Orofacial pain – an update on diagnosis and management

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In brief

Provides a comprehensive overview of common non-dental facial pain which will be of interest to non-specialist dentists.

Provides guidance with regards to diagnosis, management and when to refer facial pain patients.

Highlights the importance of adopting a biopsychosocial approach to facial pain management

The diagnosis and management of orofacial pain may be challenging due to complex histories, pathophysiology and associated psychosocial co-morbidities such as depression and anxiety. Neuropathic facial pain conditions such as burning mouth syndrome (BMS), persistent idiopathic facial pain (PIFP), atypical odontalgia (AO) and trigeminal neuralgia (TN) require early recognition by primary care clinicians and referral to secondary care. Acute pain-related temporomandibular disorder (TMD) may be managed in the primary care setting, with identification of those at risk of developing chronic TMD receiving an early referral to secondary care. Adopting a biopsychosocial approach, consisting of physical therapies, pharmacotherapy and psychological support can lead to effective management and may limit the negative impact of facial pain upon quality of life and daily functioning.

Introduction

The term 'orofacial pain' is used to describe pain arising from the regions of the face and mouth. These pains may occur due to diseases of regional structures, nervous system dysfunction, or as a result of referral from distant sources.[1] Orofacial pain of greater than three months duration may be described as being chronic.[2]

Macfarlane *et al.*[3] conducted a cross-sectional population-based survey in the UK, in which 26% of participants reported orofacial pain. At the four year follow up, 54% continued to report orofacial pain, highlighting the potential for chronicity of orofacial pain.[3] Furthermore, a more recent study by Macfarlane *et al.*[4] reported a facial pain prevalence of 1.9% in the UK, of this 48% were reported as being chronic. These findings are significant, as it has been well documented that chronic orofacial pain may be accompanied by distress, physical disability and negative psychosocial impact.[5–7] Moreover, there are economic implications for managing chronic pain, with patients often utilising greater healthcare resources, through assessment by multiple clinicians, and investigations which may not be of benefit to the patient.[8–11] Durham *et al.*[12] have conducted a study into the costs associated with persistent orofacial pain. The authors used the graded chronic pain scale (GCPS), which takes into account pain intensity and pain-related disability.[12,13] Healthcare costs were found to increase by an average of £366 when moving from a low to a high GCPS status; highlighting the biopsychosocial impact of orofacial pain and the associated economic impact.[12]

Thus, it is important that patients with orofacial pain receive an early diagnosis with instigation of appropriate management.[9] The overall management strategy for orofacial pain may be extrapolated from the guidelines produced by the British Pain Society for the management of adults with chronic pain.[14] These principles follow a biopsychosocial approach and consist of three domains: physical exercise/relaxation, pharmacotherapy and clinical psychology.[15]

Adopting this approach of early diagnosis and a holistic approach to management is central to limiting the negative psychosocial impact of orofacial pain,[9,15,16] whilst ensuring care remains effective and efficient.[9]

The aim of this paper is to summarise the diagnostic classifications, epidemiology, pathophysiology and management of the key orofacial pain conditions – burning mouth syndrome, persistent idiopathic facial pain, atypical odontalgia, pain-related temporomandibular disorder (TMD) and trigeminal neuralgia.

Burning mouth syndrome (BMS)

Classification and diagnosis

Burning mouth syndrome (BMS) is a condition characterised by burning sensation or discomfort affecting the mouth, occurring in the presence of clinically healthy oral mucosa.[17–19] BMS commonly affects the tongue, however,

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patients may also report more extensive discomfort affecting other areas of the oral cavity.[17,19,20] Patients may alternatively report sensations such a tingling or numbness;[21] while additional symptoms of xerostomia and taste disturbance may also be encountered.

Scala *et al.*[20] have described that 'primary' BMS occurs when organic causes for oral burning cannot be identified; whereas 'secondary' BMS may arise as a result of local or systemic pathology. Therefore, the diagnosis of burning mouth syndrome is made following a comprehensive pain history, with the exclusion of medical, dental and drug-related causes for the symptoms.[19,20] Clinical examination is important, in order to exclude local factors which may lead to oral burning sensation.[20,22] Oral mucosal conditions such as lichen planus, candidosis and geographic tongue may also give rise to oral burning sensations.[20] Allergic reactions to dental materials and food may lead to an oral burning sensation, thus patch testing may be indicated for patients with a history and presentation in keeping with a type I hypersensitivity (allergic response), or presenting with a suspected type IV hypersensitivity reaction (such as a lichenoid lesion).[22,23] Assessment of saliva flow may also be performed in cases where xerostomia is suspected as being the underlying cause of discomfort.[18,20]

In order to investigate systemic causes of BMS, patients should receive haematological and biochemical investigations to exclude anaemia and haematinic deficiency (low folate, B_{12} or iron) which may result in oral burning sensation.[16,24] Testing of serum zinc levels has also been advocated.[16] One study has demonstrated low serum zinc levels in patients with BMS;[25] however, it was concluded that there is limited evidence to suggest that this is a causative factor in the development of BMS. Random blood glucose and HbA1c may be required to help exclude diabetic neuropathy.[16] In patients where connective tissue disorders, or other autoimmune conditions such as Sjögren's syndrome are suspected, immunological investigations such as autoantibody screens may be performed.[16]

In summary, the diagnosis of BMS is based upon pain history, normal clinical examination and laboratory investigations.[19,20]

Epidemiology

BMS is reported to affect 0.7–15% of the population.[26] The variability in the prevalence is suggested to be due to the differing criteria used in the diagnosis of BMS, with some studies also including secondary BMS.[26] BMS more commonly affects women (with a varying ratio between five and ten females to every male).[17,18,24,26,27] It has been documented in the literature that BMS peaks between the fifth and seventh decades.[17]

BMS is a chronic condition which usually persists for many years, occasionally with episodes of remission.[22] Sardella *et al.*[28] reported 3% of patients experienced complete remission after five years of onset of the condition.

Pathophysiology

Recent studies have suggested that several neuropathic mechanisms act at different levels of the nervous system to contribute to the pathophysiology of BMS.[19] It has also been suggested that BMS is multifactorial in origin, occurring as a result of a complex interaction between local, systemic and psychosocial factors.[26] Further supporting the proposals for neuropathic mechanisms in BMS, an elegant hypothesis promulgated by Woda and colleagues suggests that a significant proportion of BMS may be attributed to neuropathic changes secondary to perimenopausal hormonal dysregulation.[18] Moreover, a study by Lauria *et al.*[17] found that tongue biopsies from BMS patients demonstrated a lower density of epithelial nerve fibres in comparison to the control group. Morphological changes affecting epithelial and subpapillary nerve fibres were noted, suggesting that BMS may be due to small fibre trigeminal sensory neuropathy. Similarly, studies have demonstrated involvement of the central nervous system in the development of BMS,[18,26] with positron emission tomography (PET) scanning of BMS patients demonstrating decreased levels of dopamine in the putamen.[29]

Additionally, understanding the impact of psychosocial factors in the development of BMS is of paramount importance.[20,30] Lamey *et al.*[30] reported that BMS patients may demonstrate a higher incidence of adverse early life experiences and chronic fatigue. Moreover, it has been documented that BMS patients may exhibit higher levels of depression and anxiety.[30,31] Further to this, brain dopamine hypofunction is shared between BMS and psychiatric comorbidity – suggesting that patients with BMS are more likely to develop anxiety and depression, and *vice versa*.[31]

Burning mouth syndrome is a chronic neuropathic pain condition that can have a significant negative impact on quality of life. Several studies have shown reduced quality of life in BMS patients compared to controls.[24,32]

Management

BMS is a chronic, often long-term pain condition and thus an important aspect of management is providing reassurance, hope, educating patients about their condition,[6] and facilitating self-management.[33] Bonathan *et al.*[6] have demonstrated that provision of information regarding chronic facial pain conditions, delivered in a sensitive manner, can aid in alleviating patients' feelings of helplessness towards their condition. Moreover, this educational approach can facilitate self-management.[6,34] Consequently, patients with BMS should be encouraged to develop self-management strategies involving physical activities, relaxation and distraction.[34]

A recently published Cochrane review[19] on the management of BMS suggested that there is currently a dearth of high quality evidence to support, or refute any specific treatments for BMS. The review concludes that further clinical trials should be conducted, looking at medications used in other neuropathic pain conditions and psychological therapies. In light of the association of BMS with depression and anxiety[19,30,31] it has been suggested that antidepressants may be beneficial in the management of BMS.[19] The blockade of the central nervous system (CNS) receptors by antidepressants may result in increased activity of descending inhibitory pain pathways.[19] Tricyclic antidepressants (TCAs) such as amitriptyline may be of benefit in managing BMS.[19,35] However, there is limited evidence to support, or refute the use of antidepressants for the management of BMS. Similar findings have also been reported for the use of anticonvulsants such as gabapentin, and the use of benzodiazepines.[19] Although robust evidence for the medical management of BMS is lacking, there is evidence for the use of antidepressants and anticonvulsants in the management of neuropathic pains in general – amitriptyline, duloxetine, gabapentin and pregabalin are considered appropriate first line medical therapies for neuropathic pains according to the National Institute for Health and Care Excellence (NICE).[36] In view of the evidence supporting BMS as a neuropathic pain, it would be reasonable to consider such neuropathic pain medications in the management of BMS.

Psychological therapies such as cognitive behavioural therapy (CBT) have been seen to reduce pain intensity in patients with BMS.[37]

A combined approach with medical and psychological therapy, with an emphasis on self-management may help to limit the negative

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psychosocial impact of BMS and improve quality of life.[19,20]

Persistent idiopathic facial pain

Classification and diagnosis

Persistent idiopathic facial pain, previously termed 'atypical facial pain',[16] has been described by the International Classification of Headache Disorders (ICHD)[38] as being '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.'

PIFP commonly presents unilaterally and may initially be limited to one side of the face, commonly affecting the maxillary region, though it may spread to involve a larger area.[39] The pain is normally poorly localised, not following the distribution of a peripheral nerve and is often of dull and aching character,[39] though sharp exacerbations may also occur.[38]

The ICHD diagnostic classification for PIFP includes the features described previously, with the addition of normal clinical neurological examination and exclusion of a dental cause.[38]

The diagnosis of PIFP is primarily based upon pain history and clinical examination.[8] Radiographic examination should also be carried out to exclude dental causes.[8]

Epidemiology

The reported estimated incidence of PIFP is given as 1 per 100,000, though this may not be representative of the true incidence due to difficulty in applying the classification criteria.[39] The incidence of PIFP is higher in women than in men[8,39] and most often occurs between the ages of 30–50 years old.[39]

There is a lack of data with regards to remission rates for PIFP; however, it may be inferred that this condition follows a similar natural history as other chronic orofacial pain conditions, with long-term pain symptoms.[10]

Pathophysiology

PIFP is reported as being a neuropathic pain condition.[39,40] This is supported by publications that report these symptoms often develop following dental treatment, suggesting underlying neuropathic pathology.[39,40] Moreover, it is suggested that there is involvement of central sensitisation pain mechanisms.[40]

Patients with PIFP may demonstrate greater incidence of psychiatric co-morbidities such as depression and obsessive-compulsive personality characteristics.[31] These conditions may occur prior to the development of PIFP and may similarly run a chronic course.[31] Further supporting these associations, some studies have identified brain dopaminergic hypofunction in PIFP patients, in a similar way to other chronic pain conditions.[41]

Management

Early diagnosis of PIFP, in conjunction with patient education is central to the management of PIFP.[39] This approach is of paramount importance, as invasive procedures may result in traumatic neuropathy and worsening of symptoms[40].

Medications may be considered to manage the symptoms associated with PIFP.[39,40] In view of the overtly neuropathic nature of PIFP, one could consider consulting the NICE guidelines for neuropathic pain[36] – which suggest first line management with either: amitriptyline, duloxetine, gabapentin or pregabalin. If sufficient benefit is not achieved, then it is suggested that patients may change to one of the alternative medications, or take a combination therapy. Moreover, one may also include the intermittent use of tramadol (an opioid) for breakthrough pain. However, solely using medications may be insufficient for managing PIFP.[39,42]

As described previously, patients with PIFP may also present with significant distress, psychiatric co-morbidities, and impaired quality of life.[6,31,39] Although these issues may be partly addressed by using the previously described medications, it is important to consider a holistic approach, incorporating patient education and psychological therapies such as CBT to facilitate self-management.[10]

Atypical odontalgia

Classification and diagnosis

AO has been reported as being a subform of PIFP.[38,39] However, as AO may occur following trauma, it may also be classified as a form of painful post-traumatic trigeminal neuropathy.[38]

AO is suggested as being continuous dull pain, affecting the teeth, or commonly at the site of a previous dental extraction.[39,42] These symptoms occur in the absence of clinical and radiographic findings.[39,42] It has been reported that these symptoms may develop following dental treatment.[39,43,44] The pain remains persistent despite dental treatments, including extraction, and may even migrate to adjacent teeth.[39]

Epidemiology

AO may affect a younger age group and demonstrate less variation in incidence between genders.[38]

A study by Pigg *et al.*[42] examining the long term prognosis of patients with AO, reported that a third of patients demonstrated improvement in their symptoms over time; however the majority of patients continued to experience long term discomfort.

The prevalence of persistent pain after successful root canal treatment has been reported to be 12%.[45]

Pathophysiology

The pathophysiology of AO is suggested to be of neuropathic origin.[39,42,46] This is further supported by studies which identify AO developing following dental treatment.[43,44]

A study by Baad-Hansen *et al.*[46] found changes in intraoral somatosensory function in patients with AO – with a higher frequency of hypersensitivity to intraoral stimuli in patients with AO, in comparison to healthy controls.

Some have suggested that PIFP and painful post-traumatic trigeminal neuropathy (such as pain resulting from a neuropathic injury for example, lower third molar surgery)[47] share many characteristics, and can be considered part of the same continuum.[40,41,48]

Management

Similar to the other neuropathic pain conditions described in this paper, early diagnosis and patient education is important in the management of AO.[39,42] Accurate and timely diagnosis of AO is crucial to avoiding futile and unnecessary dental and surgical interventions.[39]

Management of AO is largely similar to other neuropathic facial pain conditions.[39] As described previously, medical management following the NICE guidelines for neuropathic pain[36] may be implemented. Similarly, AO may be also be associated with significant levels of depression and anxiety, thus psychology therapies in conjunction with medical management may be required.[10,39,42]

Pain-related TMD

Classification and diagnosis

TMDs refer to conditions affecting the temporomandibular joint (TMJ), and/or the muscles of mastication.[49]

The original research diagnostic criteria for TMD (RDC/TMD)[50] classified TMD into

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Table 1 Classification of TMD[50]
Myofascial pain (affecting muscles of mastication)
With limited opening
Without limited opening
TMJ disc displacement
With reduction of the disk (with clicking)
Without reduction of the disk, with limited opening
Without reduction of the disk, without limited opening
TMJ arthritides
TMJ osteoarthritis
TMJ osteoarthrosis
TMJ arthralgia

three diagnostic groups which are detailed in Table 1.

The RDC/TMD classification has since been superseded by the more recent diagnostic criteria for temporomandibular disorders (DC/TMD).[22] In summary, the DC/TMD suggests that pain-related TMD is: pain involving the TMJ; muscles of mastication, which are tender to palpation; pain is evoked by function; and the pain is not attributed to another pain diagnosis.

The diagnosis of TMD follows a thorough history and examination. The history should include pain character, precipitating/exacerbating factors and previous trauma.[51] Moreover, a comprehensive medical history is required, in order to ensure that conditions that may give rise to TMD symptoms, such as rheumatoid arthritis and Ehlers-Danlos syndrome are detected.[15]

Clinical examination should include palpation of the TMJ and assessment for joint noises.[51] The muscles of mastication should also be palpated, in order to assess for tenderness or hypertrophy. In patients aged over 50 with new onset TMD symptoms, the temporal pulses should be checked,[51] and one could consider conducting an erythrocyte sedimentation rate (ESR) and C-reactive protein (CRP),[52] to help exclude a possible diagnosis of giant cell arteritis (temporal arteritis). A dental assessment should also be performed in order to rule out dental pathology.[15]

It has also been suggested that psychological assessment is required, due to the impact that chronic TMD may have upon quality of life and the development of chronic pain-related disability.[53] The graded chronic pain scale (GCPS),[13] may be used to assess pain-related disability in TMD patients. The hospital anxiety and depression scale (HAD) may be used to screen for anxiety and depression.[54]

Special investigations, such as imaging, may also be performed when diagnosing TMD. Panoramic radiographs may enable detection of dental pathology.[51] A study by Crow *et al.*[55] reported that condylar changes and degeneration were also detected on panoramic radiographs of healthy controls. Thus, it is has been suggested that imaging should be conducted only following assessment of the clinical findings.[51,56] Magnetic resonance imaging (MRI) may be used to assess disc position, osteoarthrosis and inflammatory changes.[57] Computed tomography (CT) and cone beam CT may enable detection of osseous changes.[57] However, there is limited evidence with regards to the benefit of CT or MRI in TMD.[57] Therefore, it is important that consideration is given to the overall impact that imaging will have upon the management of each individual TMD case.[55–57]

Epidemiology

The reported prevalence for TMD is that it may affect up to a third of the population during their lives.[58] Current literature reports that TMD is one of the three most common chronic pain conditions, along with headache and back pain.[58] The prevalence of TMD is seen to be higher in women;[58] the incidence of TMD peaking in the second and third decades.[59] Moreover, TMD may also be classified as acute or chronic.[60] Acute TMD is often attributable to an identifiable cause, such as prolonged dental treatment, and the symptoms are normally short-lived and self-limiting.[51] The recently published prospective cohort series, 'Orofacial Pain: Prospective Evaluation and Risk Assessment' (OPPERA), suggested that the annual incidence of new onset TMD symptoms in a cohort of 18–44-year-olds was 3.9% per annum.[61] In chronic TMD, the pain is of a longer duration, exceeding three months;[51] which is reported to occur in approximately 20% of TMD patients.[62] These prolonged symptoms may lead to depression and chronic pain-related disability.[53]

Pathophysiology

The pathophysiology of TMD is multifactorial, arising from a complex interplay between various anatomical, physiological and psychological factors.[15,49,53,63]

Table 2 summarises the pathophysiological factors associated with pain-related TMD.[15,63]

Moreover, it has been reported that TMD may arise due to both central and peripheral sensitisation mechanisms.[64] Unlike the other facial pain conditions, TMD is not considered to be a neuropathic pain, rather it is best described as a 'central sensitisation' pain syndrome; whereby, peripheral nociceptor inputs produce a reversible, but prolonged and increased activity in the central nociceptive pathways – resulting in pain hypersensitivity and hyperalgesia.[65]

Management

The majority of patients presenting with TMD can be effectively diagnosed and managed in the primary care setting;[15,51] however, those presenting with chronic TMD, significant psychosocial risk factors and other chronic pain-related co-morbidities, may benefit from early referral to secondary care.[9,15,51]

Initial management of TMD should focus upon patient education to encourage the development of self-management strategies.[33,66] These self-management strategies include physical exercises and relaxation, for example, yoga,[15,67] which has been shown to benefit patients with other chronic pain conditions with a musculoskeletal component, such as fibromyalgia.[68] Educating patients about their condition is vital in facilitating self-management – one study demonstrated the benefits of education over splint therapy in the management of TMD.[69] Similarly, physiotherapy may enable muscle relaxation and improvement in function.[70]

Psychological therapies, such as cognitive behavioural therapy may also facilitate self-management, through the development of techniques to manage pain associated with TMD.[8,51]

A Cochrane review has demonstrated a lack of high quality evidence with regards to the role of medications in the management of TMD.[71] Acute TMD exacerbations may be managed effectively with simple analgesia, such as a non-steroidal anti-inflammatory drug (NSAID).[51] Similarly, benzodiazepines may be used to manage acute TMD accompanied with limited opening, though in light of the potential for dependency, a short course of treatment is recommended.[72] TCAs such as amitriptyline or nortriptyline may be effective in managing chronic TMD which is refractory to conservative measures;[51,72] the benefit may be seen even in the absence of depression.[72]

Occlusal splints have been widely used in the management of TMD.[15,51] A systematic

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Table 2 Pathophysiological factors associated with pain related TMD[15,63]

Factor	Level of evidence			
	Strong	Moderate	Low	No association
Nervous system	Endogenous pain modulation	Autonomic nervous system	Neurodegenerative	
	Peripheral/central sensitisation			
Trauma		Dental interventions	Cervical (debatable)	
		Facial macro trauma		
Demographics	Gender	Age	Ethnicity	
Psychological	Catastrophising	Stress	Personality disorders	Socioeconomic (debatable)
		Depression		
		Childhood events		
Dento-skeletal			Occlusion	Orthodontics
Functional			Parafunction (daytime)	
Lifestyle			Nutrition	
			Smoking	
Sleep		Sleep disorders		Sleep bruxism
Genetics		Genotypic		Inheritable
Co-morbidities/ secondary	Fibromyalgia	Headache	Infection	Secondary gain (debatable)
		Lower back pain		
		Irritable bowel syndrome		
		Chronic widespread pain		

review and meta-analysis conducted by Fricton *et al.*,[73] reported that hard splints have some weak evidence to support their use in the management of TMD pain and the prevention of tooth wear. However, these modest benefits were not any greater than other management strategies for example, self-management, medications and acupuncture. Moreover, hard occlusal splints are expensive to produce and require complex adjustments,[74] and hence soft splints may be considered for patients at low risk of periodontal disease and tooth wear secondary to parafunction.[74] Anterior bite plane devices, such as the nociceptive trigeminal inhibition device (NTI), demonstrate similar efficacy in comparison to full coverage splints,[51] and also carry a significant risk of occlusal changes (such as anterior open bite) if worn for a prolonged period of time.[51,73] Therefore, anterior bite plane devices are not recommended according to current national guidelines.[51] Furthermore, it has been suggested that the benefits derived from splint therapy may be secondary to placebo effect,[73] and splint therapy may lead to hypervigilance and propagation of parafunction.[51] Therefore, splint therapy should not be used in isolation, and could be considered along with other self-management strategies.[15,73]

There is no evidence base for the role of occlusal adjustment in managing chronic TMD.[75] Similarly, a recent Cochrane review did not find any evidence for the role of orthodontics in the management of TMD.[76]

Botulinum toxin type A ('Botox') has also be used in the management of chronic TMD.[51] However, with regards to the management of pain-related TMD, there is a lack of evidence as to the effectiveness of botox.[77] Moreover, a randomised controlled trial has suggested no difference between botox and placebo in the management of pain-related TMD.[78]

The first line management for pain-related TMD normally consists of conservative measures as previously described.[15,49] Surgical interventions may be considered for patients demonstrating disc displacement, or degenerative joint pathology associated with pain and functional problems which are refractory to conservative measures.[51] Surgical interventions should be avoided in patients with chronic TMD without significant functional impairment, as such interventions are unlikely to yield benefits and may exacerbate their symptoms.[51] Minimally invasive interventions, such as arthrocentesis may be performed,[79] alternatively arthroscopy which carries the benefit of fibreoptic guidance for lavage of the joint space may be considered to improve symptoms and function in some patients.[80]

TMJ replacement surgery is only considered for those with severe degenerative disease.[49,51] NICE have produced guidelines with regards to case selection and provision of TMJ replacement surgery.[81]

Trigeminal neuralgia

Classification and diagnosis

Trigeminal neuralgia (TN) is a neuropathic condition affecting one or more branches of the trigeminal nerve.[82,83] The pain is episodic and of brief duration, occurring unilaterally, with abrupt onset and termination. The pain is often excruciating and may be described as stabbing, or like an electric shock, and may occur spontaneously, or be triggered by mild stimuli such as touch, eating or wind.[82,83]

The International Headache Society (IHS)[84] have previously classified TN into two categories – classical TN and symptomatic TN. Classical TN is described as occurring secondary to neuroavascular compression, commonly of the superior cerebellar pontine artery. Symptomatic TN refers to TN indistinguishable from classical TN, other than it arises as a result of a structural lesion other than a vascular compression, such as multiple sclerosis (MS) or a space occupying lesion.[84] A more recent working group has suggested maintaining the classical and symptomatic sub-classifications, and has added a third diagnostic category for TN – 'idiopathic' TN (whereby no compression, or pathology is identified).[85]

TN may have a significant impact upon quality of life, with a significant impact upon the ability to perform daily tasks and negative effects upon health status related to the pain severity.[82] Studies have reported that patients may experience social isolation due to the severity of pain and even loss of employment.[86] Similarly, patients may also demonstrate depression and anxiety as a result of their TN.[82,83]

The diagnosis of TN is primarily based upon the history, as there are no objective

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Table 3 TN medications[87,88,92]

Medicine	Daily dose range	Side effects	Recommendations	Comments
Carbamazepine Evidence rating A: Effective/ Should be used	200–1600 mg	Contraindicated with unpaced AV conduction abnormalities	Begin with small doses, depending on tolerability; increase and decrease slowly	Adverse drug interactions eg, warfarin
		Neurological side effects (dose related)		
		Hyponatraemia/blood disorders - monitor bloods at regular intervals		HLA-B*1502 allele in individuals of Han Chinese or Thai origin – increased risk of SJS/TEN
		Rarely SJS/TENS		
Oxcarbazepine Evidence rating B: Probably effective/Should be considered	300–1200 mg	Neurological side effects	Use on a four times a day basis	Generally better tolerated than CBZ
		Hyponatraemia with higher doses		
		Very rarely blood disorders		
		SJS/TEN		
Baclofen Evidence rating C: Possibly effective/May be considered	50–80 mg	Neurological side effects	Being slowly, divided doses	Withdraw drug to avoid side effects Useful in patients with MS
Lamotrigine Evidence rating C: Possibly effective/May be considered	200–400 mg	Neurological side effects	Initially very slow escalation. Can use in conjunction with CBZ	Cutaneous reactions common if increase dose too quickly
		Blood disorders		
		Rarely SJS/TENS		
Gabapentin with ropivacaine Evidence rating C – Possibly effective/may be considered)	1800-3600 mg (RCT utilised up to 900 mg) + 2 ml of mg/ml ropivacaine	Neurological side effects	Ropivacaine injected weekly into trigger spots	Use of ropivacaine reduced dose of gabapentin required. (Small RCT with newly diagnosed patients likely to go into remission)
Medicines not evaluated in randomised controlled trials				
Phenytoin	200–300 mg	Neurological side effects	Can use with CBZ. HLA-B*1502 cross reactivity with CBZ	>300 mg can lead to severe side effects
		Blood disorders		
		Rarely SJS/TEN		
Sodium valproate	600–1200 mg	Neurological side effects	Monitor liver function for first six months	Often used by neurologists
		Blood disorders,		
		Rarely hepatic dysfunction		
Pregabalin	150–600 mg	Neurological side effects – dose dependent	Use twice daily, avoid abrupt withdrawal	Long-term cohort study shows promise
		Peripheral oedema with higher doses		

HLA-B*1502 – Human Leukocyte Antigen-B*1502.
AV – Atrioventricular
SJS/TEN – Stevens Johnson syndrome/toxic epidermal necrolysis

investigations or tests that can confirm the diagnosis.[83,87] A full dental examination with dental radiographs should also be performed to exclude dental pathology.[86,87]

MRI should be conducted for patients presenting with symptoms consistent with TN, to assess for possible underlying pathology such as MS plaques and tumours.[88] MRI may also demonstrate the presence of neurovascular compression of the trigeminal nerve in the posterior cranial fossa.[86]

Epidemiology

A primary care based study has reported an incidence of 27 per 100,000 for TN.[89] The incidence is seen to be higher for females across all age groups, with a peak incidence between 45 to 59 years.[89]

The disease progression of TN is relatively unknown, due to a lack of published cohort data regarding the long term behaviour of TN.[87] The common notions that TN pain worsens over time, and medications gradually become ineffective, were recently refuted by a cohort study of classical TN patients on medication.[90]

Pathophysiology

The pathophysiology of TN is reported as being neuropathic in origin.[83] Devor *et al.*[91] described the 'ignition hypothesis' – whereby the development of TN occurs as result of damage to the trigeminal axons in the nerve root or ganglion; which frequently occurs due to vascular compression of the nerve in the root entry zone. The

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Table 4 TN surgery[87,88,92]

Procedure	Pain relief duration (Kaplan-Meier estimate)	Mortality	Morbidity	Comments
Peripheral that is, cryotherapy, neurectomy, laser ablation, acupuncture,thermocoagulation, injections of alcohol/phenol (Evidence rating U – data inadequate/ treatmentunproven)	50% at 12 months	Nil	Localised sensory loss, haematoma formation, infection	Can be performed under local anaesthetic Suitable for medically unfit (for general anaesthetic (GA)
Gasserian ganglion that is, radiofrequency thermocoagulation, glycerol rhizolysis, balloon compression (Evidence rating C – Possibly effective/ may be considered	50% at six years	Very low	Sensory loss >50%, dysaesthesia <6%, anaesthesia dolorosa 4%, eye complications 4%, meningitis 0.2%, up to 50% have masticatory deficit following balloon compression	Can be performed under heavy sedation, or short GA Often suitable alternative for patients unfit for MVD Glycerol rhizolysis provides shortest pain relief duration
Gamma knife (Evidence rating C – Possibly effective/ may be considered	52% at 3 years	Nil	Problematic sensory loss 6–13% often six months later Anaesthesia dolorosa very rarely	The only non-invasive technique. Pain relief can be delayed up to six months
Microvascular Decompression (Evidence rating C – Possibly effective/ may be considered	73% at five years	0.2–0.5%	Major post-operative morbidity 4%, 10% ipsilateral hearing loss, transient diplopia, sensory loss 7%	Highest improvement in quality of life

sequelae results in hyperexcitable neurones that demonstrate a phenomenon described as 'after discharge', which occur secondary to external stimuli and continue after the stimulus has ceased. This 'after discharge' triggers adjacent neurones, resulting in the symptoms of electric shock type pain. The resultant refractory period that follows is due to potassium influx hyperpolarisation, resulting in the neurone being refractory to further stimuli.

Management

TN is generally managed medically, with carbamazepine being the first-line medication.[88,92] Stevens-Johnson syndrome (SJS) and toxic epidermal necrolysis (TEN) may occur as a result of treatment with carbamazepine, with patients of Asian and Oriental ethnicity being at greater risk.[93] The HLA B*15:02 and HLA A*31:01 alleles are linked to these reactions and it is suggested that at risk patients should undergo genetic testing if carbamazepine is being considered.[93] Oxcarbazepine is considered to be the second line medication in TN management,[88,92] and is normally considered to have fewer side effects and potential drug interactions than carbamazepine.[83] Novel TN medication research is being undertaken regarding the use of the selective sodium channel blocker BIIB074[94] (an as yet unnamed drug that was previously known as raxatrigine).[95] Due to its selective action on peripheral neural receptors, it is suggested that BIIB074 may provide TN patients with pain relief and fewer side effects when compared to existing, centrally active anticonvulsants.[94,95]

Patients who have been newly established on systemic medication and are experiencing an acute exacerbation of TN, may benefit from local anaesthetic blocks into trigger points – to provide short term analgesia while awaiting oral medications to take effect.[87]

Although the majority of TN patients are managed using medications, reduced drug efficacy and side effects may lead to the medical management of TN being unsuccessful.[96–98]

Table 3 describes the medications that may be considered for managing TN.[87,88,92]

Surgery may also be considered in the management of TN, though a review by Gronseth *et al.*[92] stated that there is insufficient evidence to determine when surgery should be offered. A study on patient decision-making in the management of TN reported that patients may opt for surgery over medication.[99]

The surgical management of TN may be categorised into three groups according to site: peripheral; Gasserian ganglion level; and posterior fossa root entry zone.[87] Table 4 describes the surgical management options available for TN.

Microvascular decompression is considered to provide the longest duration of pain relief.[88,92] However, though it has been documented in the literature that TN may be managed effectively surgically, there is a lack of high quality comparative studies involving the different surgical techniques.[87]

Difficulties faced in the management of TN patients include – delays in diagnosis, side-effects from medication, and a lack of psychological support.[98] Classically, TN has tended to be managed using a very biomedical model – with medications and surgery. Current thinking suggests that it is important to enhance the care of TN patients by using a biopsychosocial approach and multidisciplinary team working.[98] There is a significant negative psychosocial impact associated with TN – with 45% of TN patients having a negative impact on activities of daily living, over 30% being depressed, and over 50% having anxiety.[100] This evidence supports the suggestion that there is a significant role for pain management psychology in the treatment of TN patients.[101] Additionally, it has been shown that patients may benefit from attending TN-focused patient support groups.[102]

Conclusion

Orofacial pain conditions occur due to complex pathophysiology, often associated with psychological co-morbidities. Chronic orofacial pain may have a significant impact upon quality of life and daily functioning. Early diagnosis and referral to secondary care is of paramount importance to ensure evidence-based management is instigated. A

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biopsychosocial approach to pain management may address the multifactorial aetiology of orofacial pain conditions, whilst limiting the economic and health-related burden associated with these conditions.

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