Review paper

Title: Myofascial Pain Syndrome: A Concise Update on Clinical, Diagnostic and Integrative and Alternative Therapeutic perspectives

Running title: Myofascial Pain Syndrome

ABSTRACT

Background: Myofascial pain syndrome (MPS) is a common multifactorial condition that primarily presents with a cluster of key symptoms and comorbid with a variety of systemic diseases and regional pain syndromes. **Objective:** This study aims to concisely review clinical, diagnostic and integrative therapeutic aspects of myofascial pain syndrome. Methods: E-searches (2000-2019) using keywords and Boolean operators were made and using exclusion and inclusion criteria, 50 full articles that focused on several clinical aspects of MPS were retained for this review. **Results:** Myofascial pain syndrome is considered a multidimensional musculoskeletal disorder with poorly understood etiopathogenesis and pathophysiology and characterized by tender taut muscle and active or nascent myofascial trigger points (MTrPs), muscle twitch response, specific pattern of referred pain and a number of autonomic symptoms. A variety of pharmacological and nonpharmacological therapies with variable efficacy are used in the management of MPS, the latter modalities such as education, stretching and exercises, moist hot and cold packs and dry needling and myofascial massage or MTrP massage are used first line options. **Conclusion:** Myofascial pain syndrome and MTrPs initiated by repeated strains and injuries co-occur with diverse physical diseases and regional pain syndromes, and need to be diagnosed by means of history, gold standard palpation and physical examination, systemic evaluation and relevant laboratory investigations and advanced techniques. Though several integrative interventions are specified in the management of MPS, manual therapies including myofascial massage or myofascial trigger point massage are found to be reasonably effective in MPS. This study calls for exploring etiopathogenesis and basic pathophysiological mechanisms underlying MPS and MTrPs in future.

Keywords: Myofascial pain syndrome, myofascial trigger points, taut muscle, myofascial massage therapy, comorbidities, regional pain syndromes.

INTRODUCTION

Myofascial pain syndrome (MPS) with acute or insidious onset is a dysfunction of muscle and surrounding fascia, and characterized by local and referred pain arising from hard and tender myofascial trigger points (MTrPs) located within the involved taut band of muscle [1-3]. Notably, pain referred from active tender MTrPs of MPS also determines connectivity with regional pain syndromes, and comorbid with several systemic conditions [2,4,5]. MPS classified as a musculoskeletal disorder with both sensory and motor abnormalities can be a primary disorder associated with local and referred pain and other accessory symptoms of variable intensity. Conversely, MPS might be a secondary muscle and fascia disorder attributed mainly to neurogenic or mechanical forces impacting the activity of a nociceptive focus in a deep somatic or visceral organs, structures and comorbid systemic conditions [2, 4-6]. Unlike acute onset MPS, chronic MPS of 6 months or more tends to generalize, reflects poor prognosis and never transforms into fibromyalgia, which is a distinctive algogenic (pain) disorder [7]. Patients with both types of MPS respond well to a variety of interventions such as myofascial massage and other manual therapies and injection techniques, acupuncture and cupping (Hijamah), infrared and ultrasound therapies, Kinesio taping and postural, ergonomic, and structural modifications, meditation, and other holistic treatments directed towards possibly correcting its underlying etiopathogenesis and pathophysiological changes [2.8-10]. According to Hong, MTrPs share many qualities with acupuncture points; their location and distribution, pain and referred pain patterns, local twitch responses in terms of de qi, and pathophysiological mechanisms [11], at myofascial nerve endplates, spinal cord and CNS [12]. Local twitch response reflects rapid relief from intense pain of MTrP. Various studies including an experimental study reported important biochemical

changes concerning MPS pain induction through motor nerve endplate dysfunctions [1,2,13].

AIM

This study concisely reviews and broadly updates myofascial pain syndrome (MPS) with a brief focus on conventional and complementary and alternative therapies including deep therapeutic massage, myofascial massage or MTrP (MTP) massage therapy. Unlike global substantial research on MPS yet inconsistencies concerning its diagnostic criteria, structure of MTrP, etiopathogenesis and pathophysiology, interventions and overall outcome persist in the relevant literature. Furthermore, there is exceedingly scanty literature on myofascial pain syndrome in Saudi Arabia [9]. This research will fill up some gaps in the pragmatic knowledge of professionals including physiotherapists, rehabilitation workers, osteopaths and chiropractors concerned with myofascial pain and MPS practices in Saudi Arabia and other Arabian Gulf countries.

METHODS

Search Strategy

The relevant literature published in English prior to 2019 was searched in PubMed, MEDLINE, Google Scholar, ScienceDirect and OvidSP databases. The Boolean operators and keywords used in multiple electronic searches were “myofascial pain syndrome AND types OR myofascial pain OR etiological factors OR etiopathogenesis OR working mechanisms OR comorbidities OR diagnosis AND laboratory investigations AND imaging procedures AND ultrasound AND electromyography AND treatment interventions AND myofascial massage OR MTrP therapy. The search strategy and the keywords were modified as appropriate according to the searched database. In addition, references included in full text articles focused mainly on myofascial pain syndrome and myofascial massage were reviewed for inclusion in this critical review.

Search Results

Hundreds of thousands articles concerning MPS and MMT (n=27,310) were retrieved and reviewed independently by two researchers (NAQ & HAS). Our main focus was on freely accessible full articles describing MPS, its socioclinical features, etiologies,

comorbidities, diagnostic criteria, relevant investigations, and treatments including technique of MTrP (MTP) therapy or myofascial massage (MM) therapy or deep therapeutic massage; the three terms used interchangeably. These articles were reviewed critically and the brief sketches of important contents were incorporated in this review. The additional inclusion criteria were papers containing salient socioclinical features and treatment intervention of MPS including MTP or MM intervention. All types of related studies such as systematic reviews and meta-analyses randomized clinical trials, observational studies, case series and single case reports were included for reviewing. Screening of retrieved records excluded 24,592 papers. More than two thousands records were reviewed for eligibility purpose (n=2,718). After removing duplications (n=914), unrelated articles (n=1002), no abstract (n=159), articles cited in SR and MA (n=63), full articles not accessible (n=210), and irrelevant information (n=315), 55 articles were left for further review. Finally, both reviewers agreed to include 50 published studies.(Fig. 1).

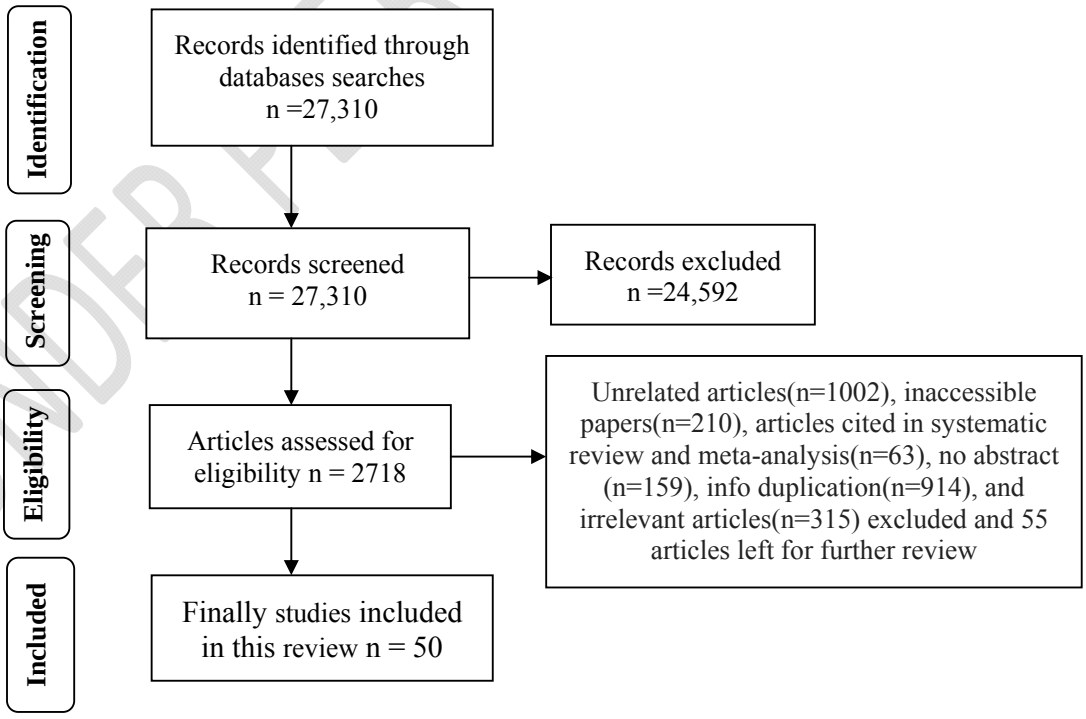

Figure 1 Prisma diagram summarizing the flow of search results

RESULTS

Epidemiology

The prevalence of MPS varies globally in relevant published literature attributed to methodological differences including settings such as pain clinics, gender, general population, acute or chronic course, under-diagnosis and misdiagnosis [14-16]. The prevalence of MPS in general population is unknown, though the life-time prevalence of musculoskeletal pain is reported to affect 85% of the population [17]. Approximately 9 million people suffer from MPS in the United State [3]. Furthermore, 30% to 85% of patients with myofascial pain syndrome tend to present with musculoskeletal pain. The prevalence of chronic MPS is reported 20% and people with age 27 to 50 years are commonly affected by MPS. In elderly population the prevalence tends to increase (85%). Although the gender difference in the prevalence of MPS are unclear [3], women (65% versus 37%) are liable to suffer more from this condition [18,19]. The MPS prevalence and gender needs relevant research in future. For proper and precise orientation directed towards physiotherapists and other practitioners, Table 1 provides short description of key terms and theories commonly used in MPS, MTrPs, MP and myofascial massage or MTrP therapy.

Table.1. Definition of key terms and theories concerning MPS, MTrP and Myofascial massage [1,5,6,20]

Key Terms	**Definition**
MPS	A complex syndrome of sensory, motor and autonomic symptoms, caused by myofascial trigger points
Myofascial massage therapy (MMT)	A type of bodywork that focuses on the myofascial (MF) unit, including muscle, connective tissue (CT) and the neuromuscular junction
Direct methods	A myofascial massage that focuses on meeting resistance in the tissues with an equal and opposite force.
Indirect methods	A myofascial massage that focuses on meeting a resistance by softening into a sense of ease
Neuromuscular approach	An orientation to myofascial massage in which the therapist focuses on localmuscular or neural dysfunctions, including trigger points, ischemia, inflammation, hypertonia, and neural impingement. The thumb or finger glides or drags to detect taut bands or muscular nodules and ischemic compression to treat trigger points, also called neuromuscular therapy (NMT) or neuromuscular technique.
Direct CT approach	An orientation to MMT in which the therapist releases muscle tissue by using sustained pressure with coached micromovements on the connective tissue/fascia
Indirect CT approach	An orientation to MMT in which the therapist releases muscle tissue with movement in the form of jostling, compression, or traction applied to the connective tissue/fascia. Indirect technique move up to a restricted point, but not beyond and then move back from that boundary.
Craniosacral approach	An orientation to myofascial massage in which the therapist applies very light pressure at the cranium, sacrum, and spine to free restrictions in the dura mater, and balance the flow of cerebrospinal fluid. Used to relieve pain in the head, spine, and pelvis, and to release trauma throughout the body.
MTrP	Knots of exquisite tenderness and hyperirritability in muscles or their fascia, localized in taut bands, which mediate a local twitch response of muscle fibers under a specific type of palpation – called snapping – and, if sufficiently hyperirritable, give rise to pain, tenderness and autonomic phenomena as well as dysfunction in areas usually remote from their site, called targets.

Simons' theory	The production of MTrP basically requires muscle overload and overuse, derived from working with a rabbit model later supported by human studies.
Non-tender nodules	Some MTrPs are not tender on palpation and found proximal to or remote from site of pain
Soft tissue pain	Here palpable nodule is not tender or no nodule is palpable: not explained by radiculopathy and muscle strain.
Cinderella Hypothesis	MPS disorder symptoms are reported to arise from muscle recruitment patterns during sub-maximal level exertions with moderate or low physical load, often applied by office workers, musicians and dentists having myalgia and MTrPs.
Henneman's size principle	Smaller type 1 muscle fibers are recruited first and de-recruited last during static muscle exertions, and consequently these "Cinderella" fibers are continuously stimulated and metabolically overloaded compared to larger motor muscle fibers which do not work hard and spent less time being activated, making "Cinderella" fibers more susceptible to muscle damage and calcium perturbation-key factors in MTrP development

Pathophysiology

To know exactly the contributory etiological factors underlying pathophysiology of any health condition must include the exploration and contribution of biological and non-biological factors or else it will remain poorly understood. Despite tremendous scientific research on MPS, its precise pathophysiology is still elusive and intangible with so many questions remain unanswered requiring respective researches [1,10]. Over more than two decades, many theories and hypotheses along with western concepts concerning pathophysiology of MPS and milieu of MTrPs were formulated which include but not limited to constant energy deficiency (Simon's energy crisis theory and integrated hypothesis concerning milieu around MTrP) involving adenosine triphosphate (ATP), sarcoplasmatic reticulum injury, and mitochondrial dysfunctions, unregulated calcium release in the involved muscle fibers, oxygen deficiency and collection of other toxic materials in involved taut muscle fibers [1,12, 21,22]. In addition, repetitive and overuse of muscle fibers, interalia, results in muscle fatigue and hypoxia (oxygen deficiency in muscles) and ischemia and pain. The pain and ischemia develops through a number of mechanisms; inflammatory mediators, neurogenic inflammation, and peripheral nerve sensitization (muscle nociceptor sensitization) that sensitizes the limbic system (especially anterior insula) in the CNS. Peripheral nerve system and CNS sensitization are crucial mediating mechanisms of myofascial pain (MP) and MTrPs. Of note, neurogenic inflammation is linked with release of BK, 5-HT (serotonin receptors), norepinephrine (NE), nerve growth factor (NGF), and adenosine causing hyperalgesia and tenderness of MTrP. Consequently, there is also perturbation of various neurotransmitters including serotonin, acetylcholine, glutamate, and prostaglandins [1,2,12,13]. Furthermore, intracellular energy deficiency (energy crisis) disturbs calcium pump activities that cause increase

in intracellular calcium and, hence, sustained muscle contraction and production of taut muscle bands and MTrPs [1-3, 12,13]. In addition, tenderness at the MTrP concerning MPS is also attributed to the release of neuropeptides, cytokines, and inflammatory substances (substance P), calcitonin gene–related peptide, interleukin-1a, and bradykinin, and protons that create local acidity (acid sensing ion) [1,21,22]. The loose connective tissue where hyaluronic acid (HA) is found in the highest concentrations acts as a muscle lubricant in the absence of muscle strains/overuse. Conversely, HA is produced in higher amount during overuse of muscles, its viscosity is increased that impairs its muscles sliding function, stimulates mechanoreceptors and nociceptors causing pain and limited movements [1,23]. In vivo studies of MTrPs, biochemical differences were found not only between active and latent MTrPs but also healthy muscle tissue [1,24]. In addition, an in vivo microanalysis technique used by Shah and colleagues (2008) further showed that the levels of IL-1b, IL-6, IL-8, tumor necrosis factor α, substance P, bradykinin, calcitonin gene-related peptide, and norepinephrine increased within an active MTrP in the upper trapezius muscle compared with subjects with latent or no MTrPs [25,26]. Corticospinal excitability (central sensitization) is considered another biomarker of MPS [27].

Furthermore, studies in MPS patients treated by ozone therapy found improvement in muscle oxygenation, inhibition of inflammatory mediators such as tumor necrosis factor alpha (TNFα), and TNF receptor2. Induction of analgesic effect was by means of phosphodiesteraseA2 blockage [8]. Importantly, using ozone in low concentration also acts on the enzymatic scavenger system including catalase, glutathione-peroxidase, and superoxide dismutase, and breaks down oxygen-free radicals and, therefore, could be an effective intervention in patients with MPS [8] and ozone tends to work through correcting aforesaid system processes. Further details of how ozone (O_3) therapy works in diverse musculoskeletal disorders including temporomandibular pain disorder (MPS), see this source [28].

In animal models, endogenous opioid system including enkephalin and endorphins are reported to mediate the reduction of pain, weakness and muscle motion concerning MTrPs in taut muscles [29] and, hence, endogenous opioid system (or exogenous/synthetic opioids given) is also implicated and used in the pain management of MPS. Overall, despite innovative research done in myofascial pain (MP), MPS and MTrPs and related treatment interventions, yet pathophysiology of

MPS is not understood fully and similarly no specific first line treatment is available to manage patients with MPS and MTrPs [1,2,3,12,13,30]. Similarly, many biochemical and mechanical processes of how tout muscle is formed with the ultimate production of latent and active MTrPs linked with no tenderness or variable tenderness and pains are not clearly identified. It is wise to know that the pathophysiology of myofascial pain (MP) arising from sources other than MTrPs is rather different and details are available here [14]. Overall, further research is needed to explore the research avenues concerning etiopathogenesis and pathophysiological processes of MPS and other look-a-like pain syndromes [1,2,12,13,30].

Diagnostic Evaluation

A typical case of myofascial pain syndrome requires a comprehensive plan: a pertinent history, physical examination (palpation), and systemic evaluation, a battery of laboratory investigation, advanced neuroimaging techniques, ultrasound, and histopathological studies (Figure 2), all components will guide to selection of suitable treatment intervention. Concerning myofascial pain (MP), a detailed history of characteristics of pain and possible factors inducing pain such as repeated injuries and muscular strain is highly important; acute or chronic MP is usually dull and aching but rarely sharp and stabbing. Acute sharp pain may occur on top of chronic pain simulating or visceral pain [1,2,20]. For example, somatic referred pain from active MTrPs in the abdomen can feel like irritable bowel, bladder pain, or endometrial pain. Referred pain from active MTrPs reflects a sensory component presenting as tingling sensation, hot or cold perceptions and piloerection (goose-bumps), and are distributed along the nerve innervating the taut muscle with myofascial trigger points. Referred MPfrom MTrPs is also experienced in several other regions including the head (headaches), the neck (neck ache), or the hip. For comprehensive description of MP, regional pain syndromes, MPS, referred pain from MTrPs and comorbid conditions(Table 2& 3)see this source [1-4,7, 17-19,31]. Overall, the salient features of MP, MPS, referred pain from and pain of active MTrPs tend to help in the diagnosis of MPS and differentiating it from regional pain syndromes.

On physical examination, recognized clinical signs and symptoms of tender MTrPs within the taut muscle,and local tenderness along with referred pain to the specific areas and local twitch responsegive further clues to the recognition of myofascial pain syndrome. [1-3,7,31]. The MTrP is always located on a taut band of muscle. An

active MTrP that causespain is mostly tender to palpation. When MTrP within a taut muscle is activated mechanically by palpation or by needling, it contracts sharply indicating a local twitch response (LTR). The taut muscle bandlimits stretch of a muscle and produces symptom of weakness and limitation of motion that is rapidly reversed as thetrigger point is deactivated or released by myofascial massage/MTrP massage. Active MTrPalso impact autonomic nervous activityproducing possible diagnostic features, such as, vasodilationor constriction, goose bumps, or piloerection.The active MTrP also induces pain to distant sites/zonesas ‘referred pain, in addition to CNS sensitization linked with lower pain threshold causing intense tenderness and pain (hyperalgesia or allodynia) in taut muscles and MTrP. In addition, painful area expands to surrounding MTrPs zone and taut musclewith a possible increase in newer MTrPs. Active MTrPs can be spontaneously painful unlike its counterpart latent MTrPs, which remain nascent until repeated physicalinjuries or deep palpation convert them to active MTrPs[1-3].Most patients with MPS suffer from local muscle pain (MP) and referred pain in specific patterns along a nerve distribution. In some patients, symptoms of MPS occur after repeated muscle injuries or overuse activities while certain patients with MPS develop symptoms without identifiable precipitating and perpetuating factors [1-3].

Concerning procedure for identifying trigger points, Gerwin (2014) described distinctively multiple palpation steps including first to identify the areas affected by pain, then muscles with TrPs, and then tenderand latent TrPs along the taut muscle bands [2]. Of note, the painoriginating from taut muscle and MTrPs differs from usual muscle pain. Lastly compression of MTrP for 5-10 seconds will induce pain or numbness, piloerection or goose bumps or pilomotor reflex or vasodilation or constriction, hot or cold sensationsaway from the MTrP, which are collectively called symptoms of "referred pain",develop through CNS sensitization impacted by autonomic system[1-2]. The signs and symptoms of MTrP-referred pain tend to improve following myofascial massage (MM) of the most to the least hardest and tender MTrPs [1,2,20]. Further details of the palpation of the taut muscle band, heart of the MTrP (the hardest part to be massaged for effective improvement), diagnostic inactivation of MTrPs are give here [1-2,20].In addition, objective identification of innervations zones and MTrPs by intramuscular needling, magnetic resonance elastography, infrared thermography, ultrasound imaging combined with vibration

sonoelastography (shear wave elastography), computerized tomography, laser Doppler flowmetry, high-definition ultrasound (HDUS) and surface electromyography (endplate noise/spontaneous electrical activity (SEA) due to release of acetylcholine and an increase in miniature endplate potentials) and local twitch response (LTR) can be found here [1,2,20, 32-36].

The histopathological reports of MTrPs also provide some equivocal support to the diagnosis of MPS [1]. Light microscope examination ofMTrPs showed local contraction of muscle fibers (muscle knots) and narrowing of space between muscle fibers, i.e., endomysium. Electron microscopic finding concerning taut muscles and MTrPs demonstrated decreasing number of mitochondria and shortening of sarcomere (functional unit of striated muscles)[3].In a study, Zhuang and associates (2014) reported the histopathological and electron microscopic features of active MTrPs; hyperchromatic rounded contracture nodules, spindle-shaped muscle fibers, and markedly increased levels of inflammatory cells [37]. In a nutshell, the best cost-effective method of diagnosing MPS and MTrPs is by palpation (gold standard) supported by comprehensive history and pertinent laboratory investigations; however, objective means of diagnosing MPS and MTrPs are relatively expensive, time-consuming and not available in all healthcare settings.

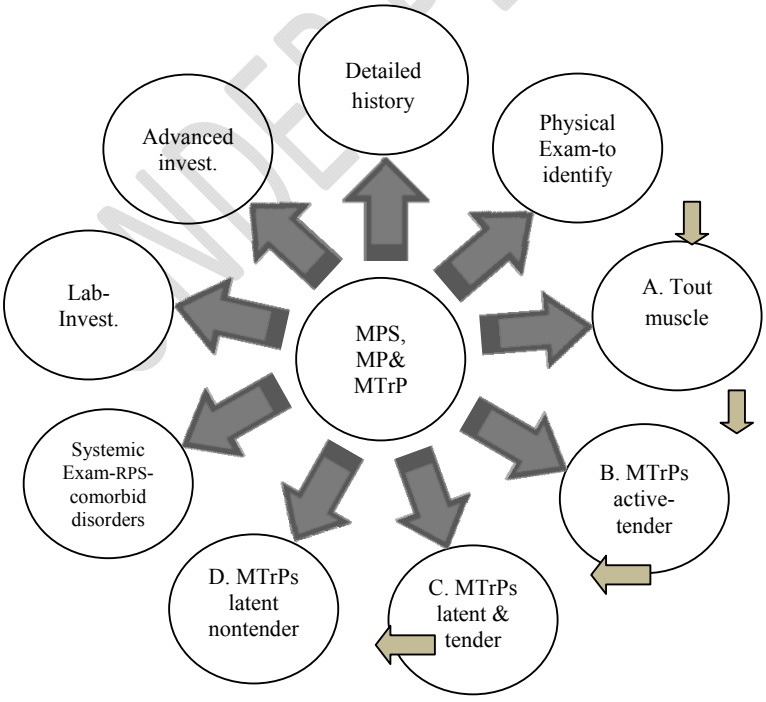

Figure 2: Diagnostic evaluations of MPS (RPS=Regional Pain syndromes; MP=myofascial pain)

Table 2 Differential diagnosis of RPS that overlap/comorbid with MPS, adapted from these sources [1,2,3,14,17-19,38]

Differential diagnosis of RPS that overlap/comorbid with myofascial pain syndrome		
Pain Region	Examine for S/S of RPS	Muscles with MTrP referred pain patterns reproducing the pain of RPS as described briefly in column 2
Head and neck	Headache details and clinical features as dizziness, photophobia, and phonophobia; +ve neurologic signs as weakness, absent tendon reflexes, and sensory loss, and range of neck motions, loading tests for facet joints, and imaging for spondylosis and instability..	Upper trapezius, levator scapulae; posterior cervical muscles as splenius capitis and cervicis, semispinalis, and oblique capitis inferior; sternocleidomastoid; facial Muscles as masseter and temporalis.
Shoulder	Shoulder and acromioclavicular joint dysfunction signs as shoulder impingement, and rotator cuff syndrome signs	Trapezius, supraspinatus, levator scapulae, infraspinatus, posterior serratus superior, rhomboids, subscapularis, teres major and minor, latissimus dorsi, deltoid, pectoralis major and minor.
Chest (no cardiac)	H/O and signs of tracheobronchial and esophageal disease (carcinoma, cardiac disease-angina).	Pectoralis major, abdominal obliques rectus femoris, and back muscles.
Low back	Spondylo-arthropathies spondylolisthesis; disc disease; spinal stenosis; myelopathies-cord compression, tethered cord; hypermobility syndrome	Psoas; quadratus lumborumparaspinal muscles-iliocostalis, longimus thoracis, multifidi, abdominal oblique, and rectus femoris.
Pelvic/hip	Internal organ disease-painful bladder, irritable bowel, endometriosis, menstrual cramps, prostatitis, vulvovaginitis, carcinoma; radicular pain from the lumbosacral spine.	Abdominal muscles, psoas, quadratus lumborum; gluteal muscles- piriformis muscle; thigh adductors-the pectineus muscle; hamstrings-the upper semitendinosis muscle; the short extensor muscles of the thigh- obturators and gemellae.
Knee	Intrinsic knee joint disease, radicular pain from the low back	Quadriceps muscle- the vastus medialis for medial knee pain; vastus lateralis for lateral knee pain; hamstrings and gastrocnemius muscles for back of knee pain.
Ankle/foot	Intrinsic joint pain, radicular pain from the low back	Anterior and posterior leg muscles; gastrocnemius, soleus, fibularis, anterior tibialis, long flexor and extensor muscles of the leg; intrinsic foot muscles.
S/S=signs and symptoms; RPS=regional pain syndrome; MTrP=myofascial trigger points; H/O=history of		

Comorbidities

Evidently, MPS and MTrPs co-occur with a variety of clinical conditions such as regional pain syndromes with myofascial pain (MP) andsystemic diseases. The physical diseases include but not limited to mild hypothyroidism,cancer, parasitic infections and Lyme disease, acute and chronic radiculopathy,nerve entrapment syndrome, endometriosis, painful bladder syndrome, facet arthropathies, migraine and tension headache, carpel Tunnel syndrome, and Ehlers-Danlossyndrome(Table 2&3)[1-3,14,17-19,38].Overall, comorbidities and regional pain syndromes share biopsychosocial etiological factors and guide practitioners to address these co-occurring conditions concerning their precise pathophysiology, diagnosis, and

treatment interventions in order to improve recovery and good outcome of each condition crisscrossing with MPS.

Differential Diagnosis

Many physical diseases are reported to present with regional myofascial pain (MP)associate withmyofascial pain syndrome (Table 2&3). The common disorders include tendinopathy, arthritis, bursitis and nerve entrapment, which need to be excluded by clinical examination and pertinent investigation. Notably, differential diagnosis depends on patterns and location of pain, presence of MTrP, taut muscle and twitch response. For example, patients who have suffered from medial elbow pain should be evaluated for possible medial epicondylitis or cubital tunnel syndrome.For patients who have chronic multiple TrPs, fibromyalgia should be considered and to be excluded. Fibromyalgia is a condition of widespread chronic pain. There are 2 major ways which fibromyalgia differs from chronic MPS. First, patients with fibromyalgia have diffuse muscle tender points without taut bands and referred pain. As a result, physicians should carefully palpate the pain area, from tendon to muscle to tendon. Second, patients with fibromyalgia usually have comorbid conditions/symptoms such as depressive mood, insomnia, dizziness, dysmenorrhea, and numbness, which are rarely found with MPS. Evidently,patients with fibromyalgia also tend to show better response and quality of life to acupuncture compared to shame acupuncture or medications but this study was without participants having MPS [39]. Thus, the evaluation of a patient withapparent MPS must consider those conditions that have a similar presentation (Table 2 &3).

Concerning the prognosis of MPS, it depends mainly on symptom duration and comorbid diseases. In acute MPS, symptoms usually resolve spontaneously.If not, patients with acute MPS may require physical modalities, stretching exercise, myofascial massage therapy, MTrPs needling or local anesthetic injection. Conversely, chronic MPS last much longer than acute form and requires sophisticated treatment intervention with greater timeline as chronicity and comorbid conditions empower MPS resistance to treatment.

Management

The goals of MPS treatment are pain relief and correction of precipitating perpetuating factors [1-3,40]. There are many pharmacological, nonpharmacological and CAM modalities to deal with MPS. All patients with MPS need educational tips concerning stretching and strengthening of muscles, exercises, moist heat/cold packs and ergonomic modifications specially to maintain neutral posture (instead of poor or abnormal or awkward postures) and avoidance of work place strains, repetitive tasks and forceful exertions. The counterstrain methods aimed at stretching muscles were developed to release MTrPs, improve functions, and reduce pain, which are: a positional release technique, ischemic compression, and transverse friction massage often combined with exercise. Other effective methods are manual therapies such as post-isometric relaxation, trigger point compression, muscle energy technique, myotherapy, and myofascial massage therapy [1-3,20,40]. Furthermore, extracorporeal shock wave (ESWT) and low energy laser therapy significantly reduce pain in patients with MPS [1-3,41].

These physical and manual therapiesunder the umbrella of CAM modalities are considered first line treatments in acute MPS [1-3,6,9,10,16,20]. Nonsteroidal anti-inflammatory drugs and other analgesics (ibuprofen, diclofenac, aspirin, etc) and muscle relaxants (Methocarbamol, Baclofen, oxazepam, diazepam etc) are often prescribed to patients with MPS, and myofascial pain (MP) linked with regional pain syndromes [1-4,6,19,40], for reducing muscle spasm and common pain. These medications have a number of adverse effects on longterm use and their effectiveness is weak like placebo compared to other modalities such as myofascial massage therapy and acupuncture and should be used only for reducing acute myofascial pain related to regional pain syndrome (RPS) and MPS.

Currently, several invasive methods are used effectively in controlling the pain of MPS and regional pain syndrome (RPS). In a meta-analysis, transcutaneous electrical nerve stimulation (TENS) or inferential current (IFC) is reported to produce a short-term (during therapy time) therapeutic effect concerning chronic low back pain and neck pain [42]. Conversely, TENS has no long-term benefit, i.e., post-therapy or 1-3 month later. However in a RCT, when TENS is combined with ultrasound phonophoresis (and compared with diclofenac phonophoresis, phonophoresis alone, and Sham ultrasound) three of them rapidly deactivated tender MTrPs and reduced pain intensity (by increasing pain threshold) but range of motion remained unaffected [43]. Besides local anesthetic injection into MTrPs (such as, procaine, lidocaine,

bupivacaine, prilocaine etc), dry needling (or needling with saline used earlier) is a useful technique (but reportedly painful) in which a small needle is effectively used to release MTrPs and associated symptoms including pain and referred pain [41]. The injection of local anesthetics are reported to have severe adverse effects such as muscle necrosis, fatal anaphylactic shock (in a susceptible person), and dose-related toxic effects. Therefore, low doses of such anesthetics are advised for preventing aforesaid effects. Practitioners should take precautionary measures while using these drugs; availability of tourniquet, IV diazepam, equipment for artificial respiration, cardiac defibrillator. Spraying overlying skin with ethyl chloride and stretching affected muscles is another effective technique that deactivates MTrPs (targeting muscle "energy crisis") [44]. Fluoromethane spray is not used because it is highly inflammable linked with accidental death and toxic effects on the ozone layer [1]. Currently, medical acupuncture needles associated with minimal pain and tissue injury are frequently used effectively in the treatment of patients with MTrP and MPS [41,45]. Surprisingly, needling of surrounding zone of MTrP or directly into it has similar therapeutic effect [1].

In a RCT, ozone therapy, lidocaine and dry needling were compared in patients with MPS; ozone and lidocaine were associated with better results compared to dry needling [8]. Several studies have reported prolonged relaxation of involved muscles,reasonable tolerability and safety, better quality of life and good outcome with Botulinum toxin injection (& Prabotulinumtoxin A) given in MTrPs associated with MPS compared to medications such as methylprednisolone (steroid), lidocaine and dry needling technique[46-49]. Botulinum A mediates the inhibition of acetylcholine release in MTrP. Currently therapeutic ultrasound combined with massage and stretching is regularly used for MPS treatment with good outcome [43,50]. Overall, the successful management of patients with chronic MPS and MTrPs requires multidimensional non-invasive (CAM therapies) and invasive interventions also directed towards contributory factorsand comorbid conditions.This review has some limitations including selection and publication biases, and is not comprehensive. The strength of this review is that it will fill up the knowledge gaps of concerned practitioners. A comprehensive paper that will include a report of 11 cases of MPS managed in a small hospital setting in Riyadh, Saudi Arabia will be forthcoming soon.

Table 3Several Clinical perspectives, diagnostic tests and management of MPS [1-3,40,45-49]

Clinical Features& Diagnostic Criteria (DC)	Etiological Factors	Comorbid Conditions& Differential Diagnosis	Diagnostic Tests	Treatment intervention
Acuteor chronic pain linked with referred pain;Pressure on taut muscle lasting 5-10 second results in reproduction of pain-D/C	Repeated strain and trauma; poor ergonomics-overuse & abnormal postures	Migraine&tension headache; spinal and disc pathology, post-herpetic neuralgia, &joint dis.	Mainly detailed history,palpation &physical and systemic examination	#Education and home programs,management and avoidance of contributory factors in chronic MPS
Hyperirritable MTrPs due to repeated muscle injury or comorbid diseases or unknown factors-D/C	Structural factors-spondylosis, scoliosis, osteoarthritis	Prostatitis, Endometriosis Dysmenorrhea, Urologic syndromes, Joint dysfunctions,	Lab. tests: exclude thyroid dis., high cholesterol& vitamin deficiency as D&B 12, infections and iron anemia	#Stretching, exercises and ergonomic modifications, MTrP release and contract relax technique.
Tender and latent MTrPs found within the contracted muscle belly called taut bands-D/C	Metabolic, infectious,psychological, MS, and visceral disorders	Hypothyroidism, Vitamin D and B12 deficiency, and iron deficiency anemia.	Plane x-ray excludes bony defectsas stenosis of foramen, scoliosis & spondylosis	NSAIDs) and muscle relaxants*, and various first & second generation antidepressants
Active &latent MTrP thatis found in some patientwith MPS and be activatedby pressure applied >10s-D/C.	Other systemic diseases, deficiency of vitamin D, 12 & iron, Lyme disease.	Autoimmune celiac and other diseases of malabsorption& Hypermobility syndrome	Ultrasound excludes bursitis &tendinopathy.	Physical and manual modalities- ESWT and low power laser therapy.
Palpation of MTrP may cause referredpain to other areas in a specific pattern of involved nerves indicating sensory abnormalities-D/C.	Tendinopathy, arthritis , bursitis, nerve entrapment	Temporomandibular joint disorder, fibromyalgia, painful bladder syndrome, and pelvic pain syndrome,	Electromyography; end-plate noise in MTrPs	TENS**& therapeutic ultrasound*, Hijamah (cupping therapy) and acupuncture.
LTR-on palpation of active MTrP-muscle abnormality-D/C. Pain relieved by stretching or injection of MTrP - Minor criterion	Cubital tunnel syndrome, insomniaand depression.	Vitamin B12 deficiency, Parasitic infection, Carpal tunnel syndrome	High definition ultrasound reveals MTrPs as hypoechoic.	Dry needling and local anaesthesia injection into MTrPs***.Lidocaine is better than dry needling, ozone therapy
Weakness, motion restriction and autonomic signsmatching Simmons' criteria	Radiculopathy or RPS as shoulder or hip, parasitic and Candida infections.	Irritable bowel syndrome Vulvovaginitis, Tendonitis, Whiplash disorders, and computer-related disorders	Medical imaging: to exclude other MS disorders. Stool examination to exclude parasite infection,	Botulinum toxin VS methylprednisolone combined with physiotherapy&Lidocaine injection vs BTX-A vs dry needling

#first option of interventions; *evidence is inconclusive;**short-term effect on pain; ***relatively invasive therapies but more effective in pain reduction; PTH=parathyroid hormone; MS=musculoskeletal disorders

SUMMARY

Myofascial pain syndrome, a multifactorial musculoskeletal pain disorder, is characterized by acute or chronic intense pain, muscle tenderness, restricted motion, weakness, and autonomic nervous symptoms concerning referred pain.MPShas major and minor diagnostic criteria including taut muscle, latent or active myofascial trigger points, local twitch response and other signs/symptoms such as numbness and goose-bumps. The prevalence of MPS varies in accordance to the age, gender, clinical settingsand general population, and often under diagnosed and misdiagnosis is commonplace. Comprehensive history and physical examination (palpation) are the

best methods for diagnosing MTrPs and MPS; however, various advanced techniques relatively expensive further support the diagnosis of MPS. Furthermore, a battery of laboratory investigations excludesdiverse systemic diseases and nutritional deficiency conditions and regional pain syndromes, which often co-occur with MPS. Although a variety of interventions with variable effectiveness are used in the management of MPS, first line definitive treatment is yet to be reported in the literature. Management of systemic diseases, regional MP syndromes (shoulder, head and neck pain, nonspecific low back pain, sacroiliac joint, knee joint etc) overlapping with MPS, and perpetuating factors (repeated injuries and strains) determines the overall treatment success of myofascial pain syndrome. The main pharmacological options for the management of MPS are analgesics such as NSAIDs (diclofenac), myorelaxants (oxazepam) and antidepressants (traditional, SSRIs and SNRIs and NDRIs), local anesthetics (Lidocaine), methylprednisolone (steroid), and Botulinum toxin A with variable efficacy. Local anesthetic and Botulinum toxin A injection targeting MTrPs of MPS have superior efficacy. Important Non-pharmacological complementary and physical therapies used successfully in patients with MPS include patient education, stretching, exercise, spray and hot/cold pack therapies, ischemic compression therapy (blockage of blood in an area of the body is made purposely, and upon release a resurgence of blood flow to the local area), deep therapeutic massage or myofascial massage or myofascial trigger point massage, TENS or interferential current (IFC) therapy, ultrasound phonophoresis, low-energy laser therapy (electricity is replaced by light here), ESWT, dry needling, and medical acupuncture and biofeedback therapy. Each patient with MPS is unique in its presentation with ill-defined pathophysiology, therefore, the treatment intervention directed towards MPS needs to be personalized and holistic in order to achieve better outcome with good quality of life. Evidently, myofascial massage, local anesthetic injection into MTrP, medical acupuncture and dry needling along with stretching exercises are most effective complementary and integrative therapies in the management of myofascial pain syndrome.

CONCLUSION

Myofascial pain syndrome, a common pain condition, co-occurs with diverse medical diseases and linked with regional pain dysfunctions, and perpetuated by a number of factors is characterized by salient features and has major and minor diagnostic criteria. The etiopathogenesis and pathophysiology of MPS and MTrPs is ill-

understood despite enormous research. Conventional approaches and complementary, alternative and integrative modalities have been used with variable success in the management of MPS with good quality outcome. This review calls for conducting rigor researches to explore basic pathophysiology of MPS and MTrPs and comparative double-blind randomized clinical trials in order to improve further the prognosis and outcome of this multifactorial musculoskeletal condition.

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