Regenerative Treatments for Spinal Conditions

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KEYWORDS

• Spine • Regenerative • Intradiscal • Platelet rich plasma • Mesenchymal stem cells • Fibrin • Annular fissure • Low back pain

KEY POINTS

- Low back pain is a common and expensive cause of disability.
- Nonhealing annular fissures are the most common cause for low back pain.
- Early treatment of painful annular fissures may also help prevent progression to spinal deformity, stenosis, and disability.
- Intradiscal platelet rich plasma, mesenchymal stem cells, and fibrin are promising therapeutic options for intervertebral disc degeneration.
- Regenerative treatments may offer a more cost-effective solution for refractory discogenic pain and perhaps avoid expensive surgery altogether.

INTRODUCTION

Although there are many causes of low back pain, most experts agree that the beginning of the end of the spine starts with an injury to the intervertebral disc (IVD). When the disc begins to fail, the "degenerative cascade" begins and the subsequent sequelae of facet loading, spinal deformity, stenosis, and nerve root compression ensue.[1] Adult spinal deformity is increasingly common in the aging population, with prevalence as high as 68% in adults older than 60 years.[2] Adult spinal deformity is also a debilitating disease that greatly affects quality of life. Studies have shown that adults with scoliosis score significantly lower in self-reported outcome measures, such as the 36-item Short Form Health Survey (SF-36) questionnaire, compared with the general US population, including physical functioning, vitality, social functioning, emotional role, physical role, and mental health.[3] Adult spinal deformity has a similar

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global burden as well. In fact, a prospective multicenter international database including 8 industrialized countries found that patients with adult spinal deformity actually have lower health-related quality of life scores when compared with patients with common chronic conditions. such as self-reported arthritis, chronic lung disease, congestive heart failure, and diabetes.[4]

The rising health care costs, the physical impact, and functional decline related to adult spinal deformity engender a need for more preventive measures and cost-effective treatments, such as preventive and regenerative interventions. Despite spending billions of dollars in various treatments, both surgical and nonsurgical current treatments have failed to meet patient expectations and curb the ever-escalating health care costs related to managing this condition. The concepts of cutting out discs, fusing the spine, burning disc nerve endings, and injecting steroids around inflamed structures all fail to address the underlying pathophysiology and do little to change the natural history of disc degeneration. It is our opinion that we need to be less aggressive with our surgical treatment of the spine, and more aggressive with intervening earlier in the disease process with regenerative treatments. Hopefully this approach will not only lead to better patient outcomes, but also to a more sustainable, cost-efficient way to manage this significant societal burden. In this article, we focus our review on the current literature that exists regarding the clinical and translational studies on regenerative treatments for healing the IVD.

DISCOGENIC PAIN

The IVD is composed of a central nucleus pulposus, consisting of hydrophilic proteoglycan and type II collagen, and the outer annulus fibrosus, made of a fibrous ring of mostly type I collagen.[5,6] Due its intrinsic hydrostatic pressure, the nucleus pulposus can bear heavy compressive loads, whereas the annulus fibrosus resists heavy tensile stresses.[7] Biomechanical studies have shown that torsion and flexion contribute to degenerative changes in the lumbar discs.[8] Disc herniations can be due to progressive degenerative changes from repetitive stress, or acute in nature due to trauma.[8] With repetitive stress, the annulus fibrosus fibers swell and disrupt as the annulus fibrosus undergoes myxomatous degeneration and cyst formation.[8] At the same time, the nucleus pulposus dehydrates, turns fibrotic, and eventually undergoes necrosis and herniation. The nucleus pulposus can herniate through annular fissures or endplate disruptions. The adult IVD is the largest avascular structure in the human body and relies on passive diffusion from adjacent endplate vessels for nutrition,[9] resulting in poor inherent healing potential. In fact, only 3% of disc bulges and 38% of focal protrusions resolve spontaneously.[10] Broad-based disc protrusions, extrusions, and sequestrations have a better prognosis, with approximately 75% to 100% resolving spontaneously.[10]

Nonhealing annular fissures of the IVD have been implicated as one of the major causes for chronic low back pain. A concomitant upregulation of proinflammatory cytokines, such as interleukin-1 (IL-1) and tumor necrosis (TNF) alpha, leads to chemical sensitization of the rich network of nerve fibers that supply the outer annulus fibrosus, resulting in pain with normal activities of daily living.[11–13] As the degenerated disc cells upregulate IL-1 expression, the native disc cells also increase matrix degrading enzyme production expression.[5] TNF-alpha expression from the degenerated tissue also upregulates matrix degrading enzymes and stimulates nerve ingrowth. Furthermore, annular fissures may also contribute to a chemical radiculitis due to the release of inflammatory mediators into the epidural space.[14] As the IVDs degenerate, there is