, 3 to 29 months after the first consultation, the VAS scores dropped significantly further to 2.6 ± 0.5. Analysis of the individual results showed that 10 patients were totally cured and needed no further treatment, 6 patients had no benefit at all, and the remaining 9 patients had some improvement but were not considered to be cured since they did not wish to stop the treatment. Blood level tests that were performed 1 and 3 hours after the topical application revealed the presence of small amounts of the drug (3.3 ng/mL ± 0.66 and 3.3 ng/mL ± 0.52, respectively). The hypothesis that clonazepam acts locally to disrupt the neuropathologic mechanism that underlies stomatodynia is proposed. The risk factors that are recognized for this condition could decrease the density and/or ligand affinity of peripheral benzodiazepine receptors. This, in turn, could cause spontaneous pain from the tissues concerned.
J OROFACIAL PAIN 1998;12:272–278.

key words: burning mouth syndrome, stomatodynia, orofacial pain, peripheral benzodiazepine receptor, clonazepam

Burning mouth syndrome is a general term that covers different conditions. Sometimes a burning sensation accompanies a well-defined disease such as lichen planus or local denture stomatitis.[1–3] In these cases, the burning sensation must be considered a symptom. It is more than a symptom, however, when burning or other sensations of dysesthesia are reported without any sign of organic pathology in the oral or pharyngeal mucosa. In these cases, where there are no clinical signs, the pain characteristics and the patients concerned are similar,[4–6] and the condition could constitute a distinct disease. The authors therefore prefer to avoid the term "syndrome," and throughout this article the older term "stomatodynia," which does not imply a distinct disease, syndrome, or symptom, will be used.

There is no recognized treatment for stomatodynia as defined above. The fact that many treatment modalities have been proposed in the literature[1,3,7–10] illustrates that none are very effective. In a chance observation, one of the authors' patients noticed that burning oral pain was suppressed by sucking a clonazepam tablet. The systemic use of this anticonvulsant benzodiazepine has already been suggested as a treatment for stomatodynia.[11] A clinical protocol based on the premise of local activity of clonazepam was developed and tested by two consultants who specialize in the management of orofacial pain. This article presents a preliminary evaluation of this protocol.

Materials and Methods

The study was undertaken with patients who had been referred by physicians or dentists after unsuccessful attempts to alleviate their pain. Both a physician and a dentist examined all patients. The basic criteria for inclusion in the study were the presence of an isolated complaint of pain or dysesthesia in the oral mucosa and a normal clinical examination. The additional presence of pain or dysesthesia in the oropharynx or of other abnormal sensations such as taste impairment or a false impression of xerostomia did not exclude the patient. An examination of the neck, head, and mouth was performed, with particular emphasis on the oral mucosa and dental status. Patients who presented with possible organic conditions, either local or systemic, that could be considered[1,7] a causative factor for the abnormal sensations were excluded. For example, patients with a history of recent antibiotic therapy that could have caused a candidal infection or patients who presented with a dry mouth that could be explained by radiation therapy were not included in the study. People with current or past psychologic records were not excluded because a psychologic component such as depression or anxiety is the only element that has been convincingly proven to have an association with stomatodynia.[12–16] No accompanying psychometric evaluation was used, however. Patients who were undergoing psychotherapeutic treatment were not asked to interrupt it. All topical medication given to treat the stomatodynia was suppressed. Twenty-one women and four men, all Caucasian, were studied. Their mean age was 62.2 ± 12.0 (± standard error), with a range of 39 to 83 years. Their symptoms were evaluated with regard to 11 characteristics.

Symptom Characterization

Quality of Pain. The words that were most frequently used to spontaneously describe the symptoms were: burning (n = 20), annoying (n = 11), a granular or sandy feeling (n = 9), dryness (n = 6), and swelling (n = 5).

Pain Localization. The sensation was restricted to the tongue (n = 21), the palate (n = 12), the gingivae (n = 5), the oropharynx (n = 3), the lips (n = 2), or elsewhere in the mouth (n = 3).

Pain Symmetry. Pain sensation was bilateral and symmetrical (n = 20) more often than it was unilateral (n = 5).

Frequency and Duration of Pain. Most patients (n = 21) reported daily symptoms that were continuous (n = 15) rather than variable or progressively increasing during the day (n = 10). Only four patients had some days without oral discomfort.

Altering or Trigger Factors. Stress (n = 10) or temperature variation inside the oral cavity (n = 7) were frequently aggravating or trigger factors. Mastication or some types of food also often modified the pain, resulting in either an increased (n = 7) or a decreased (n = 9) sensation. Both an increase and a decrease depending on the type of food were described in two cases.

Sleep. All but one subject had a normal sleep pattern that was not disturbed by pain. However, several patients used sleep-inducing medication.

Course of the Disease. The pain had been present for 6.4 ± 1.9 years on average, with a very large range (from 3 months to 16 years).

Circumstances Under Which the Pain First Presented. The beginning of the pain was frequently (18 cases) related by the patient to a strongly stressful event such as the death of a close relative or the rapid onset of psychologic or physical disease.

Pain in Other Parts of the Body. In some patients the symptoms of stomatodynia were associated with other manifestations of pain such as backache (n = 9), diffuse myalgia (n = 1), or vaginal burning (n = 3).

Other Orofacial Pain. Although clearly distinguishable, symptoms could be associated with other pain in the orofacial region such as tension-type headache (n = 1), postherpetic facial pain (n = 1), and atypical facial pain (n = 2). Three patients presented with symptoms of temporomandibular joint disorder. Because these general and orofacial conditions affected some of the same patients, a total of 13 patients had stomatodynia as their only source of pain.

Accompanying Psychopharmacologic Treatment. Only six patients were not undergoing pharmacologic treatment with psychotherapeutic drugs. The

drugs most frequently used were benzodiazepines (n = 13, with two patients taking oral clonazepam daily with no effect on their stomatodynia), antidepressants (n = 8), or other psychotherapeutic drugs (n = 4).

A vertical, 10-cm visual analogue scale (VAS) was also completed. Patients were asked to indicate the mean pain intensity for the week preceding the consultation. After informed consent had been obtained, the patients were instructed to suck ¼ of a clonazepam tablet (0.5 mg) and to hold their saliva within the mouth, taking care not to swallow during 3 minutes. After that time they were instructed to spit the saliva out. Ingestion was avoided in view of the test hypothesis that drug activity was based at a peripheral site. Since the drug appeared to act within a few minutes of application and lasted for a limited number of hours, the drug administration had to be repeated two or three times a day depending on the time course of the pain sensation during the day. The patients were free to adjust their own dose between ¼ and ½ of a tablet, and they were asked to continue the treatment for 10 days after the last pain sensation. They were also carefully informed that the pain could return, even if it had been suppressed for several weeks or months. They were instructed that in this case they were to recommence the treatment and once again to maintain it for 10 days after the last symptom.

Patients were seen for a second time 4 weeks after the beginning of the treatment. Their oral cavity was again examined. A VAS score was recorded and they were asked about positive and negative effects. If necessary, the doses and timing of clonazepam administration were modified according to the time course of pain during the day. At 3 to 29 months after the first consultation, a third appointment allowed another VAS score to be recorded. In rare instances a telephone interview was used, particularly when the treatment was suspected to be totally efficient or totally ineffective based on a previous consultation. The three meetings were termed T0, T1, and T2. Depending on patient needs, additional appointments were added between T1 and T2. The VAS scores were averaged at T0, T1, and T2 (mean ± SEM) and compared with a paired *t* test unilaterally between T0 and T1 and bilaterally between T1 and T2.

Clonazepam blood level tests were performed for 12 patients who needed routine blood sampling for other reasons. Samples were taken 1 hour (six patients) or 3 hours (six patients) after the patients had sucked 1 mg of clonazepam for the first time following the protocol already described. The blood samples were analyzed for histoimmunology and high-performance liquid chromatography, and values were given as the mean ± SEM.

Results

Typically, after clonazepam application the patients described a weak burning sensation followed 5 to 10 minutes later by suppression of the stomatodynia pain that lasted from 3 to 5 hours. The onset and offset of the therapeutic effect was rather brisk and it was only by repeating the intake that the whole day could be covered. In some cases an effect was noted only after increasing the dose from ¼ to ½ of a tablet and/or after repetition of the application for several days. Other patients reported no effect at all regardless of the dose or the number of days of treatment. No side effect of any kind was reported, except by those patients who experienced a weak burning sensation in the mouth that lasted for a few minutes after clonazepam application.

When averaged, the VAS score before treatment was 6.2 ± 0.3 (2 to 10 range). The average VAS score was reduced to 3.0 ± 0.5 at 4 weeks after the start of the treatment, and it dropped to 2.6 ± 0.5 at the second appointment (3 to 29 months later). This corresponds to a 52% reduction in pain score. As shown in Fig 1, the response to treatment varied from one patient to another, but the difference between the means was significant both between T0 and T1 ($P < 0.001$) and between T1 and T2 ($P < 0.05$).

Averaging may have hidden some interesting features. Analysis of individual results clearly distinguished three situations. The first group of patients (group 1, n = 6) noticed no benefit at all, and their treatment was consequently discontinued. A second group (group 2, n = 9) was composed of those who experienced only partial improvement. These patients went on with the treatment without interruption. A third group (group 3, n = 10) was made up of patients who described total relief.

In these patients the treatment was stopped for a few weeks after a period of 1 to 3 months had elapsed. Reappearance of pain, albeit decreased, led to recommencement of the treatment and subsequent definitive suppression of the pain. No relation was observed between the three response groups and individual symptom characteristics such as initial pain intensity or the presence of pain sensation other than stomatodynia. However, it seemed that the six patients who were not undergoing psychotherapeutic drug treatment responded better than the others; five of these patients were totally cured (group 3) and the sixth experienced some improvement (group 2).

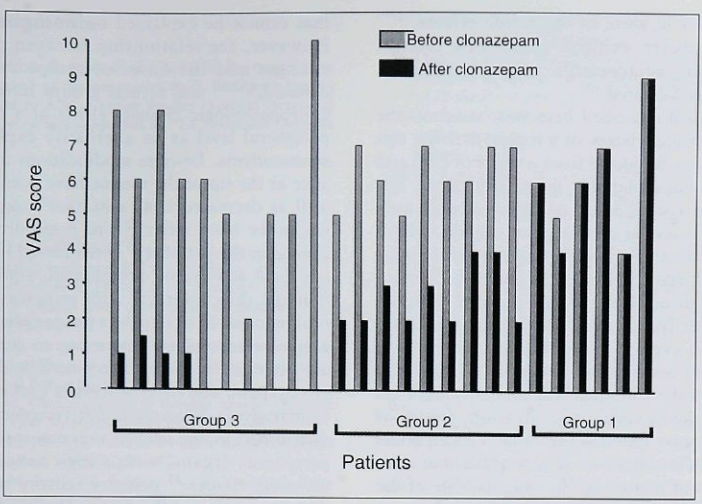

Fig 1 Effect of clonazepam in the 25 test patients. For each patient the VAS scores were recorded before treatment (gray) and 3 to 29 months after the first prescription (black). Group 1 = unsuccessful treatment, group 2 = partially successful treatment, and group 3 = very successful treatment.

Blood samples were taken 1 hour after clonazepam application in six patients and at 3 hours in six others. Only traces of clonazepam were revealed. The drug could not be detected in 3 of the 12 samples. The detection level of the dosage (2 ng/mL) was far below the therapeutic concentration of 0.02 to 0.07 μg/mL.[17] If the values of the three samples in which no trace of the drug could be detected are considered as 2 ng/mL, then the average serum concentration after topical administration of the tablet was 3.3 ng/mL ± 0.66 (n = 6) and 3.3 ng/mL ± 0.52 (n = 6) at 1 and 3 hours after application, respectively. No attempt was made to correlate drug level with analgesic activity.

Discussion

The symptoms observed in this study are highly reminiscent of the descriptions of stomatodynia that can be found in the literature[4–6] and it is likely that most, if not all, of the present cases were true stomatodynia and not a symptom of burning pain associated with other illness.

After following the proposed protocol, about one third of the patients experienced total relief from pain and needed no further treatment, one third had partially improved, and another one third experienced no improvement at all. When the outcome of all the patients was averaged, the improvement amounted to 52%. These results must be discussed with regard to two opposing ideas. On one hand, this article presents 25 cases that were examined in an open study. Therefore, the placebo effect cannot be ruled out by the present observations, and obviously these results must be confirmed by a controlled, double-blind, and randomized trial. On the other hand, the overall success rate was unexpected in a group of subjects without any known etiology for their pain and who had been resistant to many treatments in the past. It must be emphasized that the general feeling of clinicians facing stomatodynia is that they face a therapeutic dead end. This is a result of the low success rates displayed by proposed treatments and also of the low compliance associated with treatments based on antidepressant therapy, which are frequently used as the

only solution in spite of their side effects.[18,19] There is, however, evidence that a new class of antidepressant, serotoninergic reuptake inhibitors, may be better tolerated.[10]

The protocol described here was based on the hypothesis of the efficacy of a topical activity; this hypothesis was suspected from a series of trial and error that is not reported in the present paper. The use of drops was discarded during these early tests in favor of sucking clonazepam tablets, which allowed contact of a concentrated product with the painful area. A systemic effect following absorption through the tongue cannot be ruled out, however. The avoidance of first hepatic degradation could explain the increased effect seen in our protocol when compared to that described with oral intake. Although the amounts were far below the therapeutic concentration, traces of clonazepam were found in the blood 1 and 3 hours after drug administration. It is possible that after several days of treatment, the long half-life of the product[17] resulted in higher blood levels because of a cumulative effect. The low concentration observed would then be explained by the fact that blood samples were taken at the very beginning of treatment. A specially designed trial to compare the pharmacokinetics of topical versus oral intake is needed to address this issue. In any case, it must be borne in mind that the presence of clonazepam in the blood does not exclude the possibility of activity at the peripheral level through a topical mechanism.

Some peculiarities of the observed therapeutic effect favor the hypothesis of a topical mechanism:

- The duration of 3 to 5 hours and the fast onset of analgesia (in less than 10 minutes) cannot be explained by the pharmacokinetic properties of systemic clonazepam (half-life of 25 to 60 hours and serum peak between 3 and 12 hours[17]).
- No side effects were noticed aside from a transient local sensation of burning.
- Two subjects who found relief by the topical application of clonazepam had experienced no beneficial effect after systemic administration.
- Several patients reported no effect on pain located in remote areas that were not easily reached by the saliva such as the pharynx or the maxillary or mandibular bone, although the same patients experienced relief from pain in the oral mucosa.

It is generally believed that psychologic factors predominate in the etiology of burning mouth syndrome that cannot be explained by an organic cause.[9,18] However, the relationship between psychologic changes and the onset of symptoms has been debated,[6,12,20] and several groups have advocated neuropathologic changes either at a central or a peripheral level as an alternative explanation for stomatodynia. Discrete modifications in heat tolerance at the tip of the tongue have been found,[21] as well as decreased taste sensation[9] and abnormalities in the blink reflex.[22] The possibility of organic change in the periphery[5] is reinforced by the apparent local activity of clonazepam, which indicates that the drug interacts with receptors within the oral mucosa. In this respect the peripheral benzodiazepine receptors are interesting to consider. They are activated by benzodiazepine ligands, including clonazepam, and their properties evoke a link with stomatodynia. Benzodiazepine receptors are widely distributed in the central nervous system and the peripheral organs, with a high concentration in secretory tissues,[23] primary sensory neurons, the digestive tract, and the skin.[24] The risk factors associated with stomatodynia, including stress, anxiety, female sex, climacteric factors, and aging,[1,5,9] are also the most important factors that influence the peripheral benzodiazepine receptor density or activity (generally causing a decrease in activity). Changes occur by decreases in the density of receptors[25–29] and ligand affinity,[30] and by an increase in the level of the main endogenous ligand, the diazepam binding inhibitor.[31] It has been suggested that alteration in the density of receptors is a sensitive indicator of stress, with chronic stress triggering a down-regulation of the receptors.[32] The functions of both the diazepam binding inhibitor and the benzodiazepine receptors in the peripheral tissues are poorly understood, but among many other roles, they are known to be involved in cholesterol transport across the mitochondrial membrane. This affects many cellular mechanisms, notably the synthesis of steroid hormones.[29] This is not the only function of benzodiazepine receptors,[33] as can be inferred from the fact that many cells equipped with these receptors are not implicated in steroid hormone synthesis (see Krueger and Papadopoulos[34]). This leads to the hypothesis that the decreased density and/or affinity of receptors, together with an increased concentration of diazepam binding inhibitor, may be related to the painful sensation of stomatodynia. The decrease in density and/or affinity of receptors could be triggered by a cumulative effect of the risk factors mentioned above.

Acknowledgments

We are indebted to B. Laurent and R. Dallel for constructive and critical reading of the manuscript, to D. Faulks for English corrections, and to A.M. Gaydier for her excellent secretarial services. This work was supported by "La Fondation Dentaire de France."

References

1. Lamey PJ, Lewis MAO. Oral medicine in practice: Burning mouth syndrome. Br Dent J 1989;167:197–200.
2. Tammiala-Salonen T, Hiidenkari T, Parvinen T. Burning mouth in a Finnish adult population. Community Dent Oral Epidemiol 1993;21:67–71.
3. Bergdahl J, Anneroth G. Burning mouth syndrome: Literature review and model for research and management. J Oral Pathol Med 1993;22:433–438.
4. Grushka M. Clinical features of burning mouth syndrome. Oral Surg Oral Med Oral Pathol 1987;63:30–36.
5. Zakrzewska JM. The burning mouth syndrome remains an enigma. Pain 1995;62:253–257.
6. Grushka M, Sessle BJ. Burning mouth syndrome. Dent Clin North Am 1991;35:171–184.
7. Tourne LPM, Fricton JR. Burning mouth syndrome. Oral Surg Oral Med Oral Pathol 1992;74:158–167.
8. Basker RM, Sturdee DW, Davenport JC. Patients with burning mouths: A clinical investigation of causative factors, including the climacteric and diabetes. Br Dent J 1978;145:9–16.
9. Ship JA, Grushka M, Lipton JA, Mott AE, Sessle BJ, Dionne RA. Burning mouth syndrome: An update. J Am Dent Assoc 1995;126:843–853.
10. van Houdenhove B, Joostens P. Burning mouth syndrome. Successful treatment with combined psychotherapy and psychopharmacotherapy. Gen Hosp Psychiatry 1995;17: 385–388.
11. Huang W, Rothe MJ, Grant-Kels JM. The burning mouth syndrome. J Am Acad Dermatol 1996;34:91–98.
12. van der Ploeg HM, van der Wal N, Eijkman MAJ, van der Waal I. Psychological aspects of patients with burning mouth syndrome. Oral Surg Oral Med Oral Pathol 1987;63:664–668.
13. Zilli C, Brooke RI, Lau CL, Merskey H. Screening for psychiatric illness in patients with oral dysesthesia by means of the General Health Questionnaire-twenty-eight item version (GHQ-28) and the Irritability, Depression and Anxiety Scale (IDA). Oral Surg Oral Med Oral Pathol 1989;67:384–389.
14. Forabosco A, Criscuolo M, Coukos G, Uccelli E, Weinstein R, Spinato S, et al. Efficacy of hormone replacement therapy in postmenopausal women with oral discomfort. Oral Surg Oral Med Oral Pathol 1992;73: 570–574.
15. Rojo L, Silvestre FJ, Bagan JV, de Vicente T. Prevalence of psychopathology in burning mouth syndrome. Oral Surg Oral Med Oral Pathol 1994;78:312–316.
16. Lamey PJ, Lamb AB. The usefulness of the HAD scale in assessing anxiety and depression in patients with burning mouth syndrome. Oral Surg Oral Med Oral Pathol 1989; 67:390–392.
17. Kamoun P, Frejaville JP. Guide des Examens de Laboratoire. Paris: Flammarion, 1993.
18. Onghena P, van Houdenhove B. Antidepressant-induced analgesia in chronic nonmalignant pain: A meta-analysis of 39 placebo-controlled studies. Pain 1992;49:205–219.
19. Eschalier A, Mestre C, Dubray C, Ardid D. Why are antidepressants effective as pain relief? CNS Drugs 1994;2:261–267.
20. Eli I, Kleinhaus M, Baht R, Littner M. Antecedents of burning mouth syndrome (glossodynia)—Recent life events vs psychopathologic aspects. J Dent Res 1994; 73:567–572.
21. Grushka M, Sessle BJ, Howley TP. Psychophysical assessment of tactile, pain and thermal sensory functions in burning mouth syndrome. Pain 1987;28:169–184.
22. Jääskeläinen SK, Forssel H, Tenovuo O. Abnormalities of the blink reflex in burning mouth syndrome. Pain 1997;73:455–460.
23. Parola L, Yamamura HI, Laird HE II. Peripheral-type benzodiazepine receptors. Life Sci 1993;52:1329–1342.
24. Anholt RRH, de Souza E, Oster-Granite ML, Snyder SH. Peripheral-type benzodiazepine receptors: Autoradiographic localization in whole-body sections of neonatal. J Pharmacol Exp Ther 1985;233:517–526.
25. Rocca P, Ravizza L, Maina G, Bergamasco B, Ferrero P. Peripheral-type benzodiazepine receptors in blood cells of anxious patients. In: Biggio G, Concas A, Costa E (eds). GABAenergic Synaptic Transmission. New York: Raven, 1992:229–233.
26. Gavish M. Hormonal regulation of peripheral-type benzodiazepine receptors. J Steroid Biochem Mol Biol 1995; 53:57–59.
27. Hadjiivanova C, Zandjieva S, Petkov VV. Age-related changes in central and peripheral benzodiazepine binding sites. Acta Physiol Pharmacol Bulg 1992;18:17–20.
28. Holmes PV, Stringer AP, Drugan RC. Impact of psychological dynamics of stress on the peripheral benzodiazepine receptor. Pharmacol Biochem Behav 1992; 42:437–444.
29. Weizman R, Gavish M. Molecular cellular and behavioral aspects of peripheral-type benzodiazepine receptors. Clin Neuropharmacol 1993;16:401–417.
30. Marazziti D, Pancioli-Guadagnucci ML, Rotondo A, Giannaccini G, Martini C, Lucacchini A, Cassano GB. Age-related changes in peripheral benzodiazepine receptors of human platelets. J Psychiatry Neurosci 1994; 19:136–139.
31. Guarneri P, Guidotti A, Costa E. On the processing of diazepam binding inhibitor in human brain. Adv Biochem Psychopharmacol 1990;46:201–211.
32. Gavish M, Bar-Ami S, Weizman R. Pathophysiological and endocrinological aspects of peripheral-type benzodiazepine receptors. In: Giesen-Crousse E (ed). Peripheral Benzodiazepine Receptors. London: Harcourt Brace Jovanovich, 1993:210–234.
33. Alho H, Vaalasti A, Podkletnova I, Rechardt L. Expression of diazepam-binding inhibitor peptide in human skin: An immunohistochemical and ultrastructural study. J Invest Dermatol 1993;101:800–803.
34. Krueger KE, Papadopoulos V. The role of mitochondrial benzodiazepine receptors in steroidogenesis. In: Giesen-Crousse E (ed). Peripheral Benzodiazepine Receptors. London: Academic, 1993:89–109.

Resumen

Una Posible Solución Terapéutica para la Estomatodinia (Síndrome de Quemazón o Ardor en la Boca)

La estomatodinia es una enfermedad difícil tanto para los pacientes como para los clínicos. Cuando se presenta la estomatodinia verdadera, en otras palabras, una sensación de quemazón o ardor idiopático en la boca, a los pacientes se les presentan tratamientos no muy efectivos. Este estudio abierto reporta los resultados de la aplicación local de clonazepam (0,5 o 1 mg) dos o tres veces al día en 25 personas que sufrían de estomatodinia idiopática Durante la primera evaluación, 4 semanas después del comienzo del tratamiento, la escala análoga visual (EAV) que representaba la intensidad del dolor disminuyó significativamente de 6,2 ± 0.3 a 3,0 ± 0,5. Durante la segunda evaluación, 3 a 29 meses después de la primera consulta, los valores de la EAV bajaron significativamente aun más (2,6 ± 0,5). El análisis de los resultados individuales demostró que 10 pacientes estaban curados totalmente y no necesitaban más tratamiento, 6 pacientes no se beneficiaron del tratamiento y los restantes 9 pacientes tuvieron alguna mejoría pero no se consideraron como curados ya que no quisieron parar el tratamiento. Los exámenes de sangre realizados 1 y 3 horas después de la aplicación tópica revelaron la presencia de pequeñas cantidades de la droga (3,3 ng/mL ± 0,66 y 3,3 ng/mL ± 0,52, respectivamente). Se propone la hipótesis de que el clonazepam actúa localmente para interrumpir el mecanismo neuropatológico que sirve de fundamento a la estomatodinia. Los factores de riesgo que se reconocen en esta condición pueden disminuir la densidad y/o la afinidad de ligando; de los receptores periféricos de las benzodiacepinas. Esto, a su vez, puede causar el dolor espontáneo de los tejidos envueltos

Zusammenfassung

Eine Mögliche Therapeutische Lösung für Stomatodynia (Burning Mouth Syndrome)

Stomatodynia ist eine sowohl für den Patienten als auch für den Kliniker schwierige Krankheit. Wenn wir die echte Stomatodynie betrachten, d.h. das idiopathische Mundbrennen, wird dem Patienten dürftig wirkende Behandlung angeboten. Diese offene Studie berichtet über die Ergebnisse von lokaler Clonazepam (0,5 oder 1 mg)-Applikation zwei- oder dreimal täglich bei 25 Personen, die an einer idiopathischen Stomatodynie leiden. Bei der ersten Evaluation, 4 Wochen nach Behandlungsbeginn, sanken die Werte einer visuelle Analogskala (VAS), welche die Schmerzintensität repräsentierte, signifikant von 6,2 ± 0,3 auf 3,0 ± 0,5. Bei der zweiten Evaluation, 3 bis 29 Monate nach der ersten Konsultation, fielen die VAS-Werte signifikant weiter auf 2,6 ± 0,5. Analysen der individuellen Resultate zeigten, dass 10 Patienten vollständig geheilt waren und keiner weiteren Therapie bedurften, 6 Patienten hatten keinerlei Nutzen, und die restlichen 9 Patienten hatten eine gewisse Verbesserung, aber konnten nicht als geheilt betrachtet werden, weil sie mit der Behandlung nicht aufzuhören wünschten. Tests der Konzentration im Blut, welche 1 und 3 Stunden nach der lokalen Applikation durchgeführt wurden, ergaben die Anwesenheit kleiner Mengen des Medikamentes (3,3 ng/mL ± 0,66, bzw. 3,3 ng/mL ± 0,52). Die Hypothese, dass Clonazepam lokal wirkt, indem es die neuropathologischen Mechanismen stört, welche der Stomatodynie zugrundeliegen, wird vorgeschlagen. Die Risikofaktoren, welche für diesen Zustand anerkannt sind, könnten die Dichte und/oder die Bindungsaffinität der peripheren Benzodiazepin-Rezeptoren vermindern. Dies, abwechselnd, könnte spontanan Schmerz aus den betroffenen Geweben verursachen.