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Relationship between structural changes in paravertebral muscles and the development of spine degenerative diseases

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Based on the systematic approach to the diagnosis of spinal pathology, there are no fundamental differences in the etiology of spine degenerative disease, facet joints arthritis, and other diseases. These diseases are considered multifactorial: age (aging), systemic regulatory factors (hormones, peptides, cytokines), genetic predisposition, inadequate physical activity, unfavorable environmental factors, and others lead to pathological changes in the structure of the spinal motor segment components. Recently, much attention has been paid to the paravertebral muscles changes, in which over time, as a result of injuries or degenerative processes, inevitably lead to dysfunction, which can lead to the occurrence of chronic lumbar pain. Objective. To assess the relationship between structural changes in paravertebral muscles and the development of degenerative diseases of the spine on the basis of scientific literature review. It was found that degenerative changes in paravertebral muscles, as components of spinal motor segments, develop with aging. In particular, muscle fibers are replaced by fat tissue, which is more pronounced in women compared to men. A direct correlation between chronic lumbar pain and paravertebral muscle atrophy has been reported. Systemic factors, in particular low levels of vitamin D, also can cause the development of degenerative changes in paravertebral muscles, especially in women. Obesity provokes systemic inflammation, increases fatty infiltration of skeletal muscles and increases sensitivity to pain. Reduced levels of physical activity lead to weakness and atrophy of the paravertebral muscles, which can cause degeneration of the intervertebral disc. At the same time, exercise prior to spinal surgery for degenerative diseases improves functional outcomes and reduces pain. Conversely, damage to the paravertebral muscles increase the load on the adjacent to spinal fusion segments. In general, the role of paravertebral muscles in the development of degenerative spinal diseases has not been definitively studied. Key words. Low back pain, paravertebral muscle atrophy, intervertebral disc, obesity, physical activity, vitamin D.

Виходячи з системного підходу до діагностики патології хребта, принципових відмінностей в етіології остеохондрозу, спондилоартрозу й інших хвороб немає. Ці захворювання розглядають як багатофакторні: до патологічних змін у структурі складових хребтового рухового сегмента призводять вік (старіння), системні фактори регуляції (гормони, пептиди, цитокіни), спадкова схильність, неадекватні навантаження, несприятливі чинники середовища тощо. Останнім часом багато уваги приділяють паравертебральним м'язам, зміни в яких із віком, у результаті травм або дегенеративних процесів неминуче призводять до порушення функціонування, що може спричинити виникнення хронічного поперекового болю. Мета. На підставі аналізу наукової літератури оцінити взаємозв'язок структурних змін у паравертебральних м'язах із розвитком дегенеративних захворювань хребта. Результати. Виявлено, що дегенеративні зміни в паравертебральних м'язах, як і в складових хребтових рухових сегментів, розвиваються з віком. Зокрема, м'язові волокна заміщуються жировою тканиною, що більше виражено в жінок порівняно з чоловіками. Доведено пряму залежність між хронічним поперековим болем і атрофією паравертебральних м'язів. Системні фактори, зокрема низький рівень вітаміну D, також обумовлюють розвиток дегенеративних змін у паравертебральних м'язах, особливо в жінок. Ожиріння провокує системне запалення, збільшує жирову інфільтрацію скелетних м'язів і підвищує чутливість до болю. Зменшення рівня фізичного навантаження призводить до слабкості й атрофії паравертебральних м'язів, що може стати чинником дегенерації міжхребцевого диска. Водночас, тренувальні вправи до хірургічних втручань на хребті з приводу дегенеративних захворювань покращують функціональні результати лікування та знижують больові відчуття. Навпаки, ушкодження паравертебральних м'язів підвищує навантаження на прилеглі до спондилодезу сегменти хребта. Загалом роль паравертебральних м'язів у розвитку дегенеративних захворювань хребта остаточно не з'ясована.

Key words. Low back pain, paravertebral muscle atrophy, intervertebral disc, obesity, physical activity, vitamin D

Introduction

According to the report on Global Burden of Disease Study by the WHO, lumbar pain is one of the 10 diseases that account for the most days of illness, and the prevalence of episodes per year is 15–45 % [1]. According to statistics, every year in Ukraine about 1 million patients seek medical help for degenerative diseases and traumatic spinal injuries, more than 16 thousand of them become disabled [2].

Based on a systematic approach to the diagnosis of spinal abnormality, there are no fundamental differences in the etiology of osteochondrosis, spondyloarthritis and other diseases of the spine [2]. These diseases are considered as multifactorial: it is shown that abnormal changes in the structure of the components of the spinal motor segment result from age (aging), systemic regulatory factors (hormones, peptides, cytokines), hereditary predisposition, inadequate loads, adverse environmental factors, etc. [3]. The most common cause of lumbar pain are structural changes in the intervertebral disc (45 %), arcuate (40 %) or sacroiliac joints (13 %) [4]. Regarding the role of paravertebral muscles in the etiology of lower back pain, a very limited number of articles have been published by the end of the last century [5, 6], but recently they have received increasing attention [7].

Paravertebral muscles (multifidus, rectus spinae, quadratus lumborum, large lumbar muscle) play a significant role in ensuring the mechanical stability of the spine, protecting its structures from destruction due to load [7, 8]. Changes in paravertebral muscles with age, as a result of trauma or degenerative processes inevitably lead to their dysfunction, which can trigger chronic lumbar pain [9, 10]. Numerous changes in the morphology and physiology of the intervertebral disc have been described, but this knowledge has not yet led to the formation of a generally accepted model of the disease. This situation, in turn, complicates the development of effective pathogenic methods for the treatment of osteochondrosis of the spine [2, 11].

The aim of the study: to evaluate the relationship of structural changes in the paravertebral muscles with the development of degenerative diseases of the spine based on the assessment of the scientific literature.

Materials and methods

Literature review was conducted using PubMed, Google Scholar databases.

Results and discussion

Pain syndrome

The most significant clinical manifestation of degenerative diseases of the spine is pain, the occurrence of which is largely associated with degeneration of the intervertebral disc and disruption of its structure and function [4].

Numerous studies have been conducted in recent years to determine the effect of muscle structure on lower back pain. The degenerative changes in the muscles observed in such patients are associated with an increase in adipose tissue and a decrease in muscle cross-sectional area [12]. Fat infiltration or an increase in the proportion of fat in the cross section of the paravertebral muscles, detected by radiological methods, is considered a marker of muscle atrophy, which plays a role in the development of lumbar pain [13–15]. The relationship between back pain, degenerative diseases of the spine and the content of adipose tissue in a particular muscle has been proven. In particular, in clinical studies of patients with back pain and intervertebral disc degeneration at the level of L_{IV}–L_V or L_V–S_I [14], from L_I–L_{II} to L_V–S_I [16], as well as with nonspecific chronic back pain [17] the relationship between the severity of the disease and the amount of fat in the muscle is determined. An increase in the area of adipose tissue in this muscle has also been associated with the presence of spondyloarthritis in patients with lower back pain [18].

Recently, with the help of 3D reconstruction of computed tomography scans, the relationship between lumbar muscle degeneration and disc degeneration, as well as age, has been established [15, 19]. There is a theory that multifunctional muscle dysfunction, which is detected on tomographic images in the form of fat accumulation, is the cause of recurrent lumbar pain [20]. This is due to structural changes in the muscle that do not go away after the pain stops, but continue to exist, leading to relapse. Accumulation of fat in the muscles at the level of L_{IV}–L_V is associated not only with pain, but also with a violation of the structure of the locking plate (Modic I and I/II type) [21]. In addition, the severity of disorders in the intervertebral disc is associated with changes in the locking plate and the accumulation of fat in the paravertebral muscles of both women and men over the age of 50 with lumbar pain [14].

In a systemic review that included 25 studies, structural changes in the multi-muscle were named as a predictor of lumbar pain in men in 12 months after the first episode of its occurrence, for other paravertebral muscles (spinal rectus, lumbar quadriceps and lumbar muscle) no direct evidence of a similar relationship has been established [22]. A study of elderly people with and without chronic low back pain found that L_{II}–L_V fat content in multi-part muscle was higher in patients with pain and in lumbar muscle was

independent [15, 17]. Researchers have also found gender differences in the structure of the muscle of patients with pain, namely, women have higher fat content in this muscle than men. The results of other clinical studies in patients with degenerative diseases of the spine also confirm the higher content of fat in the paravertebral muscles of women compared to men [23, 24].

The mechanism of development of degenerative changes in the multislice muscle in the presence of degenerative diseases of the spine is associated with: 1) muscle compression due to lateral stenosis; intervertebral disc herniation, prolonged ischemia and nerve damage leading to muscle atrophy; 2) compression of the sinuvertebral nerve, which causes pain and reduces the patient's mobility [25].

Assessment of 267 scientific papers published since January 2010, 34 of which met the criterion of inclusion in the study (the availability of information on the relationship between paravertebral muscles and lumbar pain, thoracolumbar abnormality or postoperative consequences), showed the relationship of paravertebral atrophy muscles with degenerative diseases of the spine [7].

At the same time, there is no reliable evidence of a direct relationship between the severity of structural changes in the muscles and the degree of degeneration of the intervertebral disc. A study in dogs with chondrodystrophy who developed spontaneous intervertebral disc herniation and low back pain found that there was no direct relationship between muscle fat accumulation and the severity of intervertebral disc degeneration [26]. Dogs with a higher index of disc degeneration have lower muscle fat than animals with a lower index. Therefore, researchers believe that chronic pain and general condition of the spine are more likely to be associated with structural changes in the muscles.

In a clinical study of patients with lumbar pain, there was also no relationship between the degree of degeneration of the intervertebral disc and the accumulation of fat in the multidisciplinary muscle [27].

Age-specific changes

The aging process is accompanied by degenerative changes in the components of the spinal motor segment, as well as loss of muscle mass (sarcopenia) and muscle degeneration. However, sarcopenia is less associated with back pain than muscle degeneration [28]. A study of 99 twin men found that with age, the amount of adipose tissue increased and the transverse area of the paravertebral muscles decreased at the level of L_{III}–L_{IV} and L_V–S_I [29]. An experiment involving 516 healthy women showed a similar tendency to increase fat content in the paravertebral muscles with age [30]. The problem of reducing muscle mass and strength with age is known and in recent years in this direction are intensive research [13, 31]. It is generally believed that the decrease in muscle mass and strength is part of the aging process, but there has been significant variability in the rate of these changes between people [32]. It has been found that with age, the content of muscle tissue in the paravertebral muscles decreases secondary to an increase in connective and adipose tissue [15], and in patients with degenerative diseases of the lumbar spine, these changes are much more evident [33].

The intervertebral disc consists of two main components, namely a gelatinous nucleus and a fibrous ring. The components of the matrix, mostly proteoglycans and collagen, undergo a slow and continuous cell-mediated renewal process. Aging cells and a history of chronic overload can upset this balance, leading to progressive tissue failure and degeneration [34, 35]. Degeneration of intervertebral discs with age is accompanied by a decrease in the number of cells and increased clustering of viable. Excessive cell death with age is associated with the activation of apoptosis due to chemical factors, as well as with impaired disc trophism and inadequate loading of the spine [36, 37].

From the third decade of life in humans the ratio of keratan sulfate to chondroitin sulfate in the intervertebral disc increases, and the ratio of chondroitin-4-sulfate changes among chondroitin sulfates, the synthesis and the concentration of proteoglycans and non-collagen proteins decreases, the proportion of proteoglycans and water reduces, and collagen increases [36, 37]. This increases the expression of collagen type I, and that of collagen II decreases sharply, especially in the gelatinous nucleus. Type X collagen is associated with histomorphological signs of degeneration (cracks and fractures) and calcification of the closure plate. Collagen III and VI types are promising effective markers of early degenerative changes, because their content increases during skeletal maturation, and in areas of the matrix prone to early disorganization, they are not detected [38]. There are three phases of changes in the matrix of the intervertebral disc associated with age: 1) growth (0–15 years) — active synthesis of aggrecan and procollagen types I and II; 2) maturation (15–40 years) — decreased synthesis of matrix components, except for procollagen type I; 3) degeneration and fibrosis (over 40 years) — increased levels of denatured collagen type II and synthesis of procollagen type I [36], limiting the supply of nutrients

due to the formation of scar tissue [39]. The described age-related structural and metabolic disorders cause changes in the mechanical properties of the tissues of the fibrous ring, a decrease in the turgor of the gelatinous nucleus, dehydration of the disc with loss of its elasticity and a decrease in its height.

Degenerative changes also develop in the arcuate joints with age, leading to osteoarthritis [40]. Depending on its severity, fat accumulates in the paravertebral muscles adjacent to the level of pathology [41].

Mechanical factors

One of the main debatable issues is the sequence and cause-and-effect relationship of biological and biomechanical changes that occur under conditions of intervertebral disc degeneration. Some authors give priority to biomechanical disorders [42]. Mechanical stress affects the turgor of the matrix, because the response of cells of the intervertebral disc to physical stimuli depends largely on its mechanical properties and varies depending on the region of the disc and the degree of degeneration. Inadequate chronic load can lead to degradation, namely: to a decrease in the content of matrix components, loss of its integrity and, accordingly, disruption of the biomechanical reaction. The altered matrix transmits inadequate signals to the cells, causing a cascade of events that can ultimately lead to tissue degeneration [36, 43]. It is believed that in women the spine is more sensitive to overload than in men [44].

Reducing the physiologically normal load on the body adversely affects the structure and function of the paravertebral muscles. After a long absence of gravity, astronauts showed a decrease in cross-sectional area and weakness of the paravertebral muscles (multi-lumbar, lumbar, rectifier, square back muscle), but a year after being on Earth, this figure returned to normal [45]. Also, astronauts in the first year after returning to Earth have an increased risk of intervertebral disc herniation, almost 4.3 times compared to persons who have not been in space [46]. At the same time, being in space does not affect the height of the intervertebral discs [46, 47]. It is likely that atrophy and muscle weakness are the cause of disc herniation.

An experiment on Javanese macaques, injected with botulinum toxin into the paravertebral muscles to simulate weakness, found that this reduces the height of the intervertebral discs at the level of L_{II}–L_V by 5–6 % 21 weeks after injection [48].

The role of the mechanical factor in the etiology of degenerative diseases of the spine is confirmed by the following data: the localization of structural changes corresponds to the segments that carry the greatest load; frequent cases of development after a single injury; prevalence of the disease among persons engaged in heavy physical labor; the disease often develops with static-dynamic disorders that lead to uneven loading of the intervertebral disc and arcuate joints; experimental reproduction of osteochondrosis using mechanical factors.

Systemic factors

Vitamin D plays a role in ensuring muscle function and maintaining normal muscle mass levels with age [49]. D-hormone acts on skeletal muscle cells through the vitamin D receptor (VDR). In patients with low back pain, vitamin D deficiency causes atrophy of the multiple muscles associated with mitochondrial dysfunction due to insufficient calcium. Among such patients, women are more sensitive than men to atrophy of the multiple muscle, which developed due to vitamin D deficiency [50].

A study in vitamin D deficient mice showed histologically the occurrence of paravertebral muscle atrophy and a decrease in the number of vitamin D receptors [50].

VDR gene polymorphism has been shown to be associated with lower back pain and, in particular, spinal abnormalities involving hernias and discopathy, locking plate lesions [51, 52]. However, discussions about these associations are ongoing [53] and there are no functional studies to assess the real impact of genetic variants of VDR on intervertebral disc degeneration.

Obesity (body mass index over 30 kg/m^2) is associated with lumbar pain [54–56]. Among the reasons for this relationship are considered, firstly, biomechanical factors, and secondly, inflammatory factors [57]. It is believed that obese people have increased levels of proinflammatory cytokines due to inflammation of adipocytes in adipose tissue, which initiates the differentiation of monocytes into macrophages that accumulate in adjacent tissues, including skeletal muscle, and secrete proinflammatory cytokines (C-reactive protein, factor tumor necrosis alpha (TNF-α), interleukin-6 (IL-6) [57, 58] These processes lead to systemic inflammation and increased sensitivity to pain.

A high-fat diet, used as an experimental model of obesity [59], is known to cause oxidative stress in rat skeletal muscle [60], inhibits mitochondrial function [61] and upsets the balance between their division and fusion [62]. This, in turn, has a negative effect on the functioning of muscles and, consequently, on their structure. Accumulation of fat in multi-muscle, according to recent clinical data, is associated with dysregulation of inflammation in it [63].

The increase in adipose tissue in muscle is probably due to leptin resistance in obesity, which contributes to the differentiation of new adipocytes and the accumulation of fat in skeletal muscle [64].

Etiological role of paravertebral muscles

Less pain and faster rehabilitation after lumbar spine spondylodesis have been reported in patients with a larger lumbar cross-sectional area before surgery [65]. Also, the best results on the VAS and Oswestry scale were obtained in patients with lower fat content in the paravertebral muscles and large lumbar muscle in 1 and 6 months after microdiscectomy [66]. In patients after removal of lumbar spine stenosis, lower fat content in the paravertebral muscles before surgery was also associated with better postoperative functional outcome on the Oswestry scale [67, 68]. This is explained by the results of a biomechanical study of the musculoskeletal model with spondylodesis at the level of L_{II}–L_V, where it was found that damage to paravertebral muscles increases the load on the segments of the spine adjacent to spondylodesis [69]. The experiments determined the best results of spondylodesis in rats that swam before and after surgery and as a result had a better condition of the paravertebral muscles [70]. These data suggest the influence of paravertebral muscles not only on the results of surgery, but also on the development of degenerative changes in the spine. However, this issue remains little studied. In particular, in a rat experiment, the authors studied the relationship between multiple muscle dissection and the development of intervertebral disc degeneration and found no decrease in the area of the gelatinous nucleus 7, 14, and 28 days after surgery [71].

Conclusions

There is a direct relationship between the presence of chronic lumbar pain and paravertebral muscle atrophy.

Degenerative changes in the paravertebral muscles, as well as in the components of the spinal motor segments, develop with age. In particular, muscle fibers are replaced by adipose tissue.

Obesity provokes systemic inflammation, increases skeletal muscle infiltration, and increases sensitivity to pain.

Decreased exercise leads to weakness and atrophy of the paravertebral muscles, which can cause degeneration of the intervertebral disc.

At the same time, it has been proven that training exercises for spinal surgeries (spondylodesis, microdiscectomy, etc.) for degenerative diseases improve the functional results of treatment and reduce pain. In contrast, damage to the paravertebral muscles increases the load on the segments of the spine adjacent to the spondylodesis.

Systemic factors, including low levels of vitamin D, also cause degenerative changes in the paravertebral muscles, especially in women.

In general, the role of paravertebral muscles in the development of degenerative diseases of the spine has not been definitively elucidated.

Conflict of interest. The authors declare no conflict of interest.

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RELATIONSHIP BETWEEN STRUCTURAL CHANGES IN PARAVERTEBRAL MUSCLES AND THE DEVELOPMENT OF SPINE DEGENERATIVE DISEASES

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