

## Orofacial Pain – An Update for General Dental Practitioners

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**Abstract:** *Objective:* To review the available literature on orofacial pain. *Material and Methods:* This literature review was performed to elucidate information pertaining to orofacial pain from various medical databases. *Result:* Pain of any origin compromises on an individual's quality of life. The prevention and management of pain is an important aspect of health care. This multidimensional phenomenon requires a multi-disciplinary approach. This review describes pain, pain pathway, differential diagnosis and its management. This review also describes the factors that must be considered in developing an effective model of care for people who experience such pain. *Conclusion:* Though evidence shows that orofacial pain is widely prevalent in the general population, research still fails to address numerous aspects of pain management and diagnosis. Therefore both the laboratory and the clinical research should be performed to increase our knowledge of the normal and abnormal mechanisms that generate orofacial pain.

**Key words:** Cancer • Gender • Masticatory system • Orofacial pain • Tempromandibular joint disorder

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### INTRODUCTION

Orofacial pain is defined as any pain related to the face and mouth involving both hard and soft tissues around this region [1]. Oro-facial pain can be acute or chronic and will be commonly of dental origin [2]. Prevalence of orofacial pain among the general population, is reported to be around 17–26%, of which 7–11% is 'chronic type of pain [3-5]. A published study (of 45,711 households) reported that 22% of the U.S. population experienced orofacial pain on more than one occasion within the span of six-month period [6].

The orofacial region perform many functions very important to life support and has an vast level of brain function and nerve supply involved in its function. The region performs functions such as breathing and smell, taste, sight, mastication (eating and chewing), swallowing and communication (verbal and non-verbal).

Evidence support the fact that the most commonly experienced orofacial pain is dental in nature [7]. The dental reasons should be well thought of as the first step even in cases where orofacial pain is poorly localized.

One of the most common reasons for seeking dental care is said to be pain and dysfunction, usually involving the teeth and surrounding tissue. Musculoskeletal, vascular and neuropathic causes of orofacial pain occur very frequently. Oro facial disorders may have pain and associated symptoms arising from a discrete cause, such as postoperative pain or pain associated with a malignancy, or may be syndromes in which pain constitutes the primary problem, such as TMJ disorder pain, neuropathic pains or headaches. TMD has been identified as one of the most commonly occurring non-odontogenic oro facial pain complaints [8]. Evidence support the fact that the most commonly experienced orofacial (odontogenic origin) pain is dental in nature [7]. The dental reasons should be well thought of as the first step even in cases where orofacial pain is poorly localized. One of the most common reasons for seeking dental care is said to be pain and dysfunction, usually involving the teeth and surrounding tissue.

The magnitude of the orofacial pain is said to be associated with the type and severity of pain, the socio-demographic features like sex and age [9].

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State of depression is more prevalent in people with chronic pain disorders. In a study by Dohrenwend *et al.* [10] depression rates due to orofacial pain was reported to be high among the study population and thus it can be stated that the consequences of orofacial pain definitely can influence a person's daily life.

**MATERIALS AND METHODS**

Literature published since 1940 were reviewed, using the keywords: Orofacial pain, Tempromandibular joint disorder, Masticatory system, Gender, Cancer in various combinations. The databases used were Medline, Pubmed central and Google scholar. The search included only papers published in the English language.

**Mechanism and Pathways of Orofacial Pain:** The ophthalmic, maxillary and mandibular branches of the trigeminal nerve innervate the orofacial region [11]. The trigeminal ganglion is where the cell bodies of most trigeminal primary afferents are located. The trigeminal ganglion is analogous to the dorsal root ganglia of the spinal somatosensory system, from which the afferents runs into the brainstem; where they terminate in the trigeminal brainstem sensory nuclear complex which includes the main sensory nucleus and the three subnuclei (oralis, interpolaris and caudalis) of the trigeminal spinal tract nucleus. The three subnuclei are involved in the orofacial nociceptive mechanisms [11, 12]. The neurons, afferent and CNS pathways are involved with the process of acute orofacial pain as well as in the pathogenesis of chronic orofacial pain conditions. This includes ectopic impulses produced in injured trigeminal primary afferents, peripheral sensitization of trigeminal primary afferents, central sensitization of central nociceptive neurons, changes in CNS segmental and descending inhibitory and facilitatory influences on trigeminal nociceptive transmission and phenotypic changes in trigeminal afferents and central nociceptive neurons [13]. Few literatures provides evidence on the

involvement of nonneural cells like in the Peripheral nervous system and Central nervous system in the initiation and maintenance of orofacial pain [14].

**Types and Classification of Pain:** Pain can be classified as acute and chronic, based on onset [7, 15] (Table 1). Somatic, neuropathic and psychogenic pain constitutes the three basic categories of pain. Abnormal stimulation of normal neural structures results in somatic pain. Structural abnormality in the nervous system leads to neuropathic pain [16]. For psychogenic pain there is no obvious physiologic or natural source. Intracranial, extracranial, musculoskeletal, neurovascular and neurogenous are said to be the type of tissue system from which pain originates. Intracranial (within the skull) or extra cranial (outside of the skull) pain includes Idiopathic pain (Atypical facial pain, Atypical odontalgia, Burning mouth syndrome), Musculoskeletal pain arising from masticatory muscle disorders, Tempromandibular joint dysfunction and Tension-type and Cervicogenic (neck origin) headaches, Neuropathic pain this can be episodic or continuous in nature, Neurovascular pain, Psychogenic pain and pain associated with other diseases eg. Dental decay and abscess, periodontal disease, tumours, ulcers in the mouth, xerostomia, trauma, distant pathology (referred pain), systemic diseases, etc.

A published article [17] provides testimony of cases in which pain was thought to be of dental origin and was managed with teeth extraction but the actual pain was associated with hemicrania continua.

**Diagnosis and Management of Orofacial Pain:** The etiology and pathogenesis of orofacial chronic pain conditions remains unresolved, making its diagnosis and management difficult. The pain history can be the key for diagnosis of any type of orofacial pain and also relies on review of laboratory studies, imaging, behavioral, social and occupational assessment; interview and examination. Nevertheless diagnosis of orofacial pain is quiet

Table 1: Pain Classification

	Acute Pain	Chronic Pain
Definition	Unpleasant sensation	defined by a perseverance of pain for longer than 6 months
Time	sudden onset, normal healing time required to overcome the causative mechanisms	Beyond the typical time for healing; not self-limiting
Management	Respond predictably to traditional approaches	May be refractory to traditional modalities, that requires a multidisciplinary approach

Table 2: Differential diagnosis

Diagnosis	Type	Characteristic
<b>DENTOALVEOLAR</b>		
Reversible Pulpitis	Mild to Moderate	Sharp pain
Irreversible Pulpitis	Mild to Severe	Throbbing
Periapical Periodontitis	Mild to Severe	Throbbing, Sharp
Pericoronitis	Moderate to Severe	Aching pain
<b>MUSCULOSKELETAL</b>		
Temperomandibular Disorders	Mild to Moderate	Dull, Throbbing, Aching or Sharp
<b>BONY PATHOLOGY</b>		
Dry Socket	Moderate to Severe	Deep, Sharp, Aching
Sinus Related		
Maxillary Sinusitis	Mild to Moderate	Boring, Dull, Aching
<b>SALIVARY GLANDS</b>		
Salivary Gland Blockades	Mild to Severe	Burning or aching pain
<b>VASCULAR</b>		
Cluster Headaches	Moderate to Severe	Boring, Throbbing
Hemicrania	Moderate to Severe	Boring
Tension Type Headache	Moderate to Severe	Pressure pain , Aching
Migraine	Moderate to Severe	Throbbing pain
Temporal Arteritis	Moderate to Severe	Throbbing pain, Dull, Aching
<b>NEUROPATHIC</b>		
Burning Mouth Syndrome	Mild to Moderate	Burning, Tingling, Itching, Tender
Postherpetic Neuralgia	Mild to Moderate	Burning, Tingling, Itching, Tender, Shooting
Trigeminal Neuropathic Pain	Mild to Severe	Burning, Tingling, Aching
Trigeminal Neuralgia	Moderate to Severe	Electric shock like pain, sharp
Glossopharyngeal Neuralgia	Moderate to Severe	Stabbing, Shooting, Sharp
<b>OTHERS</b>		
Chronic Idiopathic Facial Pain	Mild to Moderate	Dull , Aching, Sharp Throbbing
Atypical Odontalgia	Mild to Moderate	Tingling, Dull, Aching, throbbing, Sharp

complicated and requires the ability to identify the type from a given set of signs and symptoms (Table 2). In addition, the diagnosis of orofacial pain is complex by the close proximity of anatomical structures involved like the eyes, nose, teeth, sinuses, muscles, ears and the temporomandibular joints. The pain from single source might radiate and spread thereby complicating the diagnosis.

When considering about the differential diagnosis of any type of orofacial pain it is important to remember co-morbid physiologic and psychosocial abnormality that may arise as a result of persisting pain. The stress and anxiety associated with it may alter the pain experience by activation of the hypothalamic-pituitary-adrenal axis, up-regulation of the sympathetic nervous system, change in sleep pattern and bruxism. All these together complicate the diagnostic procedure.

The differential diagnosis of orofacial pain includes Oral pathologies, Temporal Arteritis, Trigeminal Neuralgia, Atypical facial pain, Burning Mouth Syndrome, Post-Herpetic Neuralgia, Cluster Headache, Hemicrania Continua, Paroxysmal Hemicrania, Masticatory Muscle Conditions, Salivary Gland pathologies, Cancer and Referred pain (Angina, ocular, Aural, chest and lung

disease). Table 2 describes the differential diagnosis of orofacial pain of different origin which will aid the clinician to identify the pain and manage it efficiently

The difficulty of understanding orofacial pain may be associated to its underlying neurophysiological mechanisms like activation of peripheral receptors, change of the size of receptive fields, neurotransmitter release, transmission and projection of nociceptive information and convergence of nonnociceptive afferents on common central neurons [18].

Consultants in various disciplines of medicine like ENT specialist neurologist, otolaryngologist, neurosurgeon, dentist, physical therapist, clinical and health psychologist play a key role in multidisciplinary diagnosis and management of orofacial pain.

The procedures for easing the diagnosis of orofacial pain includes general physical examination along with history, functional analysis of the jaw, radiology, orthopantomography, Computerized tomography(CT) Scan, MRT, diagnostic nerve blocks, NRS, VAS scales, other scales for pain assessment, Neurophysiological procedures, EMG and Psychobiological examination [19, 20].

Blood, radiological, physiological and psychological investigations, helps in confirming a diagnosis and assist in treatment planning.

Not many published literatures on the current management of patients with orofacial pain were available. When the exact etiology for a patient's pain is unavailable the management should be with an interdisciplinary frame of mind.

The management of chronic orofacial pain is more difficult than acute pain. Prior to proper therapeutic management by the professional the self-treatment with analgesic would begin. Newer modalities of treatments for orofacial pain have been developed in recent past [21].

Long-standing psychotropic medications are usually used for chronic facial pain syndromes it is known to have severe side effects and provides non total pain relief [22].

The use of NSAIDs and steroidal anti-inflammatory drugs in the pre, post and intraoperative phases is beneficial in terms of pain reduction [23, 24].

In case of oral tissue infection, antibiotics reduce inflammation and provide relief to a large extent. Triamcinolone acetonide is a potent corticosteroid which is prescribed for post treatment pain [25, 26].

Oral pain due to salivary gland obstruction can be best managed by relieving the duct pressure; this can be achieved by removal of the calculus and dilatation of the stenotic point [27].

Evidence supports that the use of oral acrylic splints has an effect on myofascial pain [28]. Mandibular mobilization exercises, manual distraction of the joint junction, mobilization of the condyle-disc complex, the correction of body posture and relaxation will provide significant pain relief in the temporomandibular region [29]. The oral administration of glycosamine and chondroitin sulfate is also recommended [21, 30].

For vascular pain usually sumatriptan is advised. The drug can be administration through the intranasal route as well [31]. verapamil, corticosteroids, valproic acid, serotonin inhibitors, topiramate and Naratriptan are also used for background treatment [32]. In paroxysmal hemicranias patients indomethacin is prescribed [33-35].

In a survey done in Germany [36], it was observed that in around 79.7% of all patients diagnostic procedures were complete within a period of 6 months and therapies for management included the use of analgesics and noninvasive, interventional and surgical procedures. The study reported treatment of malocclusion, physiotherapy, analgesics, interventional procedures, sympathetic blockades, surgical procedures, tooth extractions, other dental surgical procedures, maxillofacial and orthognathic

surgery, neurosurgery, otolaryngeal surgery, other surgery, plastic surgery, traditional Chinese treatments like acupuncture and homeopathy as current therapeutic procedures followed for orofacial pain management.

**Gender and Pain:** It was observed from the literature search that majority of reports supported the fact that women suffered from more severe, frequent and long duration pain, than men [37, 38]. Many of the chronic pain conditions like migraine, pain in rheumatic disease and some cardiac pains are more common and severe in women than in men [39]. Most population-based studies have found that pain prevalence was high among women than men [40-42]. Pain thresholds and tolerance is generally low among females than males [43, 44]. Increased sensitivity to laboratory pain in females can be related with increased risk of having clinical pain [45]. These differences likely include the basic pain mechanisms that differ in both male and female and also the differences in psychosocial factors in both sexes [46]. There is no clear fundamental reason for these findings. To certain extent the female reproductive hormones play a role in this [47]. The estrogen hormone is known to influence some clinical pain conditions like, migraine and temporomandibular disorder [48-50].

In a study by Lester, N. J. C. Lefebvre, et al [42] the results concluded that females experienced a greater number of pain sites than males. Few research finding indicates that females are over represented in a variety of chronic pain disorders compared to males [38].

Evidence from few experimental studies suggests that the endogenous opioid system differs between sexes and is estrogen receptive in females, thereby influencing pain control [51].

The activity of cytochrome P450 in female is greater than in male and this suggested that drugs are can be more easily metabolized in female. Analgesic effect of pentazocine is more potent in male than in female. These evidence strongly suggested that males and females have different pain modulatory circuits [52].

Efforts to improve our understanding of qualitative sex differences in pain modulation signify a potential step toward developing more customized approaches to pain management.

**Oro Facial Pain in Cancer:** As per the data from USA, oral cancer accounts for about three percent of all cancers Rates vary according to race, approximately 12.3% is found among blacks, 10% among whites and lowest among Hispanics and Asians which is about 5.7% and 6.0

Table: 3 Orofacial Pain in Cancer

Acute Pain	Chronic Pain
Due to disease (Cancer)	Due to persisting or progressing cancer,
Invasion of bone, nerve, muscle	Surgery
Mucosal and tissue damage	Radiation therapy
Tumor pressure	Chemotherapy
Due to cancer therapy	Temporomandibular disorders
Surgical therapy	Mucosal infection
Following radiation therapy	Mucosal atrophy or xerostomia
Following Chemotherapy	Neuropathy
Oral or Dental pain	Caries
Due to mucositis	Osteoradionecrosis or mucosal necrosis
Infection	Post-herpetic neuralgia
Neuropathy	

% respectively [53]. Orofacial pain can be a presenting symptom of primary tumors, metastatic disease, systemic cancer and distant non-metastasized cancer [54].

The mechanisms involved and possible treatment objectives, in orofacial pain due to cancer are poorly understood [55]. Patients suffering from orofacial cancer, complaints mostly of chronic rather than acute type of pain (Table 3). Approximately 30% to 85% of patients with cancer experience chronic cancer pain [56]. This might depend on type and stage of cancer. Orofacial pain can turn out to be the first sign of intraoral cancer. Pain experienced by these patients is usually secondary to cancer and is mainly by the tumour itself [57, 58]. Pain could also be secondary to therapy [58, 59] (Table). Many patients complaints of pain from more than one specific site; this shows the involvement of inflammatory and neuropathic mechanism [57, 59]. Tumors or its metastases results in tissue destruction which induces inflammation and nerve damage, leading to acute pain; in some cases, chronic pain, involving inflammatory and neuropathic mechanisms, may arise.

Distant, painful effects of tumors include paraneoplastic neuropathic syndromes and effects secondary to the release of tumour factors like growth factors, cytokines and enzymes [55].

Broadly the orofacial pain in cancer is classified as acute and chronic (Table 3). Another classification of pain in cancer patient is based on pathophysiological mechanism like nociceptive, inflammatory or neuropathetic, Location of tumour – local / distant, Initiating agent- tumour/ tumour therapy.

Squamous cell carcinoma is the most common form of oral cancer [60]. This is usually associated with pain and is present in up to approximately 85% of cases [61]. Systemic malignant disease may present first with orofacial pain or numbness and paresthesia along neurologic distribution [62].

Orofacial discomfort and paresthesia may be the initial sign of metastatic cancer. In rare cases of leukaemia oral pain will be present.

In a systematic review by Epstein, J. B. C. Hong, et al [58], pain was identified before cancer therapy mainly due to cancer also an increase in pain during therapy and the common persistence of pain following cancer treatment was reported.

Cancer pain can be related to increased morbidity, less active, poor performance, increased anxiety and depression and there by reduced quality of life [54, 63].

**Genetics and Pain:** Can genetic factors explain inter-individual differences in the susceptibility to develop chronic orofacial pain? This area in the field of orofacial pain has not been addressed much. Not all individual who are exposed to pain producing etiological factor will experience pain [64, 65]. The way the orofacial region responds to injury or pain may differ from person to person [66]. In short the duration, severity and location and its impact on quality of life are also different from person to person.

Individual differences in pain have always been a topic of great interest. In the recent past this topic has gained more importance in the field of research due to the genetic revolution [67]. The huge difference in quality of chronic pain and the large number of females complaining of chronic orofacial pain [68] suggest that the susceptibility to develop such pain may be heritable [69-72]. This could be determined by a combination of polymorphic genes and environmental factors.

Published literatures have already identified chromosomal regions and even a small number of specific genes and single mutations affecting migraines, headaches and chronic orofacial pain [73, 74]. There has been evidence from published literatures on the

involvement of genetic factors in incidence of familial migraine and trigeminal neuralgia among twin pairs and pedigrees [75-77].

When talking about the genetics of any kind of pain, it is important to differentiate role of genetics to the disease course from genes involved in pain processing. Evidence shows that many of the pain conditions as familial pattern, including arthritis, fibromyalgia (FM), migraine and tension-type headache [78].

Influences of genetics on pain perception can be identified by studying the association between specific candidate genes and responses to experimentally induced pain. Catechol-O-methyl-transferase (COMT) is one of the commonly studied candidate gene. COMThaplotypes are known to be associated with overall pain sensitivity, Activity of haplotypes of COMT in humans are reported to be inversely correlated with pain sensitivity and the risk of developing TMD [74].

Other candidate genes associated with pain responses is the  $\mu$ -opioid receptor gene (OPRM1) [79], GT cyclohydrolase, or GCH [80].

Many of the candidate gene studies have reported that polymorphisms in genes disturbing the function of both catecholaminergic and serotonergic systems can be associated with chronic pain disorders, such as fibromyalgia and temporomandibular disorder [79, 81-83].

It is important to understand the gene to environment interaction for proper diagnosis and management of any kind of pain. In conclusion, it is predictable that genes with an individual effect interact among themselves and also with other environmental factors, thereby influencing pain sensitivity and the expression of chronic pain conditions in each individual.

## DISCUSSION

New advance have made the diagnosis and management of orofacial pain conditions better and easier. Also our knowledge of the neurobiologic, molecular and genetic processes involved in orofacial pain has improved. Chronic orofacial pain on a patient is particularly can also be associated with emotional, psychologic and social disturbances that may compromise the patient's quality of life and well-being. It is important to understand pain and all of its consequences in diagnosis and case-specific, evidence-based management of conditions badly affecting the masticatory system. The multi-causal nature of orofacial pain and the complexity of condition command a multidisciplinary approach to its exact diagnosis and management.

Chronic pain affecting the craniofacial region still remains as an unsolved clinical problem because they are common, cause immeasurable suffering and incapacitation and are difficult to attain complete cure with existing therapies.

Differential diagnosis is the correct path to successful therapy and prevention, but the problem of right diagnosis remains as a major question. It is important to understand that is not easy to achieve it without a good understanding of the basics of the problem that we come across.

## CONCLUSION

Though evidence shows that orofacial pain is widely prevalent in the general population, research still fails to address numerous aspects of pain management and diagnosis. Therefore both the laboratory and the clinical research should be performed to increase our knowledge of the normal and abnormal mechanisms that generate orofacial pain.

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