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Trigeminal pain and quantitative sensory testing in painful peripheral diabetic neuropathy

Astrid Arap [a], *Silvia R.D.T. Siqueira* [b], *Claudomiro B. Silva* [c], *Manoel J. Teixeira* [d], *José T.T. Siqueira* [e,*]

[a] *Neurology Department of Medical School, Universidade de São Paulo (USP), Brazil*
[b] *School of Arts, Science and Humanities, Universidade de São Paulo (USP), Brazil*
[c] *Neurology Department, Hospital das Clínicas, Medical School, Universidade de São Paulo (USP), Brazil*
[d] *Pain Multidisciplinary Center, Neurology Division, Central Institute and Experimental Neurosurgery Division, Psychiatric Institute, Universidade de São Paulo (USP), Brazil*
[e] *Orofacial Pain Clinic, Dentistry Division/Interdisciplinary Pain Center, Hospital das Clínicas, Medical School, Universidade de São Paulo (USP), Brazil*

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ABSTRACT

Objective: To evaluate patients with Diabetes Mellitus type 2 and painful peripheral neuropathy in order to investigate oral complaints and facial somatosensory findings.
Research design and methods: Case–control study; 29 patients (12 women, mean age 57.86 yo) with Diabetes Mellitus type 2 and 31 age-gender-matched controls were evaluated with a standardized protocol for general characteristics, orofacial pain, research diagnostic criteria for temporomandibular disorders, visual analogue scale and McGill Pain questionnaire, and a systematic protocol of quantitative sensory testing for bilateral facial sensitivity at the areas innervated by the trigeminal branches, which included the thermal detection by ThermoSensi 2, tactile evaluation with vonFrey filaments, and superficial pain thresholds with a superficial algometer (Micromar). Statistical analysis was performed with Wilcoxon, chi-square, confidence intervals and Spearman ($p < 0.05$).
Results: Orofacial pain was reported by 55.2% of patients, and the most common descriptor was fatigue (50%); 17.2% had burning mouth. Myofascial temporomandibular disorders were diagnosed in 9 (31%) patients. The study group showed higher sensory thresholds of pain at the right maxillary branch ($p = 0.017$) but sensorial differences were not associated with pain ($p = 0.608$). Glycemia and HbA_{1c} were positively correlated with the quantitative sensory testing results of pain ($p < 0.05$) and cold ($p = 0.044$) perceptions. Higher pain thresholds were correlated with higher glycemia and glycated hemoglobin ($p = 0.027$ and $p = 0.026$).
Conclusions: There was a high prevalence of orofacial pain and burning mouth was the most common complaint. The association of loss of pain sensation and higher glycemia and glycated hemoglobin can be of clinical use for the follow-up of DM complications.

1. Introduction

Diabetes mellitus (DM) is a syndrome characterized by abnormal metabolism of carbohydrates, lipids and proteins that result from a severe or an absolute deficiency of insulin (Type 1) or from target tissue resistance to this hormone's cellular effect (Type 2).[1] Type 1 includes the immune-mediated form (type A), in which there is autoimmune

* *Corresponding author at*: Rua Maria Cândida, 135, Vila Guilherme, São Paulo/SP, CEP: 02071-010, São Paulo, SP, Brazil.
E-mail address: jtts@uol.com.br (José T.T. Siqueira).
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destruction of beta cells at pancreas and the idiopathic form (type B); DM type 2, characterized by insulin resistance, is the most prevalent (95% of cases).[1] It is the most common endocrine metabolic disorder, affecting 4.6 million people in Brazil (2000), number that is estimated to grow 148% until 2030, reaching 11.3 million. Worldwide, DM affects over 100 million people.[2,3]

The chronic metabolic complications include increased susceptibility to infection and delayed healing, retinopathy, nephropathy, neuropathy, micro and macrovascular diseases.[1] Peripheral diabetic neuropathy is one of the most common of all long term complication of diabetes affecting up to 50% of patients.[4] The sensory manifestations are more pronounced in the lower limbs and can be painful (burning, freezing) or not (numbness, tingling). Few studies had investigated the facial region. The signals and symptoms of cranial neuropathies usually occur in pain crises of diabetic neuropathy at other regions, and the oculomotor nerve is the most affected.[5] Xerostomia, taste impairment, dental caries, periodontal disease, fungal infections, loss of sensation, numbness and burning mouth are among the most common oral manifestations of DM,[6,7] however there are no studies investigating the trigeminal sensitivity in these patients or orofacial complaints that could indicate facial diabetic neuropathy.

In our previous study we described a sample of patients with burning mouth, and DM was among the causes of it.[8] Burning mouth is a possible symptom of neuropathic pain. In this study, our purpose was to evaluate patients with DM type 2 and painful peripheral neuropathy in order to investigate the oral complaints, including burning mouth, and facial somatosensory findings (hypoesthesia/hypoalgesia) compared to controls.

2. Materials and methods

In this case–control study, twenty-nine (29) consecutive patients with DM type 2 (study group) and 31 age-gender-matched controls (control group) were evaluated from January 2007 to January 2008 at the Multidisciplinary Pain Center and the Orofacial Pain Clinic of Hospital das Clinicas, Medical School, University of Sao Paulo, Brazil. Demographic data were compared using Mann–Whitney and Pearson's Chi-square test (SPSS 17.0; SPSS Inc., Illinois, USA). The protocol was approved by the Ethics Committee of the Clinical Hospital, Medical School, University of São Paulo and the patients signed the informed consent.

2.1. *Inclusion criteria for patients*

Clinically and biochemically definite DM type 2 by the World Health Organisation criteria[9] and recent diagnosis (until 1 month) of painful peripheral diabetic neuropathy (PPDN) in the limbs and/or thorax. Tests for autoimmune diabetes (anti-GAD) and C-peptide were negative in all patients. Diagnosis of PPDN was made by the modified San Antonio criteria requiring the presence of two of the following four criteria: (a) symptoms of PPDN; (b) signs of PPDN; (c) abnormal nerve conduction studies with at least two abnormal nerves; (d) abnormal vibration perception threshold. The presence of the latter two criteria is required.[10] Diagnosis of DM Type 2 and PPDN were performed by a single trained endocrinologist from the Multidisciplinary Pain Center of Hospital das Clinicas, Medical School, University of Sao Paulo. All patients had severe DM. The protocol of diagnosis of PPDN did not reveal any impairment at the cranial nerves in this sample. All patients were having hypoglycemic medication in the same concentration for a period of at least 1 year. All patients were having chronic PPDN pain but the mean pain intensity was not collected. None of them were having any analgesic medication.

2.2. *Inclusion criteria for controls*

Healthy subjects had no pain complaints. The controls were evaluated by the clinical and biochemical protocol of Diabetes and by the clinical protocol of orofacial pain below in order to exclude these diagnoses.

2.3. *Exclusion criteria for patients and controls*

DM type 1 and/or severe psychiatric disorders, non-fulfillment of criteria for PPDN, cognitive deficit, non-agreement in participating of the study, pregnancy, other causes for generalized or localized pain. No patient or control was excluded by these criteria.

The patients underwent a standardized protocol applied by a single trained and calibrated dentist (orofacial pain specialist). It consisted of an interview and systematic evaluation of cervical, cranial, facial, dental and other oral structures according to the following specialized diagnostic instruments.[11,12]

(1) A standardized clinical orofacial evaluation to detail: (a) chief complaint; (b) general pain characteristics (quality, duration); (c) dental history; (d) burning mouth prevalence; (e) DM parameters (glycemia, glycated hemoglobin, duration, body mass index–BMI, location of painful peripheral neuropathy); for glycemia and glycated hemoglobin, a sample of 10 mL of blood was removed in the morning period of patients at the day of examination (patients were fasting for 8 h before the exam); glycemia was measured by serum glucose concentration and glycated hemoglobin was measured by high performance liquid chromatography; BMI was calculated based on the measurements of the patients (height and weight) at the moment of examination and consists in the following formula: weight/height^2.
(2) Visual Analogue Scale (VAS) for pain intensity. The patients were asked to report the average of their pain within the last 6 months in a range of 0–10 cm, with 0 labeled as 'no pain' and 10 as 'the most pain imaginable'.
(3) McGill Pain Questionnaire to define pain quality[13], validated to the Portuguese language.
(4) The Portuguese version of the Axis 1 Research Diagnostic Criteria for Temporomandibular Disorders (RDC/TMD).[14]
(5) The periodontal evaluation was performed according to clinical periodontal assessment by bleeding on probing (BOP).[15,16]
(6) Orthopantomography of the jaw to exclude structural disease of the teeth and the jaw bone for both control and study groups, analysed by a trained radiologist.