Low back pain and neck pain are the first and fourth most common causes for disability in the United States. Costs associated with these disabilities range from $80.1 billion to $91.8 billion a year. More than 70 percent of people age 50 or younger and more than 90 percent of people older than 50 experience intervertebral disk (IVD) degeneration. Although IVD can be asymptomatic, the pain associated with it, often called discogenic pain, accounts for 25 to 80 percent of all low back and neck pain.

“Degenerative IVD is the result of a series of changes in metabolism, biomechanics and morphology,” explains Wenchun Qu, M.D., M.S., Ph.D., a specialist in physical medicine and rehabilitation and pain at Mayo Clinic’s campus in Rochester, Minnesota. IVD is characterized by cell death and degeneration of extracellular matrix. Resulting microenvironmental changes include neovascularization and nerve growth, which can lead to pain and altered biomechanical function.

Current treatment modalities for IVD include pain medication, therapies, injections, nucleoplasty and surgical diskectomy. But none of these strategies addresses the IVD degeneration. Because the extracellular matrix is synthesized and modulated by IVD cells, researchers are exploring the use of stem cells and mesenchymal stem cells (MSCs) for IVD regeneration.

In animal studies, stem cell transplantation to the disk has shown promise in decelerating or arresting the degenerative process. However, small sample size, varying study designs and conflicting outcomes in preclinical animal trials have made it difficult to assess the effectiveness of this treatment. To address this challenge, Dr. Qu and a team of Mayo researchers recently performed and published a systematic review and meta-analysis of controlled trials exploring the strategy of cell-based IVD regeneration by means of stem cell transplantation in different animal models.

**Study methods**

Mayo researchers conducted a comprehensive search of seven databases and included preclinical controlled trials (randomized controlled trials, or RCTs) and nonrandomized controlled trials (N-RCTs) that evaluated stem cell transplantation on experimental regeneration of the intervertebral disk in animals.

Mayo researchers focused on the outcomes related to the effect and mechanism in IVD regeneration, which includes disk height index, MRI T2 signal intensity, type II collagen expression and histologic disk degeneration grade. Animals of any species or breed with any type of model in IVD degeneration secondary to IVD trauma were included. Control group animals included any type of intervention. Studies that combined multiple treatments, studies that used models of nontraumatic spinal cord injury, and studies lacking original data or outcomes of interest were excluded.

Using these criteria, 22 studies were culled from the 642 unique citations identified. This pool contained nine RCTs and 13 N-RCTs. Overall, 626 disks were studied, of which 313 were transplanted with stem cells and 313 were controls.
Study results
Among the 22 studies included, stem cell transplantation was associated with significantly increased disk height index, T2-weighted MRI signal intensity, type II collagen expression and significantly reduced histologic disk degenerative grade.

“We also noted that the regeneration processes after stem cell transplantation seem to follow a cascade of events reflecting the cell and molecular processes that maintain disk functions,” explains Dr. Qu. These changes included increased production of extracellular matrix that leads to increased nucleus pulposus hydration, and subsequent prevention of loss of disk height.

Although the meta-analysis of animal studies suggests that stem cells halt the degeneration processes in IVD and promote IVD regeneration, Dr. Qu acknowledges some study limitations and that additional work must be done to provide a better understanding of the genome composition and phenotypical expression of MSCs and the nucleus pulposus-like cells involved in this process. Additional clinical trials also will be needed to understand if the benefits observed in animals can be translated to humans.

For more information

Other interesting findings:

- In 13 studies, Mayo researchers found that disk height index in the stem cell transplantation group was significantly higher than the control group (SMD = 3.64, 95% CI: 2.49, 4.78, p < 0.001, I² = 91.3%).

- The 14 studies that reported MRI T2 signal intensity outcomes showed a significant increase of MRI T2 signal intensity in the stem cell transplantation group when compared with the control (SMD = 2.28, 95% CI: 1.48, 3.08, p < 0.001, I² = 88.5%).

- In 11 studies, stem cell transplantation was associated with significantly reduced histologic disk degeneration grades when compared with the control (SMD = -2.97, 95% CI: -3.97, -1.97, p < 0.001, I² = 80.1%).

- Increased expression of type II collagen was identified in nine studies (SMD = 3.68, 95% CI: 1.66, 5.70, p < 0.001, I² = 95.8%).

Mayo researchers also found no significant changes between subgroups.

Postural Orthostatic Tachycardia Syndrome and Chronic Fatigue in Adolescents: Working Toward Recovery

Chronic fatigue is common and often multifactorial in adolescents. In some patients, fatigue is due to a concurrent medical condition, inadequate sleep habits or coexisting psychological challenges. Occasionally, however, the fatigue persists in the absence of identifiable medical conditions.

Many teens who experience chronic fatigue have additional symptoms, including tachycardia, dizziness, headaches, nausea and abdominal pain, that suggest the presence of some form of autonomic dysfunction. Postural orthostatic tachycardia syndrome (POTS) is one type of autonomic dysfunction. Specific definitions vary, but generally include chronic fatigue and two key components: symptoms of orthostatic intolerance and excessive postural tachycardia (more than 40 beats a minute) with supine to upright positioning on a tilt table. In addition to these signs and symptoms, adolescents with POTS often also experience depression and anxiety.

According to Sherilyn W. Driscoll, M.D., a pediatric physiatrist at Mayo Clinic Children’s Center in Minnesota, the social and economic consequences related to POTS are significant.

“Adolescent patients diagnosed with POTS may experience decreased school attendance, withdrawal from extracurricular activities, decreased academic performance and truancy,” notes Dr. Driscoll. “And, as patients have multiple consultations while seeking a diagnosis and treatment, this condition can also have a significant financial impact on families.”

While research continues to explore the pathophysiology of this condition, it’s important to note that effective treatment is available for these patients. Dr. Driscoll advises that once the medical evaluation is complete, providers should encourage patients and their families to move
beyond the search for medical diagnoses and focus on recovery.

“Education and motivating patients to incorporate new healthy-living practices into their lives can help remediate POTS symptoms and reduce the negative impact of POTS and chronic fatigue in adolescents,” says Dr. Driscoll.

In a recent article published in Current Problems in Pediatric and Adolescent Health Care, Dr. Driscoll and colleagues provide an overview about POTS and chronic fatigue, reviewing the relevant medical and psychological literature, and drawing upon the authors’ practice experiences. Below are a few highlights from this review article, focusing on recovery strategies.

**Patient and family education**

As they struggle to find help for a condition that is not yet well-understood, many patients with POTS and their parents experience feelings of isolation and lack of social support. Education focusing on self-management and fostering social support is helpful. Individual and group education sessions that involve both patients and their families can encourage social interaction and lessen the feelings of isolation. Sessions should encourage a systematic approach to comprehensive lifestyle changes required for managing this condition.

**Multidisciplinary care**

Patients with POTS can experience a wide range of symptoms that no single medication or treatment can relieve. Treatment plans at Mayo Clinic typically use multidisciplinary care teams that may include specialists in general pediatrics, neurology, physical medicine and rehabilitation, sleep medicine, pulmonology, cardiology, infectious disease, psychology, psychiatry, and others as needed.

**Nonpharmacologic strategies**

Improvement in sleep hygiene, aerobic exercise and strength training, and cognitive behavioral therapy for pain and symptom management can be effective recovery tools. To improve the effective circulatory volume and enhance venous return, patients are advised to avoid sudden changes in posture, prolonged recumbency, high temperatures, large meals, and vasodilating or sympathomimetic drugs. Increased intake of fluids (preferably caffeine-free) and salt is usually helpful.

Numerous studies have demonstrated the benefits of including exercise and activity in the treatment plan. Exercise increases the effective circulatory volume and improves stroke volume and conditioning. Although there are currently no widely accepted specific exercise recommendations for patients with POTS, Dr. Driscoll says that patients should start with a duration and intensity that they can manage comfortably. They should gradually work toward performing at least one hour of age-appropriate aerobic exercise daily and strength training three times a week. Patients with severe fatigue may benefit from starting with recumbent strengthening, cycling, rowing or swimming, with a gradual transition to activities in an upright posture.

**Medication management**

When nonpharmacologic therapies fail to provide adequate relief from headache, circulatory problems and gastrointestinal symptoms, patients may benefit from incorporating some medication in their therapeutic regimen. These can include fludrocortisone for fluid and salt retention; beta blockers and vasoconstrictors to reduce blood pooling and increase venous return; and selective serotonin reuptake inhibitors (SSRIs) to address intestinal flow and blood flow.

Currently, data supporting the use of medications to treat “brain fog,” nausea and abdominal pain associated with POTS are scarce.

**Biobehavioral and pain management strategies**

Some patients experience pain and fatigue symptoms that significantly limit their ability to function and participate in school or social activities (Figure). When these patients don’t get relief from typical medical or nonpharma-
Education Opportunities

Geriatrics and orthopedics residencies for physical therapists
These yearlong post-professional clinical and didactic education training programs are designed to advance a physical therapist’s preparation as a provider of patient care services.

Individualizing Medicine 2015: From Promise to Practice
Sept. 20-23, in Rochester, Minn.
This conference focuses on cutting-edge, genomic discoveries and practical applications of personalized medicine for your patients. It includes a keynote address from J. Craig Venter, the researcher who helped map the first human genome. Contact: 507-284-1499 or email imconference@mayo.edu

Fourth Annual Symposium on Regenerative Rehabilitation Hosted by Mayo Clinic
Sept. 24-26, in Rochester, Minn.
This symposium features renowned researchers and clinicians focused on regenerative rehabilitation treatments and therapies. This emerging field translates discoveries in tissue engineering and cellular therapies into treatments that benefit the functional outcomes of patients. Contact: 412-624-5293 or email whartonkm@upmc.edu

Nov. 13-14, in Rochester, Minn.
This case-oriented program provides an integrated approach to the injured athlete and includes case presentations, lectures and video demonstrations that make this course interesting to all sports medicine practitioners. Contact: 800-323-2688 (toll-free) or email cme@mayo.edu

Mayo Clinic Rehabilitation Medicine Update at San Juan
Feb. 5-7, 2016, in San Juan, Puerto Rico
This course is designed as an update of techniques and topics pertaining to physical medicine and rehabilitation and includes osteoporosis, amputee, ultrasound injection, cancer rehabilitation, brain injury, spinal cord injury, pain, EMG, hand and more.

Neurorehabilitation Summit
April 11-12, 2016, in Rochester, Minn.
This comprehensive course addresses the complex issues surrounding neurorehabilitation, including brain injury, brain rehabilitation, regeneration recovery and spinal cord injury.

Mayo Clinic Physical Medicine and Rehabilitation Board Review 2016
May 18-20, 2016, in Rochester, Minn.
This course is designed for candidates preparing for certifying and maintenance of certification examinations in physical medicine and rehabilitation and uses a combination of online learning, didactic lecture and mock oral examinations.

For more information: https://ce.Mayo.edu/physical-medicine-and-rehabilitation/pmr