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Temporomandibular Disorders

A Translational Approach
From Basic Science to
Clinical Applicability

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ISBN 978-3-319-57245-1 ISBN 978-3-319-57247-5 (eBook)
<https://doi.org/10.1007/978-3-319-57247-5>

Library of Congress Control Number: 2017951906

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Printed on acid-free paper

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The registered company is Springer International Publishing AG
The registered company address is: Gewerbestrasse 11, 6330 Cham, Switzerland

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Abstract

Among the most common pain-related temporomandibular disorders (TMDs) are disorders arising from muscular sources. Lacking a single etiology, treatment for TMD and myofascial pain (MP) is directed toward identifying and treating the source of the patient's pain. Successful management of chronic TMD problems often requires a multidisciplinary approach utilizing a team of professionals working in conjunction with the individual patient. Evidence-based conservative treatment options to reduce the signs and symptoms of TMD, with special attention on MP, will be discussed in this chapter. These include patient education and biobehavioral strategies, therapeutic exercises, manual procedures, trigger point dry needling and therapeutic modalities offered by physical therapists, pharmacotherapy, and evidence-based oral appliances offered by dentists. In addition, the role of occlusion and occlusal oriented treatments will be discussed.

8.1 Introduction

Among the most common pain-related temporomandibular disorders (TMDs) are disorders arising from muscular sources. Myalgia is a general term used to describe pain of muscular origin. The terms "myalgia," "muscle pain," "myofascial pain," "myofascial pain with referral," and myofascial trigger points (MTrPs) are often used interchangeably, but throughout this chapter, unless stated otherwise, these will collectively be referred to as myofascial pain (MP). Symptoms associated with masticatory MP that are modified by jaw function or parafunction may consist of headache (located in the temporalis muscle) as

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well as pain, tension, achiness, and tightness located in any one or combination of the masticatory muscles, and patients may or may not complain of limited mouth opening. Pertinent to TMD, MP has been found to exist in the masticatory muscles such as the masseter, temporalis, and medial and lateral pterygoids (Simons et al. 1999). Having a good understanding of variables that cause an inordinate amount of muscle contraction that can result in the development of masticatory MP is essential for both researchers and clinicians who seek to develop appropriate intervention plans for patients with MP. It is currently recommended that unless there are specific and justifiable indications to the contrary, initial treatment of TMD, regardless of whether it is an intra-articular or myalgic type of TMD, should be based on the use of nonsurgical, reversible, and evidence-based therapeutic modalities (American Academy of Orofacial Pain et al. 2013; American Association of Dental Research Adopted 1996, revised 2010). However, successful management of chronic TMD problems often requires a multidisciplinary approach utilizing a team of professionals including dentists, physicians, physical therapists, pharmacists, and psychologists working in conjunction with the individual patient. Treatment options that meet these criteria to reduce the signs and symptoms of TMD, with special attention on MP, will be discussed in this chapter.

8.2 Etiology

Understanding the etiology of MP can assist with the development and implementation of a case-specific treatment plan. However, the etiology of TMD and MP is multifactorial. Certain cases have a clear antecedent etiologic event such as trauma, biting into something hard, or even dental treatment (Carlsson 2001). Other etiologies though are less clear and not fully understood. In 1934, Costen suggested the etiology of TMD was a malocclusion, i.e., crowding, malalignment, or structural abnormality and that malocclusion was the cause of a variety of head, facial, jaw, and throat symptoms (Costen 1934). Today, research-

ers have failed to reach a consensus regarding the role of occlusal interferences in the development of TMD. Current clinical perspectives on occlusal factors related to TMD and MP will be addressed later in this chapter. Since Dr. Costen's declaration of malocclusion as a causal factor of TMD, etiological theories for the development of TMD have expanded to include, although are not limited to, genetics, joint morphology, mandibular asymmetry, and structural alignment problems between the cranium and cervical spine (Greene 2001; Klasser and Greene 2009). None of these factors have consistently been found to completely explain the etiology of TMD or orofacial MP.

One etiological factor that has gained attention as contributing to excessive muscle contraction, especially to account for chronic TMD and MP, is the biopsychosocial model of pain (Klasser and Greene 2009). A biopsychosocial model takes into account the physical source of a patient's pain as well as their psychosocial distress. Psychosocial distress has consistently been found to be associated with parafunctional behaviors and masticatory MP and can have a substantial impact on muscle contraction, pain persistence, and responsiveness to treatment (Restrepo et al. 2008; Kotiranta et al. 2015; Tosato Jde et al. 2015). However, only 12% of TMD patients have the highest level of symptoms of depression, somatization, sleep dysfunction, pain-related worry, and catastrophizing/ruminative thoughts, suggesting that psychosocial distress alone cannot explain the etiology of all TMD or orofacial MP (Kotiranta et al. 2015). While a patient's level of psychosocial distress cannot be underestimated, for the vast majority of patients with TMD and masticatory MP, psychosocial distress can be addressed at the clinical level discussed later in this chapter (Sect. 8.4.1).

Though all of the previous factors may have some merit and may be associated with the onset of MP, none have been definitively determined to explain the etiology of TMD. However, regardless of the etiology of MP, concentric, eccentric, and isometric contractions can produce MP with the same pathophysiologic process as that underlying ischemic pain (Newham et al. 1994).

Regardless of the type of muscle contraction, MP can occur if a contraction is sustained, repetitive, and/or too intense.

8.3 General Management Strategies

Lacking a single etiology, treatment for TMD and MP is directed toward identifying and treating the source of the patient's pain. Of all the diagnostic subsets of TMD (Schiffman et al. 2014), MP is the most common subtype followed by arthralgia (Manfredini et al. 2012; Kraus 2014). While MP is often diagnosed without arthralgia, arthralgia is, at times, diagnosed without MP, and MP and arthralgia can exist concurrently (Kraus 2014). The temporomandibular joint (TMJ) complex is ginglymoarthrodial and requires coordinated kinematic movement between both joints and withstands significant repetitive loading during normal daily function. Restricting joint movement that is excessive and reducing abnormal joint loading by treating MP can often facilitate reduction of symptoms associated with other intra-articular disorders.

8.4 Specific Management Strategies

8.4.1 Patient Education/ Self-Management and Bibehavioral Strategies

The most conservative and often most effective treatment for a patient diagnosed with masticatory MP is patient education (Aggarwal et al. 2010). Patient education generally focuses on educating the patient as to their diagnosis, their role in management, treatment options, and treatment expectations. An essential component of patient education pertinent to the treatment of MP however is behavior modification related to the elimination of harmful oral behaviors. Harmful oral behaviors may predispose, precipitate, or perpetuate masticatory MP. Patient education that focuses on the elimination or reduction

of harmful oral behaviors through behavior modification is the corner stone for treatment of masticatory MP.

Changing behavior relies on patient education and a patient's willingness to change their harmful behavior. Patient education goes far beyond a passive approach of simply providing the patient with a sheet of instructions of "do's and don'ts." The clinician must invest the time necessary to educate their patient on the importance of these changes in an easily understood format. The clinician can help the patient identify obstacles that may interfere with their ability to change behavior and then provide them with suggestions regarding various strategies for resolution. A primary focus of care should be on reducing or eliminating oral parafunctional activity.

Oral parafunctional activity is any oral activity that includes habitual use of the mouth unrelated to essential activities of eating, drinking, yawning, or talking. One of the more common parafunctional activities associated with MP is bruxism, defined as repetitive jaw-muscle activity characterized by clenching or grinding of the teeth and/or by bracing or thrusting of the mandible (Klasser et al. 2015). Bruxism can occur during the awake hours or during sleep in which case it is referred to as sleep bruxism. Addressing sleep bruxism presents several challenges. To date, the etiology of sleep bruxism is unknown; however, a recent hypothesis supports the roles of the central and autonomic nervous systems in the genesis of oromandibular activity during sleep (Klasser et al. 2015). Currently, there is no therapy that has been proven to be effective in eliminating sleep bruxism. Suggested management strategies for sleep bruxism include biofeedback, hypnotherapy, cognitive behavioral therapy (CBT), pharmacotherapy, and occlusal appliances (Klasser et al. 2015). These treatments can involve considerable cost to the patient, and most are not supported by the literature or have been shown to have only transitory effects. An alternative treatment for sleep bruxism is patient education. Anecdotal evidence suggests that for some patients, patient education pertaining to sleeping postures is not only cost-effective but may be helpful in reducing sleep bruxism.

In considering alternate sleep positions, patients are informed to avoid positions that prevent relaxation of head and neck muscles and positions that place excessive force on the mandible. Anecdotal evidence suggests sleep positions that include stomach sleeping and side-lying (lateral decubitus) positions with hands placed between the mandible, and pillow can apply undue pressure on the mandible. However, empirical evidence is lacking to support a causal relationship between sleeping posture and the development of sleep bruxism. Educating patients regarding modification of sleep positions using appropriate pillow type based on their body type may still be beneficial. The pillow should be soft yet supportive enough to maintain the natural contour of the neck in the supine or side-lying position. In the side-lying position, the pillow must be able to effectively support the mandible. Analyzing and addressing the ergonomics of sleeping posture can be addressed in detail by the physical therapist as part of a comprehensive plan of care.

Individuals with masticatory muscle pain have been shown to have an increased frequency of daytime clenching episodes compared to pain-free controls (Cioffi et al. 2016). Also, individuals who self-report that they have awake bruxism, sleep bruxism, and parafunctional habits have been shown to have a greater likelihood of having jaw pain than if they report only experiencing one of those factors (Fernandes et al. 2016). It is possible that the presence of awake and sleep bruxism in conjunction with parafunctional habits may extend periods of muscle activation and reduce rest periods for masticatory muscles, thus contributing to the chronicity of MP. Since sleep bruxism is not under volitional control, one treatment approach to allow increased periods of rest for masticatory muscles is to reduce or eliminate awake bruxism. However, there is no empirical evidence to support this. There is also no evidence yet that reducing awake bruxism would lead to reduced sleep bruxism. However, patients should be educated to avoid daytime triggers for bruxism such as smoking, alcohol, and caffeine (Feu et al. 2013; van Selms et al. 2013). A simple and effective way to control awake bruxism is to

educate the patient that their teeth should never make contact unless they are chewing or swallowing and, even then, contact does not always need to be made. Increased or prolonged muscle activity can lead to significantly increased occlusal loads and increased loading of the temporomandibular joints (Santana-Mora et al. 2014). Patients must be aware that during the day, they should keep their tongue relaxed and teeth apart and maintain even breathing patterns (Kraus 1994). Educating the patient on the appropriate jaw resting position can promote reduced masticatory muscle activity and rest, and patients should be instructed to return to this resting position throughout the day as they feel their jaw muscles tightening or MP increasing.

Another aspect of awake bruxism that should be addressed with the patient is bracing or thrusting the jaw forward, both of which are done with the teeth out of contact. A simple yet effective awareness exercise to lessen this behavior is to instruct the patient to move their jaw from side to side, an exercise referred to as the “wiggle at will” (Kraus 1994). It is essential that the patient understands that the goal of this exercise is not to go through a large range of motion but to perform a small rhythmical movement from side to side, ensuring that movement does not cause pain or repetitive TMJ clicking. If the patient is not coordinated to isolate small side-to-side movements with their jaw, the exercise should not be continued.

Patients must be willing to put forth the effort to increase their awareness of their jaw’s resting position and to avoid bruxing during the day by keeping their jaw relaxed. Anecdotal evidence suggests that educating patients on simple concepts of tongue position and reducing jaw bracing when confronted with daily stressors can reduce awake bruxism and subsequently MP. Patients should be made aware that when confronted with any one or a combination of daily stressors, they must be cognizant of applying the strategies taught to them to minimize increases in masticatory muscle activity. These daily stressors include periods of focused activity which include working at a computer, driving, texting, reading, or writing and activities of exer-

tion such as pushing, pulling, and lifting and periods of physical stress or psychosocial distress.

While psychosocial distress especially fear, anxiety, anger, and depression (FAAD) has consistently been found to be associated with bruxism and masticatory muscle pain, the majority of patients fall into the no pain or low pain disability groups (Kotiranta et al. 2015). The following recommendations may eliminate or reduce psychosocial distress in patients with low levels of pain disability and may reduce psychosocial distress in patients with high pain disability:

1. Treat the source of pain:

A patient's FAAD can develop as a result of pain, or if a patient is predisposed to FAAD, such emotions can be magnified because of pain (Giesecke et al. 2005). The medical model of pain management should still be applied, i.e., find the source of pain and eliminate the source of pain, thereby reducing any unnecessary psychosocial distress that may be a contributing factor to the pain. The best prevention against the development of chronic TMD-related pain and the enhancement of psychosocial distress is to diagnose and efficiently treat the patient's source of pain while in the acute phase of pain.

2. Understand the patient's journey to find pain relief:

A patient's FAAD may be associated with processes of worrying and searching for a meaning of their acute or chronic pain (Bonathan et al. 2014). Patients with MP often consult with multiple healthcare professionals (Fricton and Heir 2006; Kraus 2014), and it is not unusual for patients to consult with a primary care physician; a neurologist; a physical therapist; an ear, nose, and throat specialist; a family dentist; a chiropractor; and one or more dentists who claim to be a TMD "specialist." Still, patients may not receive a definitive diagnosis, or they may receive conflicting diagnoses and treatment recommendations at variable costs. Some patients may have been informed that if they do not receive treatment soon, their condition will worsen which can promote increased FAAD. Unfortunately,

FAAD may result from or be enhanced by a patient's experiences with different healthcare providers. This can be particularly problematic with healthcare providers who are not knowledgeable *and who do not apply appropriate* diagnostic criteria for TMD or who utilize treatment approaches that are not supported by current best evidence (Klasser and Greene 2007). Muscle pain that is magnified by FAAD can be minimized if the patient can find and trust a well-informed healthcare professional who takes the necessary time to provide a clear and easily understood description of their diagnosis and treatment options (Bonathan et al. 2014). Interprofessional collaboration in the management of patients with chronic TMD is an important component in minimizing FAAD.

3. Take into account a patient's willingness to change and how they respond to stressors:

Stressors can take on many forms including interpersonal relationships at work and home, financial stress, and health-related issues with self and family members. Stressors may be associated with myogenous TMD. The severity of TMD symptoms has been shown to correlate with salivary cortisol levels and electromyographic levels of masseter and anterior temporalis muscle activity, suggesting a relationship between physical manifestations of stressors and masticatory muscle activity (Tosato Jde et al. 2015). Educating patients regarding the negative physical effects of stressors such as premature aging and cardiovascular problems may help them to accept that stressors can lead to detrimental physical effects. However, given that stressors may not ever completely be eliminated in daily life, patient education on controlling stressors in a more positive way should be included.

8.4.2 Physical Therapy

Physical therapy is well recognized as a conservative method for the management of symptoms associated with TMD (Sturdivant and Fricton 1991; Kraus 2000; McNeely et al. 2006). Physical

therapy is aimed at preventing, correcting, or alleviating movement dysfunction. In relation to masticatory MP, individuals commonly experience movement problems of limited opening, deviations or deflections on mandibular movements, aberrant mandibular posturing, and/or pain associated with jaw function. Additionally, maladaptive head posture and sleep disturbances may be present. Patient education and self-management as described earlier in this chapter are central to any physical therapy plan of care for MP. Additional management strategies for the treatment of MP utilized by physical therapists include therapeutic exercise and neuromuscular reeducation, manual therapy, dry needling, treatment of cervical spine and postural contributions to muscle-related dysfunction, and therapeutic modalities. Though all physical therapists receive undergraduate training in musculoskeletal evaluation and treatment, emphasis on TMD may be a shortcoming. Physical therapists who have received post-professional training in the evaluation and management of orofacial pain and headache may be better equipped to deal with the acute and chronic headache and orofacial/TMD patient population (The Physical Therapy Board of Craniofacial & Cervical Therapeutics from www.ptbct.org).

8.4.2.1 Therapeutic Exercise and Neuromuscular Reeducation

Physical therapists utilize a variety of therapeutic exercise and neuromuscular reeducation activities to reduce muscle activity and pain in individuals with TMD. Therapeutic exercise involving stretching and strengthening has been found to decrease pain and improve function in patients with chronic pain conditions (Karlsson et al. 2015) and in patients with myofascial TMD (Nicolakis et al. 2002). Therapeutic exercise and neuromuscular reeducation are used in the management of patients with masticatory MP. Patients with TMD have been shown to have impaired orofacial motor function (De Felicio et al. 2012; Ferreira et al. 2014), and therapeutic exercise and neuromuscular reeducation have been shown to improve mandibular motion, alter muscle coordination during jaw movement, reduce muscle ten-

sion, increase muscle strength, and improve circulation within masticatory muscles (Simons et al. 1999; Wirianski et al. 2014). Indeed, several recent systematic reviews have supported the role of exercise for treating TMD (McNeely et al. 2006; Medlicott and Harris 2006; Armijo-Olivo et al. 2016).

The physiological mechanisms underlying the effects of exercise on pain and function may be through alteration of pressure pain threshold and desensitization of muscle tissue. Exercise has been shown to lead to alterations in the concentration of glutamate, substance P, beta-endorphin, and cortisol in individuals with chronic pain (Karlsson et al. 2015). Additionally, specific types of stretching can promote reciprocal inhibition leading to reduced resting muscle tone. A focus on neuromuscular control may improve proprioception and the motor control of masticatory muscles which can lead to reduced parafunction (Wong et al. 2011). Muscular awareness relaxation training can be used to reduce resting muscle activity in elevator muscles of the mandible and improve mandibular opening and to reduce TMJ loading (Treacy 1999).

8.4.2.2 Manual Therapy

Manual therapy is a general term that is used to describe intra- and extra-articular manual therapeutic techniques. Non-thrust mobilization techniques are usually directed toward the TMJ to address intra-articular disorders involving disc displacements or adhesions (Fig. 8.1). Extra-articular



Fig. 8.1 Example of a manual therapy technique directed toward mobilizing the TMJ



Fig. 8.2 Intraoral soft tissue mobilization of the masseter

techniques include the use of soft tissue mobilization which includes mobilization of the masticatory muscles (Fig. 8.2). The mechanism of effect of manual therapy in the treatment of musculoskeletal pain is multifaceted, but in brief, it has been suggested that introduction of a mechanical force to tissue leads to a cascade of neurophysiological responses involving the peripheral and central nervous systems that serves to reduce pain and improve clinical outcomes (Korr 1978; Bialosky et al. 2009). A number of manual techniques have been advocated for use in treating MP. Different terms have been used to describe what the clinician may be attempting such as myofascial release, neuromuscular massage, strain counter strain, soft tissue mobilization, joint mobilization and manipulation, sustained natural apophyseal glides (SNAGs), upper limb neural tension mobilization, and Graston Techniques®. No one approach has been shown to be more therapeutically beneficial than another.

Regardless of the TMD diagnostic subset, a manual approach to treatment has been shown to improve mandibular range of motion and reduce pain compared to other conservative treatments (Calixtre et al. 2015; Martins et al. 2015). For TMD of myofascial origin, patient education and behavioral modification are ongoing components of a physical therapy plan of care as previously discussed (De Laat et al. 2003). In addition, the focus of physical therapy is usually directed toward treating the source of MP. Acute muscle pain due to local ischemia

results in the peripheral sensitization of local muscle nociceptors. While acute muscle pain often resolves on its own, treatment of the affected muscles may help to speed recovery (Andersen et al. 2013). However, muscle contractions that persist will lead to a cascade of molecular events that can lead to the development of myofascial trigger points (MTrPs) within the masticatory muscles. While the existence of MTrPs has not been without controversy (Dommerholt and Gerwin 2015; Quintner et al. 2015), strong evidence to support the validity of MTrPs has come through different technologies. Magnetic resonance elastography has been used to identify the presence of a taut band within the muscle (Chen et al. 2007; Chen et al. 2016), and sonoelastography and diagnostic ultrasound have been used to visualize MTrPs (Sikdar et al. 2009). Decreases in oxygen in the vicinity of an MTrP have been shown using Doppler ultrasound (Sikdar et al. 2010), and changes in chemical milieu consistent with pain and inflammation have been shown using microdialysis of an MTrP (Shah et al. 2005).

MTrPs can be an overlooked source of musculoskeletal pain in the muscles of mastication as well as in cervical muscles (International Association for the Study of Pain 1986). The development of active MTrPs may be a source of chronic MP in TMD (see Chap. 6). In brief, it has been theorized that MTrPs can become a source of chronic orofacial pain or headache when muscle contraction persists. Abnormal depolarization of the postjunctional membrane may lead to an abnormally sustained muscle fiber contraction which can promote depletion of local adenosine triphosphate (ATP). The resulting impaired calcium uptake then leads to an increased concentration of calcium, causing a local contracture of muscle fibers. Continued contraction of muscle fibers can cause blood vessel compression and local muscle ischemia, ultimately resulting in sensitization of nociceptors and a chronic pain state (Simons and Mense 1998; Simons et al. 1999; Jafri 2014). While there is some evidence to support the presence of MTrPs in muscles, the evidence to support a direct relationship between MP and MTrPs requires additional study.

Treatment of MP and MTrPs begins with an accurate diagnosis. A MTrP is palpated as a hypersensitive nodule in a taut band of the muscle (Simons et al. 1999). For patients with TMD, the masseter and temporalis are the muscles most commonly involved, and they can cause pain both locally in a predictable or unpredictable referred pattern to other areas of the face or head (Simons et al. 1999). For example, MTrP in the superficial portion of the masseter muscle can produce local pain in the muscle itself or referred pain in the lower jaw, the molar teeth and related gingiva, the maxilla, or over the eyebrow area. In contrast, MTrPs in the deep portion of the masseter muscle can produce tinnitus in the ipsilateral ear or pain in the mid cheek area, the temporomandibular joint itself, or deep in the ear (Simons et al. 1999). Myofascial trigger points can be classified as either active or latent. Active trigger points are always tender and are associated with spontaneous pain production and when palpated may produce a local “twitch” response felt by the examiner. They prevent full lengthening of the muscle and can cause muscle weakening. In contrast, while latent MTrPs can also cause muscle weakening and an inability to fully lengthen the muscle, they do not produce pain without provocation which is usually achieved via application of manual pressure to the trigger point (Simons et al. 1999). Latent MTrPs may become active by repeated muscle contraction (Celik and Mutlu 2013), and they have been associated with changes in muscle activation including increased intramuscular electromyographic activity during synergistic muscle activation and increased antagonistic muscle activity during agonist muscle contraction (Ge et al. 2014). Latent MTrPs, like active MTrPs, can also contribute to stiffness, to fatigue, and possibly to limited mouth opening (Manolopoulos et al. 2008). Sustained mechanical stimulation of latent MTrPs has been shown to induce central sensitization in healthy subjects (Xu et al. 2010). Central sensitization has been suggested as an important component in the development of many chronic musculoskeletal pain problems including TMD and headache (Sessle 2011; Coppola et al. 2013; Quartana et al. 2015). It

should be noted that the 2014 Diagnostic Criteria (DC) for TMD does not consider the evaluation of latent trigger points (Schiffman et al. 2014). However, given the relationship between latent MTrPs and central sensitization, evaluation and treatment consideration should be given to both active and latent MTrPs in the orofacial region.

Treatment of MTrPs located in the muscles of mastication begins with patient education and behavioral modification as previously discussed. Sensitization of nerve fibers may be associated with excessive release of neurotransmitters in motor end plates which can lead to spontaneous electromyographic activity in parts of the muscle. Soft tissue mobilization may reduce this abnormal discharge (Fricton et al. 1985; Hong and Simons 1998). Soft tissue mobilization is used to promote muscle lengthening and relaxation, and vapocoolant spray may be used to enhance passive stretch of the muscles (Kostopoulos and Rizopoulos 2008). Soft tissue mobilization is usually performed with the patient lying in a relaxed, supported position using manual techniques such as stroking and gliding either extraorally or intraorally to increase mouth opening and reduce pain associated with MTrPs (Pierson 2011) and to improve the abnormal thickness of the masseter muscle that has been shown to be present in patients with TMD (Ariji et al. 2010).

8.4.2.3 Dry Needling

Dry needling is a skilled intervention that uses a thin filiform needle without injectate to penetrate the skin and stimulate underlying myofascial trigger points and muscular and connective tissues for the management of neuromusculoskeletal pain and movement impairments (American Physical Therapy Association 2013). The goal of MTrP dry needling is to release or inactivate trigger points and thus relieve pain (Fig. 8.3). Dry needling of muscle tissue has been shown to inactivate MTrPs (Hong 1994) and can be an effective method of relieving pain and improving the quality of life of patients with myofascial pain (Tekin et al. 2013). When comparing MTrP injection to dry needling for the reduction of cervical pain, both have been shown to be effective at reducing pain and improving range of motion,

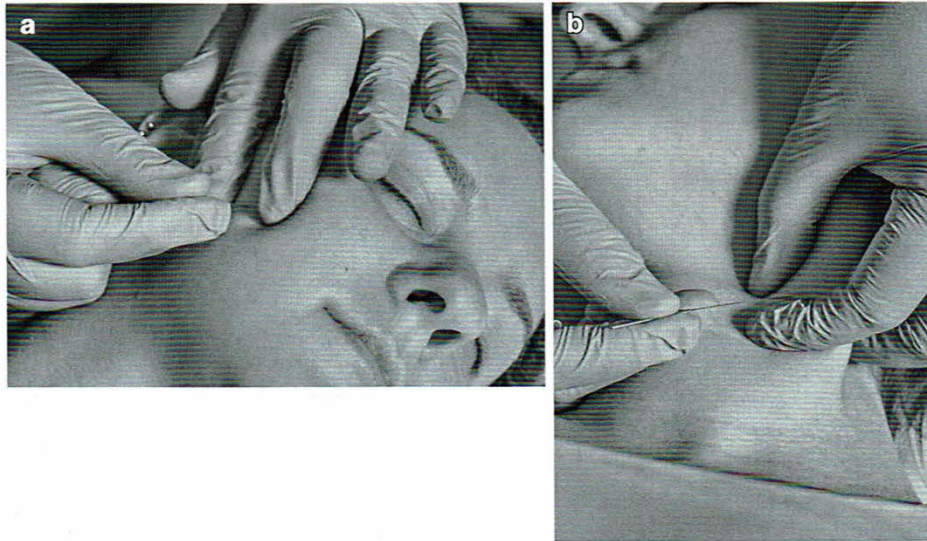


Fig. 8.3 Examples of trigger point dry needling into (a) masseter and (b) sternocleidomastoid muscles

suggesting that needling by itself constitutes the therapeutic effect and not the injected material (Ay et al. 2010).

Dry needling of MTrPs in the masseter of patients with TMD has been shown to increase pain threshold levels and maximum mouth opening distance (Fernandez-Carnero et al. 2010), and dry needling of MTrPs in the masseter, temporalis, and cervical muscles has been shown to reduce severity of symptoms in patients with myofascial pain and headache (Venancio Rde et al. 2009). Compared to trigger point injection with lidocaine or botulinum toxin, however, dry needling may be associated with increased discomfort at the insertion site during treatment and increase post-needling discomfort (Venancio Rde et al. 2009). Stretching exercises, manual therapy, and use of any modalities (Sect. 8.4.2.5) are often indicated post-needling to minimize these effects.

8.4.2.4 Cervical Spine and Postural Considerations

Symptoms of TMD and other head and orofacial pain often overlap with symptoms related to the cervical spine. Indeed, neck pain has been shown to be an associated symptom in 70% of patients diagnosed with TMD (Ciancaglini et al. 1999; Kraus 2014). The cervical spine is a primary

source of headache with a prevalence of 17.8% in a general population, similar to migraine (Nilsson 1995). The pathophysiology to explain the cervical spine as a source of headache, facial, and jaw pain is based on the well-established convergence of craniofacial and cervical afferents in the trigeminocervical nucleus and upper cervical nociceptive neurons (Biondi 2000; Piovesan et al. 2003; Bogduk 2004). Pressure-pain hyperalgesia has been found in the trigeminal region in patients with chronic neck pain, suggesting spreading of sensitization to the trigeminal region in this patient population (La Touche et al. 2010). TMD has also been associated with a higher prevalence of self-reported migraine headache and chronic fatigue (Dahan et al. 2016), and since migraine headaches have been associated with the presence of neck pain (Kaniecki 2002; Calhoun et al. 2010), the role of the cervical spine as a source of head and orofacial pain, mimicking migraine or a possible pathogenesis for migraine, cannot be ignored. Clinicians treating patients for TMD, headache, and orofacial pain must consider cervical spine dysfunction as a primary source of symptom generation or at least as a concurrent source of symptoms.

Neck pain and symptoms of TMD can be related (Ciancaglini et al. 1999). In some cases, cervical spine dysfunction or injury may precede

the onset of TMD symptoms. A prospective 15-year follow-up study showed that individuals who experienced a cervical spine extension-flexion rear-end collision without any direct trauma to the head or neck had a higher prevalence of TMD symptoms over a 15-year period when compared to a control group over the same period of time (Sale et al. 2014). TMD has also been associated with a higher prevalence of self-reported migraine headache and chronic fatigue (Dahan et al. 2016), and since migraine headaches have been associated with the presence of neck pain (Kaniecki 2002; Calhoun et al. 2010), the role of the cervical spine in contributing to TMD cannot be ignored. There appears to be a strong relationship between neck disability and jaw disability in patients with orofacial pain (Olivo et al. 2010). The cervical spine may be a source of masticatory muscle hyperactivity resulting in MTrPs. Evidence has shown cervical spine mobility, and positioning influences the kinematics of the human mandible (Visscher et al. 2000). Biomechanically, a link exists between the stomatognathic system and the cervical spine in that normal mouth opening is accompanied by an initial extension at the cervical-cranial junction (Eriksson et al. 2000). Changes in head posture have been associated with changes in masticatory muscle activity (Funakoshi et al. 1976; Boyd et al. 1987; Yotsuya et al. 2009), resting mandibular position (McLean et al. 1973; Solow and Tallgren 1976; Moya et al. 1994; Gonzalez and Manns 1996), and movement of the condyle within the glenoid fossa (Visscher et al. 2000). Urbanowicz (1991) has suggested a physiological model to show how changes in mandibular posture, specifically an increase in vertical dimension when wearing an oral appliance of the mandible, may contribute to craniovertebral extension leading to suboccipital compression. Straightening of cervical posture may reduce superior and retrusive forces on the mandible, allowing the mandible to seek an improved rest position (Goldstein et al. 1984). An improved mandibular rest position would allow for improved joint mechanics during movement and reduced muscular stress. Abnormal head posture may also affect the path of jaw motion dur-

ing chewing, talking, swallowing, and any contact of the teeth (Mohl 1976). The tonic neck reflex (TNR) is an important developmental reflex to orient the limbs in relationship to the head-body angle. The TNR can affect masticatory muscle tone through the trigeminal neck reflex, and there is an organized neurophysiologic reflex relationship between the TNR and trigeminal motor neuron activity (Funakoshi et al. 1976).

Kinematic connections between the mandible, occiput, and cervical spine and TNR influences may all play a role in increasing masticatory muscle activity. The expenditure of additional masticatory muscle activity compensating for the effects of head posture and abnormal mobility may lead to the development of MP and MTrPs. Cervical pain, tension, limited mobility, and abnormal posture may lead to the inability of the masticatory muscles to adapt to influences originating from the cervical spine as previously described, resulting in masticatory muscle pain and MTrPs. Insight into the relationship between the cervical spine (mobility and position) and masticatory muscle activity has been demonstrated in several ways. A single injection of 2% lidocaine solution to MTrPs in the upper trapezius muscle has been shown to reduce pain and electromyographic activity in the masseter in patients with facial pain (Carlson et al. 1993). In addition, experimental trapezius muscle pain has been shown to spread over a wide area and be accompanied by a temporary reduction of mouth opening (Komiyama et al. 2005). Postural reeducation has been used as part of a successful behavioral intervention program in patients with TMD who have limited mouth opening (Komiyama et al. 1996; Komiyama et al. 1999). A combination of manual therapy and exercise directed at the cervical spine has been shown to improve pain intensity and pressure pain sensitivity in patients with myofascial TMD (La Touche et al. 2009).

Physical therapy directed at treating the cervical component may have a positive impact on reducing headache and orofacial pain of cervical spine origin and masticatory MP. Physical therapy treatment may include manual therapy (Fig. 8.4), therapeutic exercise including stretching (Fig. 8.5),

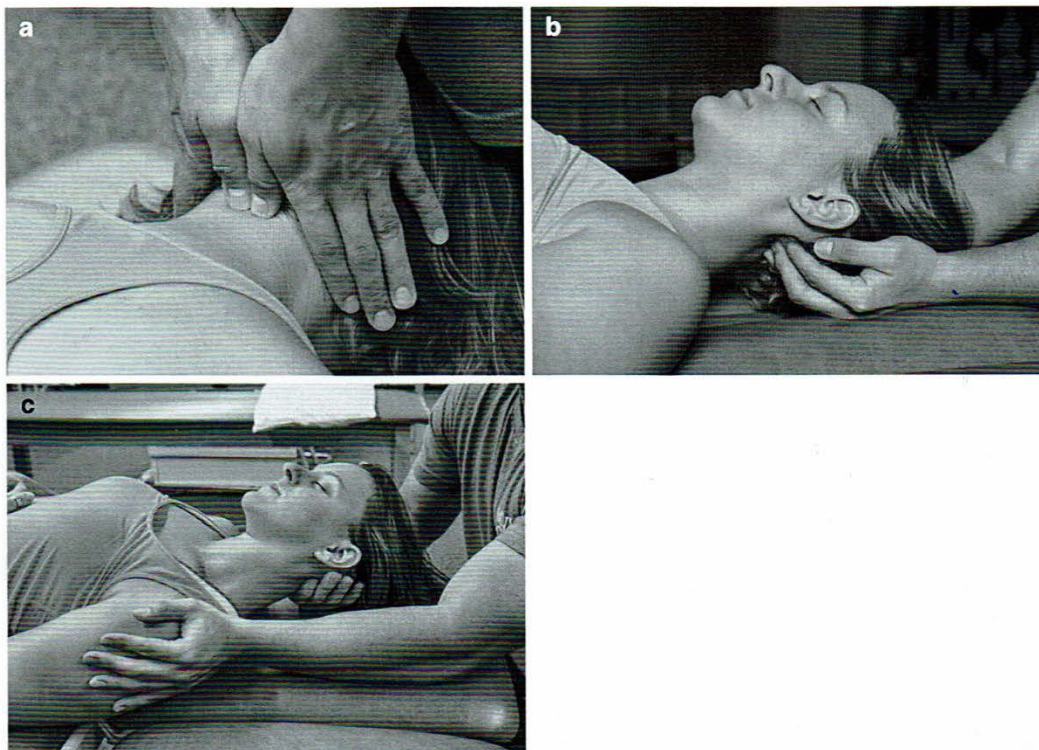


Fig. 8.4 Examples of physical therapy and manual therapy directed toward the cervical area

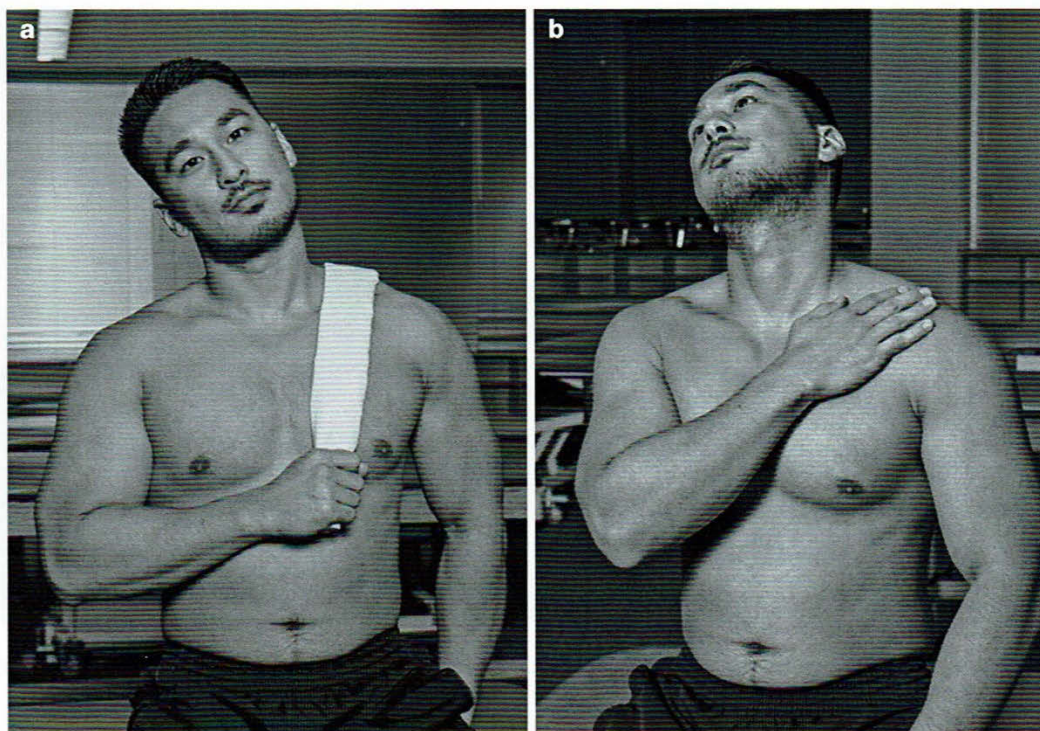


Fig. 8.5 Examples of cervical stretching exercises

dry needling, soft tissue mobilization, and postural correction activities (Fig. 8.6). Restoring cervical mobility is often a precursor to addressing postural dysfunction. Thrust and non-thrust joint mobilization can be used by the physical therapist to restore cervical spine segmental mobility, particularly in the upper cervical region. This is usually combined with activities aimed at increasing strength and endurance of the deep cervical flexor muscles (Fig. 8.7) to promote maintenance of appropriate head and neck posture (Jull et al. 2002, 2009).

8.4.2.5 Therapeutic Modalities

Modalities or adjunctive treatments to address MP include thermal agents, cryotherapy, ultrasound, iontophoresis, and cold laser, as well as the use of electrophysical modalities. Modalities are used to either prepare the patient for therapeutic exercise or manual therapy techniques or reduce any posttreatment soreness. Rarely are

modalities used as the only form of treatment. The exception would be if a patient had recent acute pain due to trauma or extreme pain and disability contributing to hyperalgesia or allodynia. Thermal modalities such as heat and ultrasound

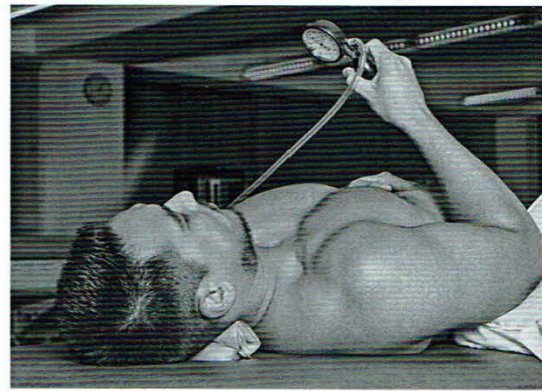


Fig. 8.7 Training of deep neck flexor muscle activation and endurance using biofeedback

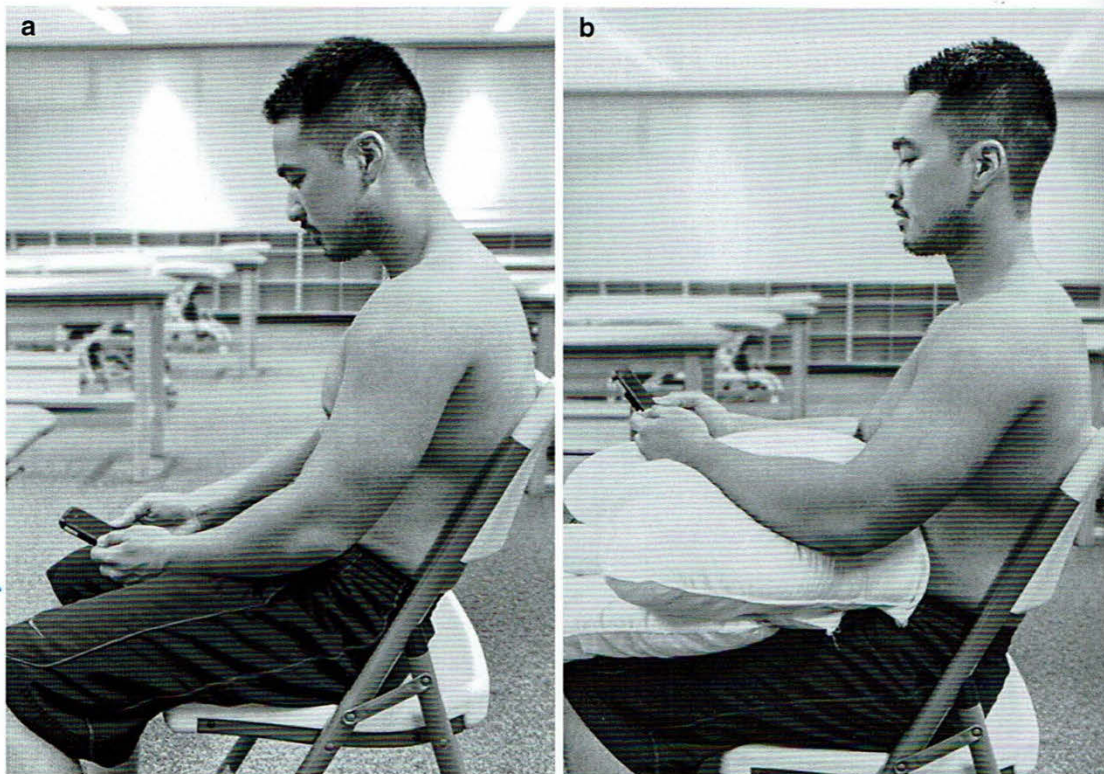


Fig. 8.6 Examples of prolonged abnormal sitting posture that can be corrected with patient education and the use of postural support for the arms

and electrophysical modalities such as iontophoresis and electric stimulation have similar goals of increasing circulation to help with ischemic muscle pain in patients with pain of muscular origin. In contrast, cold laser therapy is proposed to eliminate areas of increased muscle activity and MTrPs by increasing abnormally attenuated skin resistance to the level of the surrounding tissue (Snyder-Mackler et al. 1986). The application of heat over muscle tissue can promote reduced pain through stimulation of cutaneous thermal receptors and increased soft tissue extensibility (Cameron 2013) and lead to decreased tissue stiffness of MTrPs (Draper et al. 2010). Thermal modalities promote local vasodilation leading to increased blood flow in muscle tissue (Bickford and Duff 1953), although care should be taken when applying heat to the facial region given that pain intensity in the masseter muscle has been shown to increase when intramuscular tissue temperature is significantly elevated (Sato et al. 2015). The therapeutic effects of applying physical agents to the muscles of mastication, primarily the masseter and temporalis, can be combined with stretching exercises to promote increased muscle extensibility and jaw motion. In acute stages of muscle injury, however, the application of heat may be contraindicated, and cryotherapy or nonthermal ultrasound can be used instead to reduce inflammation and promote tissue healing. Ultrasound (Fig. 8.8) applied at intensities below a thermal level has been shown to increase intracellular calcium levels (Mortimer and Dyson 1988), increase the rate of protein synthesis by fibroblasts (Harvey et al. 1975), and increase blood flow in ischemic muscles (Barzelai et al. 2006). When ultrasound is used to promote transdermal delivery of pain-relieving and anti-inflammatory drugs such as indomethacin or hydrocortisone, this is called phonophoresis. Phonophoresis can be effective in helping to reduce pain at the TMJ (Wing 1982; Shin and Choi 1997), although its effectiveness on relieving pain due to masticatory muscle dysfunction has not been established.

Different forms of electrophysical modalities can also be used in the treatment of patients with



Fig. 8.8 Therapeutic ultrasound being delivered to the TMJ and masseter while applying a manual stretch to improve mouth opening

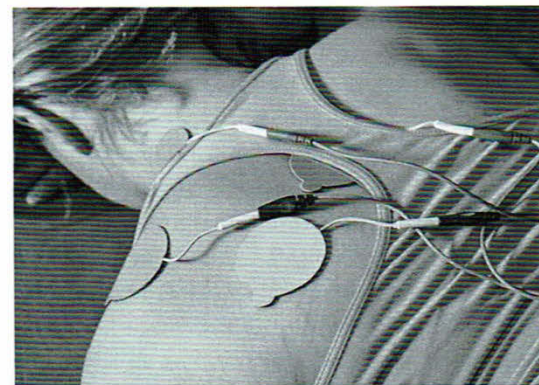


Fig. 8.9 Interferential stimulation being delivered to the trapezius area

myogenous forms of TMD. For example, transcutaneous electrical nerve stimulation (TENS) and interferential current (IFC) are typically used to modulate pain (Fig. 8.9), whereas neuromuscular electrical stimulation (NMES) is used to produce muscle contractions in innervated muscle. Pain control through the use of electrophysical modalities is achieved by different mechanisms depending on the parameters of stimulation used. For example, short-duration, high-frequency pulses can interfere with pain transmission at the spinal cord level (Melzack and Wall 1965). In contrast, lower pulse durations and higher current amplitudes can modulate pain by stimulating the production and release of endogenous opioids, endorphins, and enkepha-

lins (Sabino et al. 2008) and reduce painful muscle activity. Stimulation of muscle through NMES can promote increased blood flow which may accelerate tissue healing (Indergand and Morgan 1994).

The use of thermal, nonthermal, and electro-physical modalities to reduce myogenous pain or muscle tightness in patients with TMD may be beneficial when symptoms first develop (Gray et al. 1994), but there is little support for their use in reducing pain when used in isolation (McNeely et al. 2006). They may be more effective however when performed in conjunction with jaw mobility exercises or relaxation and awareness exercises to improve restricted mouth opening (Fig. 8.8).

8.4.3 Pharmacotherapy

The use of pharmacotherapy for the treatment of myogenous TMD pain may be as a monotherapy in some cases but is more often utilized in conjunction with other treatment options such as physiotherapy, behavioral therapy, or oral appliance therapy. The role of pharmacotherapy in TMD pain is typically to serve as an adjunct to help patients manage their discomfort to a point where it subsides or decreases to a level at which it no longer interferes with their daily activities. No one agent has been shown to be efficacious for the entire spectrum of TMD pain. Therefore, the effective use of pharmacotherapy relies on a good understanding as to the nature of pain of which the patient presents as well as a comprehensive knowledge of the agents contemplated for use. Mechanisms of action (MOA), potential adverse events (AEs), and possible interactions should all be considered in making the choice of agents to be prescribed. The prescriber should attempt to prescribe the most appropriate agent at the most appropriate dose utilizing the best route of administration for the individual being treated. As required for (PRN) dosing should be avoided in order to prevent persistent and breakthrough pain episodes (Sutters et al. 2010).

The evidence-based literature that supports the efficacy and safety of pharmacotherapy in the

TMD population is limited (Cascos-Romero et al. 2009). Very few studies have evaluated specific pharmacological treatments for myogenous TMDs by well-controlled methods. In many clinical trials of TMD treatments, patients with myogenous pain are not distinguished from those who may have arthrogeous types of TMD (Goss et al. 1985). In addition, most reports that evaluate the pharmacological treatment of TMD pain are typically observational rather than randomized controlled trials (RCTs) (Dionne 1997). A recent review concluded that even the RCTs on this topic were of low quality (Graham et al. 2013). This section will discuss some of the more common agents as well as some newer pharmacological approaches utilized to treat muscle pain. Specific classes discussed will include analgesics, muscle relaxants, antidepressants, anticonvulsants, benzodiazepines, botulinum toxin, and the cannabinoids. A brief discussion of topical applications is also included.

8.4.3.1 Analgesics

Opioids

It has long been recognized that opioids are highly effective analgesics in both acute and chronic pain states. However, the use of opioids in chronic nonmalignant pain remains controversial due to the potential for dependence, abuse, and diversion. Prolonged use of opioids has also been linked to a potential for worsening of depression frequently seen in chronic pain patients (Graham et al. 2013). The phenomenon of opioid-induced hyperalgesia (OIH) was reported as early as 1870 in morphine-addicted patients (Albutt 1870). OIH is a paradoxical effect whereby patients who are exposed to opioids experience a decline in their pain thresholds and an increase in their pain sensitivity. OIH can occur with even brief durations of therapy. The pathophysiology of this phenomenon appears to be different from tolerance (Chu et al. 2008). However, tolerance to opioid agents may in fact be a consequence of OIH (Williams et al. 2013). Other studies have demonstrated that with persistent opioid exposure, cholecystokinin (CCK) is upregulated in the rostral ventromedial medulla

(RVM), which produces both anti-opioid and pro-nociceptive effects by activating descending RVM pain facilitation. This in turn increases pain transmission and produces hyperalgesia (Ossipov et al. 2004). Watkins and colleagues recently described the potential role that glial mechanisms may play in the pathophysiology of the pro-nociceptive sequela of opioids. Their work demonstrated the opioid-induced activation of glia by way of the toll-like receptor 4 (TLR4) and other receptors, resulting in inflammation and the release of neuroexcitatory substances (Watkins et al. 2009). Ultimately, the use of opioid analgesics in the myogenous pain patient should be limited to carefully screened individuals who have failed other, more proven, and conservative modalities. Patients prescribed opioids require careful monitoring to ensure compliance, patient safety, and efficacy of the prescribed dose.

Tramadol

Tramadol is a non-opioid analgesic that weakly binds to opioid receptors and functions as a weak mu-opioid agonist. Tramadol will also inhibit the uptake of both serotonin and norepinephrine in the dorsal horns of the spinal cord similar to the effect of tricyclic antidepressants (Stoops et al. 2012; Modi et al. 2013). There are no published studies to support the use of tramadol as a single agent in myofascial pain patient populations. However, three controlled trials have studied its efficacy in fibromyalgia and demonstrated an overall reduction in pain in this patient group (Biasi et al. 1998; Russell et al. 2000; Bennett et al. 2003). A recent study by Kaneko and colleagues demonstrated an improvement in experimentally induced neuropathic and myogenous pain in the rat model (Kaneko et al. 2014). Other studies would seem to support its use in chronic widespread pain, chronic low back pain, and osteoarthritis (Schnitzer et al. 2000; Wilder-Smith et al. 2001; Kean et al. 2009; Rosenberg 2009). The combination of tramadol with acetaminophen has also been demonstrated to be effective in the fibromyalgia patient population (Bennett et al. 2003; Bennett et al. 2005). While not considered a controlled substance in the United States, there is evidence to suggest poten-

tial for abuse and dependence with tramadol (Senay et al. 2003). However, abuse potential appears to be reduced relative to opioid agents (Stoops 2014).

NSAIDs

Nonsteroidal anti-inflammatory drugs (NSAIDs) have long been utilized in the management of acute and in some instances chronic pain. They are the most commonly used drugs for pain, largely due to their availability in both prescriptive and over-the-counter preparations. They are a class of structurally diverse agents with very similar effects. They are generally well tolerated but do include cardiovascular, gastrointestinal, and renal risks. The analgesic action of NSAIDs is via the inhibition of the cyclooxygenase 2 (COX 2) enzymes. The adverse gastrointestinal effects are a result of inhibition of the cyclooxygenase 1 (COX 1) enzyme. NSAIDs are generally classified as being nonselective COX inhibitors where they inhibit both COX 1 and COX 2 enzymes, semi-selective COX 2 inhibitors, or highly selective COX 2 inhibitors in which they are seven times or more selective in their COX 2 enzyme blocking activity (Hersh et al. 2005). Currently, literature to support the use of NSAIDs for muscle pain is lacking. Several studies have demonstrated the effectiveness of NSAIDs for chronic pain and fibromyalgia in combination with other medications, but the efficacy of oral NSAIDs as a stand-alone agent in myogenous pain remains to be demonstrated (Borg-Stein and Iaccarino 2014). Recently, the Food and Drug Administration (FDA) requested that manufacturers of all NSAIDs make labeling changes to their products. The changes are to include a boxed warning, highlighting the potential for increased risk of cardiovascular events as well as the potentially life-threatening gastrointestinal bleeding associated with their use (Health and Services 2015). Even with the lack of good evidence to support their routine use, NSAIDs are commonly recommended and prescribed for myogenous pain therapy due to being readily available and mostly inexpensive (Table 8.1). Also, many patients are comfortable utilizing these agents without a

Table 8.1 Classification of commonly prescribed NSAIDs and the usual oral adult dosing for nonspecific analgesia (Crofford 2013)

Class	Subclass	Generic drug (trade name available in the United States)	Usual adult oral dose for pain	
Carboxylic acids	Salicylic acids	Acetylsalicylic acid (Aspirin)	325–650 mg PO q4h	
		Diflunisal (Dolobid)	500 mg PO q12h	
		Salsalate (Disalcid)	1500 mg PO bid	
	Acetic acids	Diclofenac sodium (Voltaren-XR)	50 mg PO bid-tid	
		Diclofenac potassium (Cataflam)	50 mg PO tid	
		Diclofenac/misoprostol (Arthrotec)	50–75 mg PO bid-tid	
		Diclofenac (Zorvolex)	18–35 mg PO tid	
		Etodolac (Lodine)	200–400 mg PO q6-8 h	
		Indomethacin (Indocin, Tivorbex)	25–50 mg PO bid-tid	
		Sulindac (Clinoril)	150–200 mg Po bid	
		Tolmetin (Tolectin)	200–600 mg PO tid	
		Propionic acids	Flurbiprofen (Ansaid)	50–100 mg PO bid-tid
			Ketoprofen (Orudis)	50 mg PO q4-6 h
			Oxaprozin (Daypro)	1200 mg PO qd
			Ibuprofen (Motrin, Advil, etc.)	400 mg PO q4-6 h
			Naproxen sodium (Anaprox, Aleve, Naprelan, etc.)	220–550 PO q12h
			Naproxen (Naprosyn)	250–500 mg PO q12h
		Fenamic acids	Fenoprofen (Nalfon)	300–600 mg PO tid-qid
Meclofenamate (Meclomen)	50–100 mg PO q4-6 h			
Enolic acids	Oxicams	Piroxicam (Feldene)	20 mg PO qd	
		Meloxicam (Mobic)	7.5–15 mg PO qd	
		Meloxicam (Vivlodex)	5–10 mg PO qd	
Nonacidic		Nabumetone	1000–2000 mg/day	
			PO divided qd-bid	
Cox 2 selective	Sulfonamide	Celecoxib (Celebrex)	200 mg PO bid	

mg milligrams; PO (per os) by mouth; q (quaque) every, each; h (hora) hour; bid (bis in die) two times a day; tid (ter in die) three times a day

healthcare provider's input. NSAIDs are most commonly used as a single agent but may be formulated in combination with other agents such as opioids.

Corticosteroids

Corticosteroids are potent anti-inflammatory agents often used for acute pain and in some cases chronic pain. They reduce prostaglandin synthesis by inhibiting both phospholipase enzyme and COX 2 but have only a minor effect on COX 1 (Sapolsky et al. 2000; Rhen and Cidlowski 2005). In addition, they inhibit tumor necrosis factor alpha and interleukins 1 and 6 which are pro-inflammatory mediators (Holte and Kehlet 2002). The analgesic properties of

corticosteroids have been shown primarily in surgical and osteoarthritic pain models and have not been well studied for muscular pain (Waldron et al. 2013; Abou-Raya et al. 2014). In a double-blinded crossover trial, Clark and colleagues found no benefit over placebo in patient diagnosed with what was known as fibrositis, a term previously used for fibromyalgia (Clark et al. 1985). Conversely, a study by Ernberg and colleagues demonstrated a positive response to the injection of methylprednisolone into localized areas of pain in the superficial masseter muscle (Ernberg et al. 1997). Another more recent study found that injection of a solution combining a local anesthetic with a corticosteroid provided relief of local muscle soreness a few days

after injection and that there was less need for oral analgesics for the primary complaint (Venancio Rde et al. 2008). One of the primary concerns with the use of corticosteroids is the potential for endogenous adrenal suppression limiting the body's ability to respond normally to a stressful event. They can also cause a suppression of the immune response making patients more susceptible to a secondary infection. Prolonged use of corticosteroids can potentially increase the risk of a number of complications, including osteoporosis and avascular necrosis (Liu et al. 2013). Limiting the cumulative dose over the course of therapy appears to reduce the risk of adverse effects (Curtis et al. 2006). Caution or avoidance should be considered in patients with diabetes mellitus. Exogenous corticosteroids have been shown to cause elevated blood glucose levels via a decrease in glucose utilization, increased glucose production, inhibition of the effect of insulin on myocytes and adipocytes, and an increase in hepatic glucose release. Gurwitz and colleagues found that subjects receiving prednisone at a daily dose of 30 mg or more had a relative risk of 10.34 of developing diabetes as compared to controls not taking corticosteroids (Gurwitz et al. 1994). Caution or avoidance is also advised if corticosteroids are contemplated for patients with an infective process. As corticosteroids can prevent or decrease the inflammatory response to multiple mechanisms, their use in the presence of infection may mask the underlying pathological process involved. For the above-described reasons, the course of treatment with corticosteroids should be limited to the shortest duration possible and preferably for only episodic use.

Acetaminophen

Acetaminophen, known as paracetamol outside of the United States, is a non-opioid analgesic that, like the NSAIDs, may be used as a single agent or in combination with other agents such as opioids. In contrast to NSAIDs, acetaminophen is not known to be associated with myocardial infarction or gastrointestinal bleeding and is usually better tolerated (Graham et al. 2013). While it is usually considered a weaker analgesic than the

NSAIDs, when acetaminophen is combined with an NSAID, the efficacy exceeds either agent used alone (Graham et al. 2013). Acetaminophen also differs from the majority of NSAIDs in that it lacks significant anti-inflammatory activity. The analgesic mechanism of action of acetaminophen has not been fully described but may be due to the inhibition of central prostaglandin synthesis and an elevation of the pain threshold (Graham et al. 2013). Other potential mechanisms of action may include the facilitation of the serotonergic descending inhibitory pathways and activation of cannabinoid receptors (Smith 2009). Hepatotoxicity is the most serious potential adverse effect associated with the use of acetaminophen, even at the recommended doses of a maximum of 4 g per day (Gupta and Jakobsson 2014). A recent recommendation from the FDA asks that providers not prescribe or dispense combination analgesic agents containing more than 325 mg of acetaminophen due to this potential for life-threatening hepatotoxicity (Mitka 2014).

Local Anesthetics

The use of local anesthetics for myogenous pain is generally reserved for times when a myofascial trigger point or a well-defined area of discomfort in the muscle can be identified. The usual route of administration is via injection, but topical preparations (transdermal) may be used as well. This application will be discussed later in this section. Trigger point injections (TPIs) have been utilized to treat a variety of painful musculoskeletal and neurological disorders for years (Ashkenazi et al. 2010). One percent lidocaine or 0.5% of bupivacaine is usually appropriate for most muscle injections (Robbins et al. 2014). To avoid ischemia and potential tissue necrosis, it is advisable to use a local anesthetic preparation without a vasoconstrictor. The MOA of local anesthetic is to decrease the permeability of ion channels to sodium ions. Trigger point injections are most often utilized to facilitate physical therapy modalities such as mobilization and stretching but may also serve as a modality to quickly relieve pain. Some debate exists as to the benefit of using local anesthetics in TPIs. Hameroff and colleagues found that based on patient's subjective report of pain relief, TPIs

with bupivacaine and etidocaine were preferred over saline injections (Hameroff et al. 1981). Conversely, a 2001 review determined that TPIs using local anesthetics proved to be no more beneficial than injecting saline or using the needle alone (Cummings and White 2001). Another more recent meta-analysis of 12 studies showed no significant difference in pain reduction for trigger point injections using local anesthetics compared with control treatments consisting of saline injections, oral analgesics, or other nonpharmacological interventions (Mosshammer et al. 2013). Other studies have suggested that dry needling alone may be as effective for inactivating trigger points as utilizing a local anesthetic (Jaeger 1987; Hong 1994). It does appear that the use of a local anesthetic significantly reduces post-procedure soreness (Hong 1994). Finally, a 2008 meta-analysis examining the effectiveness of injection therapy for low back pain concluded that evidence to support or refute the use of injection therapy is currently lacking (Staal et al. 2008).

8.4.3.2 Muscle Relaxants

Muscle relaxants comprise a group of pharmacological agents with varying MOAs that appear to act on the central nervous system (CNS) to disrupt nociceptive signaling. The specific MOA of these agents is still poorly understood. Sedation is potentially a useful benefit for this class of drugs in the TMD population (Manfredini et al. 2004). Muscle relaxants appear to be more efficacious in acute muscle pain as opposed to chronic (McQuay et al. 1995). A recent Cochrane review was able to only identify one study evaluating the efficacy of a muscle relaxant on TMD pain (Mujakperuo et al. 2010). The conclusion was that the agent cyclobenzaprine was statistically superior to placebo when combined with a self-care program for jaw pain at awakening (Herman et al. 2002). Cyclobenzaprine appears to have no direct activity on skeletal muscle. Its MOA has not been fully described but is thought to be due primarily to its sedative effects (Kruidering-Hall and Campbell 2015). Of note, cyclobenzaprine is a tricyclic amine, structurally similar to amitriptyline, with ventricular dysrhythmia as a possible adverse event (Hessler 2006).

Other common agents utilized in this class include carisoprodol, metaxalone, methocarbamol, baclofen, and tizanidine (Table 8.2). Carisoprodol undergoes hepatic biotransformation to three primary metabolites: hydroxycarisoprodol, hydroxymeprobamate, and meprobamate. Meprobamate is a potent anxiolytic with significant abuse and dependency issues (Toth and Urtis 2004). Withdrawal from extended use of meprobamate may result in severe reactions including seizures and coma. The MOA of metaxalone has not yet been fully elucidated. A direct effect on skeletal muscles or nerve fibers has not been established, but CNS depression may be responsible for its effects. Compared with other muscle relaxants, metaxalone has a relatively low risk of drowsiness or cognitive defects (Milanov and Georgiev 1994). Methocarbamol is a centrally acting agent that is a derivative of guaifenesin (Kruidering-Hall and Campbell 2015). The MOA of methocarbamol is mostly unknown but is thought to be due to sedation. A fairly unique AE of this agent is the production of brown or green urine discoloration. Baclofen is a natural analog

Table 8.2 Commonly prescribed muscle relaxants (Lo and Alan 2015)

Drug (generic/trade name)	Common dosing
Cyclobenzaprine (Flexeril, Amrix, Fexmid)	5–10 mg PO qd/tid Maximum 40 mg/day
Chlorzoxazone (Lorzone)	250–500 mg PO tid/qid Maximum 750 mg/dose
Carisoprodol (Soma)	250–350 mg tid or qhs
Metaxalone (Skelaxin)	800 mg PO tid/qid
Methocarbamol (Robaxin)	1000 mg PO qid Maximum 8000 mg/day
Orphenadrine citrate	100 mg PO bid
Tizanidine (Zanaflex)	2–8 mg tid/qid Maximum 12 mg/dose, 24 mg/day
Dantrolene (Dantrium)	100 mg PO tid/qid Maximum 400 mg/day for 3 weeks
Baclofen	20–80 mg/day divided tid/qid

mg milligrams; PO (per os) by mouth; q (quaque) every; d (die) day, each; h (hora) hour; bid (bis in die) two times a day; tid (ter in die) three times a day; qid (quater in die) four times a day

of gamma-aminobutyric acid (GABA) that binds to GABA B receptors. It appears to act presynaptically as well as postsynaptically to inhibit spinal reflexes (Kruidering-Hall and Campbell 2015). Baclofen is available as an oral preparation, as an intrathecal injection, or for use in an intrathecal pump. This later form of administration is typically reserved for cases of severe spasticity. Common AEs include dry mouth and transient sedation that tend to subside with prolonged use. Withdrawal symptoms have been reported following abrupt discontinuation of baclofen (Terrence and Fromm 1981). These may include auditory and visual hallucinations, agitation, delirium, anxiety, fever, tremors, tachycardia, and, in some cases, seizures. As with most muscle relaxants, the precise mechanism of action of tizanidine has not been fully described but may be linked to its central alpha 2-adrenoceptor agonist properties (Kaddar et al. 2012). Therefore, caution is advised when prescribing this agent to patients with impaired renal/liver function or who may have cardiac disease. Tizanidine appears to inhibit presynaptic release of excitatory neurotransmitters, reducing the excitability of postsynaptic α motor neurons. In addition, it has been demonstrated to reduce abnormal co-contractions of opposing muscle groups (Milanov and Georgiev 1994).

8.4.3.3 Antidepressants

This class of medication is typically used in the management of depressive conditions; however, due to their inhibition of the reuptake of serotonin and norepinephrine, antidepressants are commonly used for many painful conditions (Verdu et al. 2008). Antidepressants can be grouped into four main categories: the tricyclic antidepressants (TCAs), the monoamine oxidase inhibitors (MAOIs), the selective serotonin reuptake inhibitors (SSRIs), and the dual selective norepinephrine and serotonin reuptake inhibitors (SNRIs). The SNRIs demonstrate similar properties to those of the older TCAs. The TCAs and the SNRIs have both been shown to have the greatest efficacy of the antidepressants in chronic pain conditions (Mico et al. 2006). While depression is often comorbid with chronic pain, the

TCAs imipramine and amitriptyline have both demonstrated efficacy in the depressed and non-depressed subjects (Alcoff et al. 1982; Watson et al. 1982). This would seem to suggest that a unique MOA other than the antidepressant qualities is responsible for their efficacy in painful conditions. In addition, the analgesic effect of these agents is typically seen to occur more rapidly than the mood-stabilizing effect, and the required dosages for pain management have been shown to be much less than those required for mood disorders (Arnold et al. 2005; Goldstein et al. 2005). While not specific to TMD myogenous pain, several trials have explored the efficacy of amitriptyline in patients with TMD. In fact, two studies have shown a clinically significant reduction in pain utilizing amitriptyline as compared to placebo (Plesh et al. 2000; Rizzatti-Barbosa et al. 2003). Common side effects of TCAs and SNRIs include nausea, sedation, psychomotor impairment, xerostomia, and constipation (Plesh et al. 2000). These agents should be avoided in patients taking MAOIs and any other serotonergic drugs as the combination may lead to serotonin syndrome which is hallmarked by confusion, fever, shivering, diaphoresis, ataxia, myoclonus, and severe hypertension (Sporer 1995). Also of note, the prescribed dosage for pain management should be well below that required for the management of depression.

8.4.3.4 Anticonvulsants

Traditionally in the facial pain patient population, the anticonvulsant class of drugs has been utilized primarily for neuropathic pain presentations. However, as TMD pain persists, CNS changes may occur which include a sensitization similar to that seen in other chronic pain disorders such as fibromyalgia (Sessle 1995). The most commonly prescribed anticonvulsants in the orofacial pain population are carbamazepine, oxcarbazepine, gabapentin, and pregabalin. The MOA of the anticonvulsants in orofacial pain appears to be via a reduction in neurogenic inflammation and central trigeminal activation as well as an augmentation of antinociceptive activity in the CNS (Soderpalm 2002). A recent trial utilizing gabapentin for masticatory muscle pain

found it to be clinically and statistically superior to placebo in reducing the subject's report of pain and muscle hyperalgesia as well as reducing the impact of pain on their day-to-day functioning (Kimos et al. 2007). Gabapentin and the structurally similar pregabalin are possible considerations due to the relative low occurrence of side effects as compared to other agents in this class and their proven efficacy in trials involving various chronic pain syndromes (Pandey et al. 2005; Arnold et al. 2007; Tassone et al. 2007). It is important to note that in 2008, the FDA announced that all anticonvulsant drugs must display a clear warning that their use increases risk of suicidal thoughts and behaviors.

8.4.3.5 Benzodiazepines

Benzodiazepines are neuropsychotropic agents utilized primarily for their anxiolytic, sedative-hypnotic, muscle relaxant, and anticonvulsant properties. These agents produce their primary therapeutic effects through their interaction with the GABA A receptors, the major inhibitory receptors in the brain. Benzodiazepines could be considered as an alternative to the more traditional skeletal muscle relaxants, albeit with limited evidence of efficacy and potential for abuse (Chou et al. 2007). In one study of 20 TMD patients with both joint and muscle pain, clonazepam was found to be significantly more effective than placebo (Harkins et al. 1991). A larger study in patients with fibromyalgia found a decrease in the subject's rating of their symptoms after 6 weeks of receiving a combination of alprazolam and ibuprofen (Russell et al. 1991). While most would agree that benzodiazepine use should be limited to low doses over a short duration, Schenck and colleagues found that long-term, nightly use of clonazepam for the treatment of what was described as injurious parasomnias proved to have sustained efficacy with a low risk of dosage tolerance, adverse events, or even abuse (Schenck and Mahowald 1996). New data suggest that benzodiazepine use is associated with an increased risk of Alzheimer's disease as well as other dementias (de Gage et al. 2014). However, other recent reports would seem to dispute these conclusions (Imfeld et al. 2015).

8.4.3.6 Botulinum Toxin

Botulinum toxin (BTX) is a neurotoxin that when injected intramuscularly will temporarily prevent the release of acetylcholine at the neuromuscular junction resulting in a generalized decrease in muscle contraction strength. It has traditionally been utilized for the treatment of movement disorders such as spasticity and dystonia and autonomic disorders associated with cholinergic overactivity, such as hyperhidrosis and sialorrhea. In the TMD patient population, a randomized clinical trial using double-blinding and placebo control to discern its efficacy for myofascial pain found improvements in both the objective and subjective outcome variables as compared to placebo (Guarda-Nardini et al. 2008). A more recent review concluded that BTX was no more effective to treat TMD myofascial pain than other more conventional and established therapies (Dall'Antonia et al. 2013). In a recent updated Cochrane review looking at BTX for myofascial pain syndromes (MPS), the authors concluded that there is inconclusive evidence to support the use of BTX based on the data from four studies with a total of 233 participants (Soares et al. 2014). This is in agreement with their previous review (Soares et al. 2012). Another recent review by Gerwin and colleagues emphasized the need for better evidence to determine the true efficacy of BTX for MPS (Gerwin 2012). Standardization of dosing and injection site protocols will most likely prove beneficial going forward. It has recently been revealed that BTX possesses MOAs independent of its effect on muscle contractions such as the inhibition of mechanical nociception in peripheral trigeminovascular neurons (Burstein et al. 2014). The BTX molecule has been shown to inhibit the release of serotonin, dopamine, noradrenaline, glutamate, gamma-aminobutyric acid (GABA), enkephalin, glycine, substance P, ATP, calcitonin gene-related peptide (CGRP), somatostatin, and neuronal nitric oxide synthase which could partially explain its analgesic effect (Pavone and Luvisetto 2010). It should be noted that due to the reduction of contractile strength seen when BTX is injected intramuscularly, there appears to be a risk for a reduction in bone mineral den-

sity or osteopenic changes even after a single injection (Tsai et al. 2011; Raphael et al. 2014; Matthys et al. 2015). To date, this occurrence has been primarily demonstrated in the animal model with only one small pilot study appearing to replicate the effect in the human subject (Raphael et al. 2014). Further trials are needed with larger sample sizes followed over a longer duration. However, for this reason and due to the limited evidence of efficacy, it would seem reasonable to reserve the use of BTX for the more refractory cases until further data can be accumulated.

8.4.3.7 Cannabinoids

Cannabinoids have been used for medical purposes for many years. The cannabinoid (CB) receptors have emerged as a therapeutic target of interest in pain management in recent years particularly in patients where conventional therapies have failed. The antinociceptive effect of CBs can be mediated by either the CB1 receptor or the CB2 receptors depending on the type of pain. CB1 receptors are expressed at high levels in the CNS and to a degree in the spinal cord, the dorsal root ganglion, and in the periphery (Herkenham 1995). CB2 analgesia is related to peripheral mechanisms without apparent CNS effects (Zogopoulos et al. 2013). CB1 appears to be more involved with acute pain, whereas with chronic pain, it appears to be mediated by both CB1 and CB2 (Cox et al. 2007). As a whole, CBs appear to be better suited for chronic pain conditions (Beaulieu and Ware 2007). However, a recent report from Bagues and colleagues found that tetrahydrocannabinol (THC), a cannabinoid natural derivative with therapeutic use in humans, reduced the nociceptive behaviors in two models of acute muscle pain in rats (Bagues et al. 2014). While it is encouraging that some studies on the use of CBs for multiple sclerosis and spasticity-related pain (Svendsen et al. 2004; Wissel et al. 2006) report positive outcomes, overall, robust evidence for routine use in acute or chronic myogenous condition pain is still lacking. Future research and utilization of CBs in pain management will most certainly be affected at least in part by the legal climate.

8.4.3.8 Topical Applications

Topical (transdermal) medications allow for the distribution of a pharmacological agent in a very concentrated delivery area. There are some patients averse to taking oral medications that may be more agreeable to a topical preparation. Topical applications are also advantageous in patients taking multiple other medications where there is concern of drug interactions or other adverse events. Topical preparations may be used in conjunction with the systemic analog of the same agent thereby reducing the systemic dose needed and decreasing the incidence of AEs. Topical agents for pain management typically involve a local anesthetic agent and/or an analgesic but may include other pharmacological agents. Topical NSAIDs have been demonstrated to be effective in relieving muscle pain with a low incidence of adverse effects (Derry et al. 2015). Specifically, diclofenac, ibuprofen, ketoprofen, piroxicam, and indomethacin proved to be significantly more effective than placebo where subjects reported at least a 50% decrease in their pain scores (Derry et al. 2015). Topicals are usually prepared as a cream, ointment, and gel or in a patch (reservoir design) and must have the ability to penetrate the skin. Factors that may influence the ability of the preparation to penetrate the skin include the integrity of the skin, the patient's age, and the presence of any dermatologic disorders or disease. The ability of the preparation to absorb effectively is augmented by the use of carrier agents that are highly lipid soluble. Topical preparations should be avoided in individuals with broken skin, skin lesions, or atrophy or who have a known sensitivity to any of the ingredients of the agents being utilized. It is beneficial for the clinician to work with a qualified compounding pharmacist in order to ensure that the most appropriate agents are correctly prepared and utilized for the problem being addressed.

8.4.4 The Role of Occlusion and Occlusal Oriented Treatments

Over the years, there has been much controversy and debate as to the role of occlusion in the etiology and/or maintenance of TMDs. For many

years, dentists have utilized occlusal therapies for the treatment and prevention of TMDs. However, recent evidence suggests that the role of occlusion in TMDs is much less important than once believed (Turp and Schindler 2012). In fact, a recent review concluded that static occlusal factors had no significant association with TMD (Cruz et al. 2015). Yet, in the same review, dynamic occlusal factors including the absence of canine guidance, laterotrusive interferences, and a shift of ≥ 2 mm from the retruded contact position (RCP) to maximum intercuspation (MI) demonstrated a recognizable impact. Another recent study found that some occlusal features may play a small role (10.8%) in myogenous TMDs, namely, a mediotrusive interference and RCP-MI slide of ≥ 2 mm (Landi et al. 2004). The following sections will briefly look at occlusal factors pertaining to orthodontics, occlusal therapy, and oral appliances from a therapeutic viewpoint.

8.4.4.1 Orthodontics

Orthodontic therapy is a well-proven modality for the correction of occlusal discrepancies in both the growing and adult population. Given that the role of occlusal factors in TMDs is limited at best (Turp and Schindler 2012), the correction of occlusal discrepancies solely to treat a TMD should be viewed with caution. In fact, orthodontic therapy for the treatment of TMDs is not supported by the evidence (Macfarlane et al. 2009). A recent Cochrane review concluded there is no evidence from randomized controlled trials (RCTs) to support the notion that orthodontic treatment can prevent or treat TMDs (Luther et al. 2010). It should also be noted that orthodontic treatment carries with it the risk of destabilizing the stomatognathic system during the course of therapy (Greene 1982).

8.4.4.2 Occlusal Therapy

Many dental practitioners continue to believe that occlusal factors are causative or at the very least a significant perpetuating factor for TMDs and subsequently utilize occlusal adjustment as an initial treatment for these disorders, in spite of evidence to the contrary (Koh and Robinson 2004). Occlusal therapy (OT) can be a subtractive, addi-

tive, or combination procedure with the goal being to adjust the dentition in such a way as to allow the upper and lower arches to occlude in the most stable manner as possible. Occlusal therapy can also be performed to remove undesirable tooth contacts in functional movements such as nonworking side contacts allowing for cuspid-guided or group function in lateral excursive movements. It has long been thought that guidance on the anterior teeth in lateral excursive movements with the absence of posterior tooth contact resulted in a reduction of masticatory muscle electromyography (EMG) activity (Williamson and Lundquist 1983). However, these early reports mostly measured EMG activity utilizing occlusal splints as opposed to the natural dentition. In one small study of nine healthy and asymptomatic subjects, those without nonworking side contacts demonstrated a more uniform signal of the masticatory muscle EMG than those with the working side contacts (Nishigawa et al. 1997). However, it remains to be proven if these EMG patterns have any relationship to myogenous TMD. Treatment outcomes are often used as proof of concept, but to date, most studies of occlusal adjustment involve case series with a lack of control groups or placebo interventions for comparison. With the growing appreciation for evidence-based dentistry/medicine, it recognized that studies that rely on clinical observation and expert opinion can lead to strongly biased and nonsupported conclusions about treatment effects (Richards and Lawrence 1995; Raphael and Marbach 1997). Even as early as 1976, Goodman and colleagues showed that there was no difference in pain outcomes in patients treated with occlusal adjustments as compared with mock adjustments (Goodman et al. 1976). In another study, Tsolka and colleagues found no difference in treatment outcomes after real and mock occlusal adjustment (Tsolka et al. 1992). Their group attributed the positive effects of the supposed intervention to be primarily a placebo response. Given the irreversible nature of occlusal adjustments combined with the lack of evidence as to its efficacy for the treatment of myogenous facial pain, this approach cannot be recommended (Stohler 2008).

8.4.5 Oral Appliances

A 1993 survey of members of the American Dental Association found that the oral appliance (OA) was the most commonly prescribed therapy for the treatment of TMDs by both general dentists and specialists (Glass et al. 1993). Oral appliances may be soft or hard and may be made to cover a full or partial dental arch. There are a number of theories as to how OAs may benefit the patient with myogenous TMD pain, yet debate persists as to the validity of these theories (Klasser et al. 2010). There is some evidence to suggest that an OA will, at least for the short term, reduce sleep-time masticatory muscle activity (Dube et al. 2004). However, a recent review found that a hard acrylic OA, termed a stabilization splint, does not demonstrate better clinical outcomes than a non-occluding palatal appliance, a soft OA, or other conservative therapies such as physical therapy or acupuncture (Turp et al. 2004). A stabilization splint has been described as a hard acrylic OA that provides a temporary, so-called, ideal occlusion (Al-Ani et al. 2005). In contrast to Turp and colleagues, a 10-week RCT found that the stabilization appliance was more effective in alleviating symptoms of myogenous TMD pain than a palatal, non-occluding appliance (Ekberg et al. 2003). In a more recent review and meta-analysis, what was described as a properly adjusted, hard stabilization appliance demonstrated “good evidence of modest efficacy” in the treatment of TMD pain as “compared to non-occluding appliances and no treatment” (Fricton et al. 2010). Interestingly, several recent short-term studies have demonstrated a reduction in sleep bruxism with the use of a mandibular advancement type OA (Landry et al. 2006; Landry-Schonbeck et al. 2009). However, the relationship between sleep bruxism and myogenous TMD pain is debated in the literature (Raphael et al. 2012). When the existing literature on oral appliance therapy is reviewed, it becomes clear that there is a need for more RCTs looking at subjects over a longer period of time. It would also prove beneficial to standardize the trials in ways such as OA design, material used, and patterns of use. While even part-time use of

an OA can lead to unwanted permanent bite changes, it is generally recommended that their use be limited to sleep or part-time wear only (Magdaleno and Ginestal 2010). As with any therapy, careful patient selection and compliance monitoring will decrease the incidence of adverse events.

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