Atypical Odontalgia or Phantom Tooth Pain: Current Evidences for Better Understanding, Diagnosis and Management

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ABSTRACT

The phantom tooth pain or Atypical Odontalgia (AO) is a persistent orofacial pain disorder affecting teeth or tooth sockets after dental treatments like root canal therapy or extractions even when there is no any identifiable cause on clinical or radiographic examination. These conditions are thought to be associated with neuropathic, vascular or psychiatric disorders along with comorbid factors like temporomandibular joint dysfunction syndrome, burning mouth syndrome, various types of headaches etc. Peripheral and central sensitization has been considered as a possible pathophysiology of such conditions in denervated teeth and extraction sites. The pain usually radiates from the deafferentation sites to the adjacent structures. These conditions usually get undiagnosed and in most of the scenario, dentists only consider a diagnosis only after failure of multiple invasive treatments and worsening of the symptoms. Although, it is very crucial to establish a diagnostic criteria and treatment regimen for AO, still evidences are confusing and lots of clinicians are still unaware of the condition. Hence, this article reviews on AO, its terminologies, prevalence, chief complain, clinical features, pathophysiology, comorbidities, diagnostic work out, and pharmacological treatment modalities with the aim of describing the clinical characteristics, possible cause and treatment modalities. This will definitely aid in an accurate diagnosis of the conditions, before treatments are initiated to avoid overtreatments in such conditions.

Key words: Atypical Odontalgia, Central sensitization, Deafferentation Syndrome, Endodontic Treatment, Peripheral Sensitization, Phantom Tooth Pain, Psychiatric components.

INTRODUCTION

Atypical Odontalgia (AO) or phantom tooth pain is a condition where patients complains of continuous pain and/discomfort affecting teeth or tooth sockets after dental treatments like root canal therapy or extractions even when there is no any identifiable cause on clinical or radiographic examination.[1] International Association for the Study of Pain defines AO as a severe throbbing pain condition, in the tooth and persistent chronic continuous pain symptoms located in the dento-alveolar region in absence of major pathology that cannot be explained within the context of other diseases or disorders and is considered as a subgroup within persistent idiopathic or atypical facial pain.[2] International headache society defines AO as

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a subgroup of persistent idiopathic facial pain disorder.[3] Persistent dentoalveolar pain (PDAP) is a new terminology that has been put forward in order to address the shortcomings on the existing nomenclature with unclear criteria and embrace new diagnostic criteria.[4] Patients are expected to have stronger pain than normally expected from the clinical findings from the medically unexplained toothache without any pathological changes. Dental procedures like root canal treatment, oral prophylaxis, restoration or extractions can be potential risk of AO.[5] It is very challenging to diagnose and treat, for most of the dentists and frustrating for the patients. Generally, patients with AO complain of persistent pain and demands treatment which leads to many unnecessary consultations and over treatment.[6] However, these treatments usually exacerbate the pain instead of relieving it. These conditions usually get undiagnosed and in most of the scenario, dentists only consider the diagnosis after failure of multiple invasive treatments and worsening of the symptoms. It is crucial to establish a diagnostics criteria and treatment regimen for such conditions. Literature is also flooded with data regarding the same. However, evidences are still unclear, clinicians are still unaware of the conditions and in cases of Nepalese population, there is a severe scarcity of the data.

CHIEF COMPLAINT AND CLINICAL FEATURES OF THE PATIENT WITH ATYPICAL ODONTALGIA

Patient with AO complains of pain with various features. The pain can be severe, throbbing, continuous/persistent pain with or without thermal sensitivity and discomfort during function. AO is considered as a subtype of persistent idiopathic facial pain that presents with persistent facial and/or oral pain with varying presentation, which recurs daily for more than 2 hours per day for over 3 months, when there is no identifiable dental or neurological involvement.[7] Such patients often go to multiple doctors, get numerous consultations and multiple invasive procedures like curettage, scaling, endodontic treatments, extractions, apical surgeries and even alveolar debridement. Clinicians even prescribe various medicines like analgesics, corticosteroids and antibiotics with patients still having the same or even exaggerated symptoms. Nearly, one- third of the patient with AO, have received many irreversible dental procedures previously in an unsuccessful attempt to relieve the symptoms.[8] Dental treatments like endodontic therapy, apicoectomy and/or extraction sometimes relieve pain temporarily with symptoms coming back with increase intensity after sometime.[9] The symptoms usually arise after a nerve injury to the face after dental or surgical procedures. After dental extractions patient complains of pain, in edentulous area that is similar to the stump pain following limb amputation. Phantom pain phenomenon can be experienced by any individual that has undergone amputation of any anatomic structure in the body. Teeth are probably the most commonly amputated anatomic structure. Teeth have unique neural supply to its pulp and its supporting structures which can function without total amputation. Yet, orofacial phantom pain is quite neglected and very little attention has been paid to it.[10] Root treated teeth are denervated anatomic structure that is still attached to the individual. AO can thus be described as a deafferentation syndrome of persistent pain in the denervated teeth or edentulous area that has been previously occupied by teeth before it was extracted. Such pain often radiates to the facial structures adjacent to the differentiated tissue. Patients with AO presents with following clinical symptoms:

1. Orofacial pain, usually toothache.
2. The characteristics of pain being constant, dull, deep aching with few patients presenting with occasional spontaneous

pain over the toothache. Usually, sharp pain is not needed to meet the criteria.

3. There are no painful episodes while sleeping; hence, sleep is not disturbed by pain or any phantom sensations.
4. After waking up from sleep, a short (seconds to minutes) pain free period is reported. There are no any other refractory periods.
5. Patients complain of pain or continue having pain, within a month after root canal treatment, extraction, trauma or any medical orofacial procedure.
6. In or around the area of the dental or other treatment (usually face but occasionally intraoral) a hyperalgesic location with much lower pain threshold is found. That area is often further surrounded by larger area with less severe hyperalgesia.
7. No radiographic findings or laboratory test suggests other sources of pain.[11]

PREVALENCE OF AO

It has been reported that the majority of patients having persistent or chronic pain conditions are women over age 30 with pain in the posterior teeth or arch.[11] Data suggest 80-90% of all cases diagnosed with AO are females.[5] It occurs in 3-6% of patients that undergo root canal treatment.[12] Polycarpou et al. conducted a study in 175 patients and reported the prevalence of persistent orofacial pain after successful endodontic therapy is 12%. They concluded that the factors that lead to development of persistent pain after endodontic treatment are preoperative pain and its duration, preoperative tenderness to percussion, previous history of painful treatment, previous chronic pain conditions and surgical treatment received by the patients.[13] In another study by Ram S et al, at the University of Southern California Orofacial Pain and Oral Medicine Center, out of 3000 patients, 64 (2.1%) (44 women and 20 men) patients with the age between 26-93 were diagnosed with AO.[14] Except children, all age groups are affected with women in their mid-40s being the most common sufferer. Molars and premolars are more frequently involved with maxillary arch being more affected than mandibular.[12] Jacobs R et al, reported AO in 5.7% of his samples with female predominance (9:1), mostly in upper jaw (8:2) with majority in molars region (5:3). They had significantly low threshold for pain that gets aggravated even with the light touch on the affected side.[15]Another study by List et al. reported the majority of cases with AO complained of pain in upper jaw (56%) compared with lower jaw (45%) .[16] Hence, it is generally accepted that these conditions usually occur in female patients as a persistent pain for months that returns with similar characteristics over several months to year. AO's pain usually does not follow the nervous pathway or have major paroxysmal characters. It is present for all or part of day but sleep is not disturbed and often associated with psychological factors.[17]

PATHOPHYSIOLOGY OF AO (CENTRAL AND PERIPHERAL SENSITIZATION)

Generally, when patients complain of pain, the cause is odontogenic, usually pulpitis, decay, cystic changes, periodontal problems, fractures, trauma etc. which the clinicians can identify and treat. However in cases of AO, the symptoms reported by patients mimic the odontogenic origin but without any clinical or radiographic findings.[18] The pathophysiology of AO is not well known and over the past years, various mechanisms have been suggested.[19-20] Psychogenic pain, neuropathic and vascular abnormalities have been linked with its pathophysiology.[5]

The relationship of this condition with the psychological status of the patients is the topic that has been largely studied. It has been found that a large percentage of patients with depression develop AO.[21] Some studies

questions that psycological factors such as depression can be a comorbidity or secondary facor to AO's pain.[8,22-23] Ciaramella et al argued that trigeminal pain threshold can be altered by certain psychological traits or events that can initiate spontaneous or triggered pain after dental procedures in psychologically predisposed patients. They found that the patients diagnosed with AO presented with higher level of depression and resentments than normal patients that underwent dental extraction. Thus, certain psychological factors can predispose individual to the persistent chronic pain conditions after dental treatments.[23] A Miura et al reported that half of the patients in their study, with AO had a comorbid psychiatric disorder mostly depression and anxiety, with higher self-rated depression, higher affective descriptors and disturbed sleep. However, evidences are insufficient to establish psychological factors as a primary cause of AO, although psychological functioning is altered in majority of the patients. But it is evident that chronic pain conditions are associated with higher rates of psychiatric disorders.[24]

Pain of vascular origin also known as dental migrane has also been studied as a cause of AO.[25] However, the vascular cause mentioned by several authors in the past [9, 25], is now not considered as the main pathophysiology. Pain of neuropathic origin has been extensively studied and neuropathic mechanisma like deafferentiation hypersensitivity, central and peripheral sensitiation has been fould to be associated with the AO's pain.[26-27]

The normal sensory signals when altered variously, turns into neuropathic pain. These altered signals can increase nerve sensitivity to such a degree that they can fire signals without any obvious stimuli. Spontaneous ectopic discharge of peripheral nerves, altered receptors resulting into sensitization of sensory nerves and increased release of neurotransmitters are responsible for peripheral or central sensitization. Moreover, after demyelination cross excitation of these nerves can occur. After chronic or sustained pain episodes, the sympathetic nervous system can directly stimulate sensory system which increases the release of adrenergic receptors. If peripheral nerves get injured or sustain painful neural activity, the spinal cord will reorganize. The excitability of spinal and trigeminal neurons will also increases with an alteration in the descending modulatory nerves, which also develops in neuropathic pain conditions. At the same time, after injury there will be a loss of interneurons and reduction in inhibitory activity. Thus, brain does the necessary change and uses these supra-spinal influences that act as a potent amplifier to generate pain.[8, 28-29] In a systematic review by Porporatti AL et al, CNS sensitizations plays a role in somatosensory abnormalities, which are common features in patients with AO.[30]

Neuropathic deafferentation pain has been explained by Fields et al in three different mechanisms:

1. Primary afferent nociceptors that are anatomically fine but physiologically abnormal (irritable nociceptors) will cause mechanical allodynia because of central sensitization of the sensory neurons.
2. In some patients, who have developed allodynia, extensive degeneration of the C fibers has been noted.
3. In patients with constant pain and sensory loss without allodynia, deafferentation might change activation state of central nervous system sensory neurons.

One of these above mentioned, mechanism or combination can occur in the same person and with time change due to synaptic reorganization.[31]

In a hypothesis by Melzack, bodily sensations perceived by brain are started and maintained by inputs that are derived directly from bodies.

The sensations like pain can be felt without input, if there are extreme alteration in function and sensation of the sensory nerve following the injury. Thus, the neuromatrix theory by Melzack in absence of input to CNS in deafferentation after injury (example: after root canal treatment), abnormal neural activity can develop. Tissue near or at the site of the injury, sensory nerves from sympathetic chain and from higher neural processes produces prolonged firings that causes chronic pain disorders in denervated areas or even at remote body sites.[32-34]

Literature mentions dental procedures like root canal treatment or dental extractions as a potential risk factor for inducing neuropathy secondary to direct or indirect neural trauma or damage.[35, 13]

COMORBIDITIES ASSOCIATED WITH AO

International Headache Society has classified AO as a subtype of atypical facial pain or persistent idiopathic facial pain (PIFP).[7]

AO may present and share pain symptoms with other chronic orofacial pain conditions such as Temporomandibular pain disorders (TMPD), tension type headache, myofacial pain disorders, episodic tension type headache, chronic tension type headache and burning mouth syndrome (BMS).[36-38] However, statistically no significant data has been found to establish the occurrence of AO with BMS but TMPD is suggested to be a comorbid disorder for AO.[5] Although neuropathic disorder is the most accepted pathophysiology, it has been found with high prevalence of psychiatric comorbidities.[24]

DIAGNOSTIC WORK OUT

As AO mimics the pain of odontogenic origin without clinical or radiographic alteration, it became a diagnostic dilemma for the clinicians. Glenn T et al suggested that if there is no source of any infection, inflammation or pathology, then the differential diagnosis of such pain condition must include neuropathic pain disorder.[8] The diagnostic work up was suggested for the patients with suspected neuropathic disorders in three different phases as follows:

Phase I: If pain is present in vital tooth then

Step 1: Perform following tests

a. Cold Test: To rule out non vitality
b. Periapical Radiographs to check apical pathology
c. A panoramic radiograph to rule out other maxillofacial diseases
d. A through head and neck examination to identify other causative factors
e. A cranial nerve examination which might be the cause of any sensory alterations

If there are no evidences of any of the disease, abnormalities or alterations, then the clinician should proceed to phase II.

Phase II: If pain lingers for more than 3 weeks in a vital tooth with no Periapical lesion

Step 2: Remove all the restoration and inspect under magnification for cracks

Step 2.1: If there are no evidences of cracks then restore the tooth, keep the tooth slightly out of occlusion and make an orthotic appliance like occlusal splint to monitor and control the excessive tooth loading during sleep. However, if occlusal splint does not help and there are no signs of bruxism, premature contacts or sustained clenching during sleep and pain continues, stop the use of the appliance.

Step 2.2: If patients still complain of persistent pain with or without root canal treatment or in an extracted tooth site and clinicians see no evidence of cracks in a vital tooth, no periapical radiolucency, normal response to cold tests, no signs of bruxism, clenching or premature

contacts, anesthetic tests protocols for topical, infiltration then pain diary (one week) is suggested.

Step 2.3: If topical anesthetic stops pain, then neurosensory stent with topical anesthetic is advised as long as required. However, if it does not reduce pain, then the medication protocol is adopted. Re-examine, repeat radiographs and pulp tests at intervals.

Phase III: If pain lingers in a vital tooth or extraction site that has no any other clinical or radiographic findings, does not respond to occlusal adjustments or splints, topical or local anesthetics and is not responsive to anticonvulsant medications

Step 3: Following tests are performed

1. MRI of brain and
2. Psychological consultation

If positive evidences of CNS lesions or positive report on psychiatric impairment are found, then treatment can be started by appropriate specialist. However, if there are no evidences of any lesion or psychiatric impairment return to phase I and reassess and if pain is substantial, then referral to pain specialist is advised. Phase III can be started earlier if clinician finds any psychological or neurological signs and symptoms on the patients.[8]

PHARMACOLOGICAL TREATMENT MODALITIES

When there is abnormal sensitivity to noxious stimuli of the afferent nociceptors, peripheral sensitization occurs. During inflammation due to intense noxious stimuli, nociceptors become extremely sensitive which lowers the threshold of nociceptors activation. This will result in the painful or extremely painful response to usually non painful or less painful stimuli along with the intensification in the degree of response. Moreover, when there is extreme sensitization, there might be the activation of the silent nociceptors that amplifies the pain response. The treatment for the peripheral sensitization includes the drugs that act at peripheral nociceptors level such as Non-Steroidal Anti-Inflammatory Drugs (NDAIDs), opioids, cannabinoids and transient- receptor potential vanilloid (TRPV1) receptor antagonist.[39]

Persistent pain due to central sensitization occurs when afferent pain signals from peripheral nociceptors to the spinal neurons trigger large low threshold machanoreceptors at dorsal horn that produce A*β fibers mediated pain*. This will intensify the central neuron response to noxious stimuli, resulting in the altered sensitivity of neuronal cells at the level of second order neuron.[40] Hypersensitivity to pain in non-inflamed areas due to altered sensory response even to non-painful stimuli and lingering pain sensitivity even long after removal of stimuli in absence of peripheral pathology is produced in these conditions. This occurs due to altered properties of neurons in CNS where the pain is not coupled anymore and abnormal state of responsiveness with expansion of nociceptive system takes place.[41] Secondary hyperalgesia is an important aspect of central sensitization, which is produced by receptors that are usually related to sensory response to non-painful stimuli like touch that can also produce pain.[39] In peripheral nociception there is no role of neurochemical drivers but in central sensitization neurochemical drivers modulate the pain perception in CNS that results in complex cascade of events resulting in chronic and neuropathic pain conditions.[42] Drugs such as serotonin–norepinephrine reuptake inhibitors (duloxetine, paroxetine, venlafaxine), anticonvulsants (gabapentin and pregabaline), and tricyclic antidepressants (amitriptyline, imipramine and desipramine) that increase the level of biogenic amines and reduces the spontaneous ectopic discharge of pain signals are prescribed to modulate the pathways in central sensitization.[43-45]

In past, dentists usually prescribed antibiotics, anti-inflammatory, narcotics, benzodiazepines and local or general anesthesia to treat acute or chronic pain conditions, inflammation, infection, anxiety reduction and to anesthetize patients during surgical procedures. However, these medications were little or of no help in cases of chronic pain conditions like AO. Hence, the dental pharmacopoeia has now been expanded to include the vast array of drugs that can be used to treat such conditions. This array will continue to expand as more understanding in the field of orofacial pain disorders will be made and more drugs will be included to treat such conditions.

SOMATOSENSORY EVALUATION IN AO

In neuropathic pain, somatosensory changes are common clinical findings. In order to find out the underlying pathophysiology of pain in persistent orofacial pain conditions, the nature of somatosensory pain should be described. Hence, detailed orofacial clinical examination and qualitative plus quantitative somatosensory examination is indicated. Quantitative evaluation can be done by tests that aim to quantify various aspects of somatosensory function such as thermal, mechanical, electrical and chemical stimuli that used to examine the function of large and small nerve fibers. Somatosensory abnormalities are common in neuropathic pain patients like AO, where quantitative sensory testing (QST) can be used to assess its presence and severity. QST have been found to be useful in trigeminal area.[46, 19]

Sensory functions include following thresholds and tests:

1. Thermal thresholds include cold detection test (CDT), warmth detection test (WDT), cold pain test (CPT), heat pain test (HPT), and thermal sensory limen (TSL)
2. Mechanical thresholds include mechanical detection test (MDT), vibration detection test (VDT), mechanical pain test (MPT), and pressure pain test (PPT)
3. Stimulus–response functions include mechanical pain sensitivity (MPS) and dynamic mechanical allodynia (DMA),
4. Wind-up ratio shows pain summation to repetitive pinprick (WUR) and paradoxical heat sensations (PHS) during the thermal sensory limen test.[47]

Out of these tests, DMA and WUR are used to determine the presence of allodynia by activating various mechanoreceptors and generating impulses via Aβ fibers to the central nervous system (CNS). These can trigger a cascade of events and increase the excitability of trigeminal nerve. Hence, these tests determine the existence of central sensitization process in persistent pain patients. CNS sensitization occurs in somatosensory abnormalities and QST is one of the reliable evaluation methods of patients with AO.[30]

CONCLUSION

AO presents with significant intraoral somatosensory abnormalities reflecting the peripheral or central sensitization. Patients often have to go a long way before being diagnosed and get multiple unnecessary treatments without being relieved from the chronic pain conditions. Current evidence suggests a probable neuropathic pathophysiology with peripheral or central sensitization of trigeminal nerve. As these conditions are diagnosis of exclusion, one should consider the multifactorial etiology and keep the horizon board. With the new insights in the field, clinicians should be aware and be more cautious to avoid unnecessary treatments and adopt new treatment approaches. They should be able to treat not only odontogenic pathology but also psychosomatic oral discomfort of the patients. If peripheral somatic blocking occurs on local or topical anesthesia relieving the pain, it is considered as peripheral sensitization and

peripherally acting treatments protocols are advocated. However, further research should be aimed at investigation, diagnostic assessment tools, other comorbid factors, evidence-based treatments, treatment response and objective indicators

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