1) Anatomic Structure and Main Components of Intervertebral Disc

Invertebral disc has a complex anatomic and biochemical structure. It mainly consists of chondrocyte and fibrosis, which shows anatomic expansion in an avascular macromolecular matrix formed by collagen and proteoglycans.

The main components of intervertebral disc are:
- Last plaque composed of cartilage
- Annulus fibrosus (external/internal)
- Transition zone
- Nucleus pulposus

Structure of Annulus Fibrosus (External/Internal)

External annulus fibrosus composed of fibrils (Type I and in less amount Type II, III, V, VI and XI) which are regular, dense and in parallel. On the other hand, internal annulus fibrosus consists of Type II collagen. The transition zone between internal and external annuluses is a thin layer, which consists of cell-like chondrocyte.

2) Epidemiology of Degenerative Disc Diseases

It is known that 8 adults out of 10 adults in the public complain about back pain once in their lifetime. Complain due to chronic problems is seen around 5% in the public.

2a) Alterations in Disc Degeneration

Morphological alterations;
- Dehydration
- Fissuring
- Nucleus, annulus, last plaque torn

Molecular alterations;
- Decline in diffusion
- Decline in cell vigorous
- Decline in proteoglycan synthesis
- Alteration of collagen distribution

2b) Reasons of Disc Degeneration

The frequent risk factor related to disc degeneration is senescence. Beside senescence; some other risk factors such as; trauma, life style, use of cigarettes, vocational factors, tallness, obesity, lomber spinal morphology (antropometric) may also be effective in arising of disc degeneration.

Studies indicate that genetic risk factors have also important roles in degenerative disc diseases. According to these results, it is possible to say that there is a constitutional inborn tendency difference between people.

2c) Genetic Tendency in Degenerative Disc Diseases

Twin Studies

Bull and his colleagues introduced that cervical alterations on direct graft is extremely similar (concordance) for 57 twins in their research in 1969.
Although, the study did not focus on disc degeneration directly, it is observed that, while cervical radiological anatomy concordance is 77.5% in monozygotic twins, the ratio was 42.5% in dizygotic twins, which is significantly difference than that of monozygotic twins.

3) Genetic Factors in Degenerative Disc Diseases

Nelson and his colleagues examined their young patients, who were operated discectomy, in three groups according to their age (9-15, 16-19, 20-25) in their research in 1972. They observed that the patients in the youngest group has degenerative disc disease five times more comparing to that of healthy individuals in the same age group. Varlotta indicated in his research in 1991 that, when the patients under 21 years old, who have disc hernia, are compared to the healthy individuals in the same age group, it was observed that family history is five times more for the patients in the first group.

Similar results were obtained from the study of Porter, which stated that the relatives of patients who were applied discectomy, had a higher ratio in terms of back pain story. Matsui and his colleagues compared the magnetic resonance (MR) imaging and direct grafts of 24 patients with back pain, who have relatives operated discectomy, with 72 back pain patients who have no operated disc hernia story in their families: the intensity of disk degeneration and incidence of disc hernia is significantly higher in the group, whose family history had operated lomber disc hernia. It was indicated that a genetic factor determines the arising of disk degeneration may also take role in the progression of lomber disc hernia.

Studies indicate that mutations in collagen gene also take role in some familial connective tissue diseases. Knowlton and his colleagues showed that there is genetic linkage between primer osteoarthritis and Type II pro-collagen gene polymorphism in 1990. Another researcher Ala-Kokko determined that, there is a relation between specific alleles of pro-collagene Type II (Co12A1) gene found in 12th chromosome and primer generalized osteoarthritis. This collagen is the pioneer of the basic disc protein. Moreover, genotype caused by this mutation developed with moderate chondrodysplasia.

Savontus and his colleagues showed that mutations in Type II collagen repress the expression of genes related with spinal development in transgenic mice experiments in 1997. Shalman and his colleagues showed that inactivation of one of the alleles in Co12A1 gene, which constitutes the structure of Type II collagen, result in the premature vertebra last plaque ossification and moderate disc degeneration in experimental mice in the research focus on molecular mechanism of collagen IX lomber disc disease in 2001.

4) Biological Treatments in Disc Degeneration

Is it possible to postpone or decrease the degeneration?

Nowadays; various inflammation agents, growth hormones, proteinase inhibitors and intracellular regulator proteins and kind of biological materials have been being tried in order to postpone or decrease the disc degeneration. Results from both in vitro and in vivo studies are encouraging. Beside, gene therapy studies have been planned. However, the main point is whether the degeneration is going to turn back. Constitutively, prominent method for these studies is stem cell technology.

In 2006, Sakai and his colleagues transferred autologous mesenchymal stem cells derived from bone marrow to the disc degenerative rabbit model in order to understand whether stem cell application will treat degenerative intervertebral disc disease. Twenty-four weeks after the transfer of mesenchymal stem cell, it is determined that, in degenerative disc disease mice who was transferred stem cell, %91 of disc height and %81 of MR signal intensity was reached again compared to normal controls who was not operated. On the other hand; the other discs, in which Sham operation was performed, disc height and intensity of MR signal remained as %67 and %60 increases respectively. After macroscopic and histological evaluations, compared to Sham operated discs which was observed as scattered structure, mesenchymal stem cell transferred discs protected the nucleus circular annulus structure. Another study conducted by Hee and his colleagues suggested that bone marrow transplantation to the degenerative disc in a rabbit model provide enhancement in the disc height, morphological grading.
histological scoring and average dead cell count. After these studies, it was proven that, mesenchymal stem cell transfer in degenerative disc in a rabbit model provides the intervertebral disc regeneration efficiently.

Yoshikawa and his colleagues\textsuperscript{13} performed bone marrow derived mesenchymal stem cell transplantation to two female patients, who were 67 and 70 years old suffering from lumbago, leg pain, and numbness. Two years after surgeries, it was observed that intervertebral disc intensity was high on MR imaging. In recent years, these studies and similar studies showed that, mesenchymal stem cells can be used as an important source in cell therapy treatments of disc degeneration disease\textsuperscript{(14-17)}.

\begin{figure}[h]
\centering
\includegraphics[width=\textwidth]{figure1.png}
\caption{In the mesenchymal stem cell derived from adult tissue; \textbf{a}) Mesenchymal cell culture, \textbf{b}) Dendritic structures special to nerve cells.}
\end{figure}
References


