Management of Chronic Idiopathic Pain in Patients With Dental Implant Without a Clear Pathological Lesion: A Retrospective Study

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Non-nociceptive, persistent idiopathic facial pain (PIFP) is a poorly localized, continuous dull pain that occurs even in the absence of apparent pathological lesions or clinical neurologic deficiency. This study aimed to investigate the disease characteristics of PIFP that developed after dental implant treatment. The clinical characteristics of pain as well as treatment method and outcomes were retrospectively analyzed in 20 patients diagnosed with PIFP. The patients developed pain either after implant fixation or prosthetic treatment. In most patients, the pain persisted not only around the implant region but also at a distant site from the related implant (13/20, 65%). Many patients desired removal of the implants to manage the pain although the pain was not considered to be related to the implant treatment. In 12 patients, the related implants were removed, but 67% (n = 8/12) of the patients still experienced chronic pain after implant removal. Medication helped decrease the pain in most patients (n = 17). Pregabalin and clonazepam showed relatively higher efficiency than other medications for controlling the pain. The results showed that although the onset of PIFP was related to dental implant treatment, implant removal could not be considered a reliable option for the management of PIFP. Although medication controls the pain at least partially, complete pain control with medication should not be expected. These results demonstrate that an accurate diagnosis of PIFP is important for the selection of appropriate treatment.

Key Words: persistent, idiopathic, facial, pain, dental implant

INTRODUCTION

Pain that develops after dental implant treatment is typically related to postoperative surgical complications or inflammatory response.[1] However, in some patients, the pain persists after prosthetic treatment. Peri-implant disease can be associated with persistent pain after implant treatment.[2] Chronic persistent pain can develop after minor oral surgical procedures even without a clear pathological lesion in the maxillofacial region.[3–5] In cases with persistent pain that cannot be explained by specific etiological factors, painful cranial neuropathies, such as persistent idiopathic facial pain (PIFP), burning mouth syndrome (BMS), or trigeminal neuralgia need to be suspected.[6,7] The International Classification of Headache Disorders (ICHD) 2018 classified PIFP as "painful lesions of the cranial nerves and other facial pain" and defined as "persistent facial and/or oral pain, with varying presentations but recurring daily for >2 hours per day over >3 months, in the absence of clinical neurological deficit."[8]

PIFP, which is considered an "atypical" pain, is frequently diagnosed after the exclusion of all other clinical conditions that can induce facial pain in the affected sites, and is thus regarded as idiopathic and non-nociceptive.[4,6] Characteristics of PIFP include constant pain in the face or brain in the absence of any apparent lesion or cause.[6,7] Based on previous reports, PIFP can be best described as long-lasting daily pain that is poorly localized, tends to spread, and is sometimes accompanied by intense pain.[3,7] In the general population, the prevalence of PIFP is reported to be rare,[8,9] and the pathophysiological mechanism of PIFP is not clearly understood.[3,6] At present, there are insufficient objective diagnostic criteria for the determination of PIFP.[4]

In some patients, the onset of persistent idiopathic pain is related to implant therapy without the occurrence of any clear

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preceding injury, relevant pathology, or abnormality around the implant itself. However, because PIFP is experienced after implant treatment, patients typically believe that the implant is the cause of the persistent pain. Therefore, PIFP remains a diagnostic challenge for implant practitioners, and a misdiagnosis can severely influence the success of treatment and the patient–doctor relationship. The current literature on PIFP after implant treatment includes only case reports[10,11] or case series with a small number of patients,[12] resulting in limitations in understanding the disease profile of implant-related PIFP.

In this study, we aimed to investigate the disease characteristics of PIFP after dental implantation and evaluate the therapeutic efficacy of various treatments to control the pain.

Materials and Methods

Study subjects

This retrospective study evaluated data obtained from hospital records and radiological examinations of patients who presented to the authors' institute, between January 2001 and June 2019 and who were diagnosed with PIFP according to ICHD 2018.[8] The inclusion criteria were (1) age $>$ 20 years; (2) persistent, uncontrolled pain recurring daily and lasting for $>$2 hours over 3 months; (3) pain that began after dental implant surgery or implant prosthodontic treatment without any clinical neural deficit; (4) availability of clinical records and radiological examination, including panoramic radiography, cone beam computerized tomography or periapical X ray; and (5) no pain-related pathological lesion or abnormality. The exclusion criteria were (1) direct evidence of nerve injury related to the implant surgery, (2) peri-implant bone dehiscence or implant fracture, and (3) other painful neuropathies other than PIFP according to the ICHD 2018,[8] such as trigeminal neuralgia, posttraumatic painful neuropathy, glossopharyngeal neuralgia, BMS, and central neuropathic pain.

Study methods

The following data related to the pain characteristics were collected: demographic and clinical information about the subjects, dental implant site, date of implantation/prosthetics, and pain description. The description of pain or pain pattern was referred from previous literature.[5,13] The pain location was modified from other reports.[13,14] We defined "localized pain" as idiopathic pain localized to the gingiva or alveolar bone around the implants, "regional pain" as a pain nearby region of the implant sites along with the trigeminal territory, and "distant pain" as facial pain experienced far from the implant site and not restricted to a regional site, such as the cheek or neck. Previously reported medications to control PIFP,[3,4,10] such as antidepressants or anticonvulsants, had been frequently prescribed. The outcomes after the removal of implant/prosthesis, patient response to medications, and other treatment methods were also documented. Symptom onset was categorized into two periods: after surgery (before implant prosthesis) and after implant prosthesis.

In this study, the definition of treatment response was modified from another report.[14] "Effective" was defined when the patient was satisfied with the current medications or treatments and had a significant pain-free period that lasted at least 1 week. "Partially effective" treatment was defined as the patient experiencing a significant decrease in pain but still experiencing mild discomfort that did not affect daily activity. "Noneffective" was defined as the patient desiring further treatment to improve pain control other than current medications or treatments.

This study was approved by the Institutional Review Board of Kyungpook National University Dental Hospital (KNUDH 2020-07-01-00).

Results

In accordance with exclusion criteria, we excluded patients with facial pain and a history of neurologic damage after implant surgery (n = 2), trigeminal neuralgia (n = 3), or BMS (n = 3). The study enrolled 20 patients who experienced PIFP after dental implantation (mean age: 61.7 years; range: 37–80 years; 67% female). No patient had evidence of neural deficit on radiographic images. Pain developed after surgery before (n = 10) or after (n = 10) implant loading and lasted for an average of 11.7 months (range: 3–35 months). Patients had implant-related pain located in the mandibular molar region (n = 9), maxillary molar region (n = 6), maxillary anterior region (n = 1), and multiple sites of the maxilla or mandible (n = 4). In most patients, the mode of pain was often a dull, aching, tightening, or burning sensation but exhibited various patterns. In several patients, the pain was experienced near the treated sites (n = 4) or radiated to nearby regions along with the trigeminal nerve territory (n = 3). However, in most patients, the pain spread from the implant-treated region to a wider cervicofacial area (n = 13, 65%), such as the auricular region, neck, head, or extremities, and even to the contralateral side in some patients (Table 1).

All patients received initial treatment at their local dental clinic and were transferred to our hospital for management of chronic, persistent pain. Many patients desired removal of the implants that were not considered to be related to the implant surgery itself or to the abnormality of the nearby tissue or structures. Implants were removed in 12 patients, among whom only one patient experienced effective pain relief and 3 patients reported partially effective relief, whereas 8 patients (67%) continued to experience chronic pain after implant removal. In 3 patients, removal of the prosthetic superstructures was effective, but it was not effective in 2 other patients.

Pharmacologic management was performed in consideration of patient's condition, adverse effects, drug interactions, or previous prescriptions from other clinics. Medication improved the pain in most patients (n = 17; 85%). Most patients received treatment with multiple medications. Eleven patients (22%) were treated with pregabalin; of these, 7 were responders (74%, effective or partially effective). Ten patients (20%) were prescribed clonazepam, and of these, 6 were responders (60%, effective or partially effective). However, other medications such as carbamazepine showed relatively lower efficacy (noneffective = 8) to relieve the pain than other medications. Patients were also treated at the pain clinic or

Table 1

Symptom characteristics of patients with idiopathic pain after implant placement

Patient No.	Age/ Sex	Number (sites) of Related Implants	Characteristics of Pain			
			Pain Onset	Duration (Mo)	Description	Location of Pain; Other Problems
1	37/M	2 implants (#14, 15)	After surgery	9	Dull, stiff	L
2	71/M	4 implants (#26–29)	After surgery	3	Dull, aching, stabbing	L, R, D (cheek, eye lid, zygoma)
3	55/F	2 implants (#19, 18)	After surgery	6	Dull, aching	L; depression, anxiety
4	48/F	1 implant (#14)	After surgery	3	Dull, heavy, salty taste, numb	L, R, D (nose, infraorbital)
5	79/F	6 implants (All Mx)	After surgery	17	Dull, burning, stabbing	L, R; depression, sleep disturbance
6	65/F	3 implants (#18–20)	After surgery	5	Aching, tightening	L, R, D (ear, cheek, neck)
7	80/F	1 implant (#28)	After surgery	35	Dull, radiating pain	L, R, D (head, body); depression
8	62/F	4 implants (#11, 13–15)	After surgery	9	Dull, aching	L, R, D (nose, head)
9	53/F	4 implants (#18, 19, 30, 31)	After surgery	16	Dull, stiff, burning, electrical	L, R, D (tongue, lip, cheek, postauricular)
10	80/F	3 implants (#2–4)	After surgery	7	Dull, tightening, aching	L, R, D (contralateral mandible)
11	58/M	4 implants (#2, 3, 30, 31)	After prosthetic treatment	7	Gnawing, aching	L, R, D (lip, temporal)
12	46/F	3 implants (#19–21)	After prosthetic treatment	7	Cramping, gnawing	L; headache
13	71/F	2 implants (#18, 19)	After prosthetic treatment	20	Dull, aching	L, R
14	44/M	2 implants (#14, 15)	After prosthetic treatment	4	Dull, burning	L, R, D (nose, temporal)
15	71/F	2 implants (#29, 30)	After prosthetic treatment	6	Dull, burning, swelling	L
16	64/F	2 implants (#29, 31)	After prosthetic treatment	12	Dull, intermittent twinging	L, R, D (cheek, occipital, face)
17	65/F	3 implants (#29–31)	After prosthetic treatment	24	Dull	L, R, D (auricular, mandibular angle)
18	48/F	4 implants (#12–15)	After prosthetic treatment	5	Dull, cramping, tightening	L, R
19	62/M	3 implants (#2–4)	After prosthetic treatment	15	Dull, tightening	L, R, D (auricular, facial)
20	74/M	1 implant (#6)	After prosthetic treatment	23	Aching, cramping	L, R, D (zygoma, temporal)

*D indicates distant pain, pain that persists distant to the implant sites (such as cheek or neck sites); L, location (localized pain), idiopathic pain localized to the gingiva or alveolar bone around the implants; R, regional pain, pain near the region of the implant sites along with the trigeminal territory.

psychiatric or neurologic department at the university hospital. In several patients, physical therapy (n = 4) or stellate ganglion block (n = 2) was also performed at the authors' hospital (Table 2).

Discussion

PIFP is accompanied by diverse symptoms and is usually diagnosed as an exclusion diagnosis.[3,7] Some differences between PIFP and trigeminal neuralgia include a high prevalence of bilateral or multiple sites of pain, a low possibility of stabbing or touch-evoked pain, and a remission period in PIFP.[7,14,15] PIFP is frequently described as a dull, aching pain that lasts for several minutes or is continuously annoying rather than being a paroxysmal, superficial, or stabbing pain.[9,14] Most subjects in this study also experienced persistent, long-lasting dull pain that occurred daily. However, in line with a previous report,[14] some patients reported an accompanying sharp pain. Previous research has reported that the onset of PIFP is often associated with minor surgery or other dental procedures.[4,5,10,11] Patients who experience neuropathic pain after neurotrauma by dental interventions (such as extraction, implant surgery, or nerve blocks) are diagnosed with painful posttraumatic trigeminal neuropathy (PPTN).[8] PPTN is very localized and accompanied by prominent sensory changes, such as allodynia and hyperalgesia, and it can be distinguished from PIFP.[3,15,16]

Similar to previous studies, there was a higher prevalence of women among our patients, but the average age of onset was older than that in other PIFP reports.[14,17] There are only a few case reports exist on patients with PIFP after a dental implant procedure.[10–12] In the first report of PIFP related to dental implantation, a 55-year-old woman complained of a severe, constant burning pain localized to the anterior alveolar ridge after implant placement at the same area.[11] Another reported case was a 69-year-old woman who exhibited infraorbital pain immediately after maxillary dental implant insertion.[10] There was no sensory disturbance in either case. According to a report on neuropathic pain after dental implants in 26 patients, 9 patients experienced pain even without physical neurotrauma.[12] It is unclear whether the patients in this previous study can be classified as PIFP, but they reported a frequent, continuous, burning type of pain with a radiating pattern. None of our patients experienced sensory disturbance. Approximately 65% of the patients had persistent pain that spread to distant sites such as the cheek, lip, temporal area, or auricular area. Even among patients with regional pain, the region of pain was not localized to the implant site. For example, patient No. 9 complained of pain at the tongue, lip, and postauricular area after the dental implantation on the bilateral molar areas. This implies that symptoms can manifest in an area unrelated to the implant treatment itself.

The onset of PIFP is often related to minor surgery or dental treatment as an initiating event,[5,13,17] even when there is no clear injury to the peripheral nerve. From the present results, we found that PIFP occurred after implant surgery but before prosthetic treatment or after prosthetic treatment. Because there was no remarkable abnormality or identifiable triggers of facial pain, referring dentists usually prescribed analgesics and antibiotics initially and then sometimes tried to manage the pain by removing the implant body or prosthesis. After these

TABLE 2

Management of persistent idiopathic facial pain and outcome after treatment*

Patient No.	Treatment and Results After Implant/Prosthesis Removal	Medications Used for Idiopathic Pain Management	Other Treatment/Visited Clinic Other Than Dental Department
1	Implant removal (NE)	Carbamazepine (NE), Clonazepam (NE), Gabapentin (E)	
2	Implant removal (NE)	Carbamazepine (NE), Gabapentin (PE)	
3	Implant removal (NE)	Clonazepam (PE), Gabapentin (NE), Carbamazepine (NE)	
4	Implant removal (NE)	Pregabalin (E)	
5	Implant removal (NE)	Pregabalin (PE), Gabapentin (NE), Carbamazepine (NE), Clonazepam (NE), TCA (NE)	
6	No removal	Diazepam (NE), Pregabalin (E)	BT / psychiatric clinic
7	No removal	Clonazepam (NE), Pregabalin (E)	PT (E), BT / pain clinic
8	Implant removal (NE)	Pregabalin (NE), Clonazepam (NE), Carbamazepine (NE)	Neurological clinic
9	Implant removal (NE)	Carbamazepine (NE), Baclofen (NE), Clonazepam (PE)	
10	Prosthesis removal (E)	Pregabalin (E)	
11	Implant removal (PE)	Carbamazepine (NE), Gabapentin (NE)	
12	Prosthesis removal (NE)	Gabapentin (E)	PT (NE), SGB (NE) / pain clinic
13	Implant removal (PE)	Pregabalin (NE)	BT, SGB (E) / pain clinic
14	Prosthesis removal (NE)	Baclofen (E)	
15	Implant removal (PE)	Carbamazepine (NE), Clonazepam (PE)	
16	No removal	Pregabalin (E), TCA (PE)	
17	Prosthesis removal (E)	Diazepam (NE), Clonazepam (PE)	Psychiatric clinic
18	Prosthesis removal (E)	Clonazepam (PE), Pregabalin (NE)	PT (NE) / pain clinic
19	Implant removal (NE)	Clonazepam (E), TCA (E), Baclofen (NE), Pregabalin (PE), Gabapentin (PE)	
20	Implant removal (E)	TCA (NE), Pregabalin (NE), Carbamazepine (PE)	PT (PE) / pain clinic

*Treatment response was classified into three categories: E, effective; PE, partially effective; NE, noneffective.

†BT indicates behavioral therapy; PT, physical therapy; SGB, stellate ganglion block; TCA, tricyclic antidepressant.

unsuccessful attempts, the patients consulted our hospital. We were unable to find evidence of direct neurotrauma in any of the patients. However, most of the patients assumed that their pain was triggered by the implant treatment. Therefore, it was not easy to explain and make the patients understand the idiopathic nature of the pain. Previous studies have reported that 46%–67% of PIFP patients also have a psychiatric disorder[13,18] and a high level of psychological distress, such as depression or anxiety.[19,20] Most cases of PIFP are preceded by psychiatric disorders, which tend to progress in the chronic course,[21] and it is possible that physical trauma and psychological stress trigger the amplification of pain.[22] Although the relationship between PIFP and psychiatric problems is well documented, the reason for the interaction between the two remains poorly understood.[21,23] We recommended that our PIFP patients attend a psychiatric clinic. However, some of the patients did not readily visit psychiatrists, and thus this constitutes a limitation of our study.

A previously reported case demonstrated no improvement in patient symptoms after implant removal.[11] In our case series, implant removal was performed in 12 patients, but symptoms were significantly or partially improved in only 4 patients, and the remaining 8 patients (67%) did not experience any improvement after implant removal. For example, patient No. 8, who experienced long-term pain and discomfort after 4 maxillary implant treatments, strongly desired removal of all maxillary implants, including the 2 previously well-functioning implants. Changing medications and various other conservative treatments did not improve the symptoms in this patient. Finally, all 6 maxillary implants were removed in turn, but this did not result in effective pain reduction. The continuous and dull pain persisted. Based on our experience, surgical removal of the dental implant after the development of chronic pain cannot guarantee an improvement in symptoms in patients with PIFP.

Our results indicated that removal of the implant did not guarantee predictable pain control. Thus, it is reasonable to think that pain was not significantly related to the existence of the implant or prosthesis. These results suggest that development of PIFP after implant treatment is related to a psychologic disorder, such as depression, anxiety, or somatization disorders. Patients who experience pain after implant treatment usually desire the removal of the implant or prosthesis to manage their pain. However, there are two reasons why the implant should not be removed without first attempting other conservative treatments: first, an invasive surgical procedure for implant removal can potentially result in PPTN,[7] and second, implant removal frequently accompanies loss of occlusion, decreased masticatory function, and has the potential to increase depression or anxiety. In this study group, some patients might have developed pain without implant placement. Thus, in patients with PIFP, implant removal might be considered when there is clear evidence of an associated lesion around the implants. Meanwhile, other invasive surgical procedures are not recommended in patients with uncontrolled chronic idiopathic pain.

In 10 patients (Nos. 11–20) in whom PIFP developed after implant prosthesis, the implant ($n = 5$) or prosthesis ($n = 4$) was removed. The chronic pain decreased either partially or significantly in 6 patients after removal of the implant body or prosthesis. Compared with these aforementioned patients (Nos. 11–20), there was nearly no pain reduction after implant

removal among patients who developed PIFP after implant surgery (Nos. 1–10). This implies that PIFP develops after implant prosthesis might have different characteristics than PIFP that develops postoperatively. However, to relieve PIFP developing after implant surgery or prosthesis, neither implant nor prosthesis removal showed predictable outcomes.

Evidence suggests that PIFP might be a type of painful neuropathy. Therefore, use of antidepressant and anticonvulsant medications is effective for PIFP.[3] Therapeutic trials of PIFP have been reported to be efficient, but there are no randomized controlled trials or direct evidence supporting use of specific medicines. Moreover, the pathophysiology of PIFP has not been clearly elucidated, and there is no established medicine of choice for the management of PIFP. Frequently used medications include tricyclic antidepressants (TCAs)[10,11,15] and clonazepam.[11] Combinations of nortriptyline, clonazepam, and relaxation training procedures have been reported to be helpful.[4] Although the mechanism is not clearly understood, antidepressants and anticonvulsants are frequently recommended.[3,7] Some researchers have reported that anticonvulsant drugs are ineffective.[24] In our experience, 3 patients (Nos. 8, 11, and 13) did not show pain relief after treatment with single or multiple medications. In the other 17 patients, medication helped decrease the pain level. Because multiple medications were frequently prescribed in these patients, we tried to record the patients' response to pain control for each of the selected medications, but there were limitations in the numbers of each drug. Other than analgesics, several drugs were prescribed to control the pain: pregabalin (anticonvulsant, n = 11), clonazepam (benzodiazepine, n = 10), carbamazepine (anticonvulsant, n = 9), gabapentin (anticonvulsant, n = 7), nortriptyline (TCA, n = 4), baclofen (GABAergic, n = 3), and diazepam (benzodiazepine, n = 2). Among these, pregabalin (74%), clonazepam (60%), and gabapentin (57%) were significantly or partially effective in controlling the patients' pain. Because of the potential adverse effects and the general condition and age of the patients in this study, anticonvulsants are used more frequently compared with TCAs.

Many patients with atypical pain also have psychiatric disorders.[13] In these patients, significant changes are seen in cortical excitability[25] and alterations in somatosensory function were observed.[26] These changes suggest the involvement of central sensitization in patients with PIFP, which might explain why removing the implant does not significantly control the pain in most PIFP patients. Behavioral therapy, physical therapy, or psychosocial treatment is recommended for PIFP, although there is a lack of clear scientific evidence regarding these methods.[3,10] For example, in our patient no. 6, medication did not work initially. However, the patient effectively responded to a change in medication after long-term counseling and physical therapy. From our experience, to prevent unnecessary treatment, meticulous screening of the patient's medical records and adequate diagnosis are required. If needed, a consultation should be conducted with other specialists to solve psychiatric and neurologic problems. During the early phases of PIFP, effective doctor–patient communication can decrease the possibility of long-term problems.

This study has some limitations. We did not include a pain scale, such as a visual analog scale, in the results. Patients were referred from another clinic, and the initial pain scale was frequently missing from their medical records before or after each treatment. In the future, a prospective study should be performed using a standardized protocol with detailed information collected on pain intensity, quality, onset, location, and effects after various clinical treatments.

Conclusion

The findings of this study suggest that although PIFP can occur in implant patients, it is not likely to be related to the implants or prosthesis. Implant removal did not effectively relieve idiopathic pain. Although medication controlled the pain at least in part, complete pain control with medication should not be expected. These results demonstrate that an accurate diagnosis of PIFP is important for the selection of appropriate treatment.

Abbreviations

BMS: burning mouth syndrome
PIFP: persistent idiopathic facial pain
PPTN: painful posttraumatic trigeminal neuropathy
TCA: tricyclic antidepressant

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