Fibromyalgia is a syndrome characterized by chronic widespread pain, stiffness, nonrestorative sleep, fatigue, and comorbid conditions. Recognition of the condition and its associated medications and challenges, along with knowledge of treatment modifications and precautions in drug prescription, can ensure safe and effective delivery of oral health care in fibromyalgia patients. The ever-evolving research into the condition makes it necessary for the oral health care provider to be informed about the current state of the literature and treatment standards regarding the management of fibromyalgia patients. This article reviews the epidemiology, etiology, pathophysiology, and clinical presentation of fibromyalgia, as well as therapeutic advances. Also highlighted are issues that are important to the oral health care provider, including orofacial manifestations and oral health care considerations for patients with fibromyalgia. J Oral Facial Pain Headache 2014;28:107–118. doi: 10.11607/ofph.1220

Key words: dental considerations, fibromyalgia, medical management, oral health care

Fibromyalgia is a disorder characterized by widespread musculoskeletal pain and tenderness, stiffness, sleep disorder, fatigue, cognitive/memory problems, insomnia, and psychological distress. Sir William Gowers coined the term “fibrositis” in 1904.1 The current concept of fibromyalgia was established by Smythe and Moldofsky in 1977.1 The term fibromyalgia derives from new Latin (fibro meaning fibrous tissues) and Greek (myo meaning muscle and algos meaning pain). Thus, the term literally means “muscle and connective tissue pain.” It has a prevalence of about 2% to 4%2 and is more common in adult women than in men, with a prevalence of 3.4% vs 0.5%, respectively.3 The prevalence of fibromyalgia increases with age, with the highest values observed between 60 and 79 years of age.4 The disorder is an enigma to the oral health care provider due to its complex presentation and overlap with multiple orofacial disorders presenting with similar symptoms. Newer developments in its pathophysiology, treatment, and diagnostic criteria make an update on the topic of paramount importance to the oral health care provider. This topical review stems from searches of several databases (Embase, Medline, Psychinfo, PubMed, and the Cochrane Library) within a 20-year timeframe from 1993 to July 2013. All review articles and randomized controlled trials were included in the review process. The aim of this topical review is to provide direction for optimal orofacial care of patients with fibromyalgia in accord with best clinical practice.

Diagnosis

There is no single test that can fully diagnose fibromyalgia, and there is debate over what should be considered essential diagnostic criteria and whether an objective diagnosis is possible. In most cases, patients with fibromyalgia symptoms may also have laboratory test results that appear normal, and many of their symptoms may mimic those of other rheumatic conditions such as arthritis or osteoporosis. In general,
most clinicians diagnose a patient via differential diagnosis based on the patient’s symptoms, sex, age, geographic location, medical history, and other factors. The American College of Rheumatology’s 1990 diagnostic criteria for fibromyalgia were revised (and provisionally accepted in May 2010) in order to develop simple, practical criteria for the clinical diagnosis of fibromyalgia that are suitable for use in primary and specialty care (and do not require a tender-point examination) and to provide a severity scale for characteristic fibromyalgia symptoms. The Canadian Fibromyalgia Guidelines Committee (CFGC) issued comprehensive guidelines for the diagnosis of fibromyalgia (endorsed by the Canadian Pain Society and Canadian Rheumatology Association) to include patients who have diffuse body pain that has been present for at least 3 months and who may also have symptoms of fatigue, sleep disturbance, cognitive changes, mood disorder, and other somatic symptoms to variable degree, and whose symptoms cannot be explained by some other illness.

The primary modes of functional imaging that have been used in fibromyalgia include functional magnetic resonance imaging (fMRI), single photon emission computed tomography (SPECT), positron emission tomography (PET), and proton magnetic resonance spectroscopy (H-MRS). Augmented pain processing has been observed by fMRI at a lower pain stimulus in fibromyalgia patients than that required in controls. SPECT scans in fibromyalgia patients have shown a decrease in cerebral blood flow in brain structures that modulate pain perception. A recent study using voxel-based morphometric analysis of MRI brain images showed that fibromyalgia patients had decreased grey matter (atrophy) in areas involved in stress and pain processing as well as in areas consistent with cognitive difficulties. There was also decreased total brain volume compared with controls. Neuroimaging has demonstrated cerebral abnormalities and increased neural recruitment during cognitive tasks in fibromyalgia patients.

### Signs and Symptoms

According to the criteria published in 1990 by the American College of Rheumatology, fibromyalgia is defined as widespread pain of at least 3 months duration and pain on palpation of at least 11 of 18 specific tender sites on the body (Fig 1). Pain, fatigue, and sleep disturbance are observed in all patients. Additional features of fibromyalgia include stiffness, depression, anxiety, exercise intolerance, balance problems, low-back pain, skin tenderness, postexercise pain, painful menstrual periods, irritable bowel syndrome, cognitive disturbances, overactive bladder syndrome or interstitial cystitis, tension or migraine headaches, dizziness, fluid retention, paresthesias, restless legs, Raynaud phenomenon, and mood disturbances. Patients can be highly sensitive to cold temperatures, noise, odors, and light, and this may lead to sensory overload. Sjögren syndrome presents many features that overlap those found in fibromyalgia, such as dry skin, dry mouth, joint and muscle pain, swollen salivary glands, chronic fatigue, Raynaud phenomenon, and peripheral neuropathy.

Oral manifestations include xerostomia, oral ulceration, glossodynia, dysgeusia, dysphagia, temporomandibular disorders (TMD), and other types of orofacial pain.

### Pathophysiology

The exact cause of fibromyalgia is as yet unknown. However, emerging insights into the pathophysiology of fibromyalgia suggest that it is a disorder of central sensory processing but often comprising a genetic predisposition and exposure to stressors of a physical or psychologic nature. Environmental “stressors” temporally associated with the development of either fibromyalgia or chronic fatigue syndrome include physical trauma, certain infections such as hepatitis C, Epstein-Barr virus, parvovirus, Lyme disease, and emotional stress. In part, the augmented experience of pain in individuals with fibromyalgia is thought to be associated with either (a) excessive spinal or brainstem facilitation ofafferent nociceptive signaling to higher brain pain-processing regions or (b) deficiencies in descending influences from higher brain regions responsible for dampening nociceptive transmission. These factors are also usually associated with disorders that co-occur or overlap with fibromyalgia, such as major depressive disorder, irritable bowel syndrome, and TMD.

Chronic widespread pain and a lower pain threshold than healthy people are hallmarks of fibromyalgia. Alloodynia (a normally nonpainful stimulus perceived as pain) and hyperalgesia (a painful stimulus perceived as even more painful) are common responses in these patients. Central sensitization may underlie the amplification of pain and other sensory inputs (noise, odors, light) in fibromyalgia. This makes a fibromyalgia patient hyperreact to a subsequent equally painful stimulus. The central sensitization may be a result of: (1) activation of N-methyl-D-aspartic acid (NMDA) receptors in the dorsal horn of the spinal cord or medulla after repeated neuronal depolarization; (2) activation of glial cells surrounding nociceptive neurons within the central nervous system (CNS) as a result of the release of various pro-nociceptive cytokines (nitric...
oxide, fractalkine, adenosine triphosphate [ATP], and prostaglandins); (3) deficiency of inhibitory nociceptive transmission by descending serotonergic and noradrenergic projections from the brainstem to the spinal cord or medulla; (4) neurochemical imbalances, such as increased substance P and nerve growth factor; or (5) dysfunctional hypothalamic-pituitary-adrenal (HPA) axis, resulting in low morning serum cortisol levels and reduced physiologic response to stress.

Sleep deprivation is observed in up to 90% of patients. Stage 4 sleep (the deepest sleep) is markedly deficient in fibromyalgia patients, and alpha-wave activity is overrepresented. Repeated nights of disturbed sleep can cause extreme fatigue and can exacerbate pain. Cognitive dysfunction, commonly referred to by patients as “fibro fog,” contributes to memory difficulties and impaired cognition.

However, the current major hypothesis implicates aberrations in the stress axis (related to hyporesponsive HPA and autonomic nervous system) as contributing to enhanced pain due to central deregulation and exercise intolerability associated with fibromyalgia. The alteration of physiologic responses required for effective stress management (eg, increases in blood pressure) and pain inhibition via diminished production of growth hormone and insulin-like growth factor (IGF-1) further contribute to the symptoms.

Recent studies have begun to identify specific genetic polymorphisms that are associated with a higher risk of developing fibromyalgia. To date, the serotonin 5-HT2A receptor polymorphism T/T phenotype, serotonin transporter, dopamine 4 receptor, and catecholamine o-methyl transferase (COMT) polymorphisms have all been noted to be in higher frequency in fibromyalgia.

**Treatment**

The treatment of fibromyalgia is symptom based, the objective being to alleviate pain, restore sleep, and improve physical status. In general, integrated treatment plans that incorporate medication, patient education, aerobic exercise, and cognitive-behavioral therapy have been shown to be effective in alleviating pain and other fibromyalgia-related symptoms.

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**Fig 1** Common tender points in fibromyalgia are located at the lower neck in the front edge of the upper breast, muscle attachments to the lateral epicondyle at the elbow, medial fat pad of the knee, muscle insertion at the occiput, posterior neck and shoulder, muscle attachments at the upper medial scapula, upper outer buttock, and hip bone. Image reprinted with permission from Medscape Reference (http://emedicine.medscape.com/), 2014, available at: http://emedicine.medscape/article/329838-overview.
Pharmacologic Treatment

The American Pain Society in 2005 produced comprehensive guidelines for patient evaluation and management. The European League Against Rheumatism issued updated treatment guidelines in 2008 (Fig 2). Current pharmacologic treatment guidelines recommend tricyclic antidepressants (TCAs), analgesics, muscle relaxants, benzodiazepines, nonsteroidal anti-inflammatory drugs (NSAIDs), hypnotics, corticosteroids, opiates, and soft tissue injections of topical anesthetics. Most of these have demonstrated effectiveness in reducing pain, but few have been shown to be effective in improving the other major symptoms of fibromyalgia, such as fatigue, sleep disturbances, and mood abnormalities.

Antidepressants such as TCAs are the most effective medications for fibromyalgia treatment. Most TCAs (amitriptyline, nortriptyline, imipramine) increase the concentrations of serotonin (5-HT) and/or norepinephrine by directly blocking their respective reuptake. The limitations of TCAs are mostly due to their relatively narrow therapeutic index and poor tolerability. Better-tolerated selective serotonin reuptake inhibitors (SSRIs), such as fluoxetine, citalopram, and sertraline, have been shown to provide inconsistent benefit to fibromyalgia patients. SSRIs are also much more expensive than TCAs. Serotonin and norepinephrine reuptake inhibitors (SNRIs), such as venlafaxine, duloxetine, and milnacipran, tend to be better tolerated than older TCAs. Duloxetine and

Fig 2  Recommended flow diagram for pain management of fibromyalgia. Extrapolated from the European League Against Rheumatism published guidelines for fibromyalgia. Reproduced from Carville et al, © 2008, with permission of BMJ Publishing Group.
milnacipran are two SNRIs that are approved by the US Food and Drug Administration (FDA) for the treatment of fibromyalgia (in 2008 and 2009, respectively). Side effects include headache, nausea, tachycardia, hypertension and hypotension, increased risk for bleeding, and suicidality in at-risk patients. All categories of antidepressant medications, including TCAs, SSRIs, and SNRIs, may be used for the treatment of pain and other symptoms in patients with fibromyalgia [Level 1, Grade A], with choice driven by available evidence for efficacy, physician knowledge, patient characteristics, and attention to side effect profile [Level 5, Consensus].

Anticonvulsants such as gabapentin and pregabalin have been used in the treatment of fibromyalgia. Their mechanism of action likely involves reducing excitatory neurotransmitter release. Pregabalin was the first drug approved by the FDA for the management of fibromyalgia. The CFGC recommends that anticonvulsant medication use should be explained as having pain-modulating properties, and treatment should begin with the lowest possible dose followed by up-titrations, with attention to adverse events [Level 1, Grade A].

Tramadol is a weak mu-opioid receptor agonist and an inhibitor of serotonin and noradrenaline reuptake. Studies have indicated that its use can result in significantly improved pain relief and physical function. However, tramadol use has been associated with increased abuse, dependency, and presence of classic opioid withdrawal symptoms. Conventional opioid analgesics are generally not recommended in the management of fibromyalgia. The CFGC has recommended that a trial of opioids, beginning with the lowest possible dose followed by up-titrations, with attention to adverse events [Level 1, Grade A].

Newer Pharmacologic Agents. Sedative hypnotics, such as sodium oxybate (sodium salt of gamma-hydroxybutyrate, precursor of γ-amino butyric acid), used for the treatment of cataplexy and narcolepsy, have been also evaluated in fibromyalgia treatment due to sleep disturbances often being observed in fibromyalgia patients. However, a high risk of abuse, lethality at supratherapeutic doses or risk of hypnotic use, make the usefulness of these drugs questionable. FDA approval for treatment of fibromyalgia was denied due to concerns of abuse. It is conceivable that dopamine agonists such as pramipexole and tizanidine may possess beneficial effects for patients with fibromyalgia and coexisting restless leg syndrome or spasticity, respectively. Pramipexole may improve both pain and sleep in fibromyalgia patients. Tizanidine is a centrally acting alpha-2-adrenergic agonist that may possess muscle-relieving effects and reduce substance P in the cerebrospinal fluid in patients with spasticity. However, numerous side effects, including the onset of impulse control disorders like compulsive gambling and shopping, have led to concern about this drug. There is some evidence of functional growth hormone deficiency, expressed as low insulin-like growth factor 1 (IGF-1) serum levels, in a subset of fibromyalgia patients. Unfortunately, while growth hormone therapy would appear to offer this subgroup of patients some symptomatic improvement, financial considerations limit the viability of growth hormone as a long-term therapy in this population.

Newer pharmacologic approaches for fibromyalgia treatment, including 5-HT3 antagonists (tropisetron) and NMDA antagonists (dextromethorphan), have shown some promising results. However, more studies are needed before their use can be considered for fibromyalgia. The CFGC states that only pregabalin and duloxetine have Health Canada approval for the management of fibromyalgia symptoms and that all other pharmacologic treatments constitute "off label use" [Level 5, Consensus].

Nonpharmacologic Methods

Nonpharmacologic methods for fibromyalgia treatment include patient education or psychoeducation that aims to increase the patient’s understanding of the complex nature of the interaction between neurobiologic processes—behaviors such as sleep and/or activity levels—and symptoms. The CFGC suggests that psychologic evaluation and/or counseling may be helpful for persons with fibromyalgia in view of the associated psychologic distress [Level 5, Consensus]. Other modalities to address attitudes and psychologic status include motivational interviewing or group sessions.

Cognitive-behavioral therapy combines interventions from both cognitive and behavioral therapies. Cognitive therapy is based on the premise that modifying maladaptive thoughts results in changes in both affect and behavior. Behavioral therapy is rooted in the theory that inner states (thoughts and feelings) are less important than the use of operant behavioral change techniques to increase adaptive behavior through positive and negative reinforcement and to extinguish maladaptive behavior by using punishment. The CFGC states that cognitive-behavioral therapy even for a short time is useful and can help reduce the fear of pain and fear of activity [Level 1, Grade A].

Relaxation techniques likely to be helpful for fibromyalgia symptoms include, but are not limited to, progressive muscle relaxation, autogenic training, guided imagery, and meditation. There is evidence that relaxation techniques can provide effective adjunctive...
treatment for fibromyalgia. Heart rate variability biofeedback has emerged as a potential useful treatment for fibromyalgia based on reasonably good evidence that autonomic nervous system functioning in some fibromyalgia patients can be characterized by elevated sympathetic tone, poor parasympathetic tone, and an abnormal 24-hour autonomic cycle.

Exercise has overall benefits on global well-being, physical function, and pain, and it is currently recommended as the first step of a multimodal treatment strategy. Aerobic, strengthening, or water exercise may be done at home or in group programs. In a Cochrane review of 16 trials, 7 of which were high quality, supervised aerobic exercise improved physical capacity and fibromyalgia symptoms. The evidence for the effect of strengthening exercises is less clear, as studies are rated as low quality. Water exercise alone or combined with education is associated with improvements in both physical and emotional aspects of fibromyalgia, but there is uncertainty as to whether the benefit is derived from the aerobic exercise component that almost always accompanies water exercise. A Pilates exercise program over a 12-week period improved pain compared to a relaxation program, but this effect was not sustained due to poor adherence to treatment. Tai chi is an exercise activity that combines both a physical and mental component and is ideally suited to persons with fibromyalgia, with improved function and quality of life reported. When traditional yoga was compared to yoga combined with a yoga touch technique (Tui Na), improvement was more sustained in the yoga-only group. Although fibromyalgia patients often report poor exercise capacity, reduced cardiorespiratory fitness has been found to be similar to that of controls, suggesting that fibromyalgia patients overscore their perception of exertion and that a report of subjective muscle pain may be a barrier to optimal exercise activity. In the absence of a single exercise program outperforming others, fibromyalgia patients should be encouraged to choose an activity, either land or water based, that is enjoyable, easy to follow, convenient, and within their budget to improve their adherence. The CFGC recommends that persons with fibromyalgia should participate in a graduated exercise program of their choosing to obtain global health benefits and probable effects on fibromyalgia symptoms.

Fibromyalgia patients overwhelmingly have sought other forms of complementary and alternative medicine (CAM) interventions. Very little scientific evidence exists for the efficacy of such approaches. However, a few treatments have been investigated. Table 1 lists the approaches that have been studied in the treatment of fibromyalgia. The CFGC recommends that patients should be informed that there is currently insufficient evidence to support the recommendation of CAM treatments for the management of fibromyalgia symptoms, as they have mostly not been adequately evaluated for their benefit [Level 1, Grade A].

Orofacial Manifestations

Orofacial symptoms of fibromyalgia are characterized by heightened pain perception, including widespread hyperalgesia (in particular to deep-pressure stimuli), allodynia, muscle pain, enhanced temporal summation, and reduced pain-inhibiting effects of heterotopic noxious stimulation. The pathophysiologic mechanism involved in the orofacial region is likely the same as that in other parts of the body.

Altered neuromuscular control in the masticatory muscles may be correlated with perceived facial pain in patients with fibromyalgia. The fibromyalgia patient may have various masticatory muscles affected by myofascial tender points (MTPs) in such a manner as to change the occlusion, forcing the malleable to close unnaturally. TMD may coexist in the fibromyalgia patient. It is thought that fibromyalgia is probably involved in the onset and persistence of clinically significant TMD. However, it is important to distinguish the diagnostic subtypes of TMD that may coexist with fibromyalgia. Masticatory myalgia and temporomandibular joint (TMJ) pain may be related to fibromyalgia, while internal derangements of the TMJ are not likely related to fibromyalgia.

Unexplained toothache might be caused by several MTPs, chiefly in the temporalis, digastric, and masseter muscles. Pain may also be referred to the teeth from various MTPs in the upper body. Usually, MTP-induced toothache is intermittent. Each MTP seems to have its own particular toothache pattern. For example, anterior digastric MTPs may refer pain to the mandibular central incisors, and the resulting tooth pain is often mistaken for pulpitis. Unfortunately, many unnecessary endodontic procedures are performed in an attempt to treat the patient’s tooth pain, only to have the pain continue after the pulp of the tooth is gone. Anterior digastric MTPs may also cause difficulty swallowing.

Problems with swallowing, chewing pain, bruxism, jaw clicking, TMD, soreness inside the throat, and excessive saliva secretion, sinusitis-like pain, drooling in sleep, and choking on saliva have been suggested to come from a medial pterygoid MTP, which is often overlooked.

Popping or clicking of the jaw, TMD, and jaw pain and dysfunction may be associated with one or more masseter MTPs, although trapezius and temporalis MTPs are often involved.
especially in patients with complete dentures. Due to the amplification of pain and the alteration in the usual difficulty adjusting to dentures, probably would feel no pain at all. There may be more than patients with fibromyalgia, often when other patients be extremely painful and the pain may last longer in to hurt for more than a week. Endodontic therapy may muscles from the pain of cleaning may cause the jaw and probable analgesic overuse headache are re - reported by 63% and 8% of fibromyalgia patients, respectively.101

Table 1 Complementary and Alternative Medicine Interventions in Fibromyalgia

<table>
<thead>
<tr>
<th>Modality/Medicine/Supplement</th>
<th>Outcomes and adverse effects</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Massage</td>
<td>Decrease in pain and improved quality of life</td>
</tr>
<tr>
<td>2. Acupuncture</td>
<td>Improvement in fibromyalgia symptoms</td>
</tr>
<tr>
<td>3. Hydrotherapy</td>
<td>Positive effect on pain, health status and, tender point count</td>
</tr>
<tr>
<td>4. Qigong therapy</td>
<td>Improvement in all fibromyalgia symptoms</td>
</tr>
<tr>
<td>5. Phytotherotherapy</td>
<td>Improvement in all fibromyalgia symptoms</td>
</tr>
<tr>
<td>6. Craniosacral therapy</td>
<td>Improvement in anxiety, depression, and quality of life</td>
</tr>
<tr>
<td>7. Noninvasive brain stimulus therapies</td>
<td>Improvement in anxiety, depression, pain, and other mental functions</td>
</tr>
<tr>
<td>8. Hyperbaric oxygen therapy</td>
<td>Improvement in all parameters in fibromyalgia; oxygen toxicity possible adverse effect</td>
</tr>
<tr>
<td>9. D-ribose</td>
<td>Improvement in energy, sleep, mental clarity, pain intensity, and well being; no adverse effects</td>
</tr>
<tr>
<td>10. Chlorella pyrenoidosa</td>
<td>Relieves symptoms, normalizes functions, and improves quality of life; no adverse effects</td>
</tr>
<tr>
<td>11. Acetyl-L carnitine</td>
<td>Reduction in number of tender points, depression, and musculo-skeletal pain; no adverse effects</td>
</tr>
<tr>
<td>12. Melatonin</td>
<td>Decrease in tender-point count, severity of pain, improved sleep; no adverse effects</td>
</tr>
<tr>
<td>13. Anthocyanidins</td>
<td>Significant improvement in sleep disturbance; adverse effects were indigestion, nausea, and sinusitis</td>
</tr>
<tr>
<td>14. Capsaicin topical applica-</td>
<td>Significant improvement in muscle tenderness; adverse effect was burning on skin</td>
</tr>
<tr>
<td>15. Soy dietary supplement</td>
<td>No significant improvement; no adverse effects</td>
</tr>
<tr>
<td>16. S-adenosylmethionine</td>
<td>Significant improvements in fatigue, pain, morning stiffness, mood, and clinical disease activity; adverse effects were dizziness and stomach upset</td>
</tr>
<tr>
<td>17. Homeopathy (R toxico-</td>
<td>Significant improvement in tenderness, pain, sleep, tender-point count, depression, and quality of life; adverse effect was allergic reactions</td>
</tr>
<tr>
<td>19. Magnesium citrate</td>
<td>Improved tender-point score, depression, intensity of symptoms</td>
</tr>
<tr>
<td>20. DHEA (dehydroepiandrosterone)</td>
<td>No significant improvement in any parameter; adverse effects included greasy skin, increased growth of body hair, and acne</td>
</tr>
<tr>
<td>21. Cannabinoids (nabilone)</td>
<td>Significant improvement in pain and quality of life; adverse effects were dizziness, dry mouth, ataxia, and vertigo</td>
</tr>
</tbody>
</table>

A prickling “electric” face pain over the jaw area could conceivably be caused by compression of the buccal nerve by the two parts of the lateral pterygoid muscle in chronic bruxers. This sensation is frequently experienced upon waking in the morning or during times of intense stress. This symptom may also involve platysma MTPs.

Routine oral prophylaxis may be severely painful for fibromyalgia patients because of peripheral or central sensitization that amplifies pain. Tense muscles from the pain of cleaning may cause the jaw to hurt for more than a week. Endodontic therapy may be extremely painful and the pain may last longer in patients with fibromyalgia, often when other patients would feel no pain at all. There may be more than the usual difficulty adjusting to dentures, probably due to the amplification of pain and the alteration in function of the muscles of mastication while chewing, especially in patients with complete dentures.

Nonspecific headaches are reported by fibromyalgia patients in 53% to 82% of cases. Migraine and probable analgesic overuse headache are reported by 63% and 8% of fibromyalgia patients, respectively.

Xerostomia is a common complaint in fibromyalgia patients. It is yet to be determined whether this is a true oral manifestation or represents a somatization symptom. Multiple coexisting comorbid conditions (hepatitis C infection), medications (antidepressants), and autonomia have been thought to be possible causes. This may result in increased dental caries, difficulty in chewing and swallowing, and candidiasis.

Glossodynia (oral burning) is observed in a third of all fibromyalgia patients and is considered to be a result of central sensitization manifesting as hyperalgesia and allodynia. In addition, xerogenic medications (such as antidepressants, hypnotics, muscle relaxants, and anticonvulsants used to treat fibromyalgia) and hormone replacement therapy often lead to glossodynia.97

Dysgeusia is reported in 34% of patients with fibromyalgia. This may result from medications used to treat fibromyalgia, such as amitriptyline, flouxetine, venlafaxine, cyclobenzaprine, and zopiclone, or may represent a somatization symptom.
It is of paramount importance for the oral health care provider to be aware that coexistent TMD and fibromyalgia symptoms may lead to, or be the consequence of, centrally mediated alterations in pain perception, and so routine treatments for TMD may therefore not prove beneficial. The oral health care provider must involve a team of professionals, such as a physician, psychologist, and physical therapist, to treat the whole spectrum of the patient’s complaints. Occlusal splints have not shown benefits for the treatment of myofascial pain in patients with widespread pain, while full-body tactile stimulation (massage) has shown modest success in one study. Various medications used for fibromyalgia warrant careful monitoring by the oral health care provider for adverse orofacial effects. Oral ulceration and lichenoid reactions are associated with chronic NSAID use. SSRIs (eg, sertraline) have been reported to induce oral ulcerations and bruxism. These cases of bruxism have been successfully treated with gabapentin and buspirone. Pregabalin may cause dry mouth and facial angioedema. Provision of dental care for fibromyalgia patients usually requires little, if any, modifications from routine dental care (Table 2). However, care should be taken to understand the coexisting symptoms, drug interactions with commonly used dental medications, and oral lesions. Caution is to be exercised while prescribing macrolide antibiotics such as erythromycin and clarithromycin, as they may interact with the cytochrome P-450 enzyme system and increase therapeutic levels of other medications in fibromyalgia patients. Opioid analgesics may increase overall patient sedation in patients on TCAs. NSAIDs may increase the risk for prolonged bleeding in patients on SSRIs. Local anesthetics containing epinephrine have been reported to cause a hypertensive crisis in patients taking TCAs (especially amitriptyline).
Table 3  Drug Interactions for Patients with Fibromyalgia

<table>
<thead>
<tr>
<th>Fibromyalgia medications</th>
<th>Dental drugs and interactions</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Analgesics</strong></td>
<td></td>
</tr>
<tr>
<td>NSAIDs</td>
<td>Reversible decrease in platelet aggregation leading to prolonged bleeding(^{117})</td>
</tr>
<tr>
<td>Tramadol</td>
<td>Increased seizure potential and neuroexcitatory effect with cyclobenzaprine(^{120})</td>
</tr>
<tr>
<td><strong>Muscle relaxants</strong></td>
<td></td>
</tr>
<tr>
<td>Cyclobenzaprine</td>
<td>Increased blood levels/effects with ketoconazole(^{21})</td>
</tr>
<tr>
<td>Tizanidine</td>
<td>Increased CNS depression with CNS depressants such as midazolam and opioids(^{22})</td>
</tr>
<tr>
<td><strong>Anticonvulsants</strong></td>
<td></td>
</tr>
<tr>
<td>Pregabalin</td>
<td>Additive CNS depression with other CNS depressants(^{39})</td>
</tr>
<tr>
<td><strong>Sedative hypnotics</strong></td>
<td></td>
</tr>
<tr>
<td>Zopiclone and zolpidem</td>
<td>Increased levels with azole antifungals, NSAIDs, clarithromycin, diclofenac, doxycycline, and erythromycin(^{23})</td>
</tr>
<tr>
<td>Sodium oxybate</td>
<td>Increased CNS depression with other CNS depressants such as midazolam and opioids(^{24})</td>
</tr>
<tr>
<td><strong>TCAs</strong></td>
<td></td>
</tr>
<tr>
<td>Amitriptyline</td>
<td>Increased risk of hypertensive crisis with adrenaline-containing local anesthetics(^{25})</td>
</tr>
<tr>
<td></td>
<td>Increased sedative effects with other CNS depressants such as midazolam and opioids(^{26})</td>
</tr>
<tr>
<td><strong>SSRIs</strong></td>
<td></td>
</tr>
<tr>
<td>Fluoxetine and sertraline</td>
<td>Increased effect/toxicity of diazepam(^{109})</td>
</tr>
<tr>
<td></td>
<td>Increased risk of bleeding with NSAIDs and aspirin(^{117})</td>
</tr>
<tr>
<td></td>
<td>Increased effect with fluconazole, ketoconazole, and NSAIDs</td>
</tr>
<tr>
<td>Citalopram</td>
<td>Increased levels/effects with fluconazole, omeprazole, clarithromycin, diclofenac, and erythromycin</td>
</tr>
<tr>
<td></td>
<td>Increased risk of Serotonin syndrome with tramadol(^{27})</td>
</tr>
<tr>
<td></td>
<td>Increased risk of bleeding with NSAIDs and aspirin(^{117})</td>
</tr>
<tr>
<td>Paroxetine</td>
<td>Increased risk of Serotonin syndrome with tramadol</td>
</tr>
<tr>
<td></td>
<td>Increased risk of bleeding with NSAIDs and aspirin(^{117})</td>
</tr>
<tr>
<td><strong>SNRIs</strong></td>
<td></td>
</tr>
<tr>
<td>Venlafaxime</td>
<td>Increased risk of hypertensive crisis with adrenaline-containing local anesthetics(^{28})</td>
</tr>
<tr>
<td></td>
<td>Increased levels/effects with fluconazole, omeprazole, clarithromycin, diclofenac, and erythromycin</td>
</tr>
<tr>
<td>Duloxetine</td>
<td>Increased risk of hypertensive crisis with adrenaline-containing local anesthetics(^{28})</td>
</tr>
<tr>
<td></td>
<td>Increased risk of Serotonin syndrome with tramadol(^{23})</td>
</tr>
<tr>
<td></td>
<td>Increased levels/effects with ketoconazole</td>
</tr>
</tbody>
</table>

CNS, central nervous system; NSAIDs, nonsteroidal anti-inflammatory drugs; TCAs, tricyclic antidepressants; SSRIs, selective serotonin reuptake inhibitors; SNRIs, serotonin and norepinephrine reuptake inhibitors.

However, some studies have cast doubts over such interactions and have suggested the occurrence to be merely coincidental.\(^{119}\) Other possible drug interactions in fibromyalgia patients presenting for dental care are highlighted in Table 3.

Conclusions

Fibromyalgia is a complex condition that presents multiple facets to warrant a multidisciplinary approach to management. Oral care providers may be the first to identify initial signs and symptoms of the disease or be called upon to treat a diagnosed case of fibromyalgia. A complete understanding of the disease and its orofacial considerations may assist them in better providing an acceptable level of care to such patients.

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