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- Endothelial cell cultured on HA/TCP/chitosan scaffold for bone tissue engineering
- Orthodontic treatment with skeletal anchorage system Relieving idiopathic dental pain without drugs

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Literature Review

Relieving idiopathic dental pain without drugs

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ABSTRACT

Background: Teeth are commonly obvious source of orofacial pain. Sometimes the pain source is undetectable, thus called as idiopathic dental pain. Since dentist wants to alleviate or eliminate the pains with every effort in their mind, a lot of drugs could be prescribed. Moreover, it is make sense that endodontic treatment or even tooth extraction will be done. Unfortunately, endodontic treatment may also initiate neuropathic tooth pain that is caused by nerve extirpation, thus worsen the pain. Therefore, another cause of dental pain such as referred pain, periodontal disease, or stress which related to psychoneuroimmunology should be considered. In order to prevent from unnecessary drugs or invasive treatment such as root canal treatment and extraction, correct diagnosis and preliminary non-invasive therapies should be done. Purpose: This review elucidates several therapies that could be done by dentists for relieving idiopathic dental pain which includes massage, the "assisted drainage" therapy, modulation of psychoneuroimmunologic status and dietary omega-3. Reviews: Understanding the basic pathogenesis of pain may help in elucidating the effects of non-drug pain therapy such as muscle massage, the "assisted drainage" therapy, omega-3 and psychological stress relieving. These measures are accounted for eliminating referred pain, reducing proinflammatory mediators and relieving unwanted stress reactions consecutively. Psychological stress increases proinflammatory cytokines and thus lowered pain threshold. Conclusion: As an individual treatment, this non-drug therapy is useful in relieving idiopathic dental pain; nevertheless, if they work together the result could be more superior.

Key words: Idiopathic dental pain, without drugs therapy, pain relief

ABSTRAK

Latar belakang: Gigi adalah suatu penyebab umum dari nyeri orofasial. Kadang kala penyebab nyeri tidak dapat ditemukan, sehingga disebut sebagai nyeri gigi idiopatik. Karena dokter gigi berupaya untuk mengurangi atau menghilangkan nyeri dengan segala cara maka banyak obat akan diresepkan ke pasien. Bila gagal maka sangat mungkin dilakukan perawatan saraf gigi bahkan pencabutan gigi. Akan tetapi, perawatan endodontik juga dapat menimbulkan nyeri neuropatik yang disebabkan oleh ekstirpasi saraf gigi, sehingga nyeri makin parah. Sebab itu, penyebab lain nyeri gigi seperti nyeri yang dialihkan (referred pain), penyakit periodontal atau stres yang berhubungan dengan psikoneuroimunologi perlu dipertimbangkan. Untuk mencegah kejadian konsumsi obat yang tidak perlu ataupun perawatan endodontik dan pencabutan gigi maka diagnosis yang tepat dan terapi non-invasif harus dilakukan terlebih dahulu. Tujuan: Studi pustaka ini menerangkan beberapa terapi yang dapat dilakukan dokter gigi untuk mengurangi nyeri gigi idiopatik yaitu masase, terapi assisted drainage, modulasi status psikoneuroimunologi dan diet omega-3. Tinjauan Pustaka: Pengetahuan mengenai patogenesa nyeri dapat menerangkan efek terapi nyeri non-medikamentosa seperti masase otot, terapi assisted drainage, diet omega-3 dan mengurangi stres psikologis. Berbagai terapi ini dapat mengurangi nyeri alihan, mediator proinflamasi dan mengurangi stres. Stres psikologis akan mengingkatkan sitokin proinflamasi yang menurunkan ambang nyeri. Kesimpulan: Sebagai terapi individual, terapi non-medikamentosa ini berguna untuk mengurangi nyeri gigi idioaptik, akan tetapi bila bekerja sama dapat lebih baik lagi.

Kata kunci: Nyeri gigi idiopatik, terapi non-medikamentosa, pereda nyeri

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INTRODUCTION

Pain is a common presentation in general dental practice and usually its diagnosis and treatment is straightforward to the lesion. However, patients with non-dental causes of orofacial pain also seeking a dental solution to symptoms which may closely mimic toothache. According to Linn *et al.*, 22% population experience orofacial pain, 12.2% dental pain in 6 months period. Ram *et al.*, revealed that approximately 45% orofacial pain patients went to dentist and Wirz *et al.*, reported in their study that 17% of orofacial pain was atypical odontalgia or atypical tooth pain, Other terms for this pain were neuropathic tooth pain or phantom pain.

Usually, the patient has self-diagnosed the problem as toothache and expects quick and efficient resolution of their problem. ^{1,4} In practice, patient's symptoms and complaints do not present so neatly and obviously as in textbooks, thus dentist may misleading the diagnosis and lead to irreversible treatments such as endodontic treatment or tooth extractions. These therapies are common attempts to decrease pain, but also cause more complications for patients and legal affairs for dentists. ⁴

Nixdorf *et al.*,⁵ study showed that 27.27% patients suffered from persistent tooth pain after root canal therapy which may be exaggerated by pulpal extirpation and became neuropathic tooth pain (NTP). Interestingly, the prevalence of persistent pain occurred in the maxillary teeth were 87.5% compared to 12.5% in the mandibular teeth, and 68.8% relieved by tricyclic depressants.⁶

Conventionally, relieving pain with drugs targeting biological factors by lowering the "pain triggers" mediators such as prostaglandins $(PGs)^{7-9}$ or tumor necrosis α $(TNF-\alpha)$. Nevertheless, prolonged or abuse of these drugs have adverse effects. Therefore, a new non-invasive periodontal therapy that proposed termed as the "assisted drainage therapy" which had been verified significantly reduced either local of systemic $TNF-\alpha$ in an animal study is worthy to be tried. ¹¹

The effect of psychological stress towards inflammation and pain had been investigated in researches which refer to a "new" science so called Psychoneuroimmunology that was founded and developed by Ader in 1975. Cortisol produced in chronic stress could potentiate proinflammatory cytokines rather than acts as antiinflammatory. ¹² Moreover, stress may deteriorate body immune sytem ¹³ and general health. ^{14,15} Some researchers revealed that dietary omega-3 fatty acid regulating and attenuating the stress response, ¹⁶ as well as lowers proinflammatory cytokines. ^{17,18}

The aim of this article was to review the diagnostic procedures and treatment for orofacial pain, especially idiopathic dental pain without drugs. They should be done by dentists to avoid unnecessary drugs and dental treatments which may harmful to the patient, and may lead to medicolegal lawsuit in the future.

What is orofacial pain?

Orofacial pain is every pain that happens in the orofacial region. Nevertheless, according to Okeson⁷ who wrote many books about orofacial pain, the definition of orofacial pain is evolving. At the present time the orofacial pain encompasses: masticatory musculoskeletal pain; cervical musculoskeletal pain; neurovascular pain; neuropathic pain; sleep disorders related to orofacial pain; orofacial dystonias; intraoral, intracranial, extra cranial, and systemic disorders that cause orofacial pain.⁷

The complexity of pain source detection in the trigeminal system

Pain sensation from the intra and extra oral structures of the head and face are carried to the central nervous system (CNS) by the trigeminal system. Pain transmission in the orofacial region is complicated because rather than a single nerve pathway. "Trigeminal system" refers to a complex arrangement of nerve transmission fibers, interneurons, and synaptic connections which process incoming information from three divisions of the Trigeminal nerve.² The involvement of trigeminocervical complex makes the pain source detection more difficult. ^{19–21}

Another factor complicating diagnosis and management is the very complexity and multidimensionality of pain, with its basis in biological processes but its impact on the emotional, psychological and social wellbeing of the patient (Figure 1).²² The orofacial region has biological, emotional

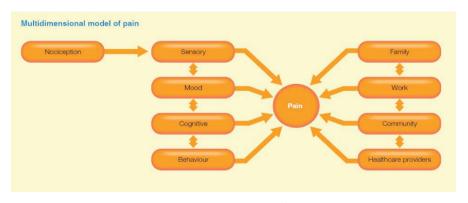


Figure 1. The complex interrelationships among variables that affect pain.²²

and psychological importance in eating, drinking, speech and the expression of our feelings, and facial appearance is also very important for most humans.⁴

Modulators of pain perception

Psychological factors (i.e. stress, anxiety)²² and biological factors (i.e. female sexual hormones)²³ may also modulate pain perception. ^{19,20,22} The intensity of pain from physical injury relates to the attention given, if it is fully absorbed to other subject during the injury (distraction), no pain at all may be felt. Moreover, recent concept of pain is changing; pain management should include body, mind and person. Consequently, good therapy to pain begins with an attitude of caring and concern for the person more than for his or her body. ^{7,21}

Diagnosing source of pain and site of pain in the orofacial region

If someone accidently cut his finger, the source of pain is the same with the site of pain, because brain gives the same perception of pain for this area. In another type of pain, so called heterotopic pain or referred pain, the source of pain is different with the site of pain. In an inflammatory or pain process, a signal is sent only when a certain critical level of insult is reached, e.g. deep caries or an early pulpitis. Brain may appreciate that there is a toothache somewhere but cannot localize it, and due to convergence factors, the brain experiences more difficulty in localizing the pain.⁷

The importance of referred pain in dentistry could be noted from a study in 400 patients with posterior tooth pain. Referred pain was reported to be 89.9% and most common site for referred pain was neighboring teeth (80%), and the frequency of pain radiating to opposite dental arch was 24%. Some criteria may helpful in determining the cause and source of non-odontogenic tooth pain (Table 1).

Spesific pains in dentistry

There are several pains that mimicking tooth pain even though it may not related to pulpalgia i.e.: atypical odontalgia/atypical tooth pain/idiopathic tooth pain;³ flareups (pain during endodontic treatment and post endodontic pain;^{24,25} periodontal pain paradox.¹¹ It was interesting that endodontic treatment itself do not guarantee as all-round pain reliever since Oshima⁶ study, NTPs among post endodontic patients, 87.6% occurred in the maxilla (Figure 3), since pulpal extirpation may also caused NTP which lead to persistent tooth pain.²

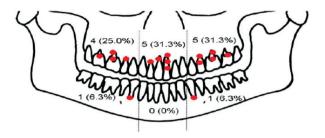


Figure 3. Distribution of pain locations (indicated by closed circles). Patient number and % number are shown.⁶

Atypical odontalgia that presents approximately 17% of orofacial pain.³ It mimics the symptoms of an acute toothache–severe throbbing, continuous pain starting in one quadrant and even crossing the midline. This condition is also called NTP, "phantom pain" or "dental migraine" and is often associated with patients suffering from unipolar depression. Over 80% of the patients are female and over 90% of the time the pain is in the teeth, jaws or gingiva. Almost a third of the pain is precipitated by dental procedure. Tricyclic or monoamine oxidase inhibitor antidepression therapy relieves the pain in many cases.^{2,6}

Table 1. Diagnostic categories-orofacial pain- non odontogenic (adapted from Linn¹)

Condition	Characteristics	Investigations
Muscular	Chronic dull ache following muscular	Tender muscles
(MPD, muscle tension headaches, neck	distribution	Imaging normal
paint, whiplash, fibromyalgia)	Muscular dysfunction	Diagnostic block no effect
Arthralgia	Pain, clicking, locking related to	Radiograph or CT may show bone morphology changes
(Internal derangement, osteoarthritis)	the TM joint	MRI show disc abnormality
Psychogenic	Abnormal often exaggerate	Objective tests normal
Atypical facial pain	description of symptoms	Subjective test atypical
Atypical odontalgia	Abnornal response to treatment	Known previous psychiatric history and treatment
Pathology	Deep constant pains	Abnormal imaging
Chronic infection	Signs of inflammation	Abnormal blood test
- Sinusitis		– white cell shift
- Osteomyelitis		- C-reactive protein
Malignancy	Usually painless unless advanced	Abnormal CT
– Oral SCC	Neuralgic pain	– biopsy
– Brain tumour		
Neuromuscular	Abnormal involuntary movements	Abnormal EMG
Dystonia	with muscle pain	
Dystinesia		

Flare up means development of pain and swelling during or after endodontic treatment. Various reasons have been attributed to these acute exacerbations of chronic conditions like: alteration of local adaptation syndrome; microbial factors; changes in periapical tissue pressure; effects of chemical mediators; immunological phenomena; and numerous psychological factors.²⁴

According to Utomo *et al.*, ¹¹ there was a particular tooth pain symptoms which was "out of the box", and caused by non-specific pain causes. It was proposed termed as the "periodontal pain paradox" (paradox means unusual inverse effect). Sharp pain could be triggered by rinsing with tap water in room temperature; moreover, hot or cold foods or drinks increased the pain even more. Interestingly, scaling did not elicit pain, It was suggested caused by an increase sensitivity of the periodontal afferent sensory fibers since chronic gingivitis had higher PGE₂ in the gingival crevicular fluid if compared to normal gingival. ^{26,27}

General pain control techniques

Based on the "gate control theory", painful stimuli can be altered at the spinal level, which means that pain is altered before it is felt. This theory is important in nondrug pain control which based on a mechanism that painful stimuli pass through a "gate" on the way to the central nervous system.^{7,28} To inhibit pain sensation, the gate can be closed by three main methods: non-painful sensory input can close the gate (i.e. stimulation by warmth and massage on trigger points, TPs) which can help control pain (Figure 4); the brainstem can project inhibitory impulses that close the gate to transmission of painful impulses (i.e. guided imagery or distraction is able to close the gate for other incoming stimuli); decreasing anxiety and increasing feelings of control over the situation.⁷ It is important to be remembered that TP-induced toothache is usually intermittent.^{7,8}

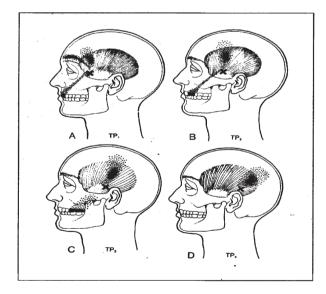


Figure 4. Referred pain patterns from trigger points, TP (x) in the temporalis muscle. A) anterior fibers; B and C: middle fibers; D= posterior fibers.⁷

Pain therapy without drugs

There are several pain relieving therapies without drugs that are: physical therapy, therapies which related to Psychoneuroimmunology, and control of biological factors. The goal of physical therapy is the inactivation of myofascial trigger points, muscles relaxation, muscle rehabilitation, and postural education. ¹⁵ Physical therapy techniques are useful in treating muscle dysfunction and pain i.e. massage, superficial (warm) and deep heats (ultrasound). These modalities reduce muscle tension, decrease inflammation and inactivate myofascial TPs. ^{7,8} Other therapies which related to Psychoneuroimmunology could be stress relieving, empathy, caring, behavioural considerations and improving the immune system ^{12–15},

A new periodontal treatment so called the "assisted drainage" therapy (ADT) which is scaling and root planning that combined with subgingival massage had been successfully relieved periodontal pain paradox symptoms. In an animal study it was verified that this therapy was able to reduce either subgingival tissue or systemic (serum) TNF- α and SP in minutes. In addition, in this study, subgingival massage in chronic gingivitis animal model this therapy also released stress proteins such as heat shock protein 70 (HSP70) which suggested caused by increased of local temperature. Heat shock protein 70 was beneficial for reducing periodontal inflammation, such as gingivitis since it act as antiinflammatory agent. 29

Down-regulate the inflammatory response with stress relieving and omega-3

Ader¹² who founded Psychoneuroimmunology in 1975 said that human stress response has a number of checks and balances built in to ensure that various components do not become overactive. Unfortunately, in the case of severe or overwhelming stress, the normal checks and balances fail, causing inflammation levels to be abnormally high. Cortisol, which is normally anti-inflammatory, can change function under severe stress and potentiate the actions of IL-1 and IL-6. ^{15,19}

Kiecolt-Glaser *et al.*, ¹⁶ noted that prior trauma "primes" the inflammatory response system so that there is heightened and more rapid rise in inflammation in response to stress. One key to improving the health of trauma survivors is downregulating this stress response and increasing resilience to stress. Researches suggests a body-related adjunct to traditional trauma treatment that specifically downregulate the inflammatory response system by stress–relieving (i.e. music listening), consuming omega-3. ^{16,17,19} Omega-3 (from fish) in reduced inflammation by competing with AA which is a long chain omega-6 (from meat, egg and dairy products). Excess AA has been associated with increased inflammation because it is converted into PGs and reduced the anti-inflammatory effects of omega-3. ^{16–18}

Other than directly reduced inflammatory reaction, researchers have examined the impact of eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA), the long-chain omega-3, on stress. They may have an adaptogenic role in stress by regulating and attenuating the stress

response. In higher levels of EPA/DHA population, they had a lower inflammatory response to stress. ¹⁶

DISCUSSION

Pulpalgia is the most painful complaint found in dental patients. Nevertheless, regarding the complexity of orofacial pain and referred pain, the diagnosis of the source of pain should be carefully done by dental practitioners. Literatures showed that diagnosing pulpal pain is uneasy because if the inflammation is limited to the pulpal tissues, it may be difficult for the patient to localize the offending tooth. It was due to the limited distribution of the discriminative touch receptors (proprioceptors) in the pulp. ^{7,19,25} Therefore, even though endodontic treatment is considered as a potent dental pain treatment and treatment of choice for irreversible pulpal pathosis, pain may still persist and become idiopathic dental pain or NTP in several cases. ⁶

Endodontic treatment itself may cause idiopathic dental pain (that may misinterpreted as "flare ups") at least by several reasons: nerve extirpation cause peripheral axonal injury; patients has to open their mouth for a long time that may cause muscle spasm. Other persistent pains may cause from the referred pain (i.e. TMJ pain, sinusitis) or habits (i.e bruxism). Misdiagnosis of dental pain may be caused by referred pain in accordance to Oshima *et al.* study, 87.6% of NTPs were in maxillary teeth, which may be caused by sinusitis or temporal muscle (TPs) (Figure 4). Consequently, diagnosing the dental pain should not limited to the dental and periodontal tissues examination; palpation of masticatory muscles to find muscle spasms and TPs is mandatory.

Additionally, orofacial pain is not just a simple matter because pain or related dysfunction that occurs in the face, mouth or jaws, especially when it becomes persistent or chronic, it can be associated with emotional, psychological and social disturbances that compromise the patient's well-being and quality of life. ^{7,22,23} Thus, the management of a patient with chronic orofacial pain requires that the clinician appreciate this biopsychosocial basis, biological factors as well as understanding the basic knowledge of psychoneuroimmunology. ^{12–15} Eventhough treatments that based on this concept is difficult to be done, treatment with empathy, caring and patience may help in reducing emotional stress. ¹⁵

Biological factors of pain mostly affect women regarding the sexual hormonal fluctuation.²⁸ The transmission and modulation of pain signals may differ in men and women.²³ Normal hormonal variations and changes related to women's reproductive functions can be sex-specific sources of pain. It was interesting that Meana *et al.*,³⁰ revealed that in women's chronic pain management, physical therapy and cognitive-behavioral approaches i.e. ensuring patients that they can involve in controlling their own pain such as massaging TPs, coping skills training such as relaxation and divert attention from pain (distraction) have been

shown to be important components in treatment other than drugs alone.

The importance of understanding the referred pain symptoms and treatment had been reported by Okeson⁷ and Mardani *et al.*⁸ They revealed that most of posterior tooth pain also showed referred pain in the head and neck area. It was interesting that Okeson⁷ and Lavelle *et al.*²⁸ suggested massage therapy in myofascial TPs which related to particular tooth to reduce referred pain (Figure 4). Massage therapy to TPs is able to relief pain via the "gate control" theory, increasing blood circulation thus increase tissue oxygenation, stimulates endorphin (a morphine-like substance) release, as well as relief of mental stress and anxiety Therefore, in idiopathic dental pain, especially if there is no obvious pathological finding, the non-drug tooth pain-reliever as in our concept i.e. massaging TPs is worthy to be tried.

Treating TPs for many pain symptoms had been known for centuries, nevertheless a "new" concept had been developed by Travell and Simmons in 1983. Massaging TP is able to relief idiopathic tooth pain by relieving masticatory muscle spasm, this kind of tooth pain is usually termed as "muscular toothache". This confusing symptom can be caused by several TPs, chiefly in the temporalis, digastric and masseter muscles. Each TP has its own particular toothache pattern. Therefore, during a long dental procedure, which often activates these TPs, the patient should take periodic rests for exercise and relieve the jaw muscles.

It should also be kept in mind that the level of inflammatory mediators inside the circulation of our body is different between individuals. ^{15,19} Our body produces anti-inflammatory such as cortisol, thus to keep in homeostasis, our body has the propensity to compensate noxious stimuli, proinflammatory mediators or neutralize antigens by itself. ^{5,8,9} Based on Psychoneuroimmunology concept, in stressful individuals, cortisol level increased and plays a synergistic role with proinflammatory cytokines instead of suppressing them. ^{12,15,16} This idea was supported with the facts that antidepression therapy relieves the pains. ^{2,6} Therefore, excess of circulating proinflammatory cytokines and Omega-6, ^{16,18,19} must be solved first or treated concomitantly with other non-drug pain therapies before conducting invasive dental procedures.

The use of Omega 3 diet for reducing inflammation is also agreed by Sharav and Benoliel¹⁹ since it has the possibility as an alternative to NSAIDs for long term use. Moreover, because high levels of EPA and DHA were related to lower levels of proinflammatory cytokines (IL-1 α , IL-1 β , IL-6, and TNF- α) and higher levels of anti-inflammatory cytokines, such as IL-10. ^{14,19} It decreases the PGs which is involved in lowering the pain threshold. ¹⁶ The conversion of AA into PGs is done by the cyclooxygenases that is activated by TNF- α . ³¹ Since the assisted drainage therapy is able to decrease local and systemic TNF- α in minutes, ²⁹ application of this method is mandatory before conducting invasive treatment.

The most difficult management of orofacial pain was the psychogenic origin pain since it was related to anxiety, depression and other emotional disturbances which needed a lot of stress-relieving drugs. Nevertheless, continuous consumption of these drugs may also cause adverse reactions, therefore alternative stress management should be discovered. Other than stress relaxation therapy, dietary omega 3 had been reported as stress-reliever supplement by Kiecolt-Glaser. 16 Nevertheless the exact dose of DHA and EPA for anxiety and depression was still in controversy. Recently, in a meta-analysis study, Sublette et al., 32 in 2011 revealed that EPA was more effective than DHA for stressrelievers, that was supplement containing EPA \geq 60% of total EPA + DHA, in a dose range of 200 to 2,200 mg/day of EPA in excess of DHA. Since daily dose for regular use is 150 mg DHA and 1000 mg EPA, twice of daily dosis was considered enough as stress-relievers.

To summarize, the non-drug therapy for idiopathic dental pain consisted of several methods: the "assisted drainage" therapy that was able to diminish tooth pain by reducing local as well as systemic proinflammatory mediators, PGs, and acts as stimulator of HSP70 excretion; physical therapy including massage of the masticatory muscles that was able to reduce pain via "gate control" mechanism; omega-3s which down regulate the stress response as well as lowering levels of proinflammatory cytokines, and PGE2; and other stress relieving procedures. Therefore, it is concluded that the non-drug therapies for idiopathic dental pain is logical and should be conducted before and during treating pains in the orofacial region that manifest as dental pain. As an individual treatment, non-drug therapy is useful in relieving idiopathic dental pain; nevertheless, if they work together the result could be more superior.

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