

## **Chronic/ Persistent idiopathic facial pain**

Joanna M Zakrzewska MD

Consultant / Honorary Professor

Division of Diagnostic, Surgical and Medical Sciences

Eastman Dental Hospital

UCLH NHS Foundation Trust

256 Gray's Inn Road

London

WC1X 8LD

UK

Corresponding author

Joanna M Zakrzewska

Division of Diagnostic, Surgical and Medical Sciences

Eastman Dental Hospital

UCLH NHS Foundation Trust

256 Gray's Inn Road

London

WC1X 8LD

[j.zakrzewska@ucl.ac.uk](mailto:j.zakrzewska@ucl.ac.uk)

Tel. 020 3456 1195

Fax 020 3456 1105

**Key words: facial pain, persistent idiopathic facial pain , cognitive behaviour therapy, antidepressants**

## **Synopsis**

Persistent or chronic idiopathic facial pain, often called atypical facial pain, is often used as a diagnosis of exclusion. It is a chronic pain in a non anatomically distributed area of the face and mouth which can be episodic or continuous and described as a nagging dull pain which at times is severe. It is associated with other chronic pain conditions, psychological abnormalities and significant life events. Investigations are all normal and early treatment can prevent chronicity. A multidisciplinary biopsychosocial approach with the use of antidepressants and cognitive behaviour therapy provides the best chance of pain relief and improved quality of life.

## **Key points:**

1. Persistent idiopathic facial pain is a poorly localised often continuous nagging pain of the face for which no cause as yet has been identified.
2. Patients are often over investigated in their quest to obtain a diagnosis and current conventional investigations are all normal.
3. Systematic reviews highlight the paucity of randomised controlled trials of high quality with a combination of antidepressant and cognitive behaviour therapy providing the best pain relief and decreased interference with life.
4. A multidisciplinary biopsychosocial approach provides for the best outcomes as these patients have significant co-morbidities including other chronic pain, personality disorders and a history of significant life events.

## **Introduction**

There has been considerable controversy about the condition currently called persistent idiopathic facial pain (PIFP) by the International Headache Society Classification ICHD <sup>1</sup>. The term persistent as opposed to chronic is preferred as it implies that relief may be a possible outcome. It is often called atypical facial pain (AFP) <sup>2</sup>. In this text both terminologies PIFP and AFP will be used but it is assumed that these are the same disorders. It may include more than one condition e.g atypical odontalgia, persistent dentoalveolar pain. In the neurosurgical literature it has been termed atypical facial pain and Burchiel emphasized that it excludes disorders for which a cause has been identified and that this is a somatoform disorder diagnosed by psychological testing <sup>3</sup>.

The ICHD Description: is “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. See box 1 for criteria .

### **Box 1: ICHC diagnostic criteria for persistent idiopathic facial pain**

Patients are diagnosed into this category frequently as an exclusion diagnosis however with improved appreciation of the need to take careful history patients who were previously put in this category may in fact have other identifiable causes of pain such as neuropathic pain and myofascial pain and so do not belong here <sup>4, 5</sup> et al.

The cause remains unknown but it has been suggested that it could be a consequence of deafferentation and central sensitization but is still not clear if peripheral or central mechanisms are involved <sup>4, 6</sup>. Not surprisingly psychological factors are identified but these could also be as a consequence of having a chronic pain, lack of diagnosis and attitude of health care professionals. Gustin et al have shown that psychological and psychosocial factors are universal to chronic pain and are no different between orofacial pain patients relative to diagnosis <sup>7</sup>.

## **Epidemiology**

A study in primary care in the Netherlands found an incidence rate of 4.4 [95% CI: 3.2–5.9] for atypical facial pain with a predominance in females 75% and mean age of 45.5 (SD 19.6) <sup>8</sup>. A review of 97 patients with facial pain attending a neurological tertiary centre in Austria classified 21% as having PIFP <sup>9</sup>. In a UK community based study chronic orofacial pain was identified in 7% of the population and these patients often have other unexplained symptoms such as chronic widespread pain, irritable bowel syndrome and chronic fatigue and show high levels of health anxiety, reassurance seeking behaviour and recent adverse events <sup>10</sup>.

### *Risk factors:*

- psychological distress
- maladaptive response to illness
- female
- retrospective perception of unhappiness in childhood <sup>11</sup>, <sup>12</sup>.

On the other hand in the large Finish birth cohort study, 5,696, a question on facial pain was added and a correlation was found with optimism which was important factor in reducing facial pain <sup>13</sup>.

Using the Chronic Graded Pain Scale Chung et al <sup>14</sup> showed in a population study of elderly Koreans that disability was high in nearly 50% of patients with chronic facial pain but lower than for other forms of facial pain such as burning mouth and joint pain.

*Major predictors of outcome:*

- patients' illness beliefs such as serious consequences of continued pain
- low personal control <sup>15</sup>
- optimism <sup>13</sup>

### **Clinical features**

If there is a history of trauma, extensive dental work prior to the pain e.g 6 months, then the pain may be neuropathic and so should not be classified under this category. Trained staff may be able to establish a more accurate diagnosis which avoids the label of PIFP <sup>16</sup>. Taking a careful history which includes family history, social history and performing psychological testing is imperative as comorbidity is very common <sup>17, 18</sup>.

Table 1 lists the key features

Pfaffenrath I <sup>19</sup> and Zebenholzer <sup>20</sup> have both used the ICHD criteria to determine if the criteria are correct and both suggested alterations. Zebenholzer <sup>20</sup>

put forward very simple criteria for PIFP under which most chronic orofacial pains could be classified .

## **Investigations**

Many of these patients will have had numerous investigations including MRIs and yet is it questionable whether they should have MRI scans as these are normal. Lange <sup>21</sup> showed that patients with PIFP do not have neurovascular compression of their trigeminal nerve at the root entry zone. However PIFP patients have brain morphology changes consistent with those who have chronic pain <sup>22</sup> but studies suggest that somatosensory processing is not used to maintain the pain <sup>23</sup>. Conditions such as temporal arteritis may need to be excluded in patients over 50 years by appropriate investigations.

Forssell <sup>4</sup> 2007 when comparing trigeminal neuropathic pain patients with AFP showed that in up to 75% of AFP patients demonstrated abnormalities on neurophysiological testing. If qualitative sensory testing QST and neurophysiological recordings are abnormal this may result in changing the diagnosis to a probable neuropathic pain <sup>5</sup> . It is important that these patients have some form of psychological testing the easiest of which are psychometrically tested questionnaires such as Brief Pain Inventory –Facial <sup>24</sup> , Hospital Anxiety and Depression Scale <sup>25</sup>, pain catastrophizing scale <sup>26</sup> , Chronic Graded Pain Scale <sup>27</sup>. These tests often show high levels of disability. A study of German University centres managing chronic facial pain showed that only 32% ( 6/19) did psychological testing <sup>9</sup>.

## **Overall management**

Often by the time these patients present in a specialist clinic they have been to numerous dentists and medical practitioners, attended at several secondary care centers, had a significant number of investigations and some treatments that may have included irreversible dental treatments<sup>19</sup>. Studies in a German secondary care sectors have shown inadequate management<sup>9</sup> and similar findings have been reported in the UK<sup>28</sup>. A qualitative study of doctors' dentists and patients in the UK showed that current management of PIFP was ineffective and unsatisfactory from everybody's perspective<sup>29</sup>. They identified especially relationships between clinician and patient and lack of psychological support.

Figure 1 shows an algorithm used in a large UK facial pain clinic which is based on what evidence is currently available.

**Figure 1 here**

### **Pharmacologic Treatment Options**

There are no high quality evidence based treatments. When List did a systematic review of pharmacological treatments for facial pain they found very few studies and many of them were mixed including both temporomandibular disorders and atypical facial pain<sup>30</sup>. Probably the first trial was by Lascelles in 1966 who used monoamine oxidase inhibitors in a cross over trial of 40 patients with PIFP and depression with some success<sup>31</sup>.

Treatment is often specialty biased<sup>32</sup>. A survey among UK medical and dental practitioners showed that the most common drugs used were antidepressants<sup>2</sup>. Some selective serotonin reuptake inhibitors (SSRIs) or selective noradrenalin and serotonin inhibitors (SNRIs) are used<sup>33</sup>. Anticonvulsants drugs have not been shown to be effective.

Patients with significant psychiatric co-morbidity will benefit from an assessment with a liaison psychiatrist prior to being referred to a cognitive behavior program.

Those studies that have been the subject of RCT are shown in table 2.

**Table 2 lists drug therapies that have been used in RCTs**

**Nonpharmacologic Treatment Options**

A systematic review of psychological therapies identified 17 trials in orofacial pain but there was a high risk of bias so only weak evidence was found to support their use <sup>34</sup>. A controlled patient blinded study in 41 PIFP compared active hypnosis for 5 one hour individual sessions with relaxation and showed that significant pain relief was obtained in susceptible adults but there was a need for further psychological support to help with coping strategies and other psychological issues <sup>35</sup>.

It is crucial to stress that a cause cannot be found in all cases and this does not mean that the pain is not real. Patients need to move away from looking for a cause and develop coping strategies, pacing and targeting goals which would reduce interference with quality of life <sup>36</sup> and these sessions may be short <sup>37</sup>. Reassurance with an explanation is required rather than just a statement that “things will get better”. Written patient information is helpful and these can be found on the European Federation Chapters [wwwhttp://www.efic.org/index](http://www.efic.org/index). European Year against pain 2013/14 . Techniques such as mindfulness, mediation and yoga can be helpful. Sleep hygiene often needs to be improved as poor sleep increases vulnerability to pain. These techniques are likely to have a positive outcome on their

other chronic pain as cognitive behavior therapy has been shown to be effective in chronic pain. <sup>38, 39</sup>

### **Combination Therapies**

Harrison <sup>40</sup> showed that the best outcome were obtained with a combination of an antidepressant with cognitive behavior therapy see table 2 .

### **Surgical Treatment Options**

In their series of 256 patients treated with Gamma Knife surgery Balamucki <sup>41</sup> included 20 with PIFP and in this group 60% had pain relief with 15% coming off all medication and up to 42% indicated that their quality of life had improved. However there was a recurrence rate of 33%. Radiofrequency thermocoagulation nor microvascular decompression gave satisfactory long term pain relief in 16 patients <sup>42</sup>.

### **Evaluation of Outcome and Long-Term Recommendations**

There is little data on prognosis. Feinmann <sup>43</sup> followed up patients who had undertaken a trial of dothiepin and at 4 years showed that improvement had been maintained albeit with continuation of dothiepin, withdrawal at 6 months had resulted in return of pain. Long term antidepressants may be needed as well as psychological support to reduce further health utilization.

### **Summary/Discussion**

There remains little high quality evidence on PIFP. Potentially this diagnosis is being used less often as more detailed history and examinations are done which enable more accurate diagnosis e.g neuropathic pain, burning mouth syndrome, temporomandibular disorders. These patients have increased vulnerability to chronic pain and will present with many other medically unexplained symptoms and personality disorders. Their health utilization is high as they seek to obtain a diagnosis, exclude a serious cause for their disease and then get treatment. They feel abandoned as once clinicians have excluded a serious or treatable cause they are reassured and discharged from clinics. Reassurance on its own is insufficient and it must be associated with written information and coping strategies. There is a paucity of high quality trials confounded by the wide range of diagnostic criteria used. Some trials will include a variety of chronic orofacial pain conditions and do not report on them separately. A systematic review showed weak evidence for psychological therapy on its own but one RCT showed that when combined with antidepressants improved outcomes are possible. PIFP is a long term condition especially if not managed early and patients need to be positively reassured that they are believed and that they have a real pain but its cause currently remains unknown.

**Conflict of interest : known**

## **References**

- (1) Anon. The International Classification of Headache Disorders, 3rd edition (beta version). *Cephalalgia* 2013;33(9):629-808.

- (2) Elrasheed AA, Worthington HV, Ariyaratnam S et al . Opinions of UK specialists about terminology, diagnosis, and treatment of atypical facial pain: a survey. *Br J Oral Maxillofac Surg* 2004;42(6):566-571.
- (3) Burchiel KJ. A new classification for facial pain. *Neurosurgery* 2003;53(5):1164-1166.
- (4) Forssell H, Tenovuo O, Silvoniemi P et al Differences and similarities between atypical facial pain and trigeminal neuropathic pain. *Neurology* 2007;69(14):1451-1459.
- (5) Forssell H, Jaaskelainen S, List T, et al . An update on pathophysiological mechanisms related to idiopathic oro-facial pain conditions with implications for management. *J Oral Rehabil* 2015;42(4):300-322.
- (6) Jaaskelainen SK, Forssell H, Tenovuo O. Electrophysiological testing of the trigeminofacial system: aid in the diagnosis of atypical facial pain. *Pain* 1999;80(1-2):191-200.
- (7) Gustin SM, Wilcox SL, Peck CC, et al . Similarity of suffering: equivalence of psychological and psychosocial factors in neuropathic and non-neuropathic orofacial pain patients. *Pain* 2011;152(4):825-832.
- (8) Koopman JS, Dieleman JP, Huygen FJ, et al. Incidence of facial pain in the general population. *Pain* 2009;147(1-3):122-127.
- (9) Wirz S, Ellerkmann RK, Buecheler M, et al Management of chronic orofacial pain: a survey of general dentists in german university hospitals. *Pain Med* 2010;11(3):416-424.

- (10) Aggarwal VR, McBeth J, Zakrzewska JM, et al The epidemiology of chronic syndromes that are frequently unexplained: do they have common associated factors? *Int J Epidemiol* 2006;35(2):468-476.
- (11) Macfarlane TV, Blinkhorn AS, Davies RM, et al . Oro-facial pain in the community: prevalence and associated impact. *Community Dent Oral Epidemiol* 2002;30(1):52-60.
- (12) Aggarwal VR, Macfarlane GJ, Farragher TM, et al Risk factors for onset of chronic oro-facial pain--results of the North Cheshire oro-facial pain prospective population study. *Pain* 2010;149(2):354-359.
- (13) Sipila K, Ylostalo PV, Ek E, et al. Association between optimism and self-reported facial pain. *Acta Odontol Scand* 2006;64(3):177-182.
- (14) Chung JW, Kim JH, Kim HD, et al. Chronic orofacial pain among Korean elders: prevalence, and impact using the graded chronic pain scale. *Pain* 2004;112(1-2):164-170.
- (15) Galli U, Ettlin DA, Palla S, et al Do illness perceptions predict pain-related disability and mood in chronic orofacial pain patients? A 6-month follow-up study. *Eur J Pain* 2010;14(5):550-558.
- (16) Nobrega JC, Siqueira SR, Siqueira JT, et al. Diferential diagnosis in atypical facial pain: a clinical study. *Arq Neuropsiquiatr* 2007;65(2A):256-261.

- (17) Sipila K, Ylostalo PV, Joukamaa M, et al. Comorbidity between facial pain, widespread pain, and depressive symptoms in young adults. *J Orofac Pain* 2006;20(1):24-30.
- (18) Feinmann C, Harris M, Cawley R. Psychogenic Facial pain, presentation and treatment. *Br Med J* 1996;288:436-438.
- (19) Pfaffenrath V, Rath M, Pollmann W, Keeser W. Atypical facial pain--application of the IHS criteria in a clinical sample. *Cephalalgia* 1993;13 Suppl 12:84-88.
- (20) Zebenholzer K, Wober C, Vigl M, Wessely P, et al Facial pain and the second edition of the international classification of headache disorders. *Headache* 2006;46(2):259-263.
- (21) Lang E, Naraghi R, Tanrikulu L et al. Neurovascular relationship at the trigeminal root entry zone in persistent idiopathic facial pain: findings from MRI 3D visualisation. *J Neurol Neurosurg Psychiatry* 2005;76(11):1506-1509.
- (22) Schmidt-Wilcke T, Hierlmeier S, Leinisch E. Altered regional brain morphology in patients with chronic facial pain. *Headache* 2010;50(8):1278-1285.
- (23) Lang E, Kaltenhauser M, Seidler S, et al. Persistent idiopathic facial pain exists independent of somatosensory input from the painful region: findings from quantitative sensory functions and somatotopy of the primary somatosensory cortex. *Pain* 2005;118(1-2):80-91.

- (24) Lee JY, Chen HI, Urban C et al. Development of and psychometric testing for the Brief Pain Inventory-Facial in patients with facial pain syndromes. *J Neurosurg* 2010;113(3):516-523.
- (25) Zigmond AS, Snaith RP. The hospital anxiety and depression scale. *Acta Psychiatr Scand* 1983;(67):361-437.
- (26) Sullivan MJ, Bishop S.R., Pivik J. The pain catastrophizing scale: development and validation. *Psychological Assessment* 1995;7(4):524-532.
- (27) Von Korff M, Dworkin SF, Le Resche L. Graded chronic pain status: an epidemiologic evaluation. *Pain* 1990;40(3):279-291.
- (28) Beecroft EV, Durham J, Thomson P. Retrospective examination of the healthcare 'journey' of chronic orofacial pain patients referred to oral and maxillofacial surgery. *Br Dent J* 2013;214(5):E12.
- (29) Peters S, Goldthorpe J, McElroy C et al. Managing chronic orofacial pain: A qualitative study of patients', doctors', and dentists' experiences. *Br J Health Psychol* 2015;20(4):777-791.
- (30) List T, Axelsson S, Leijon G. Pharmacologic interventions in the treatment of temporomandibular disorders, atypical facial pain, and burning mouth syndrome. A qualitative systematic review. *J Orofac Pain* 2003;17(4):301-310.
- (31) Lascelles RG. Atypical facial pain and depression. *Br J Psychiatry* 1966;112(488):651-659.

- (32) Madland G, Feinmann C. Chronic facial pain: a multidisciplinary problem. *J Neurol Neurosurg Psychiatry* 2001;71(6):716-719.
- (33) Benoliel R, Eliav E. Neuropathic orofacial pain. *Oral Maxillofac Surg Clin North Am* 2008;20(2):237-54, vii.
- (34) Aggarwal VR, Lovell K, Peters S, et al J. Psychosocial interventions for the management of chronic orofacial pain. *Cochrane Database Syst Rev* 2011;(11):CD008456.
- (35) Abrahamsen R, Baad-Hansen L, Svensson P. Hypnosis in the management of persistent idiopathic orofacial pain--clinical and psychosocial findings. *Pain* 2008;136(1-2):44-52.
- (36) Madland G, Newton-John T, Feinmann C. Chronic idiopathic orofacial pain: I: What is the evidence base? *Br Dent J* 2001;191(1):22-24.
- (37) Harrison S, Watson M, Feinmann C. Does short-term group therapy affect unexplained medical symptoms? *Journal of Psychosomatic Research* 1997;43(4):399-404.
- (38) Vlaeyen JW, Morley S. Cognitive-behavioral treatments for chronic pain: what works for whom? *Clin J Pain* 2005;21(1):1-8.
- (39) Morley S, Eccleston C, Williams A. Systematic review and meta-analysis of randomized controlled trials of cognitive behaviour therapy and behaviour therapy for chronic pain in adults, excluding headache. *Pain* 1999;80(1-2):1-13.

- (40) Harrison SD, Glover L, Feinmann C, et al . A comparison of antidepressant medication alone and in conjunction with cognitive behavioural therapy for chronic idiopathic facial pain. Proceedings of the 8th World Congress on Pain, Progress in Pain Research and Management; Seattle: IASP Press; 1997 663-672.
- (41) Balamucki CJ, Stieber VW, Ellis TL et al. Does dose rate affect efficacy? The outcomes of 256 gamma knife surgery procedures for trigeminal neuralgia and other types of facial pain as they relate to the half-life of cobalt. *J Neurosurg* 2006;105(5):730-735.
- (42) Teixeira MJ, Siqueira SR, Almeida GM. Percutaneous radiofrequency rhizotomy and neurovascular decompression of the trigeminal nerve for the treatment of facial pain. *Arq Neuropsiquiatr* 2006;64(4):983-989.
- (43) Feinmann C. The long-term outcome of facial pain treatment. *J Psychosom Res* 1993;37(4):381-387.
- (44) Forssell H, Tasmuth T, Tenovuo O, et al . Venlafaxine in the treatment of atypical facial pain: a randomized controlled trial. *J Orofac Pain* 2004;18(2):131-137.
- (45) al Balawi S, Tariq M, Feinmann C. A double-blind, placebo-controlled, crossover, study to evaluate the efficacy of subcutaneous sumatriptan in the treatment of atypical facial pain. *Int J Neurosci* 1996;86(3-4):301-309.
- (46) Harrison SD, Balawi SA, Feinmann C, et al. Atypical facial pain: a double-blind placebo-controlled crossover pilot study of subcutaneous sumatriptan. *Eur Neuropsychopharmacol* 1997;7(2):83-88.

(47) Feinmann C. Psychogenic facial pain: presentation and treatment. *J Psychosom Res* 1983;27(5):403-410.

Figure 1

Care- pathway used for persistent idiopathic facial pain at a large UK facial pain unit.

Box 1: ICHC diagnostic criteria for persistent idiopathic facial pain

*Diagnostic criteria:*

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

Table 1 Features of persistent idiopathic facial pain PIFP

<b>Character</b>	Dull aching nagging sharp
<b>Site and radiation</b>	Deep, poorly localized non anatomical , intraoral, extraoral , change over time
<b>Severity</b>	Varying but can be intense
<b>Duration and periodicity</b>	Long slow onset continuous, intermittent
<b>Provoking factors</b>	Stress, fatigue
<b>Relieving factors</b>	Rest
<b>Possible associated factors</b>	Multiple other bodily pains Pruritus Dysmenorrhea Life events Personality disorders Anxiety, depression Sleep disturbance

**Table 2 RCTs of drug treatments for PIFP**

<b>Drug</b>	<b>Trial details</b>	<b>Efficacy</b>	<b>Side effects</b>	<b>Comment</b>	<b>Reference</b>
Venlafaxine 75mg oral daily	RCT cross over, 2 weeks each arm 30 patients	Modest on pain relief , 3 patients > 30% pain reduction but not intensity nil on anxiety depression	Little difference between placebo and active sweating and dryness	Underpowered and low dose of venlafaxine	Forssell et al 2004 <sup>44</sup>
Fluoxetine 20mg Placebo Cognitive behavior therapy CBT with or without fluoxetine	RCT 4 arms for 3 months 178 patients	Only fluoxetine on its own was effective in reducing pain intensity. Addition of CBT reduced distress and	None stated Largest drop out rate was in CBT	59 did not complete and some patients had TMD	Harrison <sup>40</sup> et al 1997

		level of interference CBT on its own reduced interference only			
Sumatriptan 6mg Subcutaneous one dose	RCT cross over one day interval of 3-6 weeks between cross over 19 patients,	Temporary improvement only one reported sustained relief	All reported side effects headache, abnormal sensations	Assessed 60 and 120 minutes only	Harrison et al 1997 <sup>46</sup> Al Balawi <sup>45</sup> , et al 1996
Dothiepin 25-150mg with biteguard, placebo and biteguard, dothiepin, placebo	RCT 4 parallel groups 50 TMD, 43 AFP, 57 unclassified	Some pain relief with dothiepin but large drop out	Drowsiness, dry mouth, no details about withdrawals	Mixed cohort, inconclusive	Feinmann <sup>47</sup> 1983

