



Treatment of Discogenic Low Back Pain: Current Treatment Strategies and Future Options—a Literature Review

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Abstract

Purpose of Review Many studies have demonstrated that discogenic low back pain is the most common type of chronic low back pain (CLBP), one of the major causes of disability, and has a major socioeconomic impact. Our aim is to review present therapeutic interventions for discogenic low back pain.

Recent Findings There are a multitude of treatments used in clinical practice to treat CLBP, but there is continued debate and lack of consensus among clinicians and the policy makers as to which modality is the best approach. Based on controlled evaluations, lumbar intervertebral discs have been shown to be the source of chronic back pain without disc herniation in 26 to 39% of patients. Treatment modalities include noninvasive treatments such as drug therapy, multiple physical modalities, and multidisciplinary biopsychosocial rehabilitation; interventional modalities such as intradiscal therapies and epidural injections; and regenerative modalities with disc injections of various solutions; and, finally, surgical approaches such as fusion and artificial disc replacement, all of which are accompanied by significant discussion, limited evidence, and lack of consensus.

Summary The results of this evaluation show that the evidence for drug therapy in chronic discogenic low back pain is limited; for multidisciplinary biopsychosocial rehabilitation, it is moderate; and for multiple physical and behavioral therapies, the evidence is limited. For intradiscal therapies, it is poor; for epidural injections, it is moderate; and for regenerative therapies, evidence levels of 3 to 4. The evidence for surgical fusions and disc replacement is similar, without superiority when compared with multidisciplinary biopsychosocial rehabilitation, well-designed physical therapy, or epidural injections.

Keywords Intervertebral disc · Degeneration · Diagnosis · Treatment · Discogenic low back pain

Introduction

Chronic low back pain (CLBP) is one of the most significant medical and social problems in the world today [1–4, 5•, 6•, 7•]. Dieleman et al. [3] showed that among the conditions with

highest spending levels from 1966 to 2013, low back and neck pain were at the top, followed by diabetes. They also showed that in 2013, low back and neck pain accounted for the third highest amount. The estimated health care spending of \$87.6 billion, with overall musculoskeletal disorders spending of \$183.5 billion. Thus, determination of an appropriate strategy for managing CLBP and the disability related to it is crucial. Options range from simple exercise instructions to complex fusions [5•, 6•, 7•, 8, 9•, 10–15].

Lumbar degenerative disc disease without disc herniation, also known as discogenic pain, continues to be a difficult diagnosis with limited evidence and continued discussions that lack of consensus. The most commonly utilized modalities by interventional pain physicians, apart from structured exercise programs, comprehensive treatment modalities, epidural injections, and opioids are all associated with substantial debate and controversy [11–20]. Opioids have been associated with a significant number of deaths, even though the majority of them are related to illicit opioids, whereas epidural

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injections and interventional techniques face criticism for lack of proof of effectiveness which has led to a reversal of growth patterns and a decline in some modalities of interventions [16–26]. However, the discussions and debate continue in reference to evidence in managing not only discogenic pain but also all types of low back pain and other painful conditions, including vertebral compression fractures, despite numerous publications showing variable evidence, with discordant conclusions [27, 28–32, 33, 34–56].

Discogenic low back pain does not involve low back pain caused by lumbar disc herniation; however, it does refer to low back pain mediated or modulated by changes in the internal structure of the lumbar intervertebral disc [5, 9, 57–60]. Discogenic pain originates from the development of fissures in the annulus fibrosus with consequent vascularization of growing granulation tissue and growth of nociceptive nerve fibers along the tear area [58]. With age, the intervertebral disc undergoes significant changes, including loss of water content from the nucleus pulposus, disc thinning, decreased levels of hyaluronic acid, keratinized sulfate, with increase in low molecular weight glycoprotein, fibril degeneration, and collagen fiber deposition. These changes lead to loss of elasticity of the nucleus pulposus, disc structure relaxation, cartilage cystic change, and fibrous ring cracks.

The intervertebral disc is the largest structure without blood supply in the body. The nucleus pulposus tissue is wrapped by the annulus and isolated from the peripheral blood circulation. Studies have found that degeneration of the intervertebral disc tissue reveals a high concentration of a variety of cytokines. When the annulus fibrosus ruptures, the nucleus pulposus is identified by the autoimmune system after exposure, which induces an autoimmune reaction and produces pro-inflammatory substances, including interleukin and tumor necrosis factor. Among them, interleukin-1 (IL-1) can stimulate prostaglandin E₂ (prostaglandin, E₂, PGE₂) and 5-serotonin (5-hydroxytryptamine, 5-HT) synthesis and can increase the body's sensitivity to pain. Interleukin-6 (IL-6) can stimulate local inflammatory cell aggregation, activation, and inflammatory mediator release [5, 57–60].

After the degeneration of the intervertebral disc, in the process of repairing the annulus fibrosus, granulation tissue and nerve endings of nerve walls can grow into the annulus fibrosus or even the nucleus pulposus. The nerve endings that extend into the annulus are unmyelinated nerve fibers, susceptible to stromal changes, inflammatory mediators of the stimulus, and pain information along the nerve sensory terminals. Damaged spinal nerve root pain signals can increase muscle stretch reflex activity, while inflammation-induced pain substances on the nerve stimulation can increase the stretch reflex of this muscle, which induces low back muscle spastic pain [58].

Diagnosis

Magnetic resonance imaging (MRI) usually demonstrates degeneration of the disc, the so-called black disc syndrome. MRI usually shows high signal area behind the annulus fibrosus, which has an important diagnostic value. It usually indicates annulus fibrosus rupture, histologically representing vascularized granulation tissue. The diagnostic criteria for internal disc disruption (IDD) established by the International Association for the Study of Pain include emergence of a concordant pain response during discography, internal annular disruption demonstrated by computed tomography after discography and at least one adjacent disc without concordant pain [5, 8, 60]. The term discogenic low back pain, which is currently used in the literature, is in fact a specific IDD-induced low back pain. At present, IDD has been described as a distinct clinical entity to be distinguished from other painful processes, such as degenerative disc disease and segmental instability [5]. In one study, according to discography, Peng et al. [59] classified discogenic low back pain into 2 types which are supported clinically and with theoretical evidence, including annular disruption-induced low back pain and internal endplate disruption-induced low back pain.

Clinically, these 2 types of low back pain should be confirmed by lumbar discography. Painful intervertebral discs during contrast injection indicate that the contrast agent leaks through the radial annulus either to the disc or to the vertebral body through the radial endplate, both of which induce the patient's usual low back pain response. Theoretically, any lumbar vertebra that receives innervation and its adjacent soft tissue structure may be the origin of low back pain [60]. Manchikanti et al. [5], in an update of the systematic appraisal of the accuracy and utility of discography in chronic spinal pain, showed variable prevalence of 16.9 to 26% for discogenic pain and 16.9 to 42% for internal disc disruption. They utilized 5 diagnostic assessment studies evaluating prevalence of discogenic pain in CLBP without disc herniation [61–65]. Manchikanti et al. [5] provided level 2 evidence for lumbar provocation discography based on methodologic quality assessment criteria. Significant controversy was raised by Carragee et al. in reference to false-positive rates of discography [66]. Wolfer et al. [66] performed a systematic review in 2009 addressing issues related to Carragee's criticism. After reviewing all the studies, Wolfer et al. addressed this issue and performed a systematic review and meta-analysis of lumbar provocation discography in asymptomatic participants, with identification of 11 studies meeting inclusion criteria, yielding contradictory results to the opinions of Carragee et al. Wolfer et al. [66] analyzed chronic pain patients without low back pain and showed that the false-positive rate was 5.6% per patient and 3.85% per disc. Thus, Wolfer et al. [66] concluded chronic pain does not appear to be a confounding factor and patients with chronic pain possess

the ability to distinguish between pathologic and nonpathologic discs, namely positive and negative discs. They also extensively analyzed other groups including those with iliac crest pain after bone grafting, chronic neck pain, somatization disorder, and post discectomy. Overall, they showed low false-positive rates in patients with iliac crest pain after bone grafting of 12% and 7.1%, whereas false-positive rate in patients with chronic neck pain was 0% compared to post discectomy patients, 15% and 9.1% either per patient or per disc. Overall, the meta-analysis led Wolfer et al. [66] to recommend a more stringent, low pressure, positive criteria, since it was associated with a low false-positive rate.

Treatment

Natural History

The natural course of discogenic low back pain is of great clinical significance in the development of a treatment plan for discogenic low back pain. A prospective clinical study during a 4-year follow-up period indicated that the natural history of discogenic low back pain was chronic but persistent; 68.8% of patients had no change in pain and disability, as in the original case. This result indicates that most of the patients underwent a longer period of low back pain, and the original did not change significantly [67].

Drug Therapy

Multiple challenges persist in managing discogenic pain with drug therapy including balancing the effectiveness and adverse effects of each class of drugs. Multiple systematic reviews assessing the value and effectiveness of pharmacologic management of CLBP with various drugs showed that non-steroidal antiinflammatory drugs (NSAIDs) [16–20] and opioids [16, 17, 68–71] are the most commonly utilized drugs in managing CLBP. Recommendations derived from these systematic reviews not only include consideration of NSAIDs as a treatment for CLBP with favorable effectiveness but also associated with significant adverse effects. It has been estimated that approximately 60 million Americans regularly use NSAIDs on a chronic basis, but with significant gastrointestinal complications in up to 2% of the users, and with a reported 120,000 hospital admissions and over 17,000 deaths per year [72]. Among these drugs, acetaminophen has fair evidence for pain relief but has been reported to be responsible for almost 1000 deaths in the USA alone [72].

Effectiveness of muscle relaxants has not been well studied [68–71]. In addition, antidepressant therapy has been assessed in multiple systematic reviews [68–71]. However, the results of the systematic review showed lack of effectiveness of antidepressants, even though they have been shown to be effective

in various types of CLBP. Further, patients with associated depression may benefit from antidepressant therapy providing analgesia in addition to antidepressant effects. Effectiveness and role of antiepileptic drugs also have been studied. However, their role is well defined for widespread pain with highly variable effectiveness in only a small proportion of patients with low back pain [71, 73]. Benzodiazepines have been used in CLBP; however, multiple issues related to benzodiazepines have curtailed such uses and the use of benzodiazepines is limited to anxiety and the combination with opioids may result in multiple adverse consequences [74, 75].

Systematic corticosteroids have been studied mostly for radicular pain rather than CLBP with lack of proven effectiveness. Opioids are the most commonly used drugs in CLBP; however, their use has encountered extensive controversy and criticism with multiple adverse consequences contributing to the current opioid epidemic [16, 17, 19, 20]. Thus, low-dose opioids may be recommended in highly select patients, when not only pain relief, but increased functional status is demonstrated without development of tolerance, dependency, and other side effects. In addition to the traditional drugs, multiple herbal drugs also have been used [8].

Physical and Rehabilitation Therapy

Multiple interventions related to structured exercise program and physical therapy and rehabilitation modalities have been utilized in managing chronic discogenic pain. Many of these modalities are utilized by multiple disciplines and often in conjunction with drug therapy, interventional modalities, and surgery. A systematic review of various physical modalities in rehabilitation [76] showed that the only modality with significant effectiveness was multidisciplinary biopsychosocial rehabilitation. They showed lack of significant evidence for the effectiveness of exercise therapy, back schools, education, massage, behavioral treatment, transcutaneous electrical nerve stimulation (TENS), traction, and low-level laser therapy.

However, another systematic review by the same authors [77] showed improved pain intensity and disability with an improvement in long-term function compared with usual care with exercise therapy. A systematic review of back schools for nonspecific low back pain [78], with inclusion of 19 randomized controlled trials (RCTs), showed moderate evidence, suggesting that back schools, in an occupational setting, improved function with reduction in pain and also showed improved return to work status. Others also have showed that massage was significantly better than physical therapy at improving back pain and disability, even though it was associated with higher costs [79]. Traction, manipulation, massage, and acupuncture yielded overall mixed results [11, 78–80].

Overall, multidisciplinary biopsychosocial rehabilitation appears to be the favorite and recommended treatment among researchers, even though in practice, this has not been used

frequently. The literature shows discordant results in reference to the effects of biopsychosocial rehabilitation; however, there is more evidence in favor of multidisciplinary biopsychosocial rehabilitation [76, 81].

In practical terms, education, structured exercise therapy, and behavioral management have been recommended due to their noninvasiveness, low cost, and effectiveness in conjunction with other treatments.

Interventional Therapies

Epidural Injections

Multiple publications have indicated the effectiveness and cost utility of epidural injections in axial low back pain, which is considered as discogenic low back pain after eliminating pain secondary to facet joints and sacroiliac joints and also without evidence of disc herniation. Systematic reviews assessing the effectiveness of epidural injections in managing low back and lower extremity pain in various conditions have shown significant effectiveness based on RCTs for axial low back pain [7, 28, 46, 82–84]. Cost utility was similar to disc herniation, central spinal stenosis, and post surgery syndrome [48, 85]. Further, it was also shown that lumbar interlaminar epidural injection was superior to caudal epidural injections and the effectiveness in discogenic pain was similar to disc herniation and superior to central spinal stenosis and post surgery syndrome [7, 84]. Epidural injections were also shown to be superior to fusion and disc arthroplasty [6]. Manchikanti et al. [82, 83] studied the role of epidural injections with or without steroids in 2 RCTs with either an interlaminar approach or a caudal approach in discogenic pain without disc herniation after exclusion of facet joint and sacroiliac joint pain. Overall, caudal epidural or interlaminar epidural approach showed significant improvement in pain and function (50% improvement of pain and functional status). They also separated the patients into responsive and non-responsive groups. The patients who were responsive with at least 3 weeks of relief with the first 2 procedures fared better than overall when all patients were considered. Consequently, significant improvement was observed in both approaches with 72% showing significant improvement in the nonresponsive group and 80% showing significant improvement in the responsive group of patients receiving local anesthetic only, whereas the response was 67% in the nonresponsive group and 70% in the responsive group of patients receiving local anesthetic with steroids at the end of the 2 years in the lumbar interlaminar epidural injection group. In the caudal group, however, significant improvement was observed in 54% in nonresponsive group, 84% in the responsive group with local anesthetic only, whereas it was 60% or 73% in the nonresponsive and responsive groups respectively of the patients in the

local anesthetic and steroid groups at 24 months. Overall, there was no significant difference whether steroids were added or not. All patients received intermittent injections with the return of the pain and decrease in functional status, with total procedures of 6 over a period of 2 years on average. Overall, superiority was demonstrated for interlaminar approaches. Further, cost utility analysis showed a cost of \$3628 per quality-adjusted life year (QALY) improvement with caudal epidural injections [85], whereas it was \$3303 per QALY with interlaminar epidural injections [46].

Percutaneous Intradiscal Therapies

Percutaneous intradiscal therapies are administered to alter the internal mechanics of the disc or the nerve supply either by application of heat, radiofrequency, or injection of various chemicals into the disc. These modalities include intradiscal electrothermal annuloplasty (IDEA), biacuplasty, intradiscal radiofrequency, and injections of intradiscal methylene blue or other chemicals. Intradiscal procedures applying heat have been collectively termed as “thermal annular procedures” [9], and the Centers for Medicare & Medicaid Services (CMS) has described these procedures as thermal intradiscal procedures with issuance of a noncoverage policy due to lack of evidence for all thermal intradiscal procedures.

The intradiscal electrothermal therapy (IDET) was the first modality introduced with heat therapy, with extensive literature, but only 2 RCTs [86, 87]. Pauza et al. [86] in an RCT with publication of 6 month results showed significant improvement with pain and function compared to sham therapy. These results have been considered to show lack of efficacy due to its modest effect with 56% of the IDET group improving by more than 2 Visual Analog Scale (VAS) scores, whereas 38% of the control group also improved. Thus, the proportion of patients in the treated group improving with 50% improvement was only 40%, whereas it was 33% of the control group. The second RCT [87] showed no significant benefits for IDET over sham therapy. Both studies were criticized by opponents and proponents of the studies.

The transdiscal radiofrequency or biacuplasty utilizing 2 radiofrequency probes inserted into an affected intervertebral disc also has been studied. The proposed mechanism of action for intradiscal biacuplasty is the coagulation of the nociceptors within the posterior aspect of the disc [9]. In a single placebo-controlled RCT [88], the results showed significant improvement in pain, functional status, and disability in the intradiscal biacuplasty group at 6 months compared with patients who received sham treatment. The trial has been criticized for its limitations. In addition, percutaneous intradiscal radiofrequency thermocoagulation using radiofrequency current was also studied with heating of the intervertebral disc in 2 RCTs comparing it with sham control [89, 90].

Helm et al. [9] in an assessment of thermal annular procedures in treating discogenic pain, in a systematic review, with inclusion of 49 studies with only 4 RCTs concluded that there was strong evidence of efficacy of biacuplasty in the treatment of chronic refractory discogenic pain. They also showed level III or moderate evidence in support of IDET, and there was no evidence supporting the Discrode. Consequently, it was given a level V evidence status, which is also considered as limited. Further, recently, Guo et al. [91] performed a meta-analysis of intradiscal methylene blue injection for discogenic low back pain with inclusion of 5 studies. They concluded that intradiscal methylene blue injection can reduce pain severity and improve the disability scores in individuals with discogenic low back pain. The results of the meta-analysis indicated that the effects of intradiscal methylene blue injection between preoperation and post operation on discogenic low back pain were significant based on 3 month pain scales and Oswestry Disability Index (ODI). A recent RCT [92] showed lack of effectiveness of intradiscal methylene blue injection.

Regenerative Medicine Therapies

Regenerative cell-based therapies have been proposed in recent years in the management of low back pain, specifically in discogenic pain, with injection of medicinal signaling cells or mesenchymal stem cells (MSCs) and platelet-rich plasma (PRP). There have been multiple systematic reviews published based on a few well conducted RCTs [10]. In a recent systematic review, Sanapati et al. [10] identified 12 studies with lumbar disc injections and 5 studies with epidural injections. Evidence based on a single-arm meta-analysis of RCTs and observational studies, disc injections of PRP and MSCs showed level III evidence, compared to epidural injections with a single RCT and other available studies showing level IV evidence.

Spinal Cord Stimulation

Dorsal or spinal cord stimulation (SCS) is a minimally invasive pain management option for refractory chronic pain. It has been shown that SCS is an efficacious, safe, and cost-effective alternative to treat CLBP, including the reduction of pain medications (including opiates), improving function and quality of life [93]. In a prospective observational study conducted in an urban pain management center, it was found that SCS may provide effective pain relief, improve disability, and reduce opioid usage in patients with discogenic pain as well [93].

Surgical Treatment

Interbody Fusion

Interbody fusion includes anterior lumbar interbody fusion, posterior lumbar interbody fusion, and/or transforaminal lumbar interbody fusion. In recent years, there has been development of extreme lateral interbody fusion [94]. In terms of instruments, the development of pedicle screw systems and intervertebral fusion devices has improved the success rate of intervertebral fusion. A recent randomized, prospective clinical study clearly revealed that lumbar fusion is superior to nonsurgical treatment for discogenic low back pain [95]. Guo et al. [96] conducted a clinical controlled study, also demonstrating that anterior discectomy with translaminar facet screws and posterior discectomy with pedicle screw fixation could effectively relieve pain more than radiofrequency. But surgical intervention should still be considered the last treatment of low back pain. At present, interbody fusion has become the gold standard in the treatment of discogenic low back pain, but clinical follow-up results suggest that there is still fusion failure, chronic pain, adjacent segment degeneration, and other late complications [97]. However, comparative analysis of evidence with fusion showed significant improvement with epidural injections compared to fusion.

Prosthesis Replacement

Prosthetic replacement uses artificial prostheses to restore the height of the intervertebral space as well as the disc biomechanical structure and load capacity. Benefits include segmental stability and segmental movement purposes. This technique restores not only the lumbar vertebrae natural “weight” bearing but also motor function. This technique completely removes intervertebral disc tissue, which eliminates inflammatory stimulation and autoimmune reaction, thus relieving pain symptoms. Discogenic low back pain is the best indication for prosthetic replacement. Prosthetic replacement includes prosthetic disc nucleus (PDN) and artificial disc replacement (ADR). At present, PDN products tend to be close to the biomechanics of the human nucleus pulposus. PDN use has a major limitation as it must require the integrity of the annulus to avoid prosthesis prolapse. ADR can maintain the physiological state of the activity of the vertebral body. Compared with interbody fusion, prosthesis replacement is a relatively new technology. Thavaneswaran et al. [98] have pointed out that in the short and medium terms, ADR and lumbar fusion safety and efficacy are similar. But, the scope of application of prosthetic replacement is significantly smaller than intervertebral fusion, and there is no sufficient evidence to prove that its long-term efficacy is better than intervertebral fusion. The spine surgical community should be, therefore, prudent to adopt this technology on a large scale,

despite the fact that total disc replacement seems to be effective in treating low back pain in selected patients and in the short term is at least equivalent to fusion surgery [99]. A prospective, multicenter, randomized, controlled clinical trial has revealed that a single-level active total disc replacement is safe and effective for the treatment of symptomatic lumbar degenerative disc disease at 2 years [100]. However, comparative analysis with epidural injections showed lack of effectiveness of prosthesis.

Dynamic Fixation System

Dynamic fixation systems are divided into nonfusion of dynamic fixation and fusion of dynamic fixation. Nonfusion of dynamic fixation refers to implant in fusion without bone graft to help spinal motion segment movement and change load transfer. The purpose is to change the way of motion segment carrying load and to control the abnormal activities between segments to maintain transfer of physiological load segment in order to achieve pain relief and prevention of adjacent segment degeneration. Fusion of dynamic fixation makes the lumbar vertebrae stable and promotes fusion of fixed segments, which can effectively disperse the internal fixed load conduction. A clinical trial has proved safe enough to be used in surgical patients affected by lumbar spine instability. Dynamic fixation system was able to provide significant improvements in disability and pain scores with a reasonable percentage of complications [101].

Conclusion

Treatment for chronic discogenic low back pain has traditionally been limited to either conservative management or invasive procedures including spinal fusion and recently spinal arthroplasty. If conservative treatment fails, then surgical fusion is commonly considered. However, the present evidence shows the effectiveness of epidural injections, intradiscal therapies, and intradiscal injections of PRP and MSCs. Additionally, biological therapy is at present the focus of research and theoretically may restore height and structure of the disc. Biological treatment methods include intervertebral disc growth factor injection, transgenic therapy, and cell injection therapy. Basic and clinical studies have found that intervertebral disc MSC transplantation may be a promising treatment.

Discogenic low back pain caused by dysfunction will be an increasingly serious public health problem. Intervertebral disc replacement needs development of new materials and structures to make it more consistent with biomechanical characteristics of the disc, while observing its long-term efficacy. The current focus of clinical and basic research is in used tissue engineering, which tries to carry out gene therapy and protein-based growth factor treatment, as well as clear stem

cell transplantation after the phenotypic changes and the expression of cytokines and related genes. The results of the present investigation suggest that continuous development of biological technology might provide an important and significant role in the treatment of discogenic low back pain.

Compliance with Ethical Standards

Conflict of Interest Lei Zhao and Laxmaiah Manchikanti declare no conflict of interest. Dr. Kaye is a speaker for Merck. Dr. Abd-Elseyed is a consultant for Medtronic, StimWave, Avanos and Sollis.

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