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Evaluation of the sensation in patients with trigeminal post-herpetic neuralgia

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BACKGROUND: Post-herpetic neuralgia (PHN) is one complication after herpes zoster infection, which may affect the facial superficial sensitivity.
METHODS: Eighteen patients with PHN were interviewed and evaluated according to a systematized sensitivity approach, including mechanical, thermal and pain.
RESULTS: The pain location was V1 in 15 patients. All trigeminal branches from both facial sides were evaluated; we compared the affected with the opposite side. There was a significant difference at V1 with cold ($P = 0.038$), vonFrey ($P = 0.008$) and pinpricks ($P = 0.022$); at V2, the statistical difference occurred with cold ($P = 0.034$), heat ($P = 0.019$) and pinpricks ($P = 0.037$); at V3, differences occurred with cold ($P = 0.042$) and heat ($P = 0.036$). Only V1 and oral mucosa (V2–3) presented pain threshold differences between both sides ($P = 0.001$, $P = 0.021$).
CONCLUSION: Age, predominance of trigeminal PHN in V1 and continuous burning pain was common and similar to literature. Sensation was hampered with evident deficits of all sensory modalities in the affected trigeminal areas, especially V1.
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Keywords: herpes zoster; orofacial pain; post-herpetic neuralgia; quantitative sensory testing; trigeminal neuralgia

Introduction

The primary infection of the herpes zoster virus (HZV) causes chicken pox, a disease that affects mostly children, which is acquired by the respiratory way (1). The virus disseminates and forms stains, warts and vesicles spread all over the skin, and oral ulcers (2). Headaches, faringitis, anorexia and fever may occur (3). Generally, it is obvious to identify, but in 4% of cases, it may not be clinically recognized. The complications are variable, and include neurological abnormalities (4), as post-herpetic neuralgia (PHN), but usually they present spontaneous remission after the disease is cured (1, 4, 5).

Herpes zoster virus infection may affect the trigeminal nerve in 15% of 20% of the cases, and the ophthalmic branch (V1) is the most affected. The infection of the maxillary (V2) and mandibular (V3) branches is characterized by oral ulcers (6). Trigeminal PHN is *chronic pain, in one or more trigeminal branches, after acute infection by HZV* (7). It is more prevalent in older people, after 70 years old, and it is characterized by severe burning sensation, which highly affects the quality of life of patients (7). Neuropathic pain is attributed to demyelinization, walerian degeneration and/or sclerosis of the peripheral nervous system (PNS; 8), and also central alterations-like cell atrophia (9). Pain is spontaneous and continuous, and can last several years after the virus infection, usually accompanied by paraesthesia, hyperaesthesia, allodynia and sensorial deficits at the affected area that may correspond to the pain intensity (10).

Until this moment, there is a lack of systematized studies on trigeminal PHN that objectively evaluated facial sensitivity, including oral mucosa.

The objective of this study was to evaluate the mechanical, thermal and pain sensitivity of the trigeminal nerve in patients with facial PHN, who were referred to an orofacial pain clinic of a large teaching hospital.

Patients and methods

Eighteen consecutive patients were evaluated from August 2004 to November 2004 in the Orofacial Pain Clinic, Hospital das Clínicas, Medical School, University of São Paulo (EDOF-HC). They were diagnosed by the IASP criteria for PHN (7), and corresponded to all consecutive patients during this period of evaluation.

A standardized diagnostic protocol was applied to all patients by a trained dentist. It consisted of an interview

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and systematic evaluation of cervical, cranial, facial, dental and other oral structures according to the following specialized diagnostic instruments or examinations:

1 EDOF-HC protocol (11), a standardized orofacial pain questionnaire including: (i) chief complaint, (ii) general pain characteristics (location, quality, duration, pain relief or pain triggering), (iii) presence of headache and/or body pain, and (iv) patient's medical history and co-morbidities.
2 McGill Pain Questionnaire to define pain quality (12), validated to the Portuguese language.
3 Evaluation of the sensation of the face, in six regions (the three branches of the trigeminal nerve bilaterally): (i) pinpricks, superficial algometry (Micromar®, Micromar, Diadema, São Paulo, Brazil); (ii) thermoalgometry (Electrical device developed at the Functional Neurosurgery Division, Hospital das Clínicas, Medical School, University of São Paulo) and (iii) mechanical sensitivity with manual vonFrey filaments, all in distinct areas of the facial skin and oral mucosa.

The protocol was approved by the Ethics Committee, Hospital das Clínicas, Medical School, University of São Paulo and the patients signed the informed consent.

Statistical analysis

The statistical analyses were performed using the Wilcoxon (13), non-parametric test to measure differences in proportions among the sides. As indices of significance, values ≤5% ($P \leq 0.05$) were considered.

Results

General characteristics of the sample

Eighteen patients (four male and 14 female) were evaluated with the mean age of 72.11 years (range: 55–86). Eleven patients (57.9%) reported previous signals before HZV vesicles started: pain, itching and erythema; the mean duration of the vesicles was 29.9 days (range: 7–180). Four patients (21.0%) presented oral vesicles; 10 patients (52.6%) were affected on the right side and eight (42.1%) on the left side of the face.

Pain location was ophthalmic branch (V1) in 15 (13 only in V1), maxillary branch (V2) in six (two only in V2), mandibular branch (V3) in three, V1–2 in one, V2–3 in one, V1–3 in one and V2–3 and Ramsay-Hunt syndrome in one (5.3%).

Pharmacological treatment was: amitryptiline in nine (47.4%), clorpromazine in six (31.6%), gabapentin in four (21.0%), carbamazepine in three (15.8%) and imipramine in two (10.5%).

Table 1 PHN patients' distribution concerning pain intensity and frequency

	Pain intensity, n (%)			
Frequency	*Mild*	*Moderate*	*Severe*	*Total, n (%)*
Continuous	2 (10.5)	4 (21.0)	6 (31.6)	12 (63.2)
Intermittent	2 (10.5)	3 (15.8)	2 (10.5)	7 (36.8)
Total	4 (21.1)	7 (36.8)	8 (42.1)	19 (100)

PHN pain characteristics (EDOF-HC)

The mean visual analogue scale (VAS) of this sample was five (in a scale from 0 to 10). The pain descriptor was burning in 14 (73.7%), itching in seven (36.8%), jumping in six (31.6%), searing in four (21%), shock-like in three (15.8%), pricking in three (15.8%), tingling in two (10.5%), throbbing in one (5.3%). Pain intensity and frequency are outlined in Table 1.

Superficial sensitivity

The results of the ophthalmic branch (V1) are outlined in Table 2, results of the maxillary branch (V2) in Table 3, and of the mandibular branch (V3) in Table 4. The results of algometric test for pain threshold are outlined in Table 5.

The pinprick evaluation for pain also demonstrated significant differences between the affected and the opposite side, at the oral mucosa (Table 6).

Table 2 Superficial sensitivity of V1 ($n = 18$)

Modalities	*Affected side*	*Opposite side*	*P-value (Wilcoxon test)*
Cold	−0.72 ± 0.93 (−2.00 to 1.00)	−0.11 ± 0.47 (−2.00 to 0.00)	0.038
Heat	−0.44 ± 1.01 (−2.00 to 1.00)	−0.11 ± 0.47 (−2.00 to 0.00)	0.192
vonFrey	−0.72 ± 0.89 (−2.00 to 1.00)	0.00 ± 0.00 (0.00–0.00)	0.008
Pinpricks	−0.87 ± 0.97 (−2.00 to 1.00)	−0.11 ± 0.47 (−2.00 to 0.00)	0.022

V1, ophthalmic branch.

Table 3 Superficial sensitivity of V2 ($n = 18$)

Modalities	*Affected site*	*Opposite side*	*P-value (Wilcoxon test)*
Cold	−0.33 ± 0.59 (−2.00 to 0.00)	0.00 ± 0.00 (0.00–0.00)	0.034
Heat	−0.44 ± 0.77 (−2.00 to 0.50)	0.03 ± 0.12 (0.00–0.50)	0.019
vonFrey	−0.19 ± 0.62 (−2.00 to 1.00)	0.00 ± 0.00 (0.00–0.00)	0.244
Pinpricks	−0.38 ± 0.80 (−2.00 to 1.00)	0.06 ± 0.16 (0.00–0.50)	0.037

V2, maxillary branch.

Table 4 Superficial sensitivity of V3 ($n = 18$)

Modalities	*Affected side*	*Opposite side*	*P-value (Wilcoxon test)*
Cold	−0.24 ± 0.51 (−1.70 to 0.30)	0.02 ± 0.08 (0.00–0.30)	0.042
Heat	−0.29 ± 0.54 (−1.70 to 0.70)	0.00 ± 0.00 (0.00–0.00)	0.036
vonFrey	−0.12 ± 0.33 (−1.30 to 0.10)	0.00 ± 0.00 (0.00–0.00)	0.074
Pinpricks	−0.22 ± 0.68 (−2.00 to 1.00)	0.02 ± 0.08 (0.00–0.30)	0.150

V3, mandibular branch.

Table 5 Algometric test for pain threshold of V1, V2 and V3 ($n = 18$)

	Affected side	*Opposite side*	*P-value (Wilcoxon test)*
V1	73.39 ± 26.85 (10.00–100.00)	41.56 ± 13.68 (22.00–68.00)	0.001
V2	42.94 ± 27.15 (10.00–100.00)	33.61 ± 16.85 (5.00–83.00)	0.446
V3	40.94 ± 21.88 (12.00–100.00)	33.61 ± 12.40 (10.00–64.00)	0.287

V1, ophthalmic branch; V2, maxillary branch; V3, mandibular branch.

Table 6 Pinprick evaluation for pain thresholds at the oral mucosa ($n = 18$)

	Affected side	*Opposite side*	*P-value (Wilcoxon test)*
Oral mucosa	−0.33 ± 0.58 (−2.00 to 0.20)	0.01 ± 0.04 (0.00–0.20)	0.021

Discussion

In this study, we could observe that PHN predominated in older patients, and the ophthalmic trigeminal branch was the most affected. These characteristics are common to trigeminal PHN (14). On the other hand, the prevalence of female (3.75:1) diverges from other studies (7), but it is similar to Brazilian data on PHN in other body parts (4). The mean pain duration was 52.9 months, which corresponds to chronic pain with difficult treatment (15). Burning pain is the chief characteristic of PHN, but itching was reported by 36.8% of the patients and this condition can be associated with loss of peripheral innervation (16). Possible involved mechanisms are central afferent neurones specific for itching with hyperactivity, selective preservation of non-specific peripheral fibres for itching from adjacent dermatomes to the area affected by the virus and/or disarrangement between excitation and inhibition of secondary sensory neurones (16).

Sensitivity evaluation clearly demonstrated significant difference on the respective affected trigeminal areas by PHN, when compared with the opposite side. The most affected branch was V1 for cold ($P = 0.038$), mechanical stimuli ($P = 0.008$) and pain with pinpricks ($P = 0.022$). In a similar way, V2 was significantly affected on cold ($P = 0.034$), heat ($P = 0.019$) and pain with pinpricks ($P = 0.037$), and V3 was affected on cold ($P = 0.042$) and heat ($P = 0.036$). The reasons for heat and pain perception differences are unknown. Ammer et al. (17) observed thermal asymmetry in patients with acute and chronic herpes zoster, and correlated thermal imaging with pain intensity and dysaesthesia, concluding that it is a common finding for acute episodes in these patients. The greatest number of patients with V1 affected (68.4%) showed the correspondence of the infection at V1 by HZV and the permanent injury of terminal endings at this branch. This is supported by the statistical difference of hypoalgesia at V1 ($P = 0.001$) that was not observed in other trigeminal branches.

This study is different from others that evaluated the facial sensitivity of PHN but did not observe abnormalities at the affected side on pain, cold and heat thresholds. At thorax, heat, cold perception, cold pain and pain thresholds were increased when compared with the opposite side, but facial area presented a lower threshold for cold, heat and pain (8). These authors did not correlate the magnitude of sensory dysfunction and pain intensity or allodynia, in contrast to Rowbotham and Fields (18). These controversies may be attributed to different populations and/or different methodologies, for example, in the last study they excluded patients with PHN at face. In another study (19), there was a correlation between sensory deficit and the pain area, similar to ours.

Other relevant data from this study refer to hypoalgesia at the oral mucosa when compared with the other facial side ($P = 0.021$), which is contrast to what we observed on the algometric test of V2 and V3. One possible explanation would be the lower sensitive innervation density at the oral mucosa, which increases its sensory threshold and nociceptive input differentiation. The lower sensory perception of the oral mucosa, especially in older patients (many of them using dental

prosthesis), may generate more often oral trauma and the need of periodical appointments (20).

The presence of vesicles at the oral mucosa in 21% of the patients with PHN (V2/V3) supports the importance of differentiating it from common oral ulcers-like ApHTHA or gingival diseases, and we have case reports on that issue (2). The vesicles at the oral mucosa play a role in the differential diagnosis; prodromal signals including vesicles were present in 57.9% of this sample.

In conclusion, by the methodology used in this study we observed that, although the affected trigeminal branch by PHN was the ophthalmic in the largest part of the patients, there was a significant difference of pain and thermal sensitivity in all branches when compared with the opposite side. All these differences were present even in adjacent trigeminal branches that were not affected by PHN.

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