Original Article

JOMP
Journal of Oral Medicine and Pain

eISSN 2383-8493
J Oral Med Pain 2022;47(2):87-94
https://doi.org/10.14476/jomp.2022.47.2.87

Clinical Features of the Persistent Idiopathic Dentoalveolar Pain Compared with Inflammatory Dental Pain

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Received June 21, 2022
Revised June 22, 2022
Accepted June 22, 2022

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This study was supported by grant (no. 04-2016-0084) from the Seoul National University Dental Hospital Research Fund.

Purpose: This study aimed to evaluate the differences between clinical and quantitative sensory testing (QST) results among persistent idiopathic dentoalveolar pain (PIDP), inflammatory dental pain, and control group subjects to identify discriminative clinical features for differential diagnosis.

Methods: Thirty-three patients (5 PIDP-a without surgical procedures 10 PIDP-b with surgical procedures, 8 dental pain patients, and 10 controls) were evaluated for clinical features and QST results. Cold pain threshold, heat pain threshold, mechanical pain threshold (MPT), mechanical pain sensitivity, and pressure pain threshold (PPT) were performed. Psychological factors were assessed using Symptom Checklist-90-Revision (SCL-90-R) and a chart review was conducted to evaluate additional discriminative clinical features such as pain quality and treatment prognosis.

Results: The dental pain group had lower PPT than the PIDP-b and the control group. The PIDP-a group showed higher MPT and PPT than the PIDP-b and dental pain group but the difference was not statistically significant. Differences in SCL-90-R SOM (Somatization), O-C (obsessive-compulsive), ANX (anxiety), and PSY (Psychoticism) values were statistically significant among groups. PIDP-a and PIDP-b groups showed remaining symptoms after treatment and the pain tended to spread widely, whereas, in toothache patients, symptoms disappeared after treatment. However, factors that confound the diagnosis, such as an increase in pain during chewing and a decrease in the pain threshold at the affected site, could also be identified.

Conclusions: PIDP and dental pain groups have distinct clinical symptoms, but there are also factors that cause confusing in diagnosis. Therefore, various clinical examination results should be carefully reviewed and comprehensively evaluated in the differential diagnosis process.

keywords: Diagnosis, differential; Pain threshold; Prognosis; Quantitative sensory testing; Somatosensory disorders; Toothache

INTRODUCTION

Persistent idiopathic dentoalveolar pain (PIDP) was previously termed atypical odontalgia, persistent dentoalveolar pain disorder, and phantom toothache [1]. In the International Classification of Orofacial Pain (ICOP), it is defined as dentoalveolar area pain lasting more than three months without a specific preceding cause [2]. As mentioned in the definition of PIDP, diagnosis is difficult due to complains of pain without any clear objective signs,

and there is a risk of irreversible treatment such as root canal treatment (RCT) and extraction due to misdiagnosis. Therefore, when diagnosing a patient complaining of a toothache, it is very important to differentiate between odontogenic and non-odontogenic pain, but there is no clear gold standard for differential diagnosis yet [3].

Quantitative sensory testing (QST) evaluates the functions of A-beta, A-delta, and C fibers using temperature, mechanical, vibrational, pressure, electrical, and chemical stimulation to quantitatively identify somatosensory changes [4]. In the past, there were various measures and evaluation criteria, but the German Research Network on Neuropathic pain developed a standardized method [5]. The characteristics of somatosensory changes in patients with various types of neuropathic pain were evaluated using QST, and the results are also used for diagnosis and treatment effect evaluation by estimating the underlying mechanism, phenotyping, or classification of diseases. Research included those of the orofacial area including PIDP and burning mouth syndrome (BMS) [6-8]. However, variations in QST measures depending on the subject are the most significant disadvantage [9]. Abnormal findings are observed even in the normal control group, or normal results are sometimes observed in PIDP patients [6,10]. Therefore, in ICOP, the subtype of PIDP is divided into with or without somatosensory change [2]. So, QST cannot be used as a definite tool for differential diagnosis of PIDP and caution is required in interpreting examination results.

The mechanism of PIDP is still unclear and it is explained that it may occur due to micro nerve damage and deafferentation through surgical procedures such as RCT or extraction [3,11]. However, some cases of PIDPs lack precedent procedures. There could be a distinguishable difference between the two subjects according to the presence of micro nerve damage and this difference may be a feature that can be detected before irreversible treatment.

Therefore, in this study, the differential diagnosis factors were identified by comparing the clinical characteristics and QST results of PIDP and inflammatory dental pain patients, and assessed whether surgical procedure experience affects clinical characteristics and QST by dividing into PIDP groups depending on surgical procedures history.

MATERIALS AND METHODS

1. Subjects

This study was conducted on patients who came to Seoul National University Dental Hospital for treatment with dentoalveolar pain and normal controls recruited for the study who provided consent. The study was approved by the Institutional Review Board of Seoul National University Dental Hospital (SNUDH) (#CRI17001). Of a total of 35 patients (5 PIDP without surgical procedure, 10 PIDP with surgical procedure, 10 dental pain, and 10 control), 2 patients with dental pain were excluded because they were lost at follow-up and a total of 33 patients were analyzed.

PIDP was defined as a patient with persistent pain in the dentoalveolar area for more than 3 months without specific signs according to the ICOP definition. Among them, the group with no experience in surgical procedures such as RCT or extraction was designated as PIDP-a, and the group with experience in surgical procedures was designated as PIDP-b. A patient with dental pain was defined as a patient with pain due to the findings of inflammation in the pupal, periodontal, and gingiva areas by ICOP classifications. For accuracy of diagnosis, subjects of this group were limited to those with objective findings such as periapical lesions confirmed on imaging tests. At this time, subjects with traumatic events such as root fractures were excluded. Healthy controls were recruited who had no pain in the orofacial area, including teeth, for the past 6 months. Common exclusion criteria for all three groups were other neuropathic pain (such as BMS, polyneuropathy), oral mucosal lesion (such as oral lichen planus), uncontrolled diabetes mellitus, and moderate to severe psychological disorders.

2. Psychological Assessment and Chart Review

Symptomatic checklist-90-revision (SCL-90-R) test was conducted and a chart review was performed retrospectively to evaluate the clinical features of the patient. The patient's pain characteristics (pain intensity, quality, duration), treatment method, prognosis, consultation with other departments, and treatment experience before visiting SNUDH was recorded.

3. Quantitative Sensory Testing

Nociceptive stimuli of temperature, mechanical, and pressure were applied to the subjects, and the results were recorded. TSA 2001-II (MEDOC, Ramat Yishai, Israel) with an intraoral probe (6-mm diameter) was used to measure cold pain threshold (cold temperature at first perceived pain) and heat pain threshold (hot temperature at first perceived pain). Mechanical pain threshold (MPT) and mechanical pain sensitivity (MPS) used Semmes–Weinstein Von Frey filament (Touch-Test Sensory Evaluator Kit; North Coast Medical Inc., Gilroy, CA, USA), and MPT recorded the intensity of the filament that perceived pain at the time of stimulation. MPS applied Semmes–Weinstein Von Frey filament (Touch Test® Sensory Evaluator) 1.0, 1.4, 2, 4, 6, 8, 10, 15, 26, 60, 100, 180, and 300 g probes, and then the numeric rating scale (NRS) values were recorded upon stimulation. The pressure pain threshold (PPT) recorded the intensity at which the subject first perceived pain during pressure stimulation using electronic pressure algometer with a 1-cm^2 probe (Somedic, Hörby, Sweden).

4. Statistical Analysis

The Mann–Whitney U, Kruskal–Wallis, and Wilcoxon signed-rank tests were performed to compare the clinical features and QST data. Statistically significant was defined as a p-value less than 0.05. All statistical analyses were performed with the SPSS 19.0 software program (IBM Corp., Armonk, NY, USA).

RESULTS

A total of 33 subjects (5 PIDP-a, 10 PIDP-b, 8 dental pain, 10 control) were tested in this study. Majority (81.8%) of the subjects were women, and average age was 42.7±10.3 years (Table 1).

In SCL-90-R analysis, statistical significance was observed

Table 1. Distribution of gender and age

Variable	Group				
	PIDP-a (n=5)	PIDP-b (n=10)	Dental pain (n=8)	Control (n=10)	p-value
Gender, women (%)	80.0 (n=4/5)	90.0 (n=9/10)	62.5 (n=5/8)	18.5 (n=9/10)	0.472[a]
Age (y) (mean±standard deviation)	42.4±13.3	43.3±9.4	40.9±12.6	43.5±10.1	0.989[b]

PIDP-a, persistent idiopathic dentoalveolar pain without surgical procedures; PIDP-b, persistent idiopathic dentoalveolar pain with surgical procedures.
[a]p-values were obtained from Fisher's exact test.
[b]p-values were obtained from Kruskal–Wallis test.
p-value was considered as significant when p-value<0.05.

Table 2. Comparisons of Symptom Checklist-90-Revision results

Variable	PIDP-a	PIDP-b	Dental pain	Control	p-value
SOM	40.6±5.0	48.9±9.5	45.0±7.2	38.6±2.0	0.007*
O-C	36.6±6.4	45.6±10.8	46.9±7.6	39.6±3.9	0.040*
I-S	40.2±7.3	46.5±10.4	46.6±6.5	40.6±7.2	0.134
DEP	38.2±6.4	46.7±9.4	47.9±10.7	39.1±3.1	0.019*
ANX	39.0±5.3	46.1±11.5	44.6±8.4	37.7±2.6	0.033*
HOS	40.4±2.5	46.9±11.9	46.5±10.0	41.1±2.5	0.287
PHOB	42.6±4.3	46.9±11.0	44.6±3.1	42.0±3.5	0.314
PAR	41.2±4.1	45.2±12.7	44.6±6.1	40.6±3.1	0.402
PSY	39.6±1.8	47.4±11.8	44.9±4.3	39.7±3.3	0.028*

PIDP-a, persistent idiopathic dentoalveolar pain without surgical procedures; PIDP-b, persistent idiopathic dentoalveolar pain with surgical procedures; SOM, somatization; O-C, obsessive-compulsive; I-S, interpersonal-sensitivity; DEP, depression; ANX, anxiety; HOS, hostility; PHOB, phobic anxiety; PAR, paranoid ideation; PSY, psychoticism.
Values are presented as mean±standard deviation.
p-values were obtained from Kruskal–Wallis test.
*p-value was considered as significant when p-value<0.05.

in differences of somatization (SOM), obsessive-compulsive (O-C), depression (DEP), anxiety (ANX), and psychoticism (PSY) scores between groups (Table 2). In the post hoc test, SOM between PIDP-a and control, OC between PIDP-a and dental pain, dental pain and control, DEP and ANX between PIDP-b and control, dental pain and control, PSY between PIDP-a and control, dental pain and the control group showed a significant difference.

In QST analysis, comparison of the affected and unaffected sites was performed within the PIDP and dental pain group, respectively, and then comparative analysis was performed between the PIDP and dental pain and control groups. In the intragroup comparison, there were significant differences in MPS for PIDP, MPT, and PPT for dental pain. In the between-group (patient affected site and control group) comparison, there were significant differences in PPT (Table 3). Through post hoc testing, significance was shown in the control-dental pain group and PIDP-b-dental pain groups.

Pain duration (time from onset of pain to first visit to SNUDH), number of hospitals or departments visited before SNUDH, changes in NRS post-treatment, symptoms including pain characteristics and imaging test results, pain aggravating factors, accompanying symptoms, treatment methods, and prognosis were recorded (Table 4). Pain duration was observed similarly in all three patient groups, but the number of hospitals visited in PIDP groups was more than dental pain group, and NRS was observed to be higher than dental pain group. Another clinical difference between the PIDP patient and the dental pain group was observed during the follow-up period, these were the presence or absence of accompanying symptoms and the repeatability of symptoms after treatment. In dental pain group, increased symptoms and additional accompanying symptoms were not observed during the follow-up period after appropriate treatment. On the other hand, in the PIDP group, there was a repeated relief and exacerbation of symptoms even during medication. In addition, and as a comorbidity symptom, pain in the various areas (such as orofacial, head, ear, eye, nose, and uvula) and multiple toothaches were observed in follow-up period. While the main treatment methods for the dental pain group were surgical procedures such as RCT and extraction, the PIDP group mainly received medication. However, most of the PIDP and dental pain groups had experience taking non-steroidal anti-inflammatory drugs for pain relief. And to minimize the medication effect on QST results, in PIDP group, they were composed of those who had no experience in taking them or had taken it within one week in the case of anti-depressant and anti-convulsant.

DISCUSSION

Through this study, it was confirmed that PIDP and dental pain patients had various clinical differences, including prognosis, and significantly different items were found between groups in QST and SCL-90-R. However, due to the small sample size, caution is required in interpreting the

Table 3. Comparisons of quantitative stimulating test results related to pain stimulation

Variable	PIDP-a (n=5)			PIDP-b (n=10)			Dental pain (n=8)			Control (n=10)	p-value[c]
	Affected	Unaffected	p-value[a]	Affected	Unaffected	p-value[a]	Affected	Unaffected	p-value[b]		
CPT (℃)	13.9±5.5	13.2±6.8	0.500	17.2±4.7	12.6±5.6	0.093	15.0±42	16.3±6.3	0.237	13.4±6.4	0.465
HPT (℃)	47.7±4.4	48.0±4.8	0.686	47.1±5.8	50.6±1.9	0.314	50.1±2.6	48.8±3.8	0.310	49.0±3.7	0.608
MPT (g)	55.4±71.4	106.0±89.1	0.715	33.3±41.9	42.0±42.3	0.221	31.2±22.2	65.7±70.1	0.028*	76.7±70.9	0.131
MPS	25.3±15.4	16.6±16.9	0.066	25.5±19.2	20.1±18.5	0.017*	20.6±17.4	16.4±19.5	0.161	11.7±13.7	0.148
PPT (kPa)	56.5±39.8	92.8±51.9	0.275	53.4±17.7	82.7±89.9	0.646	24.4±10	33.9±8.9	0.049*	65.7±51.8	0.028*

PIDP-a, persistent idiopathic dentoalveolar pain without surgical procedures; PIDP-b, persistent idiopathic dentoalveolar pain with surgical procedures; CPT, cold pain threshold; HPT, heat pain threshold; MPT, mechanical pain threshold; MPS, mechanical pain sensitivity (numeric rating scale 0-100); PPT, pressure pain threshold.

Values are presented as mean±standard deviation.

[a]p-values were obtained from Wilcoxon signed rank test between affected and unaffected sites in the PIDP group.

[b]p-values were obtained from Wilcoxon signed rank test between affected and unaffected sites in the dental pain group.

[c]p-values were obtained from Kruskal–Wallis test between among PIDP, dental pain and control groups.

*p-value was considered as significant when p-value<0.05.

Table 4. Comparisons of clinical features

Variable	PIDP-a	PIDP-b	Dental pain
Pain duration (mo, min-max)	9.6±5.7 (3.0-18.0)	11.4±9.2 (3.0-24.0)	10.9±20.3 (0.2-60.0)
Number of hospitals or departments visited before coming to SNUDH	3.4±0.5 (3-4) ※Due to not finding the cause of the pain	2.6±0.8 (1-4) ※Due to not finding the cause of the pain	0.5±1.2 (0-1) ※Due to the high difficulty of treatment
Department with treatment by consult (except dental clinic)	**60%** of the PIDP patient Neurology, oorhinolaryngology, or aesthesiology and pain medicine	**50%** of the PIDP patient Neurology, oorhinolaryngology, or aesthesiology and pain medicine	**None**
NRS (before treatment, min-max)	6.1±2.1 (3.0-8.0)	5.7±1.7 (3.5-8.5)	3.4±1.9 (1.0-7.0)
NRS (after treatment, min-max)	3.5±2.0 (2.0-7.0)	3.7±1.2 (2.0-6.0)	0.2±0.4 (0.0-1.0)
Symptom of pain site	**Pain quality:** dull, nagging, itching, burning, throbbing, discomfort feeling, pressure **Pain duration:** continuously or minutes	**Pain quality:** dull, nagging, electric like, itching, burning, throbbing, discomfort, prickling **Pain duration:** continuously or minutes	**Pain quality:** throbbing, shooting pain, swelling feeling, **Pain duration:** intermittent (almost when teeth stimuli)
Sign of the pain site	PA lesion: none RCT or extraction: none	PA lesion: none, RCT state: 6 cases Extraction state: 2 cases, implant state: 2 cases	PA lesion: all case RCT state: 1 case
Aggravating factor	Chewing, mechanical stimuli, stress, fatigue	Chewing or teeth irritation, not brushing teeth after eating, in the night or before sleeping, stress, mechanical stimuli	Chewing or eating Fatigue
Comorbidity symptom	Pain of the below area in affected site - Ear - Temporal area - Mandible area	Pain of the below area in affected site - Surrounding teeth - Temporal area, zygoma area - Eye, ear, and nose area, uvula area Multiple toothache (unilateral)	**None**
Treatment	Commonly medication - Nortriptyline - Gabapentin, clonazepam	Commonly medication - Nortriptyline, duloxetine - Gabapentin, clonazepam - NSAIDs	Root canal treatment and crown Extraction and implant installation Incision and drainage Medication: NSAIDs and antibacterial agent
Follow up period (mo, min-max)	4.4±6.1 (0.8-15.0)	8.1±5.0 (2.0-15.0)	7.8±5.7 (0.2-15.0)
Prognosis	**Some symptoms persist** (even though better than before medication) Or **Repeated relief and exacerbation** of symptoms Or **Discontinuation of treatment**	**Some symptoms persist** (even though better than before medication) Or **Repeated relief and exacerbation** of symptoms ※ Factors of the aggravating symptom: stress, fatigue, sleep deficiency, dental treatment process ※ In many cases, **pain site becomes widespread during the follow-up period** (from unilateral dentoalveolar area to orofacial and headache, or bilateral multi teeth)	**All symptoms are relieved** (after appropriate treatment) **None of the relief and exacerbation** of symptoms ※ The two cases didn't treat, but the pain did not increase (NRS 0.5-1), and **none of the widespread and comorbidity** symptoms despite chronic pain status.

PIDP-a, persistent idiopathic dentoalveolar pain without surgical procedures; PIDP-b, persistent idiopathic dentoalveolar pain with surgical procedures; min, minimum; max, maximum; SNUDH, Seoul National University Dental Hospital; NRS, numeric rating scale; PA, periapical; RCT, root canal treatment; NSAIDs, non-steroidal anti-inflammatory drugs.
Values are presented as mean±standard deviation (range).

results clinically.

In general, fear, anxiety, and depression are observed in pain patients [12-14], and in this study also, increased levels of depression and anxiety were observed with statistically significantly higher scores in the PIDP-b and dental pain groups compared to the control group. However, there was no significant difference among patient groups. So, it is somewhat insufficient for clinical use in differential diagnosis. The SCL-90-R T-score of the PIDP-a group has an overall lower average compared to the control group. Whether it is a characteristic of the subjects constructed in this study or a general characteristic of the PIDP-a group should be confirmed through future research.

The QST results showed significant differences in PPT in the comparison of the patient-affected sites and control group, and a significant difference was observed in the PIDP-b and dental pain groups in post-hoc test. In addition, in the dental pain group, a significant difference between MPT and PPT affected-unaffected sites was observed, whereas this change was not observed in the PIDP group. However, the MPT distribution tendency of PIDP-a and PIDP-b showed in Table 3 and Fig. 1 is slightly different, and also other items. As for the MPT observed in the PIDP-b group, lower values were observed in both sites compared to other groups, these results could be explained by the decreased threshold for mechanical nociceptive stimuli and central sensitization phenomenon maintaining a low value even at the unaffected site which is in line with a previous study [6,15]. However, in the PIDP-a group, MPT and PPT showed a tendency to be higher than those of other patient groups. Regarding these results, we need to consider whether 1) the threshold of the PIDP group without surgical procedures is observed to be higher than the group that had surgical procedure for mechanical and pressure nociceptive stimuli; or 2) it is strongly influenced by individual variations. If there is a threshold difference it is necessary to reinforce and confirm whether the difference in micro nerve damage caused by the surgical procedure affects QST and also if individual variation is a limitation of QST [16]. Of course, there is no statistical significance, caution is needed in interpreting these results. Also, the fact that PPT showed differences between PIDP-b and dental pain groups confirmed the possibility of a simple, usable item in clinical diagnosis. However, the characteristic that QST results should be interpreted together with other clinical information and the absence of a critical point that enables differentiation between PIDP-dental pain groups suggests that there are still many difficulties in using QST alone for differential diagnosis. Also, in this study, standard normalization of the QST data was not satisfied due to the small sample size, and therefore the z-score, which is a prerequisite for standard normalization, could not be calculated. For this reason, it was difficult to directly confirm QST abnormality. Because QST is a test with psychophysical characteristics, it is affected by the subject's condition. Therefore, it is affected not only by the subject's factors such as age and gender but also by periodic changes such as circadian rhythm and menstruation cycle [17,18]. However, this study did not control for these confounding factors. Therefore, the inability to present a z-score, and the failure to consider these confounding

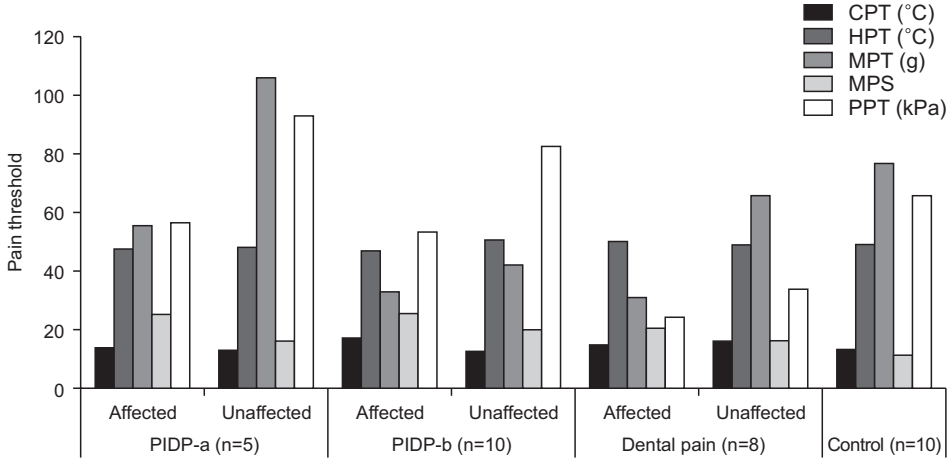

Fig. 1. Distribution of the cold pain threshold (CPT), heat pain threshold (HPT), mechanical pain threshold (MPT), mechanical pain sensitivity (MPS) (numeric rating scale 0-100) and pressure pain threshold (PPT). PIDP-a, persistent idiopathic dentoalveolar pain without surgical procedures; PIDP-b, persistent idiopathic dentoalveolar pain with surgical procedures.

factors are limitations of this study.

Through a retrospective chart review other clinical features that can distinguish the two study groups were investigated (Table 4). In general, in PIDP, changes such as central sensitization and neuroplastic change and also, it would take a long time from the time of pain onset to first visiting the hospital could be expected [19,20]. However, as shown in Table 4, there was no significant difference in the mean pain duration among groups. This may be explained that inflammatory dental pain patients visited the hospital late, and it did not take longer than expected for chronic pain accompanied by neuroplastic change to occur [21]. Therefore, if the diagnosis is accurate, it is necessary to start treatment as soon as possible. However, in PIDP patients, because the exact cause of pain cannot be found, the treatment process is often delayed [22]. The average number of visiting hospitals or other departments are higher in PIDP patients than dental pain patients which is evidence of a delayed treatment process. Usually, dental pain patients went through 0 to 1 hospital visits and received treatment right away, whereas PIDP patients usually went through 2 to 4 hospitals visits. And because PIDP pain characteristics are similar to neuropathic pain in the oral and maxillofacial area, they went through other departments including neurology, otolaryngology, and pain medicine.

Pain characteristics are shown in Table 4. Itching and burning sensations were the characteristic expressions distinguishing inflammatory dental pain. However, patients with dental pain also complain of prickling, electric pain in a state in which the pain threshold is reduced due to the inflammatory process, and in patients with PIDP, it is also said that the pain worsens when chewing and stimulating the teeth. Therefore, these clinical features can confound diagnosis, and these parts must be thoroughly reviewed in the diagnosis process.

During the post-treatment process, a clear difference could be observed between the groups. First, in patients with dental pain, pain is hardly observed when appropriate treatment is completed through RCT, extraction, or implant installation and no increase in pain was observed during the additional follow-up period. What is noteworthy here is that although dental pain patients who have not been treated for a long time experience mild pain, the change to PIDP symptoms is not observed in inflammatory dental pain patients. However, in the case of PIDP patients, even if drug treatment is effective, some symptoms often remain, and symptom relief and exacerbation appear repeatedly. In addition, more severe the remission or exacerbation of symptoms, the pain area spreaded from the dentoalveolar area to the oral and maxillofacial area, and the accompanying symptoms increased.

Therefore, it is thought that additional research is needed on the process of gradual changing from PIDP to persistent idiopathic facial pain through neuroplastic change, convergence, and central sensitization processes. Further studies are also needed to investigate the differences in mechanism between PIDP and inflammatory dental pain patients – with inflammatory toothache who have not been treated for a long time or the dental pain group that does not transition to PIDP after tooth extraction or RCT.

In conclusion, PIDP and inflammatory dental pain patients have distinct clinical characteristics, including QST results but also have similar clinical factors that confound diagnosis. Therefore, it is necessary to conduct a comprehensive evaluation using various clinical examinations and symptoms should be thoroughly reviewed at the time of diagnosis. And, in this study, some QST results showed different tendencies depending on whether or not a surgical procedure is performed, even though symptoms and prognosis are similar in the PIDP groups. However, since the sample size is small, further research is needed in the future to generalize about this.

CONFLICT OF INTEREST

No potential conflict of interest relevant to this article was reported.

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