Platelet-Rich Plasma and Epidural Platelet Lysate: Novel Treatment for Lumbar Disk Herniation

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Lumbar herniated disks present a common cause of significant axial low back and radiating leg pain. This situation poses a risk for potentially permanent neurologic compromise, including numbness, weakness, and bowel and bladder dysfunction. Traditional treatment strategies such as medications, epidural steroids, and surgery all carry potential risk for iatrogenic sequelae. Platelet-rich plasma can be processed to isolate and concentrate the growth factors contained in platelet α granules. This solution is then referred to as platelet lysate. Lumbar injection of platelet-rich plasma along with epidural injection of platelet lysate is a novel therapeutic option that can initiate or expedite the resorption of herniated lumbar disk material, which can facilitate the decompression of the affected spinal structures. This process is thought to occur through a complex interplay of cytokines and growth factors that facilitate neovascularization along with macrophage-induced phagocytosis of the disk material. In the present report, we describe 2 patients with symptomatic herniated disks who were successfully treated with epidural injection of growth factors derived from concentrated platelet lysate.

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The weight-bearing vertebral bodies of the lumbar spine are separated by fluid-filled intervertebral disks. Rupture or tearing of the outer annulus fibrosis can lead to herniation of the inner nucleus pulposus. This condition can cause significant pain and neurologic compromise from mechanical compression of the spinal canal, which can include the spinal cord and spinal nerves. Severe or prolonged neural compression can lead to permanent neurologic deficits. There are several treatment options for herniated disks including conservative (watchful waiting, osteopathic manipulative medicine [OMM], medications, and physical therapy) and invasive (surgery) options; clinical symptoms often dictate the course of care.

When pain is a prominent symptom, oral medications or epidural steroid injections (ESIs) may help reduce the inflammation contributing to pain and perineural swelling. Caution must be exercised with steroids because of known risks, including impaired bone health and endocrinopathies.¹ If pain, weakness, paresthesia, or other neurologic symptoms are static or progressive, a more definitive intervention may be warranted. Historically, surgical interventions, such as microdiscectomy or intervertebral fusions, have been used. The drawback of a microdiscectomy includes creation of a fresh wound in the annulus fibrosis that makes the disk susceptible to reherniation.²⁻⁴ Lumbar fusion, a more invasive surgical approach, increases mechanical stresses in the segments adjacent to the fusion.⁵ A conservative approach is reasonable to consider in the absence of

Table.
Physiologic Effects of Selected Growth Factors Found in Plasma and PRP^a

Growth Factor	Physiologic Effects	Mean Plasma Baseline Concentration, pg/mL	Mean PRP Lysate Concentration, pg/mL
BDNF	Promotes survival, growth, and differentiation of neurons	4960	69,000
EGF	Growth, proliferation, and differentiation of numerous cell types	41	1324
HB-EGF	Role in wound healing, angiogenesis, and neurogenesis	15	188
IL-1 RA	Selectively inhibits inflammatory effects of IL-1	72	447
PDGF-BB	Angiogenesis and proliferation of mesenchymal cells	4123	43,913
VEGF	Angiogenesis	140	572

^a Mean concentrations produced by author's laboratory compared with baseline levels.

Abbreviations: BDNF, bone-derived growth factor; IL-1 RA, interleukin -1 receptor antagonist; EGF, epidermal growth factor; HB-EGF, heparin-binding EGF-like growth factor; PDGF-BB, platelet-derived growth factor with 2 β subunits; PRP, platelet-rich plasma; VEGF, vascular endothelial growth factor.

progressive pain or neurologic compromise. It is well established that spontaneous resorption or regression of herniations can occur with time.⁶⁻¹⁰ This process of resorption may, however, take several months and is often incomplete, leaving the potential for residual pain, neural compromise, and functional deficits.⁷

The physiology of disk resorption is poorly understood, but several theories attempt to address this process. One likely explanation involves an inflammatory response to the proteins released by the herniated segment. Under this model, a complex interplay of cytokines and growth factors facilitate neovascularization along with macrophage-induced phagocytosis of the disk material.⁸⁻¹⁰ Local platelets may play a role in facilitating disk resorption through the release of proteins that help orchestrate the process. Platelets contain α granules rich in hundreds of proteins and growth factors, including platelet-derived growth factor, brain-derived neurotrophic factor, transforming growth factor, epidermal growth factor, interleukin-1 receptor antagonist, platelet-derived angiogenesis factor, vascular endothelial growth factor, insulinlike growth factor, and

fibronectin.^{11,12} These proteins have several anabolic and paracrine effects. A brief description of physiologic responses is presented in the [Table](#).¹³ Autologous platelet preparations, such as platelet-rich plasma (PRP), can be exogenously induced to release their α granules through several established methods.¹³⁻¹⁶ The resulting cytokine-rich solution is then referred to as platelet lysate (PL) or platelet releaseate. Platelet lysate can be used to induce or promote stalled or slowed physiologic processes, such as with inadequate resorption of herniated disks. Delivery of these essential growth factors may be limited, perhaps because of a suboptimal vascular supply that would inherently impair the conduit of platelets and macrophages to the local environment. We have been able to increase the concentration of autologous growth factors around persistent herniated discs by injecting PL via epidural injection.

Patients who elect to pursue treatment with lumbar PRP with epidural PL are evaluated to ensure that there are no contraindications, including current use of blood thinners (including nonsteroidal anti-inflammatory drugs [NSAIDs]), coagulopathy, active infection, active

cancer, pregnancy, or allergies to contrast agents or local anesthetics. Current lumbar magnetic resonance imaging (MRI) is thoroughly reviewed to ensure that symptoms are concordant with pathology, as well as for procedural planning. Injections are performed using a sterile technique under fluoroscopic guidance in a clinic-based procedure suite. The PRP is prepared from 180 mL of whole blood using a double centrifugation method in an in-house laboratory similar to that described by Dhurat and Suresh.¹⁷ Under the MARSPILL classification described by Lana et al,¹⁸ our PRP preparation would be considered HA-/RBC-P/Sp2/Plt 4-6/G+/Lc-R/A-. A portion of the PRP is then processed to produce PL by mechanical rupture of the platelets followed by filtration of the solution to remove cellular debris. The average PL growth factor concentrations are listed in the [Table](#). For each treatment, the super-concentrated PRP is diluted with platelet-poor plasma to a 4 to 6 times concentration from baseline. The PRP is then used to treat the posterior structures (spinal ligaments, facet joints) with the hope of providing additional stability to the spine. Each structure is injected with approximately 1 mL of PRP. Typically, 3 mL of PL is injected in the epidural space using a transforaminal, interlaminar, or caudal approach. The injection approach is based on the lumbar spine anatomy along with the clinical scenario and location of the herniation.

Through extensive clinical application, this novel procedure has been shown to safely and effectively initiate or accelerate disk resorption. In the present report, I describe 2 patients with symptomatic herniated disks that were successfully treated with epidural injection of growth factors through concentrated PL.

Report of Cases

Case 1

A 31-year-old woman presented with left leg and low back pain. She was in otherwise good health with noncontributory medical, surgical, or social histories. She reported an insidious onset of pain that began 1 year prior, with progressive and severe pain over the

previous 4 months. She described her pain as a “razor blade” sensation down her posterior lateral left leg to the knee along with associated numbness and tingling down the calf and the bottom of her foot. Her symptoms were worse when arising from a seated position as well as with forward flexion. She denied focal weakness or bowel and bladder dysfunction. She had tried physical therapy and manual manipulations with modest relief in symptoms. Her pain was also refractory to pregabalin and ESIs. She met with a surgeon who recommended a microdiscectomy with possible fusion, but she opted to avoid this procedure. On examination, she was neurologically intact but had tenderness at the L4 spinous process, and she had a positive straight-leg raise on the left. Magnetic resonance imaging revealed a large herniated and extruded disk at L4-5 with displacement of the descending L5 and S1 roots ([Figure 1A](#) and [B](#)).

After reviewing her treatment options, including the potential risks and benefits, the patient opted to begin treatment with lumbar PRP and epidural PL. This procedure was pursued with the hope of initiating or expediting the resorption of the disk material that was contributing to her severe pain. She understood that this was a novel and unproven therapy that was not recognized as falling within the standard of care for her condition. The patient signed an informed consent that reflected this fact, along with the risks, benefits, and alternatives. The PRP/PL procedure was performed using the protocol described previously, including a fluoroscopic-guided left-sided L4-5 paramedian intralaminar approach for the epidural injection of PL.

The patient had expected mild-to-moderate soreness for about 3 days after the injections controlled with hydrocodone/acetaminophen 5/325mg. The patient noted progressive improvements in symptoms and reported 50% relief of pain 4 weeks after the procedure. She had better range of motion in her left leg but still had some radicular pain and numbness in an S1 distribution, so we decided to pursue another PRP/PL treatment. The second treatment followed the same protocol.

Figure 1.

Magnetic resonance images from patient 1, a 31-year-old woman who presented with left leg and low back pain. The pretreatment sagittal (A) and axial (B) slices show a central and left paracentral L4-5 disk extrusion. Follow-up images taken 4 weeks after the second treatment with platelet-rich plasma and epidural platelet lysate injections, sagittal (C) and axial (D) slices showed significant disc resorption of disk.

At follow-up visit (4 weeks after the second procedure), the patient reported almost complete resolution of pain and function and no reported adverse effects. Repeated lumbar MRI revealed excellent resorption of the massive disk herniation, with only mild residual disk material that did not compress the spinal nerves (**Figure 1C** and **D**). At her 6-month follow-up, the patient noted brief and intermittent flare-ups in pain after heavy exertion or falls but otherwise reported significant overall improvement in pain and functional progress. Ongoing care was left to an as-needed basis.

Case 2

A 38-year-old man presented with left leg pain and numbness in an L5 and S1 dermatomal pattern. His medical history was significant for testicular cancer, which was successfully managed with cisplatin chemo-

therapy and systemic steroids. Chemotherapy had ended 3 months before presentation. He otherwise had an unremarkable medical, surgical, or social history. The patient initially described severe left leg pain after a deadlift exercise 6 years before presentation. Lumbar MRI at the time showed a left central disk extrusion at L4-5. He was treated conservatively and noted a spontaneous improvement in pain over the course of 3 months. The patient noted an insidious return of similar symptoms that occurred during chemotherapy 4 months before the current presentation. The pain was severe and was worse with the Valsalva method, forward flexion, sitting, and standing erect. He denied bowel or bladder dysfunction. Symptoms were progressive despite 4 months of conservative care, including activity modifications, NSAIDs, opioid medications, and an ESI. At the time of presentation, he was taking

hydrocodone and NSAIDs without much relief. On examination, he was in visible discomfort with an antalgic gait and pain with lumbar flexion. He had a positive straight leg raise on the left and decreased strength with left great toe extension (L5 myotome). All other lower-extremity myotomes were intact and equal. He was also found to have numbness in the left L5 dermatome. Repeated lumbar MRI showed large left paracentral and caudally extruding L4-5 disk herniation (Figure 2A and B) that mirrored the previous findings on comparison.

At the initial visit, we agreed to pursue a repeated ESI with the hope of reducing acute pain. The procedure was performed using a left L5 transforaminal approach. The patient reported an excellent reduction

in pain but had residual paresthesia and weakness. Treatment options were revisited, including watchful waiting, medications, ongoing physical therapy, repeated ESIs, regenerative medicine, and surgery. He had previously met with a surgeon who recommended a microdiscectomy, but he did not want to undergo a surgical procedure. Because of his history of extensive steroid use from cancer treatment, he wanted to avoid further ESIs. He understood that the increased steroid burden may have precipitated the exacerbation in symptoms and decreased the chances of spontaneous disk resorption because of impaired immune function. The patient opted to pursue lumbar PRP with epidural PL. This procedure was pursued with the goal of initiating resorption of the disk material. He understood that this

Figure 2.

Magnetic resonance images from patient 2, a 38-year-old man who presented with left leg pain and numbness in an L5 and S1 dermatomal pattern. The pretreatment sagittal (A) and axial (B) images show a left paracentral and caudally extruding L4-5 disc herniation. Three months after the second treatment with platelet-rich plasma and epidural platelet lysate injections, sagittal (C) and axial (D) slices showed significant disc resorption.

was a novel and unproven therapy that was not recognized as falling within the standard of care for his condition. The patient signed an informed consent that reflected this fact, along with the risks, benefits, and alternatives.

The first PRP/PL procedure was performed approximately 1 month after the initial visit using the protocol described previously. Platelet lysate was injected into the epidural space using a left L4-5 paramedian intralaminar approach under fluoroscopic guidance.

The patient was next evaluated 2 months after the procedure, and he reported having a day or 2 of post-procedure stiffness and soreness. After that period, he noted progressive improvements in left leg pain and paresthesias. He continued to have intermittent paresthesia and lateral calf pain with certain lumbar movements, including flexion. We agreed to repeat the PRP/PL to facilitate ongoing improvements. (This procedure was repeated using the same paradigm.)

Three months after the second treatment, the patient described resolution of pain, numbness, tingling, and weakness along with improved function. He had no reported adverse effects. Repeated lumbar MRI showed almost complete resorption of disk material, with no evidence of ongoing neural impingement (**Figure 2C and D**). Follow-up was left to an as-needed basis.

Discussion

The cytokines contained in the α granules of platelets have the potential to initiate or accentuate several physiologic responses that may otherwise be suboptimal for clinical improvements. One such process includes resorption of herniated lumbar disk material. Through observation of clinical improvement and objective measures (including imaging), I have found that epidural injection of concentrated platelet growth factors has the potential to facilitate disk resorption to help improve pain and function by decreasing the mechanical compression of the spinal nerves. Although resolution of disk material can occur spontaneously, this process can

take several months. Spontaneous resorption of herniated disks that have been present for several years would not be expected, as described in the second case. Oftentimes, severe pain or neurologic compromise warrants a more aggressive approach than watchful waiting.¹⁷ Platelet-rich plasma/PL seems to be a safe alternative to opioids, ESIs, and surgery. Patients treated with the protocol described herein have injections at approximately 1-month intervals. End-of-care is determined by clinical response, including patient satisfaction with improvement in pain and function. If clinically indicated, repeated MRI is performed approximately 1 month after the last treatment. Patients are monitored throughout their treatment course for adverse effects, clinical response, and changes in MRI findings. To date, more than 350 cases have been performed in my clinic with lumbar PRP and epidural PL injections. Mild-to-moderate soreness at the PRP injection sites has been reported, but when epidural PL is injected without PRP, there is generally little postprocedure soreness noted.

Conclusion

Osteopathic medicine is founded on the principal that the body has an inherent ability to heal itself. Epidural installation of concentrated PL seems to be a safe, efficient, and relatively easy treatment for patients with herniated lumbar disks that embodies the concept of facilitating enhanced natural physiologic function. As with all regenerative medicine procedures, application of PL to the epidural space is considered an investigational procedure. Future directions include safety studies, as well as research evaluating which growth factors and concentrations are optimally suited for facilitation of disk resorption. Double-blinded randomized controlled trials would be useful to prove a treatment effect beyond spontaneous resorption.

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