

SYSTEMATIC REVIEW

Temporomandibular disorders and orofacial neuropathic pain in children and adolescents: a systematic review

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Abstract

Pediatric orofacial pain (OFP) is a blanket term referring to the pain of soft and hard tissue in the face, neck and headaches affecting subjects younger than 18. OFP encompasses pain due to various causes, *i.e.*, (i) Temporomandibular Disorders (TMD), (ii) Headache, and (iii) Neuropathies. This review aims to provide an overview of these three causes of OFP. The inclusion criteria are: (1) articles in English; (2) human studies; (3) clinical trials; (4) systematic review. Data from the included studies using a customized data extraction on a Microsoft Excel sheet. PubMed, Web of Science and Lilacs were systematically searched. The time window considered for the electronic search was from 01 January 1950 to 21 October 2022. A total of 3399 articles published were found from electronic searches. Finally, six full-text articles satisfied the inclusion criteria. The included studies have been published over the past 27 years (1993 to 2020). The studies analyzed were conducted in various parts of the world: USA, Argentina, Canada, South America (Brazil), and India. A total of 308 subjects were analyzed. TMD, headache, and neuropathies are among the leading causes of orofacial pain. Lifestyle changes and psychological approaches could be curative. However, some patients need pharmacotherapy. Regarding the inadequate treatment of pain after hospital discharge due to the difficulty of following the scheduled intervals prescribed, remote monitoring through telemedicine tools could be a solution in the future. Several conditions present with pain in children and adolescents; in most of them, pain is the most prominent symptom. This review found that one of the most critical causes of OFP is temporomandibular dysfunction. Treatment is founded on a multidisciplinary approach.

Keywords

Orofacial pain; Children; Pediatric; Temporomandibular disorders; TMD; TMJ

1. Introduction

The current International Association for the Study of Pain (IASP) definition of pain as “An unpleasant sensory and emotional experience associated with actual or potential tissue damage, or described in terms of such damage” was recommended by the Subcommittee on Taxonomy and adopted by the IASP Council in 1979 [1–3]. Pediatric orofacial pain (OFP) is a blanket term referring to the pain of soft and hard tissue in the face, neck and headache affecting subjects younger than 18 years [2–6]. An essential medical and social issue is a pain in the oral and craniofacial system. A report by the U.S. Surgeon General on orofacial health states, “oral health means much more than healthy teeth. It means being free of chronic oral-facial pain conditions”. If neglected, facial discomfort is a debilitating disorder. When the cause of a patient’s facial pain is unknown, it happens far too frequently that psychopathology is diagnosed [7–9]. They are classi-

fied as “atypical”, “idiopathic”, or “psychogenic” patients. Idiopathic refers to an undefined condition and implies that there is something unknown. The same is true for words that contain the word “atypical”. Because the pathophysiologies of neuropathic and myofascial pains are poorly known. Because facial pain may have neurological, vascular, or dental causes, it has been proposed that these disorders are the most frequently misdiagnosed causes of facial pain. Trigeminal neuralgia is far less common than dental discomfort. Compared to dental and temporomandibular causes [10], neurological and vascular conditions rarely cause facial discomfort. In children, facial neuralgias are often uncommon. Neurological disorders that can cause facial discomfort in children include trigeminal, glossopharyngeal occipital neuralgia, and Bell’s palsy; however, they are incredibly unique. The International Classification of Orofacial Pain (ICOP), the first thorough classification that specifically addresses orofacial pain, was released in 2020. It results from an international collaboration between

the American Academy of Orofacial Pain, the International Headache Society, the International Network for Orofacial Pain and Related Disorders Methodology, and the Orofacial and Head Pain Special Interest Group of the International Association for the Study of Pain. The International Classification of Headache Disorders (ICHD) (3rd edition, ICHD-3) is the basis for the new orofacial pain classification, which is well-regarded and utilized by physicians and researchers worldwide. The ICOP thoroughly explains pain problems affecting the orofacial area and diagnostic standards for such diseases. Its six chapters, which aim to be all-inclusive, address pain in muscles, temporomandibular joint (TMJ) pain, neuropathic pain affecting cranial nerves, pain similar to primary headaches, and idiopathic pain. It includes both original pain (pain not brought on by another condition and secondary pain, sensitization of the tissues, structural changes, muscle spasm, or injury). In addition, a number of the chapters separate the different types of pain into acute and chronic categories, with chronic pain being defined as pain that lasts three months or more [11]. It displays a high prevalence among young subjects (20–30%) [12], with a special meaning to the young patients because of the emotional and psychological aspects [7]. OFP prevalence increase with age, especially in female. Female adolescents are the most vulnerable among pediatric subjects due to hormonal fluctuation and genetic susceptibility [13].

Orofacial pain may impact the youth's daily functioning and overall well-being. It can be associated with functional avoidance, poor sleep, depression, and emotional stress, among other adverse outcomes [14]. It may affect the overall well-being of an individual. Correct diagnosis and therapy depend on exhaustive history taking and an extensive physical and neurological examination [15, 16]. However, this can be challenging concerning the limited communication abilities and the variability in feelings and perceptions of children. Therefore, in some cases, additional diagnostic tests are indicated. The multidisciplinary approach is the cornerstone of OFP management in children and adolescents [17]. A simultaneous approach encompassing lifestyle modification, psychotherapy, physiotherapy and pharmacotherapy is often needed to reach a satisfying outcome. Further, the use of telemedicine could favour an improvement in pain management, allowing for ongoing discussion between parents and physicians [17]. Although this approach was already established, the COVID-19 pandemic has severely implemented and improved the use of telemedicine in managing patients affected by chronic disease [18, 19], among other OFPs. In this view, telemedicine allows for continuing pain management, avoiding the face-to-face examination that puts at the probability of infection for both patients and health professionals [20]. OFP encompasses pain of different origins and causes: (i) Temporomandibular Disorders (TMD) [21–25], (ii) Headache, and (iii) Neuropathies [26]. TMD and headaches are ubiquitous in children and adolescents, whereas neuropathies are rare. According to ICOP classification in our review, we excluded the leading causes of OFP, *i.e.*, dental and periodontal pain, as they are easy to diagnose by doing a systematic review of and viewing the less frequent causes of orofacial pain. This review aims to provide an overview of the different types and

causes of OFP in children and adolescents, with a systematic evaluation of the prevalence and intensity of Orofacial pain due to TMD, neuropathies and/or headaches in children and adolescents. Further, we evaluated pain evaluation and management of these conditions. Finally, we focused on telemedicine's potential role in improving OFP management.

2. Materials and methods

2.1 Eligibility criteria

We assessed for eligibility all documents based on the following Population, Exposure, Comparator, and Outcomes (PECO) model [27]:

(P) Participants: children and adolescent patients.

(E) Exposure: diagnosis of Orofacial pain due to TMD, neuropathies and/or headache.

(C) Comparison: between the different types and causes of OFP in children and adolescents.

(O) Outcome: prevalence and intensity of TMD, neuropathies and headache in children and young adults. The secondary outcome: assessing the pain evaluation and management of these conditions and the role of telemedicine in the treatment of OFP.

The following inclusion criteria were used: (1) articles in English; (2) human studies on children affected by OFP; (3) clinical trials; (4) systematic review of OFP due to Headaches, TMD, and neuropathies.

Exclusion criteria were: (1) articles that did not comply with PECO, so they did not deal with incidence on causation and telemedicine; (2) duplicate articles; (3) books; (4) letters to editors and experimental studies; (5) studies written in a language different from English; (6) full-text unavailability (*i.e.*, posters and conference abstracts); (7) studies involving animal; (8) history of temporomandibular joint (TMJ) trauma; (9) review articles (10) case series; (11) case report; (12) other causes of facial pain, odontogenic pain, muscular pain.

2.2 Search strategy

We used a systematic search strategy to go through the PubMed, Web of Science, and Lilacs databases for publications published between the beginning and 30 September 2022; Table 1 outlines this strategy. In addition, a manual search of earlier systematic reviews on the same subject was also done. In PubMed, the MeSh terms were used; however, in the other search engines, this lack was made up for by a manual search.

2.3 Data extraction

The data were extracted by two reviewers (M.M.M. and G.M.) independently from the included studies using a customized data extraction on a Microsoft Excel sheet. A consensus was reached through a third reviewer, in case of disagreement (R.F.).

The following data were extracted: (1) First author; (2) Year of publication; (3) Design study; (4) Population; (5) Age of study participants; (6) Diagnostic tool for OFP; (7) Treatment; (8) Topic of the study; (9) Main findings; (10)

TABLE 1. Search strategy.

PubMed
(((“facial pain” (MeSH Terms) OR (“facial” (All Fields) AND “pain” (All Fields)) OR “facial pain” (All Fields) OR (“orofacial” (All Fields) AND “pain” (All Fields)) OR “orofacial pain” (All Fields)) AND (“child” (MeSH Terms) OR “child” (All Fields) OR “children” (All Fields) OR “child s” (All Fields) OR “childrens” (All Fields) OR “childrens” (All Fields) OR “childs” (All Fields) OR (“paediatrics” (All Fields) OR “pediatrics” (MeSH Terms) OR “pediatrics” (All Fields) OR “paediatric” (All Fields) OR “pediatric” (All Fields)))) NOT (“case reports” (Publication Type) OR “case report” (All Fields))) NOT (“review” (Publication Type) OR “review literature as topic” (MeSH Terms) OR “review” (All Fields))) AND (English (Filter))
Web of Science
(((ALL = (children)) OR ALL = (pediatric)) AND ALL = (orofacial pain)) and Article (Document Types) and English (Languages)
Lilacs
orofacial pain (Palavras) and children (Palavras)

We did our research following the Cochrane Handbook for Systematic Reviews of Interventions and the Preferred Reporting Items for Systematic Reviews (PRISMA) standards. The International Prospective Register of Systematic Reviews (PROSPERO) has recorded the systematic review protocol number CRD42022326253.

role of telemedicine (only for the study used to explore the role of telemedicine; not available for studies included in Table 2). The following data were extracted and included in the table, and also all causes of OFP were summarized with their frequencies. In addition, the possible role of telemedicine in the treatment of this condition was evaluated in each selected article. Two authors read all articles independently, and the data were compared and contextualized in the table.

3. Results

3.1 Study characteristics

Three thousand three hundred ninety-nine studies were located after the investigation. According to the PRISMA 2020 flowchart in Fig. 1, only 6 articles were chosen to create the current systematic survey, and 3393 articles were excluded: 506 articles were eliminated because they were reviews, 489 articles were eliminated because they were case reports, and 168 articles were eliminated because they were not written in English. According to the PECO model, the remaining papers were chosen for title and abstract screening. The 82 remaining articles were selected, and the abstract was analyzed and evaluated to determine whether it was in line with the inclusion and exclusion criteria and the PECO used. In the end, only 6 articles that met the requirements were full-text read to extrapolate the data for this review. In the end, six articles were published on the search engines. Over the previous 27 years, the listed studies have been published (1993 to 2020). The research that was examined was carried out all around the world: USA, Argentina, Canada, South America (Brazil), and India. A total of 308 subjects were analyzed. Regarding the study designs, there were 6 cross-sectional studies. Among these 6 studies, only 1 included a control group, 2 used the Research and Diagnostic Criteria for Temporomandibular Disorders (RDC/TMD) and the Diagnostic Criteria for Temporomandibular Disorders (DC/TMD), and 2 studies used scale instruments (SLEDAI; DMFT-I; PI; GI; CDI; MMI; FPS; FPS-R; VAS; CAS), and 2 did not define a standardized method to describe the symptoms. Table 2 summarizes the main characteristics of all the studies included in the present

systematic review.

3.2 Main findings

35 patients with cluster headaches began at or before the age of 18 and had their first attack when they were just 10 years old. All patients met the International Headache Society’s episodic or recurrent cluster headaches criteria. Patients had cluster headaches for up to 20 years before seeking medical help, and it took numerous consultations with doctors to make the proper diagnosis. Childhood cluster headaches had similar clinical characteristics as adult cluster headaches. Over 18 years of follow-up, cluster headache patterns evolved. In 14 cases, the number and length of cluster periods rose. In a similar number of participants, the frequency of isolated headache attacks during cluster periods also increased [28].

Patients who participated in the study identified temporomandibular joint and/or masticatory muscle pain lasting more than a week as their primary concern. The following age categories were used to divide up the patients: younger than 20, between 21 and 30, between 31 and 40, between 41 and 50, between 51 and 60, and older than 60. Patients underwent clinical examinations and were required to complete the Hospital Anxiety and Depression Scale and an amnesic questionnaire (HADS). In total, 75 patients—20 males and 55 women—were enrolled in the study. TMDs were more common in female patients, 33 of whom (60%) experienced moderate-to-severe TMDs. Twelve (60%) of the 20 male patients displayed signs and symptoms of mild TMDs [29].

All juvenile patients (less than 18 years old) with trismus or restricted mandibular excursion from 1976 to 2008 had their clinical files, cephalograms, computed tomography scans, magnetic resonance images, and pathologic specimens evaluated. Cases were divided into groups based on the pathology of the soft tissues or the skeleton, with skeletal abnormalities further classified as intracapsular or extracapsular.

38 patients were found to have temporomandibular joint problems, with ages at diagnosis ranging from 1 day to 18 years. There were ten cases (26.3%) when soft-tissue abnormalities were included. The remaining 28 instances (73.7%), which had 14 congenital cases and 14 acquired cases, were all

TABLE 2. Data extraction.

First Authors	Publication year	Study design	Population (M/F)	Age	Diagnostic tool for OFP	Treatment	The topic of the study	Main findings
Maytal <i>et al.</i> [28]	1993	Cross-sectional	35	<18 yr	Headache characteristics, <i>i.e.</i> , type and site of pain and associated symptoms.	None	Childhood Onset Cluster Headaches.	Childhood-onset cluster headaches are a rare but curable type of headaches in children and adolescents that commonly go undiagnosed or misdiagnosed.
Yadav <i>et al.</i> [29]	2020	Cross-sectional	75	<20 yr, 21 to 30 yr, 31 to 40 yr, 41 to 50 yr, 51 to 60 yr, >60 yr	DC/TMD; Clinical records; Anamnestic Questionnaire; HADS	None	Influence of Psychosocial Factors and Parafunctional Habits in Temporomandibular Disorders.	TMDs are linked to increased levels of anxiety and sadness. Malocclusion and the severity of TMD do not correlate significantly, while parafunctional bruxism is mainly related to more severe TMD symptoms.
Allori <i>et al.</i> [30]	2010	Cross-Sectional	38	<18 yr	Clinical records, cephalograms, TC scans, MRI images, and pathologic specimen reports	Gap arthroplasty; Type I maxillectomy; Buccal fat pad flap	classification to differentiate between soft-tissue and skeletal abnormalities and to better characterize the extent of capsular involvement.	Extracapsular diseases, including coronoid hypertrophy and maxillomandibular bone fusion, were present in most congenital cases. Intracapsular ankyloses were observed in a small percentage of hereditary issues.
Cordeiro <i>et al.</i> [31]	2016	Cross-sectional	49	All ages	RDC/TMD; TC	None	Analyze whether RA patients have TMD and degenerative bone abnormalities in their TMJ.	The asymptomatic nature of the involvement of the TMJ in RA can hide structural damage seen in imaging. Thus, the importance of early diagnosis and treatment to reduce structural and functional damage is emphasized.

TABLE 2. Continued.

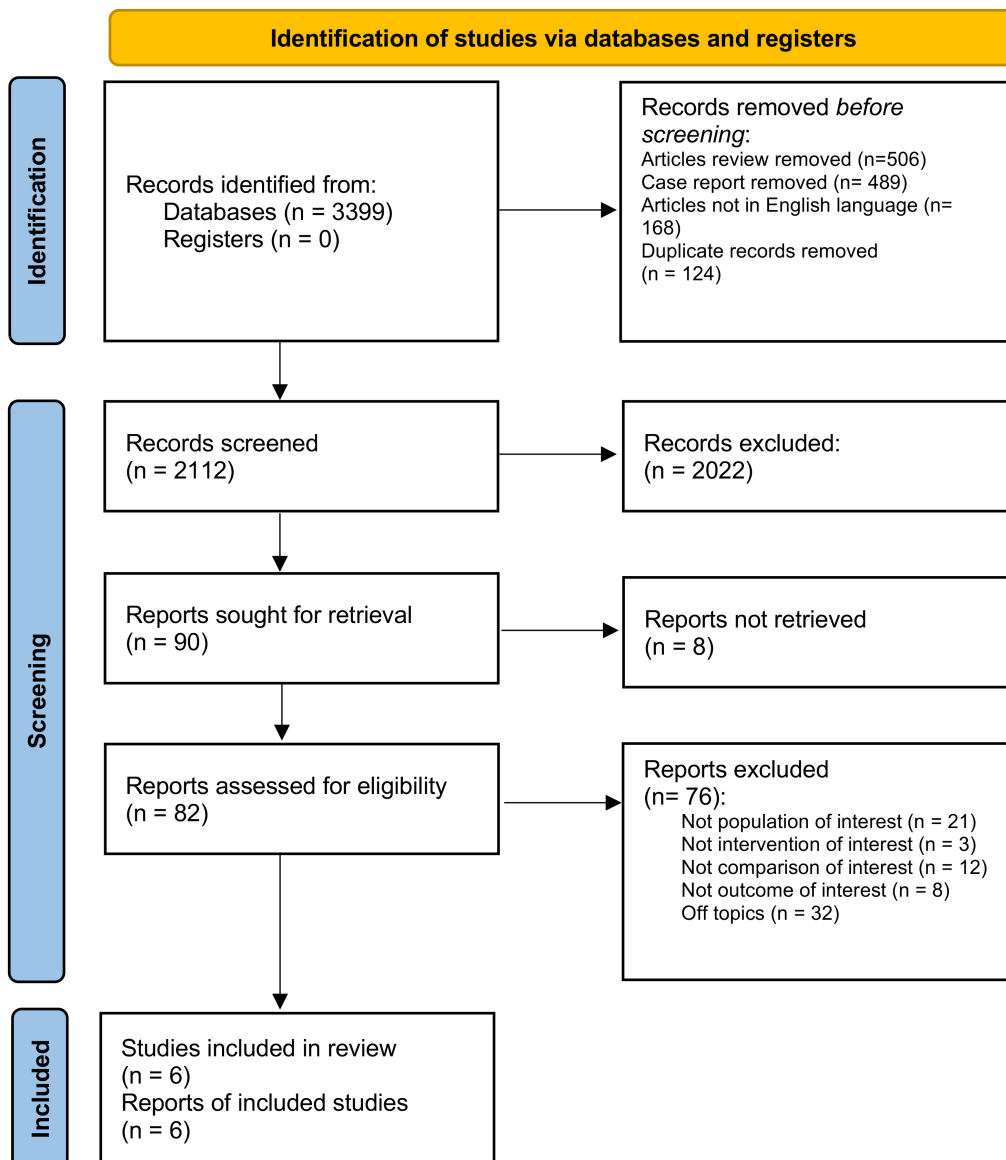
First Authors	Publication year	Study design	Population (M/F)	Age	Diagnostic tool for OFP	Treatment	The topic of the study	Main findings
Fernandes <i>et al.</i> [32]	2007	Cross-Sectional	48 + 48	6–21 yr	SLEDAI; DMFT-I; PI; GI; CDI; MMI.	None	Orofacial characteristics in JSLE patients and controls, as well as the relationship between oral and facial involvement and the disease's clinical signs, lab tests, and treatments.	Gingivitis was more common in patients with the longer-lasting disease and higher cumulative prednisone dosages, and those who used immunosuppressive medications developed TMJ dysfunction.
Hicks <i>et al.</i> [33]	2001	Cross-Sectional	15	18–44 yr	FPS; FPS-R; VAS; CAS	None	Revise the original scale used to assess the intensity of children's pain and validate the adapted version.	It has been demonstrated that the FPS-R is suitable for determining the severity of children's acute pain at age 4 or 5.

DMFTI: Decayed, Missing, Filled, Teeth Index; PI: plaque Index; GI: gingival bleeding indices; JSLE: Systemic lupus erythematosus juvenile; SLEDAI: SLE Disease Activity Index; CDI: Clinical dysfunction index; MMI: Mandibular Movement Index; FPS: Faces Pain Scale; FPS-R: Faces Pain Scale ± Revised; VAS: visual analogue scale; CAS: coloured analogue scale; HADS: Hospital Anxiety and Depression Scale; OFP: orofacial pain; TMJ: temporomandibular joint; TMD: Temporomandibular Disorders; DC/TMD: Diagnostic Criteria For Temporomandibular disorders; TC: Computed tomography; MRI: Magnetic Resonance Imaging RDC/TMD: Research and Diagnostic Criteria for Temporomandibular Disorders.

related to skeletal abnormalities (50 per cent each). Twelve intracapsular ankyloses (85.7%) and two extracapsular ankylosis (14.3%) were among the skeletal abnormalities that were acquired (extraarticular bone blocks). Five intracapsular ankyloses (35.7%) and nine extracapsular ankyloses were caused by congenital skeletal abnormalities (64.3 per cent) [30]. 49 patients of all ages and genders. People who had previously had treatment for TMD or who had a history of craniofacial trauma were omitted. Cone beam computed tomography (CBCT) examinations were performed on the individuals to check for any degenerative changes in the articular eminence and mandibular condyle. The frequency of the observed alterations is displayed, and the chi-square test is used to examine any potential correlations between the clinical and Computed Tomography (CT) findings. The orofacial region was shown to be the source of pain complaints in 75% of patients, including arthralgia, myalgia, or both. Regarding the diagnosis, RDC/TMD Group III was identified in 100% of the sample (arthralgia, osteoarthritis or osteoarthrosis). 90% of the individuals had degenerative bone alterations, with flattening and osteophytes being the most common (78.7% and 39.3%, respectively). The association test indicated that asymptomatic people have a higher propensity to develop degenerative alterations ($p = 0.01$) [31]. 48 juvenile systemic lupus erythematosus (JSLE)

patients' oral health and masticatory systems were assessed and compared to 48 healthy kids and teenagers. Review of JSLE therapy, clinical symptoms, and demographic information. Dental connection, facial profile, clinical dysfunction, mandibular mobility, plaque (PI), gingival bleeding (GI), and the DMFT index (DMFTI) were all assessed. Regarding age, gender, Brazilian social-economic class, and tooth decay index, the two groups were comparable ($p > 0.05$). Notably, JSLE patients had greater medians for the PI and GI than controls (61.5 compared to 38.10, $p = 0.003$; 26.0 versus 15.95, $p = 0.014$, respectively). The JSLE and the GI length, the cumulative dose of prednisone and the PI, and the cumulative dose of prednisone and the GI all showed linear statistical correlations ($p = 0.017$, $r = 0.11$, $p = 0.001$, $r = 0.471$, respectively). JSLE patients had greater mandibular mobility and clinical dysfunction indices than controls ($p = 0.002$, $p = 0.025$). Additionally, JSLE patients who used at least one immunosuppressive medication had a greater median mandibular mobility index than those who did not ($p = 0.0001$) [32]. Four faces were chosen to represent equal intervals between the scale values for least pain and most pain using a computer-animated version of the FPS created by Champion and colleagues (the Sydney Animated Facial Expressions Scale). Children in the second phase rated the severity of

PRISMA 2020 flow diagram for new systematic reviews which included searches of databases and registers only



From: Page MJ, McKenzie JE, Bossuyt PM, Boutron I, Hoffmann TC, Mulrow CD, et al. The PRISMA 2020 statement: an updated guideline for reporting systematic reviews. *BMJ* 2021;372:n71. doi: 10.1136/bmj.n71

For more information, visit: <http://www.prisma-statement.org/>

FIGURE 1. Flow chart.

ear-piercing pain using the updated six-face Faces Pain Scale-Revised (FPS-R). A significant positive connection between it and a visual analogue scale (VAS) assessment in kids between the ages of 5 and 12 ($r = 0.93$, $n = 76$) demonstrates its validity. In the third phase, a clinical sample of pediatric inpatients between the ages of 4 and 12 rated their pain from painful surgical and non-surgical disorders while hospitalized using the FPS-R, a VAS, or a coloured analogue scale (CAS). Strongly favourable correlations between the FPS-R and the VAS ($r = 0.92$, $n = 45$) and the CAS ($r = 0.84$, $n = 45$) in this clinical population further confirmed the FPS-R's validity. Most kids across all age ranges, even the smallest ones,

could utilize the FPS-R in a way consistent with the other measures. The FPS-R and any analogue scale's means did not significantly differ from one another [33].

3.3 Quality assessment

The risk of bias in papers was assessed by two reviewers using Version 2 of the Cochrane risk-of-bias tool for randomized trials (RoB 2). Any disagreement was discussed until a consensus was reached with a third reviewer.

4. Discussion

4.1 Temporomandibular disorders

TMD affect masticatory muscle and/or temporomandibular joint. Symptoms can vary in duration and intensity; however, they usually include moderate and prolonged pain with reduced interincisal opening, trismus and forced interincisal space [30]. It is generally associated with other symptoms such as ear-related disturbances, headache, and altered head and cervical posture. Ehlers-Danlos syndrome, psoriatic arthritis, systemic lupus erythematosus, Marfan syndrome, and juvenile idiopathic arthritis are common comorbidities [34–36]. However, several studies supported that it is primarily attributed to acquired abnormalities, specifically trauma (or surgery) and infection [30].

A study on more than 3000 subjects seeking treatment for TMD showed that 85.4% were female. The gender difference peaks in adolescence; however, female preponderance occurs at all ages [37]. Traumas, including head traumas, are among the etiological variables that frequently affect children and adolescents and may contribute to headaches and TMJ disorders. 26.0% of TMD in children and adolescents is brought on by trauma. Impact (vehicle accidents, contact sports), biting on complex objects, or extending the mouth too widely can all result in TMJ injury. In the 40-subject group, 27.5% of participants had experienced head trauma, and 81.8% displayed bite and non-bite parafunction. Probably muscle hyperactivity causes this pain of muscle origin, which is one of the causes of OFP. The main areas where OFP localizes due to temporomandibular disorders are as follows: pain affected the forehead (50.0%) and temples (43.8%), occipital regions (38.5%), as well as the frontal area (30.8%) [38].

Persistent orofacial pain is the leading cause of individuals seeking medical attention and treatment. To obtain the diagnosis, one would need to assess the pain reported by the patient on palpation of the masticatory muscles and temporomandibular joint. In children, spontaneous orofacial pain or pain on palpation has a frequency ranging from 2.59 to 35% [39, 40]. The American Dental Association recommends obtaining information regarding TMD-related pain. Although manual palpation may supply objective values, this procedure is a subjective experience, and self-report has been considered the “gold standard” [41] for pain assessment.

TMD pathogenesis is still controversial due to the complex physiology and structure of the craniofacial region. The numerous available studies suggest the involvement of both central and peripheral mechanisms [42–44].

Some factors could aggravate TMD manifestations, such as parafunctional habits, mandibular function, psychological distress, and incorrect postures [29].

However, the prevalence in children under ten is primarily determined by self-reported or proxy-reported signs and symptoms; so that reliability and validity may be evaluated and enhanced for this population, a more thorough standardized method for the gathering of clinical data and the diagnosis of TMD in children and adolescents is required [45, 46].

The Diagnostic Criteria for TMD (DC/TMD) has been used as the international standard for assessing TMDs since 2014. Axis I is used for physical diagnosis, and Axis II is used to evaluate psychosocial state and pain-related disability. To-

gether, these two axes make up the DC/TMD. The DC/TMD is validated for several diagnoses based on a standardized diagnostic methodology that includes a clinical examination and history. A diagnostic approach that uses historical and clinical data enables it to have significant diagnostic accuracy for TMD in adults and very high sensitivity and specificity for particular TMD subgroups.

The DC/TMD is only valid for users at least 18 years old, so applying it to children and teenagers necessitates some adaptation.

Due to the disparities in comprehension and communication skills between adults, teenagers, and kids, the DC/TMD has been adjusted for adolescents and children. The modified version incorporates a separate language review for both questionnaires and clinical examinations, as well as modified clinical assessment methods [47, 48].

With conservative treatment, it is often self-limited. Self-care management, and physiotherapy, are examples of traditional therapies. Young affected by TMD report a higher rate of depression, post-traumatic stress disorder or anxiety compared to pain-free subjects [49]. In this regard, there could be a link between factors aggravating TMD manifestation. Indeed, psychosocial distress favours muscle hyperactivity and bruxism, which aggravate TMD manifestation. Therefore, psychological distress management is critical in mitigating TMD manifestation and chronic pain in general.

4.2 Headache

Headache is a prevalent type of OFP in children and adolescents. 60% of young subject experiences in their lifespan significant headache and almost 10% are affected by migraine [45]. Migraine and Tension-type headaches (TTH) are the most common pediatric headaches.

Migraine is the most frequent headache in children and adolescents. It is a very disabling disease impairing quality of life and school performance, similar to subjects affected by rheumatological and oncological diseases.

Pain is usually described as uni- or bilateral throbbing of moderate to severe pain, often in the forehead. The pain usually peaks in 1–2 hours and lasts from 2 to 72 hours. Associated symptoms vary with age and gender [50]. During preschool, migraine patients complain of fatigue, vomiting and abdominal pain. In contrast, at school age, the associated symptoms are similar to those of migraine adults, such as photophobia, phonophobia and nausea. Aura precedes headaches more typically in adolescents [50].

Concerning aetiology, it is considered a disease of multifactorial nature. A genetic predisposition is recognized as most pediatric patients report positive family history. Conversely to TMD, which would realise both central and peripheral mechanisms, migraine is considered a brain pathology. The brain of migraine patients is genetically sensitive to neurochemical changes induced by exposure to numerous stimuli, such as drugs, diet, stress, or hormonal changes. Trigeminovascular activation led by these neurochemical changes results in neurogenic inflammation that, in turn, decreases the threshold of nucleus caudalis activation. The neurological mechanisms that can trigger OFP have been investigated, probably the

following. Secondary central nervous system consequences in headaches caused by transferred pain can perplex a clinician. The atypical orofacial pain sites in people with headaches may be referred to as pains because the trigeminal nerve's body part and the trigeminal nucleus's visceral part may converge. It is thought that a significant factor contributing to TMD and headache is involuntary nonfunctional tooth contact. In 60% of cases, TMD and headaches are related and coexist [51].

In tension-type headaches, pain is bilateral pressing tightness, and patients often refer to the sensation of wearing a helmet [52].

Pain intensity is mild to moderate and is directly related to age and stressors.

The headache usually appears in the school-age years [53], with an increasing prevalence throughout childhood. It reaches a peak around 11–13 years old, and after puberty [54], prevalence is much higher in females than males [54].

According to the International Headache Society's International Classification of Headache Disorders (ICHD-III), both can be classified as episodic or chronic. When headache occurs more than 15 days per month for at least three months, they are defined as chronic [55].

Finally, we should mention cluster headaches. It is a cause of severe unilateral head pain associated with autonomic manifestation. It is infrequent in children; however, some occasional cases were reported in the literature with a prevalence of 0.2% for males [56]. It is underrecognized, and often patients with headaches receive the correct diagnosis several years after the onset of the symptoms [28]. No data are available on the female gender. Symptoms, gender differences and treatment are similar to those of adults. Lacrimation is the most common symptom in children, followed by conjunctival injection.

4.3 Neuropathies

Trigeminal neuralgia, glossopharyngeal neuralgia, occipital neuralgia and Bell's palsy are neurological causes of facial pain in the child but are very rare. Neuralgia pain is characteristically intense and paroxysmal.

Only 1% of all cases of trigeminal neuralgia occur in children. In the literature, there are only a few reports. Three children described by Childs and colleagues complained of severe debilitating facial pain due to neurovascular compression of the V cranial nerve. Few cases of successful microvascular decompression in children were reported in the literature [57]. Secondary trigeminal neuralgia is also a rare entity. It could be the first manifestation of Multiple Sclerosis (especially in adolescents). In this case, it is more often bilateral. Tumours and vascular malformations are other possible causes of secondary trigeminal neuralgia [58–60]. According to estimates, typical trigeminal neuropathies (TGN) affects 1 in 25,000 people and is rare before the third decade, with 1% of cases occurring before the age of 20.

TGN rarely manifests in a child's early years. TGN has not been widely reported in the pediatric literature. According to Childs *et al.* [55], three youngsters experienced acute, incapacitating facial discomfort over two years due to neurovascular compression of their cranial nerves.

Glossopharyngeal neuralgia is a rare condition, even in

adults. Few reports were reported in children after amygdaloidectomy or tonsillectomy or with a Chiari 1 malformation [58]. Childs and colleagues said a case of glossopharyngeal neuralgia in which magnetic resonance angiography showed a prominent looping of the right posteroinferior cerebellar artery compressing the nerve at its exit from the medulla. Although glossopharyngeal neuropathies is a far more uncommon illness, it is thought that in the absence of a tumour, the idiopathic form may likewise be caused by vascular compression of the nerve as it exits the brain stem based on several anecdotal cases.

Occipital neuralgia was described in young patients with stenosis of the foramen magnum and, especially in adolescents, following traumatic injuries [59].

Bell's palsy is a possible cause of OFP in children and adolescents. It is more frequent than the described neuralgia, with an annual incidence of 3/100,000 during the first ten years and 10/100,000 between 10 and 20 years of age. Pain may be the first manifestation together with parasthesia homolaterally to the palsy. Treatment is symptomatic, and recovery is the rule in children [60]. The ignition theory partially addresses the unique characteristic of Trigeminal nerve (TN), that pain can start from a harmless trigger. In the context of these modifications, there will surely be central nervous system neuroplasticity, which will ultimately affect the clinical phenotype and therapeutic response.

According to surgical and cadaver studies, vascular contact is not always present in TN patients, which raises the possibility that different pathophysiologic mechanisms are at play.

4.4 OFP evaluation

Although children can recognize the multidimensional character of pain very early, perceiving the emotional components, the level of comprehension is lower than in adults. It should be considered that it is strictly dependent on communication abilities. A proper evaluation of the signs is a central aspect of diagnosing and monitoring the pathology's evolution. For example, in the case of TMD, children could have difficulties communicating the exact location and nature of pain. Therefore, several scales assess pain subjectively and depending on the complexity and number of questions, they can be more or less detailed.

However, it is essential to execute the evaluation by looking for the following characteristic of the pain:

- Frequency and duration.
- Location, ask the young patients to point the finger where they feel pain.
- Nature, factors that mitigate or intensify the pain, order of appearance of the symptoms and their evolution: this would be possible if the patients have sufficiently developed communication skills.
- Intensity.

Intensity evaluation in children could be very challenging due to their limited communication abilities and perception variability. Therefore, it is recommended to perform a self-evaluation and a hetero-evaluation.

Self-evaluation could be performed by the patients as well as by the parents. There are several instruments to evaluate

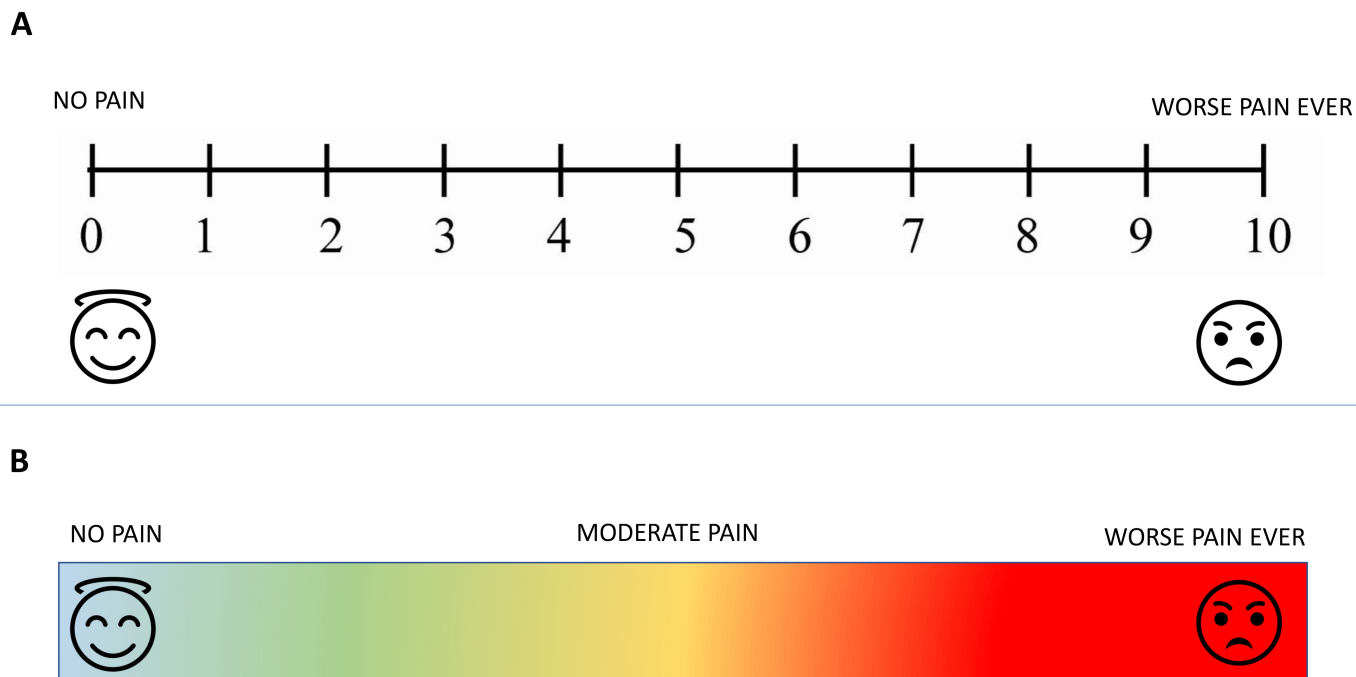


FIGURE 2. Visual Analogue Scale. (A) Visual Analog Scale. (B) Coloured Analogue Scale.

pain intensity. The Visual Analog Scale (VAS) consists of a horizontal line of 10 mm in length with the extremities that corresponds to “no pain” (left side) and “worst pain ever” (right side). Patients are invited to point to the spot on the line corresponding to the level of pain perceived. It is considered reliable for subjects aged five years or older.

The Verbal Numeric Scale [61] and the Coloured Analogue Scale [62] are similar to the VAS conceptually. In the former, the patients are invited to choose a number from 0 to 10 or from 0 to 100 to rate the pain. Concerning the latter, it is a rectangle with various colour intensities (Fig. 2).

A more recent innovative instrument is the Facial Pain Scale (FPS), in which the patients choose the one that better corresponds to their perception among six different facial expressions (from a smiling face to a tearful face). The Oucher scale is similar to the FPS and suitable for very young patients [61, 62].

The McGill Pain Questionnaire (MPQ) is more complex and articulate: here, the caregiver asks questions to the patient regarding their pain. It is structured in 3 parts: the first consist of a numerical and descriptive scale (from 1 to 5, from tolerable to unbearable) qualifying the pain. The second part consists of human shapes in both frontal and dorsal projection necessary for localizing the pain. The third part allows a description of the pain and encompasses several adjectives corresponding to the cognitive, sensory and affective components of pain [67]. This scale is more detailed and reliable.

A clinical examination, guided by the data collected through the scale, should always complete the evaluation.

The hetero-evaluation consists of observing child behaviours that could represent the presence of pain (Face, Legs, Activity, Crying, Controllability—FLACCs-scale). It could be performed by parents and healthcare professionals [63]. Therefore, the diagnosis must be made by combining

these subjective scales with a complete clinical evaluation of the patient. Numerous scales have been adopted. However, the VAS and personal scales are particularly significant in diagnosing OFP.

4.5 Treatment of OFP

The multidisciplinary approach is the cornerstone of OFP management in children and adolescents. A concurrent approach encompassing lifestyle modification, psychotherapy, physiotherapy and, lastly, pharmacotherapy is often needed to reach a satisfying outcome [64].

The first step is to acknowledge the patient and caregiver on the treatable nature of the condition and the importance of avoiding the identified triggering factors [65]. Further, often psychotherapy and especially cognitive-behavioural therapy have repeatedly been shown to be effective in the management of several pediatric pain conditions. A growing body of evidence supports that the psychological approach is a more effective treatment in the child than in adults [66].

Pharmacological approaches for pediatric OFP should be considered when behavioural changes and psychological interventions have failed or when the severity of the condition needs an immediate resolution.

The pharmacologic approach is based mainly on strategy deriving from studies on adults [67]. When TMD require pharmacological therapy, possible agents are muscle relaxers, anxiolytic, and non-steroidal anti-inflammatory drugs.

Acute pharmacological treatment for headaches is centred on using non-steroidal anti-inflammatory medications (NSAIDs), triptans and anti-nausea medications [63]. Preventive medicine includes tricyclic antidepressants (such as amitriptyline), anticonvulsants or beta-blockers [61].

Data regarding the pharmacologic treatment of neuropathies in the child are scarce. They are treated like adults. Possible

agents could be carbamazepine, lamotrigine, amitriptyline, and nortriptyline. They can also be used with refractory patients [67, 68].

4.6 The role of telemedicine in OFP management

Several studies have revealed that pain management in children and adolescents is often inadequate [69]. A recent study has shown that the main problem after hospital discharge is using treatment as needed instead of at scheduled intervals and more frequently than prescribed [67].

In this regard, the use of telemedicine could favour an improvement in pain management, allowing for ongoing discussion between parents and physicians [70]. Although this approach was already established, the COVID-19 pandemic has severely implemented and improved the use of telemedicine in the management of patients affected by chronic disease [64, 65], among other OFPs. In this view, telemedicine allows for continuing pain management, avoiding the face-to-face examination that puts a probability of infection for both patients and health professionals [67].

Telemedicine can be synchronous (real-time interaction) or asynchronous (store and forward approach). Telemedicine represents a valid option to obtain an interdisciplinary assessment, considering the relevance of collecting a detailed patient's medical history together with the need for a multidisciplinary approach. Indeed, telemedicine allows for providing education, psychological support, and self-management strategies without the need for a face-to-face visit. A recent article provides a detailed example of the potential role of telemedicine in the management of Orofacial Pain in a subject Affected by Eagle Syndrome [70]. The authors mentioned that the patient found the unique but welcome solution of the team meeting virtually from the convenience of her home, having the time and means to describe her condition, and receiving a viable treatment plan. However, these considerations are not generalizable as they result from a single case. Other studies on larger samples of pediatric patients affected by OFP are needed to ascertain the feasibility, acceptability, and effectiveness of telemedicine in managing these little patients.

4.7 Quality assessment and risk of bias

The risk of bias among the examined studies was calculated using RoB 2 and shown in Fig. 3. Regarding randomization, 50% of the studies guaranteed low bias risk. Only 30% of research correctly ruled out a performance bias, 20% of included trials adequately left out bias in selecting the reported outcomes, and only 20% of studies disclosed all outcome data. Only three out of six studies revealed a low probability of bias.

5. Conclusions

In conclusion, temporomandibular disorders, neuropathies and headaches are complex, multifactorial clinical conditions where the pain is the most prominent symptom. The appropriate diagnosis followed by a proper treatment approach, starting with cognitive therapy followed by a pharmacological approach, is necessary. To treat and manage

pain, an adequate definition of the pain and a precise diagnosis of the underlying pathology is indispensable. Concerning the limited communication abilities and the variability in feelings and perceptions of a child, this is not always easy. Several scales are available to overcome these limitations. Treatment is founded on a multidisciplinary approach. Lifestyle changes and psychological processes could be curative. However, some patients need pharmacotherapy. The pharmacological approach is based mainly on findings deriving from studies on adults. Regarding the inadequate treatment of pain after hospital discharge due to the difficulty of following the scheduled intervals prescribed, remote monitoring through telemedicine tools could be a solution in the future.

ABBREVIATIONS

OFP, Orofacial Pain; TMD, Temporomandibular Disorders; DC/TMD, Diagnostic Criteria for Temporomandibular Disorders; TMJ, Temporomandibular Joint; ICHD-III, International Headache Society's International Classification of Headache Disorders; VAS, Visual Analog Scale; FPS, Facial Pain Scale; MPQ, McGill Pain Questionnaire; FLACC, Face, Legs, Activity, Crying, Controllability-Scale; TTH, Tension-Type Headache; OFP, Orofacial Pain; TN, Trigeminal nerve; CT, Computed Tomography; TMJ: temporomandibular joint; TMD, Temporomandibular Disorders; DC/TMD, Diagnostic Criteria For Temporomandibular disorders; TC, Computed tomography; MRI, Magnetic Resonance Imaging; RDC/TMD, Research and Diagnostic Criteria for Temporomandibular Disorders.

AVAILABILITY OF DATA AND MATERIALS

Not applicable.

AUTHOR CONTRIBUTIONS

GM and MMM—designed the research study. RF and GC—performed the research. MC, RF and LF—analyzed the data. GM, GC and MMM—wrote the manuscript. All authors contributed to editorial changes in the manuscript. All authors read and approved the final manuscript.

ETHICS APPROVAL AND CONSENT TO PARTICIPATE

Not applicable.

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FIGURE 3. Risk of bias.

CONFLICT OF INTEREST

The authors declare no conflict of interest. Giuseppe Minervini is serving as one of the Editorial Board members of this journal. We declare that Giuseppe Minervini had no involvement in the peer review of this article and has no access to information regarding its peer review. Full responsibility for the editorial process for this article was delegated to GAF.

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