



A Review on Persistent Idiopathic Facial Pain (PIFP)

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DOI: 10.31080/ASDS.2022.06.1383

Received: March 28, 2022

Published: May 16, 2022

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Abstract

PIFP is a chronic pain condition recurring daily for over two hours daily for more than 3 months, in absence of neurological deficits. Pain may be localized, and may eventually spread, further affecting the quality of life of patients. The pathophysiology is not clearly identified and neither is the diagnostic criteria, which has further led to lack of research on the topic. We hereby present a narrative review; discussing the symptomatology, differential diagnosis and the diagnostic criteria available for the condition, as also the holistic management.

Keywords: Orofacial Pain; Persistent Idiopathic Facial Pain; PIFP; Idiopathic Facial Pain; IFP; Trigeminal Neuralgia; PTTN; Chronic Facial Pain; Idiopathic Facial Pain; Daily Pain, Idiopathic Facial Pain

Introduction

International Classification of Headache Disorders (ICHD, version 3) published by the International Headache Society (IHS) defines persistent idiopathic facial pain (PIFP) as 'persistent facial and/or oral pain, with varying presentations but recurring daily for more than 2 hours per day over more than 3 months, in the absence of clinical neurological deficit' [1]. In a study published in 2020, PIFP was found to be frequently misdiagnosed, imposing the unnecessary burden of ineffective medications, unwarranted procedures, and economic burden [2,11]. This is mainly because its clinical presentation is variable, often confused with other orofacial pains; its diagnostic criteria is loose and ambiguous, and the pathological mechanism is not clear [3-7]. This necessitates a discussion on understanding the disease etiopathogenesis, diagnostic guideline and treatment planning. Limited epidemiological data is available, as PIFP is a rare disease. According to a study, the incidence of PIFP is 4.4 (95% confidence interval: [3.2; 5.9])/100 000 person-years [8]. Another population-based study from Essen, Germany, found a lifetime prevalence of 0.03% [9]. Overall, women are significantly more frequently affected than men and account for about 75% to 90% of cases [8,10], with most cases are between 30 and 60 years of age at the time of first diagnosis [10].

Understanding orofacial pain

International Classification of Orofacial Pain (first edition)

The International Classification of Orofacial Pain (ICOP) has categorized orofacial pain into six groups [3]. The first three main groups represent disorders of the masticatory system in its broadest sense generally treated by dentists. The fourth to sixth groups comprise orofacial pain syndromes where the pain is not explained is not morphological correlated with the teeth, dentoalveolar structures or temporomandibular joint. It is non-dental orofacial pain and should be treated with conservative pain therapy.

Orofacial pain attributed to disorders of dentoalveolar and anatomically related structures

- Dental pain
- Oral mucosal, salivary gland and jaw bone pains

Myofascial orofacial pain

- Primary myofascial orofacial pain
- Secondary myofascial orofacial pain

Temporomandibular joint (TMJ) pain

- Primary temporomandibular joint pain
- Secondary temporomandibular joint pain

Orofacial pain attributed to lesion or disease of the cranial nerves

- Pain attributed to lesion or disease of the trigeminal nerve
- Pain attributed to lesion or disease of the glossopharyngeal nerve

Orofacial pains resembling presentations of primary headaches

- Orofacial migraine
- Tension-type orofacial pain
- Trigeminal autonomic orofacial pain
- Neurovascular orofacial pain

Idiopathic orofacial pain

- Burning mouth syndrome (BMS)
- Persistent idiopathic facial pain
- Persistent idiopathic dentoalveolar pain

In the following, we summarize the most common facial pain syndromes of clinical importance in the ICOP group's 4-6.

All the above-mentioned diseases and conditions vary in their pathophysiology and therefore in symptomatology, discussion of which is beyond the scope of this article.

PIFP

PIFP has been found to be associated with minor surgical or other invasive dental or otolaryngological procedure, which may have been performed in an attempt to manage the pain. However, the sequence of events is unsure and often not reliable [18].

Earlier known as atypical facial pain, PIFP is a rare and poorly understood orofacial pain condition. The presentation of this condition is rare characterized by continuous pain of the face and/or teeth, sometimes varying in intensity throughout the day, it is usually medium, sometimes strong. Usually deep but can be superficial as well. Poorly localized, radiating pain, described as aching, burning, throbbing and often stabbing pain. Mild to severe in intensity, rated 7-11 on VAS scale, only few patients report that their pain ceases for longer period of time, sleep is usually undisturbed by pain, and some may even report brief pain free periods on waking up in the morning before pain occurs, usually lasting for 30 minutes or lesser. Only one side may be affected, rarely it affects bilaterally (in 40% cases) in the later course of disease. Spread is non-dermatomal, Maximum intensity of pain is experienced in the cheeks and upper jaw, pain may radiate to lower jaw, occiput, ear,

shoulder or arm, but this maybe unusual [17]. No objectively identifiable neurological deficits may be seen. Rarely, swelling may be experienced on nasolabial region on affected side of face [11].

Concomitant autonomic symptoms may not be noted. Characteristics of neuropathic facial pain are usually absent; however 10% patients may show neuropathic pain [13] patient does not show sensory negative symptoms such as anesthesia or hypoesthesia [11], some amount of hypoesthesia has been reported using QST [14-17]. It has been suggested by IHS that patients with neuropathic pain following a surgery or trauma and with neurosensory changes should be diagnosed as painful traumatic trigeminal neuropathy (PTTN), this should be taken into account when managing patients and conducting studies [1].

Atypical odontalgia, now known as persistent idiopathic dentoalveolar pain (PIDAP), is a subtype of PIFP, symptoms of which are identical as described above, difference being that PIDAP remains strictly limited to one or two teeth and does not spread [12].

Psychiatric and psychosocial disability have often been associated with PIFP [19], however this has not been proven yet and studies have also found no psychiatric disorders compared to control, [20]. Studies have shown higher Anxiety and depression scores in PIFP patients with higher pain intensity [21]. 41.3% patients suffering from PIFP or Burning mouth syndrome (BMS) have been found to have axis I disorder (major depression being the commonest) before the onset of orofacial pain [19]. This therefore necessitates interdisciplinary approach in diagnosis and management of PIFP.

Pathogenesis

The pathophysiology of PIFP is not clear, studies have shown increased neuronal activity at brainstem level, [20,22,23] disturbed inhibitory function of pre-frontal cortex [24], alteration on dopamine system associated with pain transmission and modulation [25], QST results has shown hypoesthesia, indicative of neuropathic pain [14-16]. No evidence has been found for neurovascular compression of trigeminal root entry [26-28].

PIFP is therefore a heterogenous entity with definitive neuropathic pain syndrome or idiopathic pain with unclear neuropathic involvement.

Inconsistent changes in blink reflex and unchanged somatotopy and somatosensory cortex indicative of alteration in somatosen-

sory pathway, the QST profiles were not significantly different for controls in these patients [20].

Diagnosis

Diagnosis is based on diagnosis of exclusion, recently in a paper published by Benoliel R., *et al.* PIFP was classified into 6 different types, ranging from A to F [7].

	Diagnostic criteria	Notes
A	Facial and/or oral pain fulfilling criteria B and C	This is the current term for what was previously termed Atypical Facial pain or its intraoral counterpart, atypical odontalgia
B	Recurring daily for >2 hours per day for > 3 months	It can have sharp exacerbations and is aggravated by stress.
C	Pain has both the following characteristics: 1. Poorly localized, and not following the distribution of a peripheral nerve 2. Dull aching or nagging quality	Pain may be described as either deep or superficial. With time it may spread to a wider area of craniocervical region
D	Clinical neurological examination is normal	A continuum seems to exist from PIFP induced by insignificant trauma to painful post-traumatic trigeminal neuropathy caused by significant insult to the peripheral nerves. PIFP may be initiated by a minor operation or injury to face, maxillae and teeth or gums without any demonstrable local cause. However, psychophysical or neurophysiological tests may demonstrate sensory abnormalities
E	A dental cause has been excluded by appropriate investigations	The term atypical odontalgia has been applied to a continuous pain in one or more teeth or in a tooth socket after extraction, in absence of any usual dental cause. This is thought to be a sub form of PIFP, although it is more localised, the mean age at onset is younger and genders are more balanced.
F	Not better accounted for by another ICHD-3 diagnosis	Persistent Idiopathic facial pain (PIFP) may be comorbid with other pain conditions such as chronic widespread pain and irritable bowel syndrome. In addition, it presents with high levels of psychiatric comorbidity and psychosocial disability.

Table 1

According to ICHD-3 criteria for the diagnosis of persistent idiopathic facial pain (ICHD, Cephalalgia 2013, 33,782) [1].

- Facial and/or oral pain fulfilling criteria B and C
- Recurring daily for > 2 h per day for > 3 months
- Pain has both of the following characteristics
 - poorly localized, and not following the distribution of a peripheral nerve
 - dull, aching or nagging quality
- Clinical neurological examination is normal
- A dental cause has been excluded by appropriate investigations.
- Not better accounted for by another ICHD-3 diagnosis.

It is important to distinguish PIFP from other chronic daily headache syndromes, including the following

- Trigeminal neuralgia
- Postherpetic neuralgia
- Temporomandibular joint (TMJ) syndrome
- Chronic cluster headache
- Cluster-tic syndrome
- SUNCT (short-lasting, unilateral, neuralgiform headache attacks with conjunctival injection and tearing) syndrome
- Jabs and jolts syndrome
- Raeder syndrome
- Thalamic pain syndrome
- Hemicrania continua
- Side-locked migraine

Conditions like glossopharyngeal neuralgia, migraine, trigeminal autonomic cephalgia, burning mouth syndrome, giant cell arteritis can be distinguished from TN and PIFP by presence or absence of autonomic phenomenon, neurologic deficits. Evaluation of nerve root for trauma, inflammation and tumour must be considered for diagnosis of trigeminal nerve disorders, and to distinguish it from Painful traumatic trigeminal neuropathy (PTTN), PTTN is a condition in which pain occurs in a region of trigeminal nerve, there is definite injury to the nerve, not older than six months. Pain is generally localized. Besides, evaluation of musculoskeletal and odontoid structures for evaluation of orofacial disorders causing facial pain is important to rule out myofascial pain dysfunction syndrome (MPDS). Psychosocial disorders are often a comorbidity associated with PIFP or other orofacial pain and must be thoroughly investigated for diagnosis and treatment planning.

PIFP can often be confused with myofascial pain, especially in the pericranial area, and must be distinguished by the referring pattern; pain referred to eye, jaw, teeth is not common in case of PIFP.

Migraine headache, cluster headache, as well as the trigeminal autonomic cephalalgias, can also have facial pain complaints, similar to PIFP but the timing and the associated tearing or conjunctival injection, help to distinguish [7,29].

Treatment

The mainstay of medical treatment of PIFP is counseling [45]. Patients should be counseled about the chronic nature of the illness, and its nonmalignant nature. Their pain should be acknowledged, and they should feel that their concerns are being heard, their attitudes and beliefs on pain must be considered and a plan for addressing them is forthcoming [30].

Investigation should always be supplemented with - screening questionnaire for anxiety and/or depression (such as hospital anxiety and depression scale), Brief pain inventory - facial [46] Hospital Anxiety and Depression Scale [47], Pain Catastrophizing scale [48], Chronic graded pain scale [49], as they help to identify the psychological impact of the disease. Only 32% (6/19) centers managing chronic facial pain did psychological testing according to a study conducted by German university [50].

In 1982, Dr Eric Cassel wrote the article "The nature of suffering and the goals of medicine," he writes, "...Physicians' failure to understand the nature of suffering can result in medical intervention that (though technically adequate) not only fails to relieve suffering but becomes a source of suffering itself." [51] Chronic pain is manifest not just physiologically, but shaped by one's experiences, culture, social norms, and expectations, emotions, such as anger, fear, and anxiety, strongly influence pain perception. Being positive, relaxed, and distracted can reduce pain sensitivity [45].

In a systematic review, that considered 17 trials in orofacial pain, all studies were shown to have a high risk, thus backing weak evidence in support of their use [42]. In one patient blinded controlled trial, 41 PIFP patients were compared active hypnosis for 5 hour individual sessions in one group with relaxation in another group. The study found significant pain relief in susceptible individuals, but there was need for further support to evidence with respect to psychological support, coping strategies and psychological issues [40].

Patient must be trained to move away from identifying cause, and directed towards coping strategies, targeting goals that will improve the quality of life. These sessions may be short, reassurance with an explanation, supplemented with written patient information may be helpful. Context can be found on European Federation Chapters [wwwhttp://www.efic.org/index](http://www.efic.org/index). European Year against pain 2013/14. [43,44].

Considering the ambiguous nature of the disease, there are not enough RCT and therefore multidisciplinary approach with minimal or no intervention has been suggested [31]. Behavioral interventions, along with pharmacotherapy - antidepressants and anti-epileptic drugs. Proper patient education to clarify the diagnosis, patient must be discouraging from any invasive treatment.

Therapeutic trials considered for PIFP (and AFP) have been considered using tricyclic antidepressants [32], duloxetine [33], venlafaxine [34], anticonvulsants [35], low level laser therapy [36], all of which have been shown to have beneficial effects, however level of evidence is low. High-frequency repetitive transcranial magnetic stimulation (rTMS) on the right secondary somatosensory (S2) cortex in patients with neuropathic orofacial pain induced significant pain relief compared to stimulation of the sensorimotor (S1/M1) cortex and sham stimulation [37].

Occipital nerve blocks have been proven to be inefficient [39] whereas, hypnosis has been shown to have a positive effect [40]. When all treatment fails, pulsed radiofrequency for sphenopalatine ganglion has been shown to be effective [41]; however, invasive treatments always come with a risk for traumatic neuropathy and always end up increasing pain.

Considering the poor prognosis of PIFP with respect to treatment outcomes, patients afflicted with this condition have become fertile ground for studies involving "integrative medicine," which refers to the combination of complementary and alternative therapy, including nutrition, mind-body therapies, and spirituality. The emphasis is on the whole person and a "holistic" approach, in combination with evidence-based medicine.

Diet

Integrative approach to patients health is incomplete without consideration for patients diet for Hippocrates quotes, "Let food be thy medicine and medicine be thy food." Inflammation is a potential mediator in chronic pain states, caused due to injury to muscle

or deep tissue causing changes in both central and peripheral pathways, further leading to neuronal hyperresponsiveness, abnormal spontaneous discharge and increase in the receptive field [52].

Promoting a diet low in saturated fat, rich in fruits, vegetables and whole grains is recommended by the US Preventive Services Task Force for health promotion as also as part of 2005 Dietary guidelines for Americans. (53) Dietary supplementation with omega-3 fatty acid, considering the anti-inflammatory effect of n-3 fatty acids tends to suppress T-cell function, Vitamin E helps to mitigate this effect. Multi-vitamins inclusive of B vitamins, especially B6, B12, folate, thiamine, Zinc and Vitamin A (immune function), Vitamin C. (neuroprotector) [54].

Exercise

In 2003, a review found the evidence to support the role of therapeutic exercise on chronic pain, different physical exercises yield same magnitude of effect on pain, and therefore any activity can be selected as per patients preference, desired outcome and experience [55].

Osteopathic manipulative therapy and acupuncture

OMT is a way to promote healing by manipulating bones to allow free circulation of blood and balanced functioning of nerves, OMT has been found effective in treatment of migraine [56]. Acupuncture involves use of small needles placed superficially into any more than 360 points on body along the 12 meridians, that are postulated to channel qi, or vital energy/life force. Disease is said to occur due to blockage of qi in this paradigm. Acupuncture works by restoring these natural energetic flows. The use of Acupuncture and OMT has not been explored in treatment of PIFP however, there is strong evidence of the benefits of such treatment in chronic pain therapy [57-59].

Cognitive behavioral therapy

Cognitive behavioral therapy (CBT), emphasizes on effective coping strategies and acceptance of pain, is also recommended as adjunctive therapy for PIFP [61] An evidence-based review of 4 CBT trials in TMD revealed 1 trial showing no effect, and 3 that showed both short-term and long-term improvement in outcomes [60].

Religion and spirituality

The role of religion and spirituality proves to have a significant source of support for many patients with chronic pain [62]. Patients' reliance on spirituality in chronic illness and pain has re-

vealed positive outcomes with improved sense of well-being, resiliency, and decreased pain and anxiety. Prayer is proven to be one of the most commonly used complementary modalities, and religious coping a common strategy for dealing with pain [63].

The mind is a very powerful tool in pain management, whether focused, relaxed, or distracted. Therefore, methods to engage it, from meditation to biofeedback [64] through journaling [65] and art [66] music therapy [67] are additional tools that may play a useful role in crafting an individualized plan for pain management in patients with chronic facial pain.

These less studied and often underemphasized aspects, including nutrition, mind-body therapies, and spirituality essentially emphasize on the whole person and a "holistic" approach, in combination with evidence-based medicine.

Conclusion

Persistent idiopathic facial pain represents a challenging diagnostic and treatment entity. The best approach uses a multidisciplinary team, typically is a combining agents and modalities that address not just the physical body, but also include the psychosocial, emotional, behavioral, and spiritual components as they relate to the whole person, aiming to not only cure but heal thy patients restoring their humanity and integrity. In this manner, patients may not be cured, but healed in a way that restores part of their humanity and integrity.

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