A review of the degenerative intervertebral disc disease

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ABSTRACT

Degenerative disc disorders represent an important cause of morbidity in everyday clinical practice. Numerous factors may initiate degenerative processes, which most commonly affect the nucleus pulposus and ultimately influence the biomechanics of the spine. Mechanisms of degeneration and associated factors are briefly described.

Key words: fibrous annulus, nucleus pulposus, intervertebral disc, degeneration, spine.

1 INTRODUCTION

The degenerative disease of the intervertebral disc and the back pain are chronic conditions that are caused by numerous factors. They represent an important cause of both morbidity and mortality [1]. During the clinical examination, the disease may present itself as axial back pain, spinal stenosis, myelopathy or radiculopathy. The consequences of the degenerative disease of the intervertebral disc are among the main initiative factors for chronic instability of the diseased segments of the spine and also for functional disability among both sexes, which significantly affect living quality, especially in young and active population [1-3].

2 EPIDEMIOLOGICAL CONDITIONS

The incidence of low back pain varies widely among different reports. It is the fifth most common cause for the visit to the doctor and affects 7.6 to 37% of patients. Long lasting pain and movement difficulties are experienced by 10% of patients [1-3]. The degeneration of the intervertebral disc tissue starts sooner than that of other muscular and skeletal tissues and is in many cases asymptomatic [4,5]. It is reported that the initial degeneration of intervertebral disc may be present as early as in the adolescence, when 20% of young people have mild signs of the disease. With age, the incidence rises. It affects 10% of male population at the age of 50 years and up to 50% at the age of 70 years. In some reports, the degenerative disease of the intervertebral disc may be present in 90% of people; many of them have no signs of the disease [2,3,6,7].

Low back pain is strongly connected to the degenerative process of the intervertebral disc. The height of the intervertebral disc gradually falls and the consequence is changed dynamics in the affected segment of the spine. This accelerates the degeneration of other, nearby segments as well as other spinal structures, such as ligaments, joints and muscles. In the long term, this leads to narrowing of the spinal canal with the compression of the neural tissues due to the spinal stenosis, which is the main cause of pain, especially among the elderly. With the increase of elderly population, this problem is gaining significance [5].

3 STRUCTURE OF THE INTERVERTEBRAL DISC

The intervertebral disc is composed of three layers: I) fibrous annulus with its outer and inner part, II) central pulposus nucleus and III) terminal plates [4,5]. The disc is avascular, structure, made of fibrous tissue and cartilage. Microscopically, it is composed of scarce fibroblast-like cells, located in the extracellular matrix, which accounts for the most of the disc structure. Both cells and matrix are fundamental for normal function of the intervertebral disc [4].
4 HERNIATED DISC

Herniated and prolapsed discs are among the most frequent reasons for presentation to the orthopaedist or neurosurgeon (Figures 1 and 2). Herniation is bulging of the disc due to partial or complete rupture of the outer fibrous annulus. The bulging may involve anterior, posterolateral or posterior direction. The last two directions are particularly important as they cause compression of the neural structures in the vertebral canal [8]. Occasionally, spontaneous resorption of the disc may occur, leading to improvement or even cessation of lumbar pain [9]. Although disc herniation is most commonly caused due to mechanical injury and consequent rupture of the fibrous annulus, some extent of initial degeneration is necessary in order to allow the pulposus nucleus to herniate through fibrous bands of annulus into the vertebral canal. For a healthy disc to rupture, an enormous force is necessary. In many cases, the terminal plate of the vertebrae fails sooner than the fibrous belt [10-14].

5 THE PROCESS OF DEGENERATION

The border between the annulus of the intervertebral disc and its nucleus becomes more and more pronounced during the organism growth. Numerous mechanical factors, depending on duration, severity, type and position of load, affects the state of the intervertebral disc and thus the biological response to these factors [4,7]. The degenerative processes encompass the structural damage of the intervertebral disc and the changes in the number and composition of cells. With aging and advancing degeneration, the nucleus is primary affected. It becomes more fibrous and less elastic. Tiny concentric breaks emerge in the outer part of the disc from where they extend into the nucleus. The amount of fibrous tissue rises, the composition and quantity of proteoglycans changes and the number of cells changes due to apoptosis [7,14-17]. Mechanical, traumatic, genetic and nutritional factors play an important role in the degenerative process. The fibres in the fibrous annulus become increasingly disoriented and the network made of elastin and collagen fibres gradually deteriorates. Cells in the nucleus are affected by apoptosis and later on by necrosis, on the other hand they tend to proliferate excessively. These degenerative cascades are frequent and in an adult intervertebral disc, up to 50% of cells may be necrotic [10,14,15].

The main factor in the degeneration of the intervertebral disc is the loss of proteoglycans. These large molecules are degraded to smaller fragments that are lost from disc tissue. The consequence is a fall in the osmotic pressure in the disc matrix and the loss of water molecules, which affects the mechanical properties of the disc [14,18]. As degenerated intervertebral discs contain less water and have therefore inferior capabilities for sustaining pressure, they bulge and lose height. Proteoglycan loss affects also movement of other molecules into and out of the disc matrix. Serum proteins an cytokines diffuse into the matrix, affecting the cells and accelerating the process of the degeneration [5,15,16,18].

The quantity of the disc collagen and its composition are also connected with the matrix degeneration. The orientation, location and types of collagen fibres are mostly affected, while the effect on the total quantity of collagen is not so pronounced. Old collagen fibres become denatured, although new fibres are being synthesised early in the process of degeneration. The enzyme activity has an important role in the process of collagen, fibronectin and proteoglycan denaturation and breakdown. Among these, matrix metalloproteinases and cathepsins are the most important [5,6,13,15,19].

The degenerative changes of the intervertebral disc are connected to damage of nearby structures, such as ligaments, joints and vertebral muscles. This leads to functional changes and greater susceptibility to injuries [5,19]. Due to load, a degenerated intervertebral disc is lower than normal and apophyseal joints need to bear higher loads. The consequence is osteoarthritic degeneration. Strength of yellow ligaments decreases, which leads to their hypertrophy and protrusion of the ligaments into the spinal canal with consequent narrowing and compression of neural structures. The causes for pain in the course of the degenerative process are complex and in many cases a fair combination of structural and mechanical deformation as well as activity of inflammatory mediators [20]. Frequently, spinal nerve radicles are involved in the degenerative cascade, which causes chronic pain mainly due to their compression and partly due to ingrowths of tiny neural endings into the degenerated disc and their activation due to constant release of inflammatory mediators [5,20].

6 FACTORS INFLUENCING THE DEGENERATIVE PROCESS
6.1 Degeneration due to nutritional disorders of the disc

One of the important reasons for the degenerative process is also nutritional disorder of the intervertebral disc [21]. For normal function and structure of the disc, the cells need sufficient nutritional supply. Disc is avascular structure and its supply depends mainly on diffusion. Capillaries arising in the vertebral bodies extend only to the subchondral area of the disc terminal plate. This means that gasses and nutrients must diffuse through extracellular matrix in order to reach the cells. A fall in nutritional supply causes a fall in oxygen quantity and a rise in lactate concentration with consequent pH alteration, affecting the cell function and synthesis of extracellular matrix. In the long term, this leads to degenerative process [13,21-23].

6.2 Mechanical stress

Abnormal mechanical loads and micro injuries lead to disc degeneration through faster wear and tear of both acellular and cellular components, involving the processes described earlier. The common consequence is chronic pain [24]. The most important risk factors involve heavy physical labour, obesity, smoking (through atherosclerosis of minute vessels that supply the terminal plates), lack of physical activity and inappropriate flexed posture [18,24,25].

6.3 Genetic factors

There is also a genetic basis for the degenerative process of the intervertebral disc. Certain genetic polymorphisms for matrix molecules define the integrity of the extracellular matrix and these polymorphisms may also influence the course of the degenerative process [23,26]. Mutations in genes coding for matrix molecules lead to alterations of matrix morphology, consequently affecting the function and biochemical processes of the disc. However, genes alone are not the only reasons for disc disease as environmental factors are also involved, showing that intervertebral disc degeneration is probably a multifactorial disease [27-29].

6.4 Bacterial infection of the intervertebral disc

The exact pathobiology of degenerative disc disease is still unknown [28,29]. As discussed, numerous factors play a role in the degeneration, such as genetics, vascular aspects, mechanical stress, inflammatory and biochemical changes. One of recently described agents that may start the degenerative process is also bacteria. It has been proposed, according to some studies, that intervertebral disc degeneration might be initiated by a long-lasting low-grade infection, eventually leading to the disc prolapse and herniation. The \textit{Propionibacterium acnes} is the most commonly isolated infectious agent, which may be the principal cause for the disc disease. Some studies concerning the bacteriology of the intervertebral discs have been conducted and the results were contradictory. Although the positive disc cultures may have resulted from specimen contamination after disc removal, on the other hand, the degeneration processes were stopped or slowed by antibiotic treatment. It is still not known whether the genesis of disc degeneration originates in the immune system and repeated episodes of injury and reparation that could eventually culminate to the progressive tissue damage [30-33].

7 CONCLUSION

Degenerative disease of the intervertebral disc remains a significant health problem, still not understood and solved sufficiently [34,35]. Besides standard conservative and surgical treatment, techniques of regenerative therapy are very promising, although most of them still in the experimental phase [35-38]. Regenerative therapy aims to restore the degenerated disc matrix by two approaches: with growth factors enhancing extracellular matrix synthesis by the disc cells and with agents inhibiting cytokines that normally cause matrix loss [36-38].
COMPETING INTERESTS

Authors have declared that no competing interests exist.

AUTHORS' CONTRIBUTIONS

Tomaz Velnar designed the review, Gorazd Bunc collected the data, Uros Maver and Lidija Gradišnik managed the analyses and the literature searches. All authors read and approved the final manuscript.

REFERENCES

Figure 1: A T2-phase MRI scan of lumbar spine showing massive disc herniation at L5-S1 level.

Figure 2: Axial view of T2-phase MRI scan of the same segment. Thin arrow indicates herniated disc.