Step-Up Regenerative Injection Therapy for Severe Chronic Low Back Pain Utilizing Epidural Dextrose Solution (Prolotherapy), Local Platelet-Rich Plasma, and Epidural Platelet-Rich Plasma: A Case Report and Suggested Protocol

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ABSTRACT

Chronic low back pain (CLBP) is a prevalent problem that rarely resolves completely and frequently has a negative impact on mood, activity, and mobility. Conservative pharmacologic and non-pharmacologic therapies have limited efficacy, and there is an unmet therapeutic need for these patients. The authors report a case of a 38-year-old male patient with a 6-year history of moderate to severe back pain, significantly impaired mobility and neurologic deficits that were resistant to a wide range of conservative therapies. Physical exam and magnetic resonance imaging (MRI) revealed evidence of radiculopathy, with impaired sensation and strength that was consistent with a right L5 nerve root impingement. Repeated caudal epidural injection of dextrose solution caused rapid, though not durable, improvement in symptoms and mobility, with some effect on neurologic findings. Stepping up to caudal epidural platelet-rich plasma (PRP) injection combined with articular PRP injections at the sacroiliac joint and lumbar facet joints resulted in almost complete resolution of pain, marked improvements in mobility and resumption of physical activity. Also, after caudal epidural PRP injection the patient regained sensation and function over the right L5 distribution for the first time in 6 years. The injections were well tolerated, and the patient was very pleased with the therapy. The case report also includes a brief review of and suggested approach to injection therapy for the naturopathic physician treating resistant CLBP.

Key Words PRP, degenerative disc disease, disc herniation, discogenic back pain, caudal epidural, facet arthropathy, lumbar radiculopathy

INTRODUCTION

Chronic low back pain (CLBP) is a prevalent problem in North America. A recent survey found that as many as 8% of those in the general US population report CLBP that is severe and the majority experience limitations in mobility and ability to work.[1] Meta-analysis has shown that both acute and subacute low back pain have a favourable prognosis in terms of resolution of pain and disability. However, mean pain and disability scores in non-interventional cohort trials that evaluate the course of CLBP (defined as pain that is present for longer than 12 weeks) show limited improvement over time.[2] The Cochrane Database of Systematic Reviews includes meta-analyses that conclude that exercise therapies,[3] yoga,[4] and a multi-disciplinary biopsychosocial approach to CLBP[5] show mild to modest improvements in pain and disability. A Cochrane meta-analysis found that pharmacologic therapies other than opioids are either mildly effective or not effective.[6] There was good evidence for a modest reduction in pain with opioids, but the potential for dependence and the adverse effect profile of opioids, including dependence and hyperalgesia, are well-known, which necessitates close patient monitoring.[7]

A wide range of pathologic entities can be responsible for CLBP, including lumbar radiculopathy, neuropathic pain, spinal stenosis, post-surgical pain, and non-specific CLBP.[8] Controlled trials demonstrate that a wide range of injections are effective for CLBP, regardless of the cause. More evidence is accumulating to

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support the efficacy of what are termed "regenerative injections"; two examples of regenerative injectants include dextrose solutions (either isotonic or hypertonic, known as prolotherapy) and platelet-rich plasma (PRP).[9,10,11] A wide range of structures can be injected, including facet joints, intervertebral discs, and the epidural space. Caudal epidural injections of dextrose solution or PRP are intriguing because studies seem to indicate that they are efficacious in CLBP associated with multiple etiologies and the procedure is relatively simple, technically speaking, compared with facet joint or intradiscal injections.[9]

This paper describes a patient with refractory CLBP who experienced significant and prolonged improvements in pain, disability, and neurological complications associated with lumbar radiculopathy after 4 dextrose solution and 2 PRP caudal epidural injections. This case report was prepared following the CARE guidelines.[12]

CASE DESCRIPTION

The patient is a 38-year-old Caucasian man with a history of intermittent back pain for more than 10 years. His CLBP was exacerbated by a chiropractic manipulation in 2018, and since then he has experienced loss of mobility, limitation of work activities, and hypoesthesia over his right great toe. He is a construction labourer by trade and does not smoke, drink, or use any illicit substances. Prior to his back pain his recreational physical activity included weightlifting, which he had to modify or discontinue due to pain and mobility limitations. He slipped and fell on ice in February 2024, and since then, his CLBP was exacerbated to the point where he had to miss work and could only engage in swimming as a recreational activity. On the date of the first visit with the author (18 May 2024) his chief complaint was severe left-sided lower back pain (reported as 7–8/10 in severity), difficulty mobilizing, difficulty sleeping due to pain, and numbness in the right big toe. The patient's therapies at that time included pregabalin, massage therapy, acupuncture, and disc decompression as well as therapeutic exercise from a physiotherapist. The patient reported mild benefits which were not long-lasting after physiotherapy and no significant benefit from the other treatments.

On the first visit, the patient was obviously uncomfortable, and he had significant difficulty walking and standing from a seated position. On physical exam, posterior pelvic tilt and spasm in the erector spinae and gluteus complex were noted, without muscle atrophy. Gait was antalgic with notably reduced push-off strength on the left side. Diffuse tenderness and increased muscle tone were noted on palpation of the lower lumbar erector spinae and gluteus muscles, as well as tenderness over the lumbar spinal processes, sacro-iliac (SI) joint, and facet joints—the area of greatest pain was between L5 and S1. Neurological exam revealed weakness in right great toe dorsiflexion (L5) and decreased sensation to light touch and sharp stimuli over the dorsum of the right foot and great toe (L5). The Achilles reflex was diminished on the right side. Straight-leg raise was positive on the right side, with radicular pain radiating into the great toe. Slump test was positive. FABER test and Gaenslen's test were negative, and there was no report of saddle anesthesia or bowel/bladder complaints.

Magnetic resonance imaging (MRI) performed on 18 April 2024 reported the following:

- L3–L4 disc desiccation and mild diffuse disc bulge that flattens the thecal sac as well as a 6-mm left foraminal disc protrusion with an extruded component that migrated superiorly 10 mm, causing left foraminal narrowing with compression of the L3 nerve roots. Mild right foraminal narrowing and facet arthropathy were also noted.
- L4–L5 disc desiccation and mild diffuse disc bulge is present with a posterior annular tear and 2-mm disc protrusion. No spinal stenosis, but mild facet arthropathy and mild foraminal narrowing were noted.
- L5–S1 disc desiccation and mild diffuse disc bulge as well as a right paracentral tear and disc protrusion that measures 4 mm and indents the right side of the thecal sac. The protrusion compresses nerve roots posteriorly on the right side.

Based on the history, physical exam findings, and imaging the patient and author agreed on caudal epidural dextrose injections (prolotherapy). The injectant was 20 mL of 5% dextrose in water (D5W) which was administered using ultrasound guidance. The injection was repeated 3 times for a total of 4 dextrose solution injections (each one 20 mL); the injections were given at 1-week intervals, and the concentration of dextrose was increased by 5% each week (last injection was 20 mL of D20W). The patient reported a very good pain response to the injections each time, with a drop in pain levels early on (after 4 hours) such that the pain was reported as mild (1–2/10). Four to five days post-epidural dextrose solution, pain came back to a moderate level (4/10) in a consistent fashion. During this period, the patient reported more restful sleep.

After the fourth dextrose solution injection, the patient wished to step up to epidural PRP combined with PRP injections into the facet joints that were most likely contributing to his symptoms based on imaging (L4/L5 and L3/L4 facets). Two weeks after the last dextrose solution epidural (June 25, 2024), 10 mL of 5% hematocrit PRP was injected into the epidural space and 0.5 mL of 2% hematocrit PRP was injected into the facet joints under ultrasound guidance. Additional 2% hematocrit PRP (0.5 mL each site) was injected into the left base of the sacro-iliac joint and the left gluteus maximus insertion point. Platelet-poor plasma was injected into multiple trigger points (0.5 mL each) on the left side. The patient reported that 4 days after the first PRP injections his back pain had almost completely resolved, and he regained sensation in his right great toe—he had not had sensation in that toe for the last 6 years. His ambulation and mobility had greatly improved, and he was able to engage in bodyweight strength training with minimal discomfort. The patient requested an additional PRP epidural on July 10, even though his CLBP symptoms had not returned since the last epidural. 10 mL of 7% hematocrit PRP was injected caudally into the epidural space and the same facet and sacro-iliac joint sites as his first PRP treatment. Since the last PRP treatment the patient has not needed any further injection therapy. As of January

2025, he has returned to full duties at work, he feels no limitations in activity, and he ranks his back pain at less than 1/10 (more than 6 months later). Table 1 outlines additional details of the injectant composition and preparation for the dextrose solutions and PRP.

The patient improved objectively in a steady fashion throughout the course of therapy. Assessment at the appointment for the second PRP epidural showed that his gait was no longer antalgic and he mobilized on the table easily. His posture was more upright with minimal pelvic tilt or lumbar flattening. His strength had normalized, and his plantar reflexes became symmetrical. He was very satisfied with the results—it would not be an exaggeration to say that he seemed elated. To quote from a written testimonial sent to the author, he was "…shouting from the mountaintops that the pain dropped to a manageable level" after the first D5W epidural, and "Sleep actually started to become a time of repair, as [he woke] up feeling better than the day before" after the third dextrose solution (D15W) epidural. After the first PRP epidural he described, "…concentration starting to go back up… Tuesday was the first day where I could focus on something else instead of just the pain." The patient noticed no adverse effects with any of the injection therapies outside of transient stiffness and mild discomfort for 2 to 3 days after PRP injections, and he gave signed consent for his case to be published. Figure 1 illustrates the injection schedule, the injectant used, and the clinical findings at selected timepoints.

DISCUSSION

Regenerative injection therapy using dextrose solution or PRP has been used for years, and clinical trial data is accumulating to support its efficacy and safety. Caudal epidural injections using these injectants are a newer approach, with few clinical studies. A double-blind, randomized placebo-controlled trial conducted in 2016 using caudal epidural D5W injections for patients with CLBP showed a 70% decrease in pain scores hours after the injection, with gradual (days) re-emergence of low back pain; 2 weeks after the epidural, there was a 30% reduction in pain scores compared with baseline.[9] An open-label extension of this trial showed that with 12 months of follow-up, between 5 and 6 injections on average were needed for patients to maintain a statistically and clinically significant long-term reduction in pain and disability scores of 52% and 42%, respectively.[13] Two small recent trials, both randomized and controlled, found that a single epidural injection of PRP was effective at improving disability and CLBP.[14,15] Both studies used an active control (triamcinolone) and both showed that epidural PRP was superior to epidural glucocorticoid for pain and disability improvement after 24 weeks. Injected glucocorticoid is the only other epidural therapy for CLBP that the authors are aware of that lasts longer than a few days. A Cochrane meta-analysis found low- to moderate-quality evidence that epidural corticosteroid injections are somewhat effective for lumbosacral radicular pain in the short term, so epidural D5W and/or PRP injections could plausibly become an important part of non-surgical care.[16] The biological mechanism of action for epidural D5W has not been clearly defined, though the authors of the randomized controlled trial (RCT) cited above suggest a few theories based on animal studies.[13] Among them are modulation of transient receptor potential vanilloid 1 (TRPV-1) cation channels or other channels, such as the acid-sensing ion channel (ASIC); animal studies have found that dextrose solutions impact the activity of these channels, which are implicated in models of chronic pain.[17] Human studies have shown that multiple spine-associated structures, notably intervertebral discs and facet joints, experience increased nociceptive fibre sprouting in response to damage—these fibres could be impacted by local dextrose solution and its modulation of TRPV-1 and ASIC channel activity. Reduced pain sensation could also lead to improved function of spinal stabilizers such as the multifidus and erector spinae, which can be inhibited by spinal pain sensation.[8] It remains to be proven whether this or other mechanisms are responsible for the benefit of dextrose solution caudal epidurals, since no mechanistic studies have been conducted to date in animal or human models. The impact of PRP on CLBP may be due to increased disc resorption and reduced inflammation through the release of platelet-derived growth factors and anti-inflammatory cytokines, respectively. It could also be due to improved resorption of herniated disc components, as seen in animal models.[10,11] Although trials have established the efficacy of PRP in CLBP, the mechanism has not been clearly proven in human subjects, and changes on imaging are modest if present at all.[10,15]

TABLE 1 Injectant and Procedure Description

Injectant	Preparation	Cellular Composition	Volumes
Sterile dextrose in water: 5–20 g/100 mL of water	Stock D5W solution or dilution of D50W	N/A	20 mL in epidural space
Epidural PRP #1 (25 June 2024)	180 mL whole blood starting volume, final PRP volume 8 mL	5% hematocrit 2.09 × 10^6 platelets/uL 2.30 × 10^4 leukocytes/uL	10 mL in epidural space
Epidural PRP #2 (10 July 2024)	180 mL whole blood starting volume, final PRP volume 10 mL	7% hematocrit 1.88 × 10^6 platelets/uL 2.35 × 10^4 leukocytes/uL	10 mL in epidural space
PRP for facets and SIJ	180 mL whole blood starting volume, final PRP volume 6 mL	2% hematocrit 1.76 × 10^6 platelets/uL 6.88 × 10^3 leukocytes/uL	0.5 mL peri- and intraarticular

PRP = platelet-rich plasma; SIJ = sacro-iliac joint.

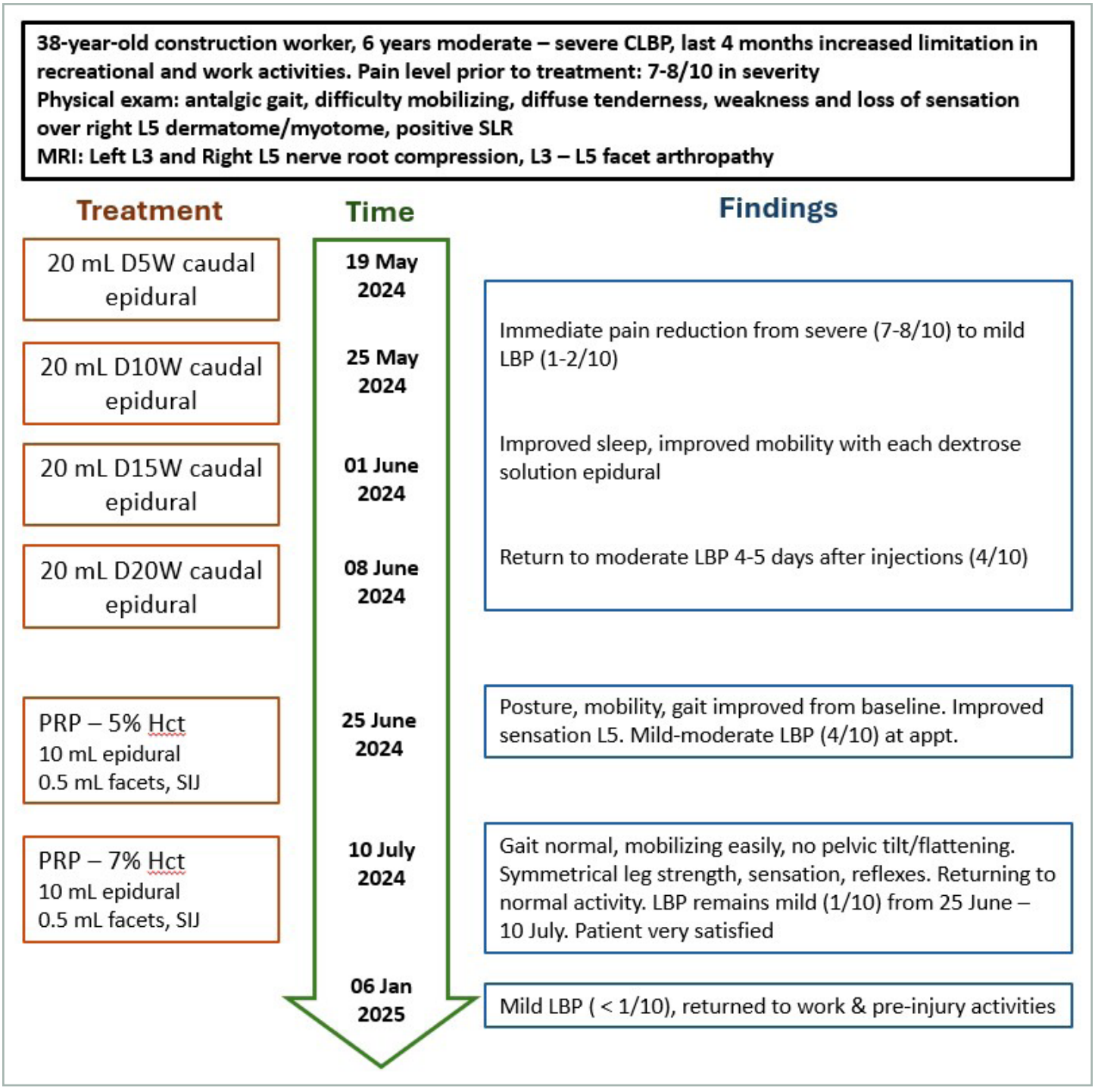

FIGURE 1 Timeline of Interventions and Salient Clinical Findings
CLPB = chronic low back pain; SLR = straight leg raise; MRI = magnetic resonance imaging; D#W = g of dextrose/100 mL of water; PRP = platelet-rich plasma; LBP = low back pain; Hct = hematocrit; SIJ = sacro-iliac joint.

One of the strengths of this regimen was its step-up nature. When the cheaper, more frequently administered therapy—epidural dextrose solution—showed good but not optimal results, the patient chose PRP injections in multiple sites—epidural, facet joints, and the sacro-iliac joint. This responsive approach may have resulted in more robust clinical outcomes. It was guided by both imaging and clinical findings and likely reflects clinical practice better than a RCT. A limitation of this case report is that one cannot be sure what aspect of the intervention was most responsible for the patient's improvement, since all of the injection strategies have evidence of efficacy.[10] There is no way of knowing whether the epidural dextrose solution would have had the same results as PRP if further injections had been conducted. There is also no way of knowing if the improvement in the patients' symptoms after PRP injections was due to the caudal epidural or the facet joint injections. However, the authors think that epidural PRP was

responsible for the bulk of the improvement, as it is unlikely that the facet joint injections would have had an impact on radicular symptoms. Another weakness of this case report is the relatively short follow-up—the last check-in with this patient was in January 2025 (just over 6 months after the last PRP injections). However, the patient was very pleased with the treatment, his CLBP has almost completely resolved, his objective neurologic findings have resolved, and he has been able to return to work. These are durable and highly clinically significant outcomes. Unfortunately, the author did not use a validated disability scale such as the Oswestry Disability Index (ODI) to quantify improvements; future case reports would benefit from incorporation of validated indices of treatment response.[18]

Finally, as with all uncontrolled studies, it is impossible to know for certain if the patient's symptoms resolved on their own independently of injection therapy or if the placebo effect was responsible. The clear temporal association between therapy and improvement of symptoms in the setting of CLBP that had been moderate to severe for years argues against spontaneous resolution of symptoms. Objective findings such as reflexes, sensation, and muscle strength showed an excellent response to therapy, in addition to reported pain. A number of trials, including a meta-analysis and a randomized trial of open label placebo injections, found evidence that placebo medications and sham procedures show clear benefit for pain and disability scores in CLBP. These trials did not report any benefit for objective neurological findings.[19,20] Undoubtedly the placebo effect provided some benefit, but the authors feel it is unlikely that it was solely responsible. To support this, placebo-controlled RCTs for both dextrose solution[9,13] and PRP caudal epidural injection[14,15] have demonstrated efficacy in CLBP.

This case report uses a similar approach, in terms of injectant and technique, to the one controlled study on epidural therapy using dextrose solution for CLBP. The patient opted to increase the concentration of dextrose for each subsequent injection, even though there is no good evidence to suggest concentrations greater than 5% dextrose are necessary. In contrast, there are many different approaches to epidural therapy using PRP. The injectant in trials differs in preparation method, injection technique, and concentration of erythrocytes, leukocytes, and platelets.[14,15] It is therefore difficult to hypothesize an optimal protocol for epidural PRP in CLBP when few trials have been done.

The system the primary author uses for PRP is the Arthrex™ system,[21] which is a self-contained, sterile system that offers modifiable and reproducible cell counts. Other advantages of systems such as this include ease of use and no need for a fume hood. The studies supporting the efficacy of epidural PRP used higher cell counts of both platelets and leukocytes. Intra- or periarticular joint injections typically involve lower cell counts of erythrocytes and leukocytes but high platelet counts, as seen in Table 1. Caudal epidural injections are technically straightforward, and practitioners can become competent at this procedure with a modest amount of training.[22] In contrast, injection of facet joints or structures associated with transverse processes are more technically difficult; the corresponding author recommends pursuing these therapies only after training with an experienced injector and while using ultrasound guidance with a device that can image these structures well. Table 2 lists commonly used injection therapies in naturopathic practice (given that regional regulations designate them as within scope), their most rational indications, a brief description of technical difficulty, and their most common adverse effects.

It is unlikely that there is any "one size fits all" protocol for non-surgical approaches to CLBP given the uncertainty of the pathogenesis, the developing nature of the literature, and individual patient variability. A number of excellent resources exist for diagnosing likely causes of CLBP and ruling out red flags,[23,24] as well as administering trigger point therapy.[25] Recent reviews for PRP[10] and dextrose injections[26] provide additional guidance regarding solution preparation and injection targets. A rational approach to CLBP begins with a thorough history and physical exam to rule out red flags or autoimmune causes. During the history and physical exam the likely cause of the pain can be determined—most causes of CLBP do not require imaging to guide treatment, though it can be helpful if one is aware of the high frequency of radiologic "findings" in the spine and adjacent structures in asymptomatic

TABLE 2 Injection Therapy Options for CLBP

Injection	Indications (based on evidence, experience)	Technical Difficulty/Cost	Notable Adverse Effects
Trigger point (saline ± anaesthetic)	Non-specific LBP, myofascial pain	Low/$	None beyond those for any IM or subcutaneous injection
Dextrose solution D5W (epidural)	Refractory CLBP, neuropathic/radicular pain up to L3	Low–medium (ultrasound guidance not necessary but useful)/$$	None beyond those for any epidural injection
Leukocyte-rich PRP (LrPRP) (epidural)	Refractory CLBP, neuropathic/radicular pain up to L3	Low–medium (ultrasound guidance not necessary but useful)/$$$$$ PRP kits range between CA$350 and CA$500	PRP injections are often significantly more painful than dextrose injections for several days after the procedure
Dextrose solution D15/D20W (specific sites or joints)	Refractory CLBP, physical exam/imaging suggests discrete structures (TVPs, facet joints) contribute to pain	Challenging; recommend ultrasound guidance/$$$	Increased risk of intrathecal injection (facets) or intraperitoneal injection (TVPs)
Low-Hct, lower leukocyte PRP (specific sites or joints)	Refractory CLBP, physical exam/imaging suggests discrete structures (TVPs, facet joints) contribute to pain	Challenging; recommend ultrasound guidance/$$$$$ PRP kits range between CA$350 and CA$500	Increased risk of intrathecal injection (facets) or intraperitoneal injection (TVPs) Increased pain with PRP injections (vs. dextrose)

LBP = low back pain; IM = intramuscular; D#W = g of dextrose/100 mL of water; CLPB = chronic low back pain; PRP = platelet-rich plasma; TVP = transverse processes; Hct = hematocrit.

patients.[23] If physiotherapy, exercise therapy, weight loss, and other conservative approaches do not bring a satisfactory result, then it is logical to pursue trigger point or other superficial local injection procedures. If CLBP is thought to be radicular/neuropathic and related to structures at L3 or lower, then epidural injections are a logical next step. The few studies that have evaluated caudal epidural injection of D5W seem to yield impressive results with few side effects. Since the cost of this procedure is low and it entails a modest level of training, it may be a logical next step prior to injection therapies that cost more (epidural PRP) and may be more uncomfortable. Finally, if imaging or physical exam suggest deeper pathology associated with the lumbar spine then higher concentration dextrose solutions or lower hematocrit, leukocyte-poor PRP may be added to the regimen.

In conclusion, this case report describes a patient with severe CLBP refractory to non-surgical treatment who was experiencing significant disability due to his pain. He responded very well to 4 caudal epidural dextrose solution injections and chose to step up to caudal epidural PRP as well as PRP injections for facet joints and his sacro-iliac joint. More than 6 months after PRP injections, the patient experienced a durable reduction in pain and improvement in mobility and activity. Given the prevalence of CLBP, this type of step-up regimen may be valuable option for many patients.

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CONFLICTS OF INTEREST DISCLOSURE

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