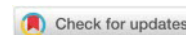


REFERRED MUSCLE PAIN, SOME CONSIDERATIONS OF ITS SIGNIFICANCE IN PRACTICE

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Abstract: Muscle pain is a common symptom in many musculoskeletal disorders. When it is local as a result of a muscle injury, correct diagnosis does not appear difficult. Referred muscle pain is a symptom associated with diagnostic and therapeutic challenges. It can be a consequence of an injury that develops elsewhere in the body: a skeletal muscle in another area or joint, or it can often be associated with a visceral injury (in this case we have referred muscle pain or secondary muscle pain). The aim of this article is to make a review of the available literature studying the nature, diagnosis, and treatment of referred pain and its relevance to clinical practice. Materials and Methods: In this review, the available scientific articles concerning the field of reflected pain are reviewed: Google Scholar, Pubmed, Science Direct Web of Science, Scopus, and scientific articles in Cyrillic) databases were reviewed. The search results included keywords that define the current problem: muscle pain, referred muscle pain, nociceptive pain, neuropathic pain, radicular pain, somatic, viscera, visceral pain, hyperalgesia, central sensitization, spinal sensitization, visceral hyperalgesia; viscerosomatic convergence; descending modulation, muscle contraction, muscle hypotrophy. Results: When searching for topical scientific results, not many publications have been found. Some of them were older, in some possible mechanisms of pathogenetic manifestation of referred muscle pain were discussed. One article suggested the existence of another possible mechanism besides the generally described ones. Several hypotheses concerning the occurrence of this secondary pain were found to exist, without giving priority to any theory. Most articles described different localizations of symptoms of referred pain and their relationship to other body structures (muscle or joint in a distant region) or internal organ dysfunction or disease. Most of the authors emphasized on the need of better knowledge of this type of pain and the distinction between local, nociceptive, radicular, and neuropathic pain that has a precise clinical characteristic and evidence of a specific injury to an underlying body structure. Conclusion: Knowledge and diagnosing of referred muscle pain is important for clinical practice. Differentiation from primary skeletal muscle pain is still a challenge, but a good knowledge of the problem can provide solutions, although the pathogenetic mechanisms of its occurrence remain unclear. It is likely that the totality of central-nervous mechanisms, the convergence of information from different somatic areas in the dorsal horn and/or its facilitation in it as well as at the level of the thalamus, and the phenomenon of hyperexcitability are essential, although the notion that referred muscle pain has a peripheral origin should not be ignored. Knowledge and targeted search for referred secondary pain could prevent some diagnostic problems and at the same time treat it with appropriate treatments, including the means of physiotherapy.

Keywords: muscle pain, referred muscle pain, visceral pain, central sensitization, muscle contraction, physiotherapy.

Field: Medical sciences and Health

1. INTRODUCTION

Muscle pain is a common symptom in many musculoskeletal disorders. When it is local as a result of a muscle injury, a precise diagnosis is not difficult (Marker-Hermann E., 2020; Giamberardino, M. A. et al., 2004; Yankai, A. et al., 2023). Muscle pain is associated with the activation of nociceptive nerve endings, associated with a decrease in tissue pH and adenosine triphosphate. Activation of these receptors in turn increases the excitability of sensory neurons in the spinal cord and leads to central sensitization. This, in turn, causes increased excitability on spinal cord level and is the cause of the onset of muscle pain, in which motoneurons of the injured muscle are inhibited on a central level. The occurrence of muscle spasm usually has a secondary origin and is due to damage to another muscle or joint. Current understanding of pain assumes that there are different types of pain, which are caused by different mechanisms and need to be treated differently depending on the origin of the pain (Mense S., 2008). Reflected muscle pain is a symptom associated with diagnostic and therapeutic challenges. It can be a consequence of an injury that develops elsewhere in the body: a skeletal muscle in another area or joint, or it can often be associated with a visceral injury (in this case referred muscle pain or secondary muscle pain) (Jin, Q. et al., 2023; Giamberardino, M. A. et al., 2004; Sikandar, S., & Dickenson, A. H., 2012).

Referred muscle pain in pathology of internal organs is a symptom that can be observed in

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myocardial infarction. Before true visceral pain develops, indeterminate pain in the lower sternal and/or epigastric, or interscapular region, accompanied by sweating, nausea, and tremor, is reported in the early stages of the disease. Subsequently, pain is localized to the chest in its anterior or posterior projection and often involves the left upper extremity. These cases are not infrequently accompanied by hyperalgesia of the m. Pectoralis major, inter-scapular space and forearm. In rarer cases, symptomatology may be seen in the area of the m. trapezius and/or m. deltoideus. Similar cases of reflected muscle pain in internal organ disease are seen in kidney colic, where it is found in the area of m. Quadratus lumborum and mm. obliquus, while in biliary colic there is reflected pain in the upper right abdominal quadrant and radiation to the back (Giamberardino, M. A. et al., 2004).

Sometimes symptoms can persist over time and a good knowledge of them can guide the clinician to the internal organ that is suffering. For example, weakness of the muscles on the inner side of the thigh may point to problems with the large intestine, such as colitis and obstipation; with flatfoot, it is necessary to monitor the condition of the muscles of the pelvic floor and female reproductive organs; back pain and shoulder forward bending may be associated with diseases of the stomach; hypertonia of the neck flexor muscles may point to problems in the maxillary sinuses, etc.

Lower back pain can be associated with morphological and functional changes in the hip muscles, such as mm. glutei, m. piriformis m. psoas major (Pourahmadi, M. et al., 2020).

All these examples draw attention to a secondary pain whose primary cause is located in another body segment, but often due to the prolonged persistence of the primary cause, a long-lasting referred muscle pain develops, accompanied by prolonged spasm and hypotrophy of the secondarily affected muscle (Giamberardino, M. A. et al., 2004).

The aim of this article is to make a review of the available literature studying the nature, diagnosis, and treatment of referred pain and its relevance to clinical practice.

2. MATERIALS AND METHODS

In this review, the available scientific articles concerning the field of reflected pain are reviewed: Google Scholar, Pubmed, Science Direct Web of Science, Scopus, and scientific articles in Cyrillic databases were reviewed. The search results included keywords that define the current problem: muscle pain, referred muscle pain, nociceptive pain, neuropathic pain, radicular pain, somatic, viscera, visceral pain, hyperalgesia, central sensitization, spinal sensitization, visceral hyperalgesia; viscerosomatic convergence; descending modulation, muscle contraction, muscle hypotrophy.

3. RESULTS

When searching for topical scientific results, not many publications have been found. Some of them were older, in some possible mechanisms of pathogenetic manifestation of referred muscle pain were discussed. One article suggested the existence of another possible mechanism besides the generally described ones. Several hypotheses concerning the occurrence of this secondary pain were found to exist, without giving priority to any theory. Most articles described different localizations of symptoms of referred pain and their relationship to other body structures (muscle or joint in a distant region) or internal organ dysfunction or disease. Most of the authors emphasized on the need of better knowledge of this type of pain and the distinction between local, nociceptive, radicular, and neuropathic pain that has a precise clinical characteristic and evidence of a specific injury to an underlying body structure.

4. DISCUSSIONS

Pain is a symptom that alerts to a problem in a particular body segment and is a common reason for a visit to the doctor. Accurate differentiation of pain and its origin is important for proper treatment (Nedyalkova-Petkova & Mihaylova, 2023; Bekir et al., 2022). Often, the diagnostic process is not complicated and with the help of a physical examination and instrumental or other laboratory testing, the source of pain is identified. At the same time, there are cases in which the diagnosis requires checking for the presence of secondary or referred muscle pain. Sometimes this type of pain may precede the clinical manifestation of the underlying disease, and the correct interpretation of this symptom may very early direct the clinician to the actual pathologic process.

For example, in low back pain (Nicol et al., 2023) according to literature data only in 20% of patients with low back pain a precise etiological cause can be found. In about 5% of patients, two or more causes may be found to be present simultaneously (Todorov, 2014). Low back pain is most

commonly caused by damage or degeneration of the intervertebral discs and intervertebral joints, which is characterized by vertebral and radicular syndrome, and in both syndromes the pain has different origins and characteristics. Radicular pain in this case is due to irritation of the dorsal root or their ganglia, or compression of various natures of the dorsal root ganglia (Bogduk, 2009; Vulfsons et al., 2017; Jin, Q. et al., 2023). In cases in which no morphological substrate is found in these structures, low back pain may be caused by thoracolumbar fascia and/or compartment syndrome, paravertebral muscles (mm. iliocostalis and longissimus dorsi) or by m. psoas and/or m. quadratus lumborum, ligaments and insertions in the form of enthesopathy, ligaments, (facet) joints, sacroiliac joints, in osteoporosis of vertebral bodies (Todorov, 2014; Becker et al., 2021) morphological and/or functional changes in the hip muscles, such as mm. glutei, m. piriformis m. psoas major (Pourahmadi et al., 2020) and others. In other cases, pain in the area of the m. Quadratus lumborum and mm. obliquus may be associated with renal pathology in asymptomatic renal calculi (Giamberardino et al., 2004). Therefore, differentiating primary, local pain from secondary referred pain is an important issue.

There are several scientific theories that attempt to explain the presence of referred muscle pain. According to some, the dorsal horn nociceptors and brainstem neurons receive information from different tissues, which converging results in the inability of higher brain centers to differentiate the actual source of pain (Arendt-Nielsen & Svensson, 2001; Yam M. F. et al., 2018). Referred muscle pain is likely determined by the distribution along the sclerotomes (muscle, fascia, and bone) and more rarely has a dermatomal representation (Whitman, Launico, & Adigun, 2023; Arendt-Nielsen & Svensson, 2001).

According to Mense S. (1993), muscle pain is more often associated with distant areas from the primary focus than skin pain. This is explained by the Convergence-Projection Theory, which postulates that the fusion of afferent information from internal organs at the spinal cord level with somatic afferent information leads to an increase in the activity of neurons in the dorsal horn due to its being read as originating from the same dermatome (Mense S., 1993). This is why it is important to know the connections at the level of the nervous system between the different cortical segments, including between somatic and visceral structures and organs (Gadet, 2019). Other plausible theories that explain referred muscle pain may be: Convergence-facilitation theory. The processing of the resultant subthreshold sensory afferents from skin receptors and from the sinuvertebral nerve is realized by the same spinothalamic structures, therefore these structures cannot localize the exact location of pain. (Simmons et al., 1993).

According to Arendt-Nielsen & Svensson, 2001) Axon-reflex theory (Yaprak, 2008) is a less likely explanation for referred muscle pain. According to them referred muscle pain is probably due to the activation of central-nervous mechanisms because it is possible to induce referred muscle pain in limbs with sensory loss. However, it should be considered that the absence of peripheral afferent for pain reduces the appearance of referred muscle pain, but it can be induced without the presence of peripheral input (Arendt-Nielsen & Svensson, 2001).

Hyperexcitability theory - the development of a central hyperexcitability mechanism may modify and modulate referred muscle pain, and substance P may possibly play a role in this regard (Arendt-Nielsen & Svensson, 2001; Polgár et al., 2020). According to Lidbeck J. (2002), dysfunctionality in central nervous information processing may explain the causes of different types of musculoskeletal pain, which in turn will allow, depending on the different pathophysiological mechanisms of pain induction, to differentiate different rehabilitation programs for pain management (Lidbeck, 2002; Martins et al., 2022, Krenn et al., 2020).

According to the Thalamic convergence theory, referred pain is not a consequence of information processing at the spinal cord level, but results from the accumulation of information in brain neurons after information from referred pain and from the damaged anatomical structure is aggregated. Computer simulations have been described that show that there may be communication between different cortical and subcortical structures (Arendt-Nielsen & Svensson, 2001; Lee & Winer, J. A. 2011).

Other authors assume that referred muscle pain has a predominantly peripheral origin. Farasyn, A. (2007) proposes the "barrier-dam" theory (Farasyn, 2007). According to this theory, if injured muscle structures (hard and/or soft myofibrosis), symptomatic and/or asymptomatic trigger points are located along the path of peripheral afferent sensory nerves in skeletal muscle, these structures can disrupt conduction along the nerve, compressing it and causing referred muscle pain. It has been suggested that these myofibrotic structures are a consequence of incomplete repair of a local inflammatory process in the setting of an impaired immune response in the tissue. This theory, for example, explains the burning pain in Meralgia paresthetica (tingling and burning pain in the outer thigh due to pinching of the n. cutaneus femoris lateralis, which is compressed at the exit of the pelvis) (Dengler N. F., 2023). By reducing the effect of the "barrier-dam" by means of deep cross-friction massage on rigid fibrosis (for at least 2 weeks), the reduction and disappearance of referred muscle pain in pseudo-sciatica is explained, which is associated

with nonspecific low back pain resulting from compression of the n. clunium superior medialis from muscle stiffening in the upper part of the m. gluteus medius et m. tensor fasciae latae (Konno et al., 2017); as well as in tension headache (in the temporal and/or orbital and/or frontal region of the head) caused by myofibrous points in the muscular body of m. sternocleidomastoideus et pars superior m. trapezius, which compress the nn. auricularis et transversus colli, et n. occipitalis; and also, in radiating tension along the dorsal part of the shoulder and upper limb, which results from squeezing at the level of the rhomboid and infraspinatus muscles of the rr. dorsales nn. thoracis (Farasyn, 2007).

It is likely that a cluster of central-nervous mechanisms, the convergence of information from different somatic areas in the dorsal horn and/or its facilitation in the dorsal horn, as well as at the level of the thalamus, the phenomenon of hyperexcitability and/or damage to peripheral muscle areas are essential for the occurrence of the referred muscle pain phenomenon.

Referred muscle pain may also be due to damage to various structures in the spine (Kurosawa, Murakami & Aizawa, 2015), such as the intervertebral discs, facet joints and sacroiliac joints (Jin et al., 2023). In these cases, it is very important to differentiate, true radicular pain (radicular-type pain, weakened or absent tendon and periosteal reflexes, muscle weakness and/or hypotrophy, and paresthesia along the course of the corresponding dermatome innervated by the peripheral nerve) and/or neuropathic pain (allodynia with hyperalgesia, spreading along the dermatomal type in the area innervated by the corresponding peripheral nerve) from referred muscle pain, because there may often be overlap of the areas of manifestation, but referred muscle pain does not spread along the dermatomal or radicular type (Farasyn, 2007); Jin et al., 2023). The pain is often dull, is described as an expanding pressure and spreads over a wide area, and sometimes has the character of hyperalgesia. Occasionally, muscle hypotrophy and hyperalgesia may also be observed in the area of reflected pain. There is no neurological symptomatology including numbness and paresthesia, as this type of pain is not caused by pathological compression on nerve roots. The shoulder and neck region are the most common areas in which secondary pain is seen when the cervical facet joints are affected, whereas dysfunction of the thoracic facet joints results in pain in the back and iliac crest region. Damage to the lumbar facet joints results in referred muscle pain in the area between the hip and thigh (reflected pain in the hip region, hip joint, and lateral thigh for the upper lumbar facet joints and in the posterior thigh region for the lower lumbar facet joints) (van Kleef et al., 2010; Manchikanti et al., 2020; Jin et al., 2023).

Referred muscle pain occurring in the lower back, buttock, groin, and thigh, even the foot, which is not radicular in origin, may be due to involvement of the sacroiliac joints (van der Wurff et al., 2006; Jin et al., 2023).

Recognition and targeted searching of the reflected secondary pain could prevent some diagnostic problems and at the same time treat it with appropriate treatments, including the means of Physical and Rehabilitation Medicine.

Due to the mentioned heterogeneity of the Referred muscle pain, a multimodal approach for its treatment is recommended, which incorporates pharmacological treatment, invasive therapy with local anesthetic blockages or intra-articular administration of corticosteroids, radiofrequency coagulation of articular nerves, methods from Physical Medicine, regular performance of therapeutic exercises and psychological support of patients (van Kleef et al., 2010; Jin et al., 2023; Li. et al., 2023).

Acupuncture, Manual medicine techniques, Trigger point injections, Laser therapy, Superficial dry needling in combination with muscle stretching, Massage, Application of heat or ice, TENS (Transcutaneous electrical nerve stimulation), Ethyl chloride spray and stretch technique, Ultrasound, Exercise may come into consideration in the treatment of referred muscle pain (Lidbeck, 2002; Yildirim, Öneş & Gökşenoğlu, 2018; Harada et al., 2019; Gibson et al., 2019; Ali et al., 2020; Chang et al., 2021; Martins et al., 2022; Krenn et al., 2020; Yankai, A. et al., 2023; Portilla et al., 2023).

5. CONCLUSIONS

Knowledge and diagnosing of referred muscle pain is important for clinical practice. Differentiation from primary skeletal muscle pain is still a challenge, but a good knowledge of the problem can provide solutions, although the pathogenetic mechanisms of its occurrence remain unclear. It is likely that the totality of central-nervous mechanisms, the convergence of information from different somatic areas in the dorsal horn and/or its facilitation in it as well as at the level of the thalamus, and the phenomenon of hyperexcitability are essential, although the notion that referred muscle pain has a peripheral origin should not be ignored. Knowledge and targeted search for referred secondary pain could prevent some diagnostic problems and at the same time treat it with appropriate treatments, including the means of physiotherapy.

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