Peripheral Painful Traumatic Trigeminal Neuropathy: Clinical Features in 91 Cases and Proposal of Novel Diagnostic Criteria

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Aims: *To field-test carefully designed criteria for pain following trigeminal nerve trauma.* ***Methods:*** *In order to characterize the clinical phenotype, posttraumatic pain patients were studied and compared with classical trigeminal neuralgia patients (CTN, defined according to the International Headache Society's criteria). Based on etiology and features, trigeminal pain following trauma was defined as "peripheral painful traumatic trigeminal neuropathy" (PPTTN). Data were analyzed with* t *tests, ANOVA, chi-square, and regression analyses.* ***Results:*** *A total of 145 patients were included: 91 with PPTTN and 54 with CTN. Findings indicated that PPTTN criteria are clinically applicable in the detection and characterization of relevant cases. In contrast to accepted characteristics for PPTTN, the observed profile included both continuous and paroxysmal pain that was stabbing and/or burning. The quality, duration, and intensity were significantly different from the CTN patients (*P < .05*). PPTTN was consistently accompanied by trigeminal sensory abnormalities (96%) that were mostly allodynia, hyper- or hypoalgesia, and only 1% of the PPTTN cases had anesthesia.* ***Conclusion:*** *Overall, the proposed PPTTN criteria have proven to be clinically useful. In view of these results, modified PPTTN diagnostic criteria are proposed for use in future research.* J OROFAC PAIN 2012;26:49–58

Key words: atypical odontalgia, neuropathic pain, persistent idiopathic facial pain, trigeminal neuralgia

Injury to the trigeminal somatosensory system at peripheral nerve, ganglion, sensory root, or central structures can induce chronic neuropathic pain[1,2] and may follow major[3,4] or even minor trauma.[5]

Unfortunately, neuropathic pain due to trigeminal nerve injury has been poorly defined. Various related terms exist in the literature, including deafferentation pain,[6–8] phantom tooth pain,[9,10] atypical odontalgia,[11,12] anesthesia dolorosa,[13–15] and persistent idiopathic facial pain (atypical facial pain).[13,16,17] The occurrence of Complex Regional Pain Syndrome[11] in the craniofacial region is unclear.[18] The term "posttraumatic neuralgia" has also been suggested in an article that employed advanced statistical processing and successfully clustered such patients based on clinical features.[19] The above terminologies have been critically reviewed.[1,20]

Criteria for posttraumatic trigeminal neuropathic pain have been suggested.[21,22] Based on recent literature, these criteria were refined

Table 1 PPTTN: Proposed Diagnostic Criteria

	Diagnostic criteria	Notes
A	Spontaneous or touch-evoked (stimulus dependent) pain affecting one or more divisions of the trigeminal nerve that: 1. Lasts from seconds to minutes.* 2. Is constant (> 8 h/day, > 15 days/mo).	Pain is mostly unilateral and does not cross the midline. *Paroxysmal pain patients may also have constant background pain. Present results show that attack duration is heterogenous and this needs reevaluation (see Discussion).
B	Develops within 3 months of an identifiable traumatic event to the painful area* or relevant innervation.† Continues for more than 3 months.	Trauma, surgery, invasive dental treatment. *Usually localized pain. †Likely to cause dermatomal pain, may spread due to central mechanisms.
C	At least one clinically evident neurologic dysfunction: Positive sign 1. Hyperalgesia 2. Allodynia 3. Swelling or flushing and/or: Negative sign 1. Anesthesia 2. Hypoesthesia	Must be a constant feature and reproducible. Nonvital tooth is evidence of nerve damage. Clinical examination may be suitable. If area is amenable, quantitative sensory testing may reveal changes. Advanced neurophysiologic testing is not always available but certainly valuable (see D), eg, nerve conduction studies, electromyography, laser-evoked potentials, blink reflex, masseter inhibitory reflex. Convincing data from C may be considered sufficient.
D	Imaging or neurophysiology demonstrating a neurologic lesion and its location	Imaging may often be historical, eg, zygomatic fractures affecting the infraorbital nerve that have been decompressed, dental implants that impinged on nerve bundles but may have been removed. Root canal therapy is considered evidence of nerve damage. Neurophysiology (see above).
E	Not attributed to another disorder	Other causes are ruled out by history, physical examination, and special investigations if necessary.
Diagnostic level	Fulfills criteria A, B, and E Fulfills criteria A, B, C or D, and E Fulfills criteria A, B, C and D, and E	Possible NP Probable NP Definite NP

Definite PPTTN cases are defined as meeting criteria A, B, C and/or D, and E. Probable PPTTN lacks sufficient neurologic documentation as required in C and D. A total lack of such documentation in the presence of A, B and E (with or without D) would classify the patient as possible PPTTN (see reference 23). NP = neuropathic pain.

and a grading of the certainty of neuropathic pain diagnosis was incorporated (Table 1).[2,23] The aim of the present study was to field-test these carefully designed criteria for pain following trigeminal nerve injury. This article thus presents the results of field-testing the proposed criteria for "peripheral painful traumatic trigeminal neuropathy" (PPTTN) in a craniofacial pain clinic. The term "neuropathy" is used in preference to neuropathic pain so as to allow the future inclusion of the clinically common non-painful trigeminal neuropathy due to trauma (and other causes).

Materials and Methods

This was a prospective cohort study where the PPTTN patients were to be compared to classical trigeminal neuralgia (CTN) patients. Inclusion criteria were comprised of a complaint of facial or head pain that was present for a minimum period of 3 months. The criteria for the first experimental group of patients were in accordance with the International Headache Society's (IHS)[13] definition of classical trigeminal neuralgia (CTN; 13.1.1). Only CTN cases with no history of previous surgery were included. The second experimental group had to meet inclusion criteria for PPTTN that the authors defined (see Table 1).

Exclusion criteria included: painless sensory deficits; anaesthesia dolorosa[13] because it includes occipital and trigeminal nerve injuries, both peripheral and central; persistent idiopathic facial pain (PIFP) due to the ambivalent nature of this entity; and burning mouth syndrome because it is unclear whether it is solely a neuropathy. By definition, all symptomatic trigeminal neuralgia cases were excluded.

Patient History

A pain intake form routinely used for the authors' research[16,21] was employed to record all relevant parameters (translated copy[24]). Patients were asked

to rate their characteristic (typical) pain intensity on a 10-cm visual analog scale (VAS). Pain quality was established by asking the patients to choose one or more of the following descriptive terms: electrical, stabbing, throbbing, pressure, burning, or any combination of the five terms.[16,21] Patients were asked to report pain duration representing that of a typical attack. The presence of autonomic signs such as tearing, redness, or swelling was noted. Patients were also asked whether the pain specifically woke them up from sleep.[21] Additionally, gender, ethnicity, medical status, and history of other therapeutic interventions were recorded.

Patients were allocated to three temporal patterns according to attack frequency and duration parameters often used in the headache literature: "daily" for patients with short and daily attacks of pain (> 15 days/month) lasting less than 4 hours, "episodic" for patients with attacks of pain lasting less than 4 hours but that occurred on ≤ 15 days monthly, and "continuous" in patients with daily constant pain (attacks ≥ 4 hours or continuous).[25] Patients with primarily paroxysmal daily pain who also reported a constant background pain were coded as having concomitant "background pain."

A trauma history was collected verbally and from relevant documentation (eg, dental or hospital records, historical imaging).

Clinical Examination

The examination included a routine physical assessment of the head and neck, the masticatory apparatus (temporomandibular joints and masticatory/neck muscles[26]), dental and periodontal tissues, and cranial nerves. The authors attempted to identify tactile trigger areas, ie, sites which when pressed caused onset of severe pain that spread beyond the area of stimulation.

The following muscles were examined bilaterally: temporalis, masseter, medial pterygoid, sternocleidomastoid, trapezius, and the suboccipital (as one group). Muscle trigger points were included as part of the assessment of muscle involvement, not to be confused with the tactile trigger areas described for CTN and PPTTN. Tenderness to muscle palpation was graded as 0 (no pain), 1 (mild), 2 (moderate), and 3 (severe), and the individual scores summated as the total tenderness score (TTS), as described previously.[21,27–31] Diagnostic imaging was requested routinely for CTN cases (brain and brainstem computed tomography [CT] or magnetic resonance imaging/angiography) and for other diagnoses as needed. Additionally, areas adjacent to the nerve injury were imaged (plain radiography, CT).

All patients were collected from the Orofacial Pain Clinic at the Faculty of Dentistry, Jerusalem, for a period of 3 years. The clinic is a secondary/tertiary referral center. Following a primary intake (in Hebrew) by a resident, all patients were examined by both senior authors (RB, YS) who designed the original criteria[20] together. The institutional review board approved the study, and patients consented to the use of their data.

Sensory Testing

Routine testing in affected and contralateral areas included the use of a sharp stimulus and a blunt stimulus. These were augmented by examining sensitivity to moderate digital pressure and dynamic testing by rubbing the traumatized and/or painful areas. Based on these tests, areas were designated a "sensory signature" according to the definitions described by the International Association for the Study of Pain,[32] as follows:

- Hypo/hyperalgesia: diminished/increased pain to a stimulus that is normally painful (eg, pinprick).
- Hypo/hyperesthesia: decreased/increased sensitivity to stimulation (eg, cotton wool, blunt instrument, digital pressure).
- Allodynia: pain due to a stimulus that does not normally provoke pain (eg, cotton wool, blunt instrument, digital pressure).

Teeth were tested by cold (ethyl chloride) application if radiographs were inconclusive. Electrical pulp testing was employed if the cold test was negative and the radiograph showed no root canal therapy. In addition, patients with extraoral sensory signs (negative or positive, eg, hypoesthesia and hyperalgesia, respectively) routinely underwent quantitative sensory testing (QST) with transcutaneous electrical stimuli delivered by the Neurometer Nervscan NS3000 device (Neurotron). The Neurometer delivers calibrated electrical stimuli to assess the thresholds of the sensory effects evoked by each of the three sensory fiber types (see below). Patients with CTN with no sensory changes on clinical examination of the trigeminal nerve did not undergo routine QST. The stimuli were applied bilaterally to the area affected and its contralateral equivalent. The skin was cleaned and electrode gel applied to the surface electrodes. Nonconductive adhesive strips held the electrodes (1-cm diameter gold-plated, Goldtrode, Neurotron) in close proximity. Stimuli were delivered at 250 Hz to assess the sensory threshold associated with A-δ fiber stimulation, and at 2,000 Hz and 5 Hz for A-β and

Table 2 Differences Between Patient Profiles in CTN and PPTTN

Parameter	CTN (n = 54)	PPTTN (n = 91)	Statistics
Gender (M:F)	25:29	34:57	χ^2, $P > .05$
Onset age (y ± SD)	58.61 ± 13.9	48.60 ± 15.2	T, $P < .001$
Location	Unilateral (100%) dermatomal	Bilateral (10%) injury related	χ^2, $P > .05$
Nerve branch affected	I = 2%, II = 30%, III = 48%, II & III = 20%	Injury related area*; may be dermatomal†	χ^2, $P > .05$
Intensity (mean VAS ± SD)	9.1 ± 1.1	7.7 ± 1.8	T, $P < .001$
		Dental 7.6 ± 1.8 / Macro 7.9 ± 1.6	T, $P > .05$
Temporal	Daily (100%)	Daily (47%) ‡Episodic (3%) ‡Continuous (50%)	χ^2, $P < .0001$
Duration	Homogenous 100% cases 0.5–2.5 min	Heterogenous: 24% cases 1–4 min; 26% cases 10–180 min; 50% cases > 4 h	T, $P < .0001$
Common quality	Electric (32%), electric + stabbing or pressure (30%)	Burning (13%), burning + stabbing or pressure (20%) Stabbing (12%), stabbing + pressure or throbbing (6%) Electric (11%)	χ^2, $P = .001$
Background pain	33%	39%	χ^2, $P > .05$
Identifiable trigger	57%	5%	χ^2, $P < .0001$
Autonomic signs	21% tearing	11% redness/swelling	χ^2, $P > .05$
Muscle pain (TTS ± SD)	0.4 ± 2.0	3.6 ± 6.3	T, $P = .001$
Wakens	29%	37%	χ^s, $P > .05$
Sensory disturbance	Rare (1 case; 1.8%)	96%	

SD = standard deviation of mean value; I = ophthalmic branch; II = maxillary branch; III = mandibular branch (of trigeminal nerve); min = minutes; h = hours; *in injuries involving peripheral fibers; †more usual in injuries to major branches of trigeminal nerve; ‡18 patients (39.1%) of the daily and episodic PPTTN patients reported a constant background pain.

C-fiber-evoked sensory threshold, respectively.[33–35] The subjects were instructed to release a control button upon the first sensation. Both operator and patients were blinded to the stimulus intensity provided.

Statistical Methods

Data were analyzed with SPSS version 19 (IBM) with α set at .05 (two-tailed). Interactions between nominal variables were analyzed with a Pearson chi-square test (χ^2). Differences between continuous variables were analyzed with a Student *t* test (T).

Neurometer results were converted to ratios (affected side/contralateral side) to account for between-patient variability, then analyzed with a one-group T for significance from the normal value of 1. Repeated-measures analysis of variance was used to test for differences between readings obtained for the three fiber groups. The relationship between the reported duration in pain attacks and disease duration was analyzed with a linear regression analysis. Within-group analyses were often performed in the PPTTN group to analyze differences between dental and macrotrauma groups.

Results

A total of 145 patients were collected during the study period: 91 cases of PPTTN and 54 of CTN. The essential features of PPTTN and comparisons with those of CTN are summarized in Table 2. Mean onset age in PPTTN (48.60 ± 15.2 years) and CTN (58.61 ± 13.9 years) was significantly different; no differences were observed in onset age between dental (50.4 ± 14.8 years) and macrotrauma (43.5 ± 15.6 years, T, $P > .05$) groups.

The initiating event in PPTTN was a dental procedure in 67 patients (16 dental implants, 11 root canal therapies, 21 surgical extractions, 15 surgeries [endodontic, exploratory], 4 maxillary sinus surgeries), and macrotrauma in 24 patients (19 road traffic accidents, 5 assaults). Of the 67 patients with dental trauma, 26 had undergone mandibular procedures with inferior alveolar and lingual nerve blocks. CTN cases all reported spontaneous onset.

Results of Imaging

All patients with pain following dental implants underwent cone beam CT of the area in order to locate and grossly assess the extent of crush damage. All implant cases showed varying degrees of impingement on the inferior alveolar nerve (crush) except for one, which showed total axotomy. All "sinus" cases were imaged with CT with no evidence of damage. Postextraction, postoral surgery patients were imaged with panoramic or intraoral radiographs; 4 of the 21 surgical extraction cases were referred for CT to assess better the extent of damage. Ten of the remaining 17 surgical extraction cases also had clear damage that involved the inferior alveolar nerve. No pathology was observed in the radiographs of patients with standard root canal therapy. In postsurgical endodontic cases, there was root apex amputation often accompanied by periapical scar formation.

All macrotrauma patients had plain radiographs and/or CTs from the time of their injury showing involvement of nerve bundles.

Pain Location

CTN was, as expected, exclusively unilateral, but 10% of patients with PPTTN reported bilateral pain (7% of the dental cases and 18% of the macrotraumas, χ^2, $P > .05$).

CTN patients reported pain in trigeminal dermatomes (see Table 2) and none of these were exclusively intraoral. The areas affected by PPTTN were dependent on the area of trauma: predominantly the mandible (n = 29, 31.9%), maxilla (n = 28, 29.6%), and exclusively intraoral (both maxilla and/or mandible, n = 18, 19.8%).

Intensity and Temporal Pattern

Pain intensity was significantly higher in CTN patients than in PPTTN patients (Table 2, T, t = –5.1, $df = 143$, $P < .001$). Within the PPTTN group, no differences were observed in VAS scores between the dental and macrotrauma ($P > .05$) groups.

Within the PPTTN group, temporal patterns were variable, from daily, through episodic, lasting minutes to hours to continuous pain (Table 2), while in CTN patients all patterns were daily (χ^2, $P < .001$). A constant low-grade background pain was present in 18 of the 46 PPTTN patients with daily or episodic pain (39.1%) and in 33.3% of the CTN patients (χ^2, $P > .05$).

Pain and Disease Duration

Reported pain duration in CTN patients was homogenous (1.5 ± 0.6 minutes, range 0.5–2.5). The PPTTN group generally had longer pain duration (T, t = 6.4, $df = 143$, $P < .0001$, Table 2). Interestingly, 22 PPTTN patients (24%) reported pain attacks of 4 minutes or less (range 0.5–4), and these were indistinguishable from CTN based on pain duration alone (T, $P > .05$). In 14 PPTTN patients (15%), pain duration was longer than 1 hour but shorter than 8 hours.

Disease duration in CTN patients was 38 ± 61 months and in PPTTN patients was 31 ± 104 months ($P > .05$). For both PPTTN and CTN patients, there was a significant (albeit weak) correlation between duration of pain attacks and time since initial onset (ie, disease duration, PPTTN: F = 6.9, $df = 1$, $P = .01$, $r^2 = .07$, CTN: F = 5.4, df = 1, $P = .03$, $r^2 = .1$).

Pain Quality

Quality of pain reported by PPTTN patients was burning, at times in combination with stabbing or pressure (Table 2). Stabbing pain was common, often appearing in combination with other descriptors (Table 2). Within the PPTTN group, there were no significant differences in quality descriptors between pain induced by dental procedures or by macrotrauma (χ^2, $P > .05$).

CTN was most commonly described as similar to an "electrical shock" type of pain, often accompanied by stabbing or other pain quality. Burning-type pain was reported by nine CTN patients (16.7%), with no correlation with the presence of background pain (χ^2, $P > .05$). The differences in pain quality descriptors between PPTTN and CTN patients were significant ($\chi^2 = 47.2$, $df = 21$, $P = .001$).

Triggering/Trigger Areas

Trigger areas were identified in 57% (n = 31) of CTN patients. Trigger areas were identified in only 5.5% (n = 5) of PPTTN patients ($\chi^2 = 48.9$, $df = 1$, $P < .001$), but none of these had the typical features of CTN trigger points such as refractory period or latency.

Muscle Pain

Comorbid muscle pain, reflected in the TTS, was significantly higher in PPTTN than in CTN patients (t = 3.5, *df* = 140, *P* = .001, Table 2).

Regional Autonomic Signs, Dizziness, and Awakening

Ten PPTTN patients (11%) reported (clinically verified) autonomic signs (AS) accompanying their pain. Five reported swelling, two reported redness, two both swelling and redness, and one tearing. Eleven CTN patients (21%) reported tearing (χ^2, *P* > .05), but the single patient with CTN in the ophthalmic division of the trigeminal nerve was not among them.

In the whole group, the presence of an AS was not related to the VAS scores (T, *P* > .05). Independent analysis of the CTN group revealed that tearing was significantly associated with the VAS scores (with tearing VAS = 9.6 ± 0.6, without VAS = 8.9 ± 1.2, t = –3, *df* = 52, *P* = .006).

PPTTN patients were the only ones to complain of dizziness (n = 13, 14.1%, χ^2 = 8.5, *df* = 5, *P* = .004), but this was unrelated to whether pain had been induced by dental (n = 9, 13.4%) or macrotrauma (n = 4, 16.7%). The presence of dizziness was also not related to the TTS or the VAS reported by PPTTN patients.

Pain-related awakening from sleep was reported by 50 of the 145 patients (34.5%) and this was not statistically different between the groups (Table 2). In general, patients with pain-related awakenings suffered significantly more severe pain (VAS 8.8 ± 1.4) than those who did not (7.9 ± 1.8, T: t = –3.2, *df* = 143, *P* = .002). Similarly, the TTS was significantly higher in patients reporting sleep-related awakenings (3.7 ± 6.9) than in those who did not (1.7 ± 4.2, T: *P* = .04).

Sensory Testing

Clinical (Qualitative Testing). Hypoalgesia was most prominent, occurring alone in 28 PPTTN patients (30.8%) or with allodynia in 21 PPTTN patients (23.1%). Hyperalgesia was found in 7 PPTTN patients (7.7%) accompanied by allodynia in a further 9 PPTTN patients (9.9%). Allodynia alone was detected in 22 PPTTN patients (24.2%). In the PPTTN group, 4 patients (4.4%) had no detectable sensory dysfunction in spite of a clear connection with a traumatic event and pain in the traumatized region.

Only one case of CTN showed clinical hypoalgesia on the affected side. This was confirmed by QST. Specifically, magnetic resonance imaging ruled out secondary (symptomatic) CTN.

QST. Only PPTTN cases were included in this analysis. QST results from 24 PPTTN cases were analyzed. Ratios obtained from PPTTN patients for A–β (2.3 ± 1.7), A–δ (2.6 ± 2.3) and C-fiber (2.6 ± 1.8)-evoked sensory thresholds were significantly higher than the expected "1" (T: t = 3.8, *P* = .001: t = 3.6, *P* = .002: t = 4.2, *P* < .001 respectively, *df* = 24 for all). Repeated-measures analysis did not reveal any significant differences between the fiber types, with (F = 2.1, *df* = 1, *P* = .16) or without trauma type as a between-subject factor (F = 1.8, *df* = 2, *P* = .18).

Discussion

This article presents the results of a thorough characterization of patients with craniofacial pain secondary to trauma. The comparative group was patients with CTN, a well-documented neuropathy whose pathophysiology probably involves the dorsal root entry zone (DREZ). The suspected pathophysiology consists of pressure from an aberrant vessel on the DREZ resulting in demyelination, dismyelination, and axonal damage.[36] In many ways, the histopathology is similar to that seen in certain traumatic neuropathies, although the latter are certainly more varied and dependent on the degree of damage.[37] Thus, the study included a peripherally based pain (PPTTN) versus a centrally based pain (CTN), the latter having a well-characterized clinical profile, and thus making it a suitable comparator.

The profile of the CTN cohort was in line with the published literature.[20] In contrast, the clinical profile of the PPTTN group was that of a moderate, stabbing, and/or burning pain in the receptive field of the traumatized nerve, and was usually unilateral. The injured nerve's dermatome was often involved with pain and clear sensory disturbance. The majority of PPTTN patients reported pain that was present on most days; however, about one-fourth reported short attacks rather than continuous pain. Hence, the PPTTN pain profile was generally significantly different from that of the CTN group. However, there was phenotyical overlap; burning pain was clearly more prevalent in PPTTN patients, although it has also been observed in CTN in this and other reports[38] and pain duration in a minority of PPTTN cases closely resembled that of CTN cases. This observation warrants modification of the originally proposed criteria for PPTTN, and refinements, particularly to criteria A and B, are presented in Table 3. Pain in PPTTN patients was accompanied

Table 3 PPTTN: Modified Diagnostic Criteria

	Diagnostic criteria	Notes
A	Spontaneous or touch-evoked (stimulus dependent) pain predominantly affecting the receptive field of one or more divisions of the trigeminal nerve. *Duration ranges widely from episodic (minutes to days) and may also be constant.	Pain tends to spread with time and is mostly unilateral without crossing the midline. Paroxysmal pain patients may also have constant background pain. Time pattern may change over the course of the disease.
B	Develops within 3 months of an identifiable traumatic event to the painful area* or relevant innervation.† Continues for more than 3 months.	
C	At least one clinically evident neurologic dysfunction: Positive sign 1. Hyperalgesia 2.Allodynia 3. Swelling or flushing and/or: negative sign 1. Anesthesia 2. Hypoesthesia	As in Table 1
D	Imaging or neurophysiology demonstrating a neurologic lesion and its location	
E	Not attributed to another disorder	
Diagnostic level	Fulfills criteria A, B, and E Fulfills criteria A, B, C or D, and E Fulfills criteria A, B, C and D, and E	Possible NP Probable NP Definite NP

Based on the present results, Table 1 has been modified and a refined set of diagnostic criteria presented for testing in further studies. As in Table 1, definite PPTTN cases are defined as meeting criteria A, B, C and/or D, and E. Probable PPTTN lacks sufficient neurologic documentation as required in C and D. A total lack of such documentation in the presence of A, B, and E (with or without D) would classify such a patient as possible PPTTN.

by comorbid regional myalgia and dizziness but rarely with regional AS. The mixed pain phenotype of neuropathic and muscular pain has been previously described[4] and needs to be accounted for in diagnosis and therapy.

Classically, PPTTN is described as continuous pain.[39,40] In the current patient population, PPTTN could be daily with attacks of short-lasting pain or continuous with or without superimposed attacks of sharp pain. These superimposed attacks were mostly spontaneous, but a small number of patients reported mechanical triggers. However, the mean paroxysms of pain are significantly longer than those in CTN. It is important to stress that some PPTTN attacks lasted < 4 minutes; thus pain duration, as a single measure, may not distinguish CTN from some PPTTN cases. Furthermore, cases were found with intermediate pain duration, a group the authors had not been expecting; thus the relevant criteria A1 and A2 should be modified. The question is where to set the cutoff points? From the present results, the heterogeneity is so large that A1 and A2 should probably be united under one criterion, namely pain that may be paroxysmal, long-lasting, or even constant. Further research is clearly needed. In both CTN and PPTTN patients, pain duration was positively (but weakly) correlated to disease duration; in other words, the longer the pain is present, the longer the pain attacks become. The significance of this finding is unclear but may reflect the effects of increased nerve damage from a neurovascular contact in CTN cases, continued deterioration of damaged nerves in PPTTN cases, and/or the establishment of central sensitization. The finding is therefore interesting but needs further investigation in larger studies.

The "sensory signature" for PPTTN was typically either allodynia or hypoalgesia, but a combination of these was also observed. QST suggested damage to all fiber types (Aβ, Aδ, C), with no significant difference between them. Thick myelinated Aβ fibers are more susceptible to damage, particularly crush injuries (see reference 3), but there was no evidence of this in the current study. A larger sample and multimodal testing may reveal differences in future studies; however, a further problem is that the injuries were not uniform. Four patients did not meet the "sensory criteria" as defined in Table 1 (C), and cannot be considered "definite" neuropathic pain.[23] Seven oral surgical cases had no clear radiographic evidence of nerve damage, making them "probable" neuropathic pain.

It is not unusual that criteria fail to accurately include all cases. The present study's criteria defined seven probable and 80 definite PPTTN patients, totaling 96% of the patients. Some would argue that a tooth with a root canal filling is insufficient evidence of nerve injury. However, in the authors' view, the presence of a root canal filling is clear evidence of axotomy at the tooth apex and, therefore, nerve damage. The lack of a response to the application of cold to a tooth due to denervation by root canal therapy supports this and is comparable to the numbness often felt in body structures following nerve injury.

The definition of clinical entities is a complex exercise. Recently, a descriptive approach that has the benefit of descriptive, literal accuracy has been advocated and employed in the redefinition of atypical odontalgia.[41] The approach is based on ontology principles and has advantages and disadvantages, a discussion of which is beyond the scope of this paper.

Some patients develop chronic pain following negligible nerve trauma such as root canal therapy or following considerable injury to nerve bundles, such as orthognathic surgery[42] or fractures of the facial skeleton.[3,5] Following injury to trigeminal nerve branches, chronic pain develops in about 3% to 5% of patients.[3,42] This compares with about 5% to 17% in other body regions.[43,44] Peripheral branches of the trigeminal nerve can be damaged during many dental procedures and surgical interventions. Damage to sensory nerves can result in sensory changes (positive or negative), pain, or a combination of the two.[45] Although transient or permanent sensory dysfunction is common and has been widely documented following implant surgery[46–48] and third molar extractions,[49,50] there are few reported neuropathic pain cases.[51,52] The incidence of nonpainful traumatic trigeminal neuropathy may be even higher as some patients may not attend for therapy if the defect is minor. Chronic neuropathic pain occurs in 3% to 13% of cases following conventional root canal therapy[5,9,53–55] and in 5% of patients following surgical root canal therapy.[56] Although beyond the scope of this paper, a recent review[45] has examined preventative and therapeutic strategies for iatrogenic nerve injuries; since 67 (74%) of the PPTTN cases in the present study were dentally induced, a conservative and informed approach may have a significant impact.

It is likely that direct dental trauma was the primary cause in the PPTTN group. It cannot be ruled out that nerve insult due to a local anesthetic or needle injury induced or augmented the pain, particularly in mandibular blocks.[57,58] Moreover, it has been the authors' experience that patients with PPTTN often "evolve" from other primary pain syndromes, such as misdiagnosed CTN[59–61] and cluster headache,[62–64] that have been invasively treated, leading to repeated nerve injury and neuropathic pain.

Additional Considerations

The CTN group included cases with lacrimation, not usually associated with CTN. Patients with CTN and lacrimation have been described in which all branches of the trigeminal nerve are involved.[65–67] These may be suspicious of short-lasting neuralgiform headache attacks with conjunctival injection and tearing (SUNCT). However, SUNCT is periorbital; in the present cases, all showed involvement of the maxillary/mandibular branches, suggesting they were CTN cases with lacrimation.

Pain-related awakening in CTN is also an atypical sign. However, recent reports[68,69] have suggested that pain-related awakening in CTN may be more common than previously thought. Background pain in CTN is also a common finding.[20]

In line with the literature, the present CTN cases showed a peak incidence at 50 to 60 years of age.[70,71] CTN may occur earlier but may indicate pathology; in patients under the age of 29 years, the prevalence of intracranial tumor or multiple sclerosis is high (≈ 100%) and decreases with increasing age.[72]

Strengths and Limitations

In summary, the criteria employed in this study were clinically applicable and significantly assisted us in characterizing patients with traumatic neuropathic pain. However, in view of the present results, these have been modified (see Table 3). Additionally, the term "peripheral painful traumatic trigeminal neuropathy" is flexible and will allow for the future definitions of peripheral nonpainful and central (painful or nonpainful) trigeminal neuropathies. Future multicenter research will allow testing and further refinement of these criteria, enabling reliable and comparable research on prevention strategies and treatment outcomes.[45]

The findings in this study of sensory changes were based on clinical and QST data. Although such data are largely efficacious,[2,73,74] it is clear that advanced neurophysiologic testing (eg, of brainstem reflexes) is superior.[75–79]

No psychosocial questionnaires were used in the patients; these may be helpful in revealing different patient profiles.

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