Atypical odontalgia: pathophysiology, diagnosis and management

Odontalgia atípica: fisiopatologia, diagnóstico e tratamento

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ABSTRACT

BACKGROUND AND OBJECTIVES: Atypical odontalgia, a subtype of persistent idiopathic facial pain, is characterized by continuous pain in one tooth or more, or inside the alveolus after exodontia, with no apparent clinical causes. These patients run the risk of going through unnecessary dental/surgical procedures which would worsen their pain. Since the pathophysiology, diagnosis, and management of atypical odontalgia are not clear, this article aims to present an integrative literature review about these aspects.

CONTENTS: A review of articles related to the topic was conducted on the Pubmed database using the keywords "atypical odontalgia" OR "phantom tooth pain" OR "idiopathic tooth pain" OR "odontalgia" OR "odontalgias" OR "atypical toothache". Applying the inclusion criteria (publications in the last ten years, in English, as clinical trials, multicenter studies, case reports, reviews, integrative and systematic reviews, 114 articles were found, and 39 were selected after the application of the exclusion criteria (articles with no relation to the topic).

CONCLUSION: Although studies suggest the involvement of strong neuropathic mechanism, the psychological/psychiatric aspects might be considered not as a primary cause, but as an aggravator of the patient´s pain. Knowledge of other pathologies is recommended in order to determine the differential diagnosis. Also, complementary image tests, qualitative somatosensorial test, and reference to an orofacial pain specialist should be considered. In case of uncertain diagnosis, it is recommended to avoid any dental procedures because the pain can get worse.

Keywords: Atypical odontalgia, Endodontic, Odontalgia.

RESUMO

JUSTIFICATIVA E OBJETIVOS: A odontalgia atípica, um subtipo da dor facial idiopática persistente, se caracteriza por dor contínua em um ou mais dentes, ou no alvéolo, após exodontia sem qualquer causa aparente e é um desafio para o dentista. O desconhecimento por parte do profissional pode levar a procedimentos odontológicos desnecessários e mutiladores, piorando e/ou cronificando a dor do paciente. Diante desse panorama, o objetivo deste estudo foi apresentar informações referentes à fisiopatologia, diagnóstico e tratamento da odontalgia atípica através de uma revisão integrativa da literatura.

CONTEÚDO: A busca na base de dados Pubmed foi realizada com os termos: "atypical odontalgia" *OR* "phantom tooth pain" *OR* "idiopathic tooth pain" *OR* "odontalgia" *OR* "odontalgias" *OR* "atypical toothache". Aplicando-se critérios de inclusão (publicações nos últimos 10 anos, de língua inglesa, tipo ensaio clínico, estudo multicêntrico, relato de caso, revisão, revisão integrativa científica e sistemática) foram encontrados 114 artigos, dos quais 39 foram selecionados após aplicação do critério de exclusão (trabalhos sem relação com o tema).

CONCLUSÃO: Embora os estudos apontem forte envolvimento de mecanismos neuropáticos, aspectos psicogênicos/psiquiátricos devem ser levados em consideração como agravante do estado de dor do paciente. Sugere-se conhecimento sobre as outras doenças existentes para se realizar um diagnóstico diferencial, exames complementares de imagem, realização do teste somatossensorial qualitativo, encaminhamento a um especialista em dor orofacial e neurologista, e em casos de dúvida, não realizar nenhum procedimento a fim de não piorar a sua dor.

Descritores: Endodontia, Odontalgia, Odontalgia atípica.

INTRODUCTION

Atypical odontalgia (AO) represents a clinical challenge for most dentists[1]. Generally, when a patient complains of pain, its origin is odontogenic, and the professional can identify and treat its cause – for example, a typical toothache due to pulpitis, caries or periodontal problem. But in some situations, pain continues in one or more teeth or in the socket after extraction without any apparent dental cause[2], and the dentist faces the challenge of determining the true non-odontogenic origin of pain and properly diagnosing it[1,3-5].

According to the 3rd edition of the International Headache Society (ICHD-3)[2], the diagnostic criterion of AO is described by continuous pain in one or more teeth or socket after extraction, without any apparent dental and neurological causes. Pain lasts for more than two hours daily and persists for more than three months and may or may not be associated with a history of dental trauma (Table 1).

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Table 1. Diagnostic criteria of the "International Headache Society 3"

A. Facial or oral pain that meets criteria B or C.
B. Recurrent daily pain for more than 2h/day for more than 3 months.
C. Pain has both characteristics: 1. Poorly located, and does not follow the peripheral nerve path; 2. Painful, "boring", light.
D. The neurological clinical examination is normal.
E. The dental cause is excluded after proper investigation.
F. The characteristics do not fall into any other diagnostic criteria of the ICHD-3.
G. Facial or oral pain in the distribution/path of one or both branches of the trigeminal nerve that meets criterion I.
H. History of an identifiable traumatic trigeminal nerve event, with evidence of positive clinical signs of trigeminal nerve dysfunction (hyperalgesia, allodynia) and/or negative (hypoesthesia, hypoalgesia).
I. Evidence of cause demonstrated by: 1. Pain is localized in the path of the trigeminal nerve affected by the traumatic event; 2. Pain developed within a period of less than six months from the traumatic event.
J. The characteristics do not fall into any other diagnostic criteria of the ICHD-3.

From A to F when atypical odontalgia falls into a subtype of persistent idiopathic facial pain. G to J: when atypical odontalgia is related to trigeminal nerve trauma.

The difficulty in diagnosing AO is because the reported pain is identical to those of odontogenic origin without clinical and radiographic alterations[4,6]. The patient may have a history of extensive dental treatment without pain relief, which makes the diagnosis more complex[7,8]. Endodontic treatment, apicectomy and/or extraction may alleviate pain temporarily, but pain increases in intensity in a few days or weeks[7,9].

The physiopathology is not well defined, and several mechanisms have been suggested in the last 50 years[3,10]. There is great controversy regarding AO and psychological factors, with studies that indicate a large percentage of individuals with depression[11] and others question whether they could be secondary factors to pain[12-16]. Vascular origin is a disorder of the pulp and ligament blood vessels and is described as a "dental migraine"[7,17].

Neuropathic origin is the most studied, being described in 1971 by Melzack based on Mitchell's phantom limb pain in 1871 (Apud[9] and described by Marbach in 1978 for the first time as "phantom tooth pain"). In addition, other neuropathic mechanisms would explain the physiopathological process: deafferentation hypersensitivity[12,18] and central and/or peripheral sensitization[3,19-21]. And, given this scenario, ICHD-3 classifies it as a subtype of persistent idiopathic facial pain (ICHD 13.12). If it is based on a history of trauma, it will be a subtype of posttraumatic trigeminal neuropathic pain (ICHD 13.1.2.3).

Although there is a well-defined diagnostic criterion by ICHD-3 for AO, there is no protocol on how to perform it[22]. Detailed clinical examination, work among various specialists, and listening to the patient about their dental history are proposed[23,24]. Some studies have shown that patients with AO have altered responses to qualitative and quantitative somatosensory tests[3,19].

Currently, there is insufficient evidence to establish a treatment protocol for AO[25]. Tricyclic antidepressants, antiepileptics, anesthetics, and botulinum toxin, although reducing the pain of the patient[3,22,25], have limited activity and have no proven effectiveness[25-27].

Generally, the dental surgeon is the first healthcare professional with whom the AO patient consults. The lack of knowledge of this situation by the dentist can lead to unnecessary and mutilating dental procedures, such as endodontic and surgical treatments ranging from apicectomy to extraction[28]. Knowing the physiopathology and the diagnostic process allows the proper treatment, avoiding further injury to the patient[29].

Given a scenario in which there is no consensus in the literature on the physiopathology, the diagnostic process, and its treatment, this study aimed to review these aspects, assisting the dentist in his/her professional activity.

CONTENTS

This is an integrative literature review with a qualitative approach to identify physiopathological, diagnostic, and treatment aspects of AO. The methodological process was divided into 5 steps, according to Whittemore and Knafl[30]: 1) problem identification; 2) literature search; 3) assessment of information; 4) critical analysis of the information; 5) presentation of results.

A search was performed in the Pubmed database. As a search strategy, the following terms were used: *"*atypical odontalgia*"* OR *"*phantom tooth pain*"* OR *"*idiopathic tooth pain*"* OR *"*odontalgia*"* OR *"*odontalgias*"* OR *"*atypical toothache". The inclusion criteria were articles published in the last 10 years, in English, clinical trial, multicenter study, case report, review, integrative scientific review, and systematic review. After reading the title and the abstract, those who had no relation to the theme were excluded. In case of uncertainty of inclusion, the full article was read.

A total of 114 articles were found, and after applying the established inclusion criteria, 48 articles were chosen. Of these, 9 were excluded because they were not related to the theme, totaling 39 studies. The material was grouped according to the emphasis of the article: physiopathology, diagnosis and treatment. Information relevant to both steps is summarized in table 2.

PHYSIOPATHOLOGY

Current evidence suggests neuropathic mechanisms to explain the physiopathology of AO[1,24,41,44,45,50] and the somatosensory tests suggest its description in central and peripheral[19,23,38,47,52].

One of the tests performed is local anesthesia, which, when observing pain reduction, suggests the neuropathic mechanism of peripheral origin (peripheral sensitization)[41]. The quantitative somatosensory testing (QST) used are based on the pain threshold using a mechanical stimulus and heat pain threshold tests, for example[40]. Sensory alterations after cold application were identified in AO patients, also suggesting the involvement of central neuropathic mechanisms[52]. Qualitative somatosensory testing (QualST) were also used to confirm neuropathic involvement[45].

Table 2. Selected studies and relevant information

Durham et al.[5]	The use of a questionnaire to diagnose neuropathic pain (S-LANSS) is desirable because it has sufficient sensitivity and specificity. However, clinical examination and investigation cannot be neglected.
García-Sáez et al.[25]	The use of botulinum neurotoxin type A has been shown to reduce pain in patients with AO. However, randomized controlled trials (RCT) are suggested to prove their effectiveness.
Miura et al.[16]	Attention to psychiatric comorbidity, common in patients with AO. There is no cause-effect relationship.
Malacarne et al.[1]	Persistent dentoalveolar pain is likely to be of neuropathic origin, but physiopathological mechanisms that explain the onset and maintenance of pain are not understood. A correct diagnosis must be established prior to any treatments.
Ghurye and McMillan[31]	The physiopathology of orofacial pain is complex, sometimes associated with psychological comorbidities. Chronic pain has an impact on quality of life. Early diagnosis and referral. Attention to the biopsychosocial approach, which confers a multifactorial etiology to chronic orofacial pain. It should be treated as neuropathy.
Tu et al.[32]	The presence of psychiatric comorbidities aggravated the quality of sleep but had little impact on pain experience. The presence of burning mouth syndrome in patients with AO contributes to more severe pain.
Takenoshita et al.[33]	AO is not purely a sensory problem, but it has psychological involvement. It has a variable response to drug use, and it is necessary to investigate the different pharmacological responses to advance the treatment of AO.
Tait, Ferguson and Herndon[34]	They consider AO, so the diagnosis occurs by exclusion. According to the authors, there is no diagnostic protocol with evidence. Treatments that are considered effective for orofacial pain are disappointing for AO.
Kobayashi et al.[35]	The authors found no relationship between pain relief and duloxetine plasma concentration, which is used to treat AO.
Benoliel and Gaul[36]	Enigmatic physiopathology. Neuropathic mechanisms are more relevant. Interdisciplinarity. Attention to psychiatric comorbidity. Careful interdisciplinary assessment is necessary to institute appropriate treatment.
Baad-Hansen and Benoliel[28]	There is no gold standard for diagnosis. A consensus on classification and taxonomy is needed. Prospective studies are necessary. Education and training for professionals are important to avoid iatrogenies. Careful interdisciplinary assessment is required to institute appropriate treatment.
Agbaje et al.[37]	QualST can be used as a clinical diagnostic tool, as well as to investigate intraoral somatosensory function in patients with AO. QualST is a simple test to verify changes in somatosensory function.
Rafael, Sorin and Eli[38]	It presents clinical characteristics and physiopathology of painful traumatic trigeminal neuropathy, and what to do to prevent it.
Toyofuku[39]	The professional must be aware of the patient's psychosomatic aspect, which is a priority as well.
Cuadrado et al.[26]	The positive response to the use of botulinum neurotoxin type A suggests that its use is effective and safe in the treatment of neuropathies, but RCT are necessary to prove its effectiveness.
Porporatti et al.[40]	QST can help in the differential diagnosis between pulpitis and AO with substantial accuracy. QST limitations: patient gets tired, it is difficult to examine painful areas
Porporatti et al.[41]	There is central sensitization involvement, and decreased pain with the anesthetic also suggests that there is peripheral involvement.
Porporatti et al.[10]	It reinforces the role of the central nervous system sensitization. The most reliable method would be bilateral QST comparing pain threshold using a mechanical allodynia stimulus or heat pain threshold tests.
Baad-Hansen et al.[42]	QST should be associated with neurophysiological tests or imaging examinations, where possible, to increase test sensitivity and specificity.
Forssell et al.[24]	There is increasing evidence of neuropathic mechanisms for orofacial pain - including AO. The authors suggest that the diagnosis be based on clinical examination, medical history, QST, neurophysiological tests, etc.
Pig et al.[43]	MRI may be of great value as it excludes inflammation processes in the mandibular and maxillary regions. When the diagnosis is uncertain, MRI raises the argument to avoid dental treatments and consider noninvasive treatments.
Yatani et al.[27]	The authors present a guide for the treatment of non-odontogenic origin. The use of tricyclic antidepressants is the most commonly used but has no proven effectiveness.
Baad-Hansen et al.[44]	The QST showed 87.3% abnormality in individuals with AO as an increase in mechanical and thermal stimuli and may be an appropriate tool for scanning patients with neuropathic pain.
Tarce, Barbieri and Sardella[23]	Diagnosis and treatment are challenging. Physiopathology is unclear. They suggest more RCT to prove the effectiveness of drugs used in the treatment of AO.
Baad-Hansen et al.[45]	QualST detect disturbances in individuals with AO, especially sensitivity to cold, touch, and bristle stimulation.
Zakrzewska[46]	It reviews the literature on pain in the lower face and mouth. It addresses classification, epidemiology, and diagnosis.
Tınastepe and Oral [47]	Neuropathic pain has complex physiopathology and may start after dental treatment such as endodontic treatment, implant surgery, and trauma when anesthetizing. Trigeminal neuralgia, mouth burning syndrome, and postherpetic neuralgia and AO are neuropathic conditions
Ciaramella et al.[15]	Some psychological factors determine predisposition to the development of chronic pain after extraction. Individuals with AO had high levels of resentment and depression.

Continue...

Table 2. Selected studies and relevant information – continuation

Nagashima et al.[48]	Duloxetine relieved the pain of patients with burning mouth syndrome and AO.
Patel, Boros and Kumar[49]	In the absence of an accurate diagnosis, do not perform endodontic and surgical treatment.
Abiko et al.[22]	They present diagnostic criteria and treatment and management protocols. There is insufficient information to establish a diagnosis and treatment protocol for AO. Psychological factors cannot be disregarded as there is a high incidence of related problems.
Thorburn e Polonowita[50]	The diagnosis occurs by exclusion. Clinical examination and history are important. With the advances in understanding the mechanisms of chronic neuropathic pain, there will be more focus on the diagnosis and treatment of AO.
Bosch-Aranda et al.[20]	AO is difficult to diagnose because the physiopathological mechanisms are unclear. Still, the evidence is not enough to indicate treatments with analgesics and antidepressants.
Pigg et al.[51]	Cone-beam computed tomography provides the identification of patients without periapical bone destruction, which facilitates the differentiation between symptomatic apical periodontitis and AO.
Zagury et al.[52]	Sensory changes for post-cold sensation were identified in patients, suggesting the involvement of central neuropathic mechanisms. Pain extending to a broader region of the site of origin, and pain occurring on the contralateral side, reinforces the idea of central sensitization. Extraoral QST does not seem to be able to detect change.
Takenoshita et al.[14]	AO patients were most often diagnosed in the stressed F4 neurotic category.
Ito et al.[53]	Milnacipran was effective in reducing pain in AO patients, regardless of the degree of depression.
Ram et al.[29]	If the patient continues to have persistent pain after the treatment, with no apparent clinical and radiographic cause, the professional should consider AO as a differential diagnosis. Dentists should be able to identify this situation and refer to an orofacial pain specialist or neurologist.
List, Leijon and Svensson[19]	Most patients with AO presented somatosensory alteration compared to few in the control group, which reflects in central and peripheral sensitization.

AO = atypical odontalgia; QST = quantitative somatosensory testing; MRI = magnetic resonance imaging; RCT = randomized clinical trials; QualST = qualitative somatosensory testing.

In addition to these mechanisms, other neuropathic physiopathological events may be involved: nerve damage and ectopic activity due to the formation of neuromas, phenotypic changes, and increased sympathetic activity in times of stress or anxiety[38]. Recent studies do not point to psychiatric comorbidity as a determining cause for triggering AO[15], but professionals should be aware of this condition[36] and cannot disregard it[22]. A high incidence of AO patients presents these comorbidities[22,33], reaching 50% in another study[16]. "Neurotic and stressed"[16] and "resentful and depressed"[15] were striking characteristics described in individuals with AO. Moreover, such comorbidities may determine a predisposition to the development of chronic pain after extraction[15]. Tu et al.[32], however, concluded that psychiatric comorbidity in patients with AO and mouth burning syndrome had little impact on pain experience.

The vascular cause presented by Rees and Harris[7] and Kreisberg[17] was mentioned in only two studies[20,22], thus not being the main physiopathological mechanism of AO.

DIAGNOSIS

There is no gold standard diagnostic protocol for AO[28,34,] and existing ones are not sufficiently reliable for diagnosis[1]. Since the physiopathology is not well defined[20,23], its diagnosis is often by exclusion[34,50].

Even in the face of insufficient information for the elaboration of a diagnostic protocol[22], after analyzing the data extracted from this study, it was possible to synthesize the main information for the professional who may be facing a diagnosis of AO:

1) Importance of medical history: patient assessment should begin with its medical history, especially with regard to pain characteristics[23];

2) Importance of the clinical examination: the odontogenic causes of toothache must be totally ruled out. For this, a thorough clinical examination is necessary[5,10,24,40]. One should not forget Rees and Harris's observations[7] emphasizing that all possibilities of caries, pulp disease and crack/fracture of the crown or root should be excluded;

3) Complementary imaging tests: despite the limitations of periapical radiographs[54,55] they should be used to assess the periapical region. Volumetric computed tomography should be performed to rule out any possibility of periapical endodontic alteration[10,51]. The use of magnetic resonance imaging (MRI), in cases of suspected non-inflammatory dental pain, can be of great value as it excludes inflammation processes in the mandibular and maxillary region. When the diagnosis is uncertain, MRI reinforces the importance of noninvasive management[43];

4) In order to facilitate and assist the diagnostic process, two tools should be highlighted:

a) Visual analog scale: diagnostic tool for pain measurement[41,45]:

b) QST and QualST: are important allies in the diagnosis of AO[24,27,40,44,45,52]. QST is performed through several stimuli, and only mechanical and thermal stimuli are related to AO. Of the patients with AO submitted to these stimuli, 83.7% had some QST abnormality[44]. Performing bilateral QST (pain side versus pain free side) also helps to detect neuropathic changes[10]. Despite the indications, QST, when used outside hospitals and university clinics, is costly and often unfeasible, requiring the calibration and training of examiners[45]. QualST detects hypersensitivity disorders to touch, cold, and bristle stimulation[46].

5) Exclude all hypotheses of non-odontogenic odontalgia. According to Yatani et al.[27] and ICHD-3, after discarding the

hypothesis of dental pain, there are numerous other conditions of non-odontogenic origin that should be ruled out;
6) Refer the patient to other specialists: Given the difficulty of properly diagnosing and the various physiopathological mechanisms that could be involved, it is recommended to refer the patient to other specialists[23,24,36,57]. Interesting to note that in 1982, Kreisberg[17] already suggested referral to the neurologist;
7) Consider psychological aspects: Although psychogenic and psychiatric factors have no determining relationship in the development of AO[16], there was a high incidence of these patients with psychiatric comorbidities[14-16,22,32,36]. The professional should be aware of these comorbidities, giving AO a multifactorial etiology[31,33]. Thus, a biopsychosocial[31] and interdisciplinary[36] and no less priority[39] approach are necessary[39];
8) A more holistic, psychosocial, and not purely mechanical approach is important. It is recommended to listen carefully to the patient's complaint and his/her history of treatments[56];
9) Knowledge and training by professionals are important to avoid unnecessary and iatrogenic procedures[28].

TREATMENT

Like diagnosis, AO treatment is challenging[23,50]. Currently, there is insufficient evidence to establish a treatment protocol[25].
Tricyclic antidepressants are the most cited drugs in case reports and case-control studies, and for many authors, they are considered the first choice in treatment[27,35]. However, these drugs cause adverse effects. Amitriptyline, for example, causes xerostomia, constipation, urinary retention, and weight gain[20] and, depending on the dose and the patient, have varied responses regarding the effectiveness in pain remission[33].
Serotonin and norepinephrine reuptake inhibitors, such as milnacipran and duloxetine, have also been used in the management of painful symptoms[35,48,53,] and although they have pain reduction, there is a need for randomized controlled trials (RCT) to prove its real effectiveness[20,21,23].
As already described, current evidence suggests neuropathic mechanisms to explain the physiopathology of AO[1,24,41,44,45,50]. Thus, treating it as a neuropathy sounds coherent[31]. However, results with therapies employed for neuropathic orofacial pain have been disappointing in AO studies[34].
More recent studies have assessed the action of botulinum neurotoxin type A (Onabotulinum toxin A) in pain control. The good results regarding pain remission point it as a promising drug in the treatment of AO. However, as with tricyclic antidepressants and serotonin and norepinephrine reuptake inhibitors, the use of botulinum neurotoxin type A should be proven to be effective through more RCT[20,25,26].
Thus, the information obtained from the articles found can be summarized:
1) In cases of doubt, not performing endodontic and surgical treatments, as AO would be unnecessary and worsen the patient's pain[49];
2) Knowledge and training by professionals in the diagnostic process are essential to avoid unnecessary and iatrogenic procedures[28];
3) Interdisciplinary work is important not only in the diagnosis, but also in the institution of the correct treatment[36,50];
4) RCTs are necessary to assess the effectiveness of tricyclic antidepressants, serotonin and norepinephrine reuptake inhibitors and botulinum neurotoxin type A[21,23];
5) Minimizing the pain of patients with the lowest drug dose is the main objective and inadvertent use without the need for several drugs should be avoided[20];
6) And again, a holistic, psychosocial, and not purely mechanical approach is important. It is recommended to listen carefully to the patient's complaint and his or her history of treatments[56].
After these reflections, it is important to emphasize that this study had limitations regarding the choice of database for the selection of studies. However, Pubmed is considered the universal English language database with indexed high impact journals.

CONCLUSION

Recent studies use the 3rd edition of the ICHD classification, in which AO falls into the "persistent idiopathic facial pain" category (ICHD-13.12). Since the physiopathological process is not defined, the establishment of a protocol to make its diagnosis is fundamental. It is suggested knowledge about the other existing diseases to make a differential diagnosis, and the use of complementary exams such as volumetric computed tomography, MRI, and QualST. Tricyclic antidepressants and serotonin and norepinephrine reuptake inhibitors are the drugs of first choice in the treatment of AO. However, currently, the use of botulinum neurotoxin type A in pain management has been assessed. All these drugs require RCT to have their effectiveness proven. Given the possibility of AO, an interdisciplinary approach in the diagnostic process and definition of its treatment is guided.

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