Regenerative injection therapy for axial pain

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Chronic pain is considered epidemic coupled with claims of inadequate treatment. While the understanding of pain, including diagnosis and treatment, is in its infancy, significant progress has been made with diagnostic and therapeutic interventional techniques during the past two decades. Though the structural basis of spinal pain is well established, some patients continue to present a diagnostic and therapeutic challenge. In addition to target-specific fluoroscopically guided techniques, Regenerative Injection Therapy (RIT), also known as prolotherapy, is a viable treatment in managing chronic spinal pain. Proponents suggest effectiveness of RIT in treating musculoskeletal pain, while opponents suggest otherwise. Multiple published studies show (RIT) is effective despite continued controversy. This review will describe various aspects of regenerative injection therapy, technical aspects and clinical effectiveness.

Chronic spinal pain is highly prevalent in the United States, placing an enormous burden on society in terms of patient suffering and cost. A search for effective treatments is a priority.1

Interventional pain management is defined as the discipline of medicine devoted to the diagnosis and treatment of pain by application of interventional techniques independently or in conjunction with other modalities of treatment.2 Interventional technique is defined as a minimally invasive procedure for precise percutaneous delivery of therapeutic/diagnostic modalities to targeted areas in managing chronic, persistent or intractable pain.3 Based on these definitions, regenerative injection therapy (RIT) is the oldest interventional technique in current use. RIT triggers influx of macrophages, fibroblasts, release of growth factors and ultimately, new collagen formation. RIT leads to strengthening of connective tissues, reduction of pain and disability. A variety of agents including phenol, dextrose, and glycerin, alone or in various combinations, mixed with local anesthetics have been used in RIT.

Nonradicular axial or somatic pain may be felt in the extremities. Kuslich and coworkers4 identified intervertebral discs, facet joints, dura of the nerve root, ligaments, fascia and muscles as tissues capable of transmitting pain in the low back. The same philosophy is applicable to thoracic and cervical areas. Pain due to nerve root irritation, facet joint, discogenic and sacroiliac joint pain are proven to be common causes of pain by appropriate diagnostic techniques.2 However, vertebrae, muscles, and ligaments are not “proven” to be common sources of spinal pain due to lack of adequate, reliable and valid diagnostic technology.5 Utilizing advanced imaging, neurophysiologic and precision diagnostic techniques, spinal pain can be identified in approximately 50% to 80% of patients.2 Nonetheless, there continues to be 20% to 50% of patients without appropriate diagnosis.2,5–9 Further, axial and periaxial pain patterns from ligaments, muscles, intervertebral discs and facet joints overlap significantly. Therefore, patients continue to present with a diagnostic dilemma and a therapeutic challenge.2,4 –14

A short definition of RIT, also known as prolotherapy, is an interventional technique for chronic pain caused by connective tissue diathesis.15–26

Terminology

Before the 1930s, all injections were under one umbrella of “Injection Treatment” with the addition of a pathological
Local anesthetics in diagnosis of musculoskeletal pain

It was understood in the 1930s that posterior primary rami provide motor and sensory supply to muscles, tendons, thoracolumbar fascia, ligaments, aponeuroses, their origins and insertions, and NO definite diagnosis could be made based on clinical presentation alone. To facilitate the differential diagnosis of musculoskeletal pain infiltration of procaine at the nociceptive tissue beds, specifically at the fibro-osseous junctions, was introduced by Leriche, Halderman and Soto-Hall, Steindler and Luck. The following criteria were established to prove a causal relationship between the structure and pain symptoms: (1) reproduction of local and referral pain by needle contact and (2) suppression of local tenderness and referral/radiation pain by procaine infiltration.

The same basic principles have been advocated since the inception of RIT as well as other currently employed injection procedures, to objectively confirm the source(s) of pain and augment clinical diagnosis by local anesthetic blocks.

Pathophysiologic considerations

Ligaments and tendons are fibrous collagenous tissue with a crimped, wave-like appearance under a light microscope. This crimped pattern unfolds during initial collagen loading. Elongated beyond 4% of the original length, ligaments and tendons lose elasticity and recoil capability to the original crimp wave appearance. They become permanently lax leading to joint hypermobility. Sub failure was reported at earlier stages of elongation in degenerated ligaments. Natural healing, at best, may restore connective tissue to its preinjury length but only 50% to 75% of its preinjury tensile strength.

Collagenous tissues are deleteriously affected by steroid administrations, NSAIDs, inactivity and denervation. In the presence of repetitive microtrauma with insufficient time for recovery, use of steroids and NSAIDs, tissue hypoxia, metabolic and hormonal abnormalities as well as other less defined causes, connective tissue divert toward a degenerative pathway. Therefore, “a judicious utilization of antinflammation therapy remains useful, albeit adjunctive, therapy.”

Connective tissue response to trauma is inflammatory/regenerative/repairative and varies with the degree of injury. In the presence of cellular damage, regenerative pathway takes place; in case of extracellular matrix damage, a combined regenerative/repairative pathway takes place. Both are controlled by hormones, chemical and growth factors. Central denervation such as in quadriplegia leads to a statistically high, accelerated degeneration. Corticosteroids do not arrest or slow the course of degenerative process.

Neoneurogenesis and neovasculogenesis are integral components of both regenerative/repairative and degenerative processes. Nerve and vascular tissue in-growth into degenerated intervertebral discs, posterior spinal ligaments, hard niduses of fibromyalgia, together with neuropeptides in the facet joint capsules, sacroiliac ligaments have been documented.

Rationale

Rationale for RIT in chronic painful pathology of fibrous connective tissue such as ligaments and tendons evolved mainly from clinical, experimental and histological research performed for injection treatment of hernia. In hernias, inflammatory response to injectate induced proliferation and subsequent regenerative/repairative healing phases lead to a fibrotic closure of the defect. This process actually reproduced the healing by second intention. Of specific interest is the intense neovasculogenesis and neoneurogenesis accompanying the inflammatory phase and regressing during the contraction phase. It is the regression of neoneurogenesis that probably explains the pain reduction. Ability to induce proliferative regenerative repetitive response in ligaments and tendons was demonstrated in experimental and clinical studies with up to a 65% increased diameter of collagen fibers.
Movements of the spine and cranium are accomplished through various well innervated joints, which are located in the anterior, middle and posterior columns. These joints are synovial, synovial and symphyseal. Synovial joints are anterior and posterior longitudinal ligaments (ALL, PLL), anterior and posterior atlanto-occipital membranes (AAOM, PAOM), supraspinous and interspinous ligaments (SSL, ISL), and ligamentum flavum (LF). Symphyseal joints are intervertebral discs (IVD). Synovial joints are atlanto-axial (AA), atlanto-occipital (AO), zygapophyseal (ZJ), costotransverse (CT) and costovertebral (CVJ) sacroiliac (SI) joint is a combined synovial–syndesmotic one. Differential diagnosis is based on understanding of the regional and segmental anatomy, pathology, as well as segmental, multisegmental, and intersegmental communications in innervation of the compartments and their contents around the spine. This is provided by ventral rami (VR), dorsal rami (DR), gray rami communicants (GRC), sinuvertebral nerves (SVN) and sympathetic chain (SC).

Lumbar interspinous ligaments make nerve innervation from the medial branches of the dorsal rami. Three types of nerve terminals in posterior spinal ligaments have been confirmed microscopically. They are the free nerve endings, the Pacini and the Ruffini corpuscles. A sharp increase in free nerve endings quantity at the spinous processes attachments (enthesis) were documented rendering them putatively nociceptive. Experimental and empiric observations suggest that similar arrangement may exist at the cervical and thoracic spinous processes also rendering them putatively nociceptive.

Based on the IASP criteria, utilizing controlled local anesthetic blocks, in patients without radiologic or neurophysiologic evidence of nerve root compression, cervical facet joints have been shown to be responsible for pain in 54% to 67% of the patients, thoracic facet joints have been responsible 42% to 48% in chronic thoracic pain, lumbar facet joints have been responsible for 15% to 45% pain in chronic low back pain, and sacroiliac joints have been responsible for 10% to 19% pain in low back pain. Utilizing IASP criteria, discogenic pain has been established in 26% to 39% of the patients. There are no studies evaluating the prevalence of the pain secondary to atlantoorcital or atlantoaxial joints. Overall, strong evidence was shown for diagnostic facet joint blocks for the diagnosis of facet joint pain, and lumbar provocative discography for discogenic pain. Moderate evidence was shown for sacroiliac joint pain, and for transforaminal epidural injections in the preoperative evaluation of patients with negative or inconclusive imaging studies, but with clinical findings of nerve root irritation, the evidence was shown to be limited. The effectiveness of multiple interventional techniques also varies substantially based on the evaluators. Moderate to strong evidence was shown for multiple therapeutic interventional techniques including medial branch blocks and medial branch neurotomies; caudal epidural steroid injections and transforaminal epidural steroid injections; lumbar percutaneous adhesiolysis and implantable therapies.

Based on the extensive review of precision diagnostic blocks, and therapeutic interventional techniques in managing spinal pain, it appears that multiple hidden or unproven pain generators continue to persist.

Spondyloarthropathies with enthesopathies are rarely, if ever, included in the differential diagnosis or therapeutic plan by the interventional pain community. The reason why the other pain generators are not included in differential diagnosis can be explained by the spinal uncertainty principle, in a simple example of two motion segments, where disc, facets and musculotendinous compartments, each considered as one putative nociceptive unit, and the total number of clinically indistinguishable combinations rises to 63 possibilities. It is practically impossible to address such a magnitude of possibilities under fluoroscopic guidance.

The primary target for RIT is the tissue bed pathology and pain, taking innervation into account. Therefore, RIT may afford evaluation of many putative pain generators from the variety of pain presentations of the axial spinal pain and, when correctly implemented, can offer an attractive, practical alternative that can be accomplished at the same office visit (Table 1).

### Indications

Multiple indications for RIT are described in Table 2. Seronegative spondyloarthropathies accompanied by enthesopathies comprise the list of syndromes and conditions...
Clinical effectiveness

There have been multiple publications including systematic reviews, randomized controlled trials (RCTs), numerous nonrandomized reports including prospective and retrospective clinical studies. Prolotherapy is most effective when it is practiced in conjunction with manipulation. Consequently, the first RCT evaluated prolotherapy in conjunction with manipulation. Thirty-five patients out of 40 in the treatment group and 16 of 41 in the control group achieved >50% improvement in pain and disability, sustained at 6 months. The treating solution was dextrose/phenol/glycerin (DPG) and the control solution was normal saline. These findings have been misconstrued as evidence of manipulation efficacy rather than prolotherapy.

The second RCT also evaluated DPG solution but with 0.25% lidocaine/normal saline control. This study reported that 30 of 39 patients in the treatment group and 21 of 40 in the control group achieved a 50% or greater improvement in pain or disability at 6 months. Overall, both treatment groups improved markedly.

A third RCT using a lidocaine control group provided three injection treatments with much lower volumes of injectate than in the other trials and without manipulation or exercises. No changes in mean pain or disability scores in either group were reported over 6 months; therefore, it was concluded that prolotherapy was ineffective.

Most recent RCT had 110 participants with nonspecific low-back pain back, average duration of 14 years. Study was conceived with a null hypothesis that prolotherapy would be no more effective than control. It compared 20% dextrose solution with normal saline injections and either flexion/extension exercises or normal activity. At 2 years both groups reported a sustained 50% reduction in pain and disability. It was concluded that in chronic nonspecific low-back pain, significant and sustained reductions in pain and disability occur with ligament injections irrespective of the solution injected or the concurrent use of exercises. Such success rates were as good as those reported for surgery, spinal cord stimulation or multidisciplinary treatment or for patients with low-back pain of shorter duration. This

| Table 2 | Multiple indications described in the literature for RIT include the following:
| 1. Painful enthesopathies, tendinosis or ligamentosis from overuse, occupational and postural conditions known as Repetitive Motion Disorders
| 2. Painful enthesopathies, tendinosis or ligamentosis secondary to sprains or strains
| 3. Painful hypermobility, instability and subluxation of the axial joints secondary to ligament laxity accompanied by restricted range of motion at reciprocal segment(s) that improve temporarily with manipulation
| 4. Vertebral compression fractures with a wedge deformity that exert additional stress on the posterior ligamentous complex
| 5. Recurrent painful rib subluxations at the costotransverse, costovertebral, sternochondral, articulations
| 6. Osteoarthritis, spondylolysis and spondylolisthesis
| 7. Post surgical cervical, thoracic, and low back pain (with or without instrumentation)
| 8. Posterior column sources of nociception refractory to steroid injections, nonsteroidal anti-inflammatory therapy (NSAID) and radiofrequency procedures
| 9. Enhancement of manipulative treatment and physiotherapy
| 10. Internal disc derangement

Contraindications to RIT include general contraindications that are applicable to all injection techniques such as:

- Allergy to anesthetic solutions;
- Bacterial infection, systemic or localized to the region to be injected;
- Bleeding diathesis secondary to disease or anticoagulants;
- Fear of the procedure or needle phobia;
- Paraspinal neoplastic lesions involving the musculature and osseous structures;
- Recent onset of a progressive neurologic deficit including but not limited to severe intractable cephalgia, unilaterally dilated pupil, bladder dysfunction, bowel incontinence, etc.;
- Requests for large quantity of sedation and/or narcotics before and after treatment; and
- Severe exacerbation of pain or lack of improvement after local anesthetic blocks.

Specific contraindications are:

- Acute arthritis (septic, gout, rheumatoid or posttraumatic with hemarthrosis);
- Acute bursitis or tendonitis;
- Acute nonreduced subluxations, dislocations or fractures; and
- Allergy to injectable solutions or their ingredients such as dextrose, sodium morrhuate or phenol.

| Table 3 | Conditions treated with RIT
| - Cervico-cranial syndrome, cervicogenic headaches (atlanto-axial, atlanto-occipital joint and mid-cervical facet joint sprains)
| - Barré Lieou Syndrome
| - Torticollis
| - Cervical, thoracic and lumbar midline spinal pain “of unknown origin”
| - Cervicobrachial syndrome (shoulder/neck pain)
| - Hyperextension/hyperflexion injury syndromes
| - Cervical, thoracic and lumbar sprain/strain syndrome
| - Costovertebral and costotransverse arthrosis, ligament strain/strain and joint pain
| - Sacroiliac joint instability, hypermobility, repetitive strain/strain, pain
| - Myofacial pain syndromes
| - Marie-Strumpell disease
| - Ligament laxity with hypermobility and pain, Ehler’s-Marie-Strumpell disease
| - Iliac crest syndromes, iliocostalis friction syndrome, iliolumbar syndrome
| - Piriformis syndromes
| - Ankylosing spondylitis
longitudinal study demonstrated that: (1) pain and tenderness at the enthesis is a significant clinical finding treatable by injection in “nonspecific” low back pain, and (2) serendipitously chosen combination of volume and concentration of injectates combined with needle placement into ligaments, produced equally beneficial results in both arms of the experiment and is highly unlikely to present a placebo effect.53-87

A systematic review by Yelland and coworkers21 echoed trends observed in the earlier RCTs and uncontrolled studies. It found that repeated ligament injections, regardless of injectate, provide long-lasting relief of pain and disability and that prolotherapy is more effective when combined with manipulation. There is substantial evidence of prolotherapy effectiveness from nonrandomized prospective and retrospective studies as well as case reports75-79 and testimonials including one from the former Surgeon General of the United States, C. Everett Koop, MD.88 Because of technicalities and heterogeneity, present literature offers moderate evidence of prolotherapy effectiveness in select patients utilizing appropriate technique and cointerventions. They concluded that more research is needed to compare prolotherapy with noninjection therapies and its effectiveness for discogenic pain.

Clinical presentation and evaluation

As is obvious from the list of syndromes, there is a wide variety of presenting pain complaints from headaches (occipital and suboccipital), neck, cervicothoracic, between the shoulder blades, scapular and shoulder regions, thoracolumbar, low back, buttocks, sacroiliac, trochanteric area and any combination of the above.13,15,17–20,49,58,63,64–70,72,75,76,89 The intensity, duration and quality of pain are variable, as well as the onset, which may be sudden or gradual. The evaluation may reveal postural abnormalities, functional asymmetries, combinations of kyphoscoliosis, flattening of cervical and lumbar lordosis, arm and/or leg length discrepancies. Variable combinations of flexion/extension, rotation and lateral bending combined with contractions against resistance provoke pain.

The pertinent subjective clinical finding is exquisite tenderness at the fibro-osseous junctions (enthesis). The area(s) of such tenderness are identified and marked to become the subject of needle probing, “needling,” and infiltration with local anesthetic. Initial needle placement at the fibro-osseous junction usually reproduces the pain that becomes worse on infiltration of local anesthetic, typically to subside within 15 seconds after infiltration. Abolishment or persistence of tenderness, local or referred pain objectifies the finding of tenderness, concludes the clinical examination and becomes the basis for clinical diagnosis and further injections with RIT.

Radiologic evaluation

Plain radiographs are of limited diagnostic value in pain-ful pathology of the connective tissue but may detect structural or positional osseous abnormalities such as anterior or posterior listhesis on flexion/extension lateral views and degenerative changes in general with deformity of z-joints.1,90

MRI may detect pathology of intervertebral disc, ligamentous injury, interspinous bursitis, enthesopathy, z-joint disease, sacroiliac joint pathology, neural foraminal pathology, bone contusion, infection, fracture or neoplasia. MRI may exclude or confirm spinal cord disease and pathology related to extramedullary, intradural and epidural spaces.90,91 CT scans may detect small avulsion fractures of facets, laminar fracture, fracture of vertebral bodies and pedicles, neoplasia, or degenerative changes.90 Bone scans are useful in assessment of the entire skeleton to rule out metabolically active disease process.90 However, medical literature continues to report back pain cannot be diagnosed in up to 85% of cases.92 Thus pivotal to the proper management of chronic spinal pain is the ability to pinpoint an anatomical diagnosis. For this purpose physical examination is neither reliable nor valid.93 Medical imaging provides little sound information.94 No technique of physical examination has sufficient reliability and validity to allow a patho-anatomic diagnosis to be made.93,94 Radiographic investigations, including magnetic resonance imaging, reveal only some conditions with certainty.93

Technical considerations

Any structure that receives innervation is a potential pain generator. Because pain maps overlap significantly, the question is, “How to navigate in this sea of unknown?” For the purpose of RIT, the following step by step approach is recommended. Patients’ “pain and tenderness” is accepted for face value without dismissal or allocation to a distant “proven” source. It is the knowledge of clinical anatomy, pain patterns and pathology that guides the clinical investigation, based on clinical experiments of many clinicians and researchers over the years.

Initially, pain generators are identified by reproducible tenderness and movements that provoke pain; the areas are marked. Tenderness over posterior column structures is considered an objective finding until proven otherwise, especially in the midline.20,58,64,89,95 Confirmation is obtained by needling and local anesthetic blocks of the tissue at the enthesis taking the nerve supply into account.

In experienced hands, using palpable landmarks for guidance, the following posterior column elements innervated by the dorsal rami may be safely injected with or without fluoroscopic guidance: tendons and ligaments entheses at the spinous process, lamina, posterior ZJ capsule, transverse process and thoracolumbar fascia insertions.

The 0.5% lidocaine solution is an effective, initial diagnostic option for pain arising from posterior column elements when utilized in increments of 0.5 to 1.0 mL injected after each bone contact initially blocking the structures innervated by terminal filaments of the MBDRs with the sequence as follows:

1) (a) In the presence of midline pain and tenderness, enthesis of various structures inserting to the spinous process are blocked initially in the midline at the previously marked level(s). (b) The area(s) reexamined about one minute after each injection for tenderness and movements that provoked pain.
2) If tenderness remains at the lateral aspects of the spinous processes, injections are performed to the lateral aspects of their apices thus continuing on the course of medial branches or dorsal rami. Step (b) is repeated.

3) Persistence of paramedial pain dictates blocks of ZJ capsules (cervical, thoracic and lumbar), costotransverse joints or posterior tubercle of the transverse processes in the cervical region with their respective tendon insertions. Step (b) is repeated.

4) Perseverance of lateral tenderness dictates investigation of the structures innervated by the lateral branches of the dorsal rami, ie, enthesis of iliocostalis at the ribs, ventral sheath of thoracolumbar fascia at the lateral aspects of the lumbar transverse processes, iliac crests insertions. Step (b) is repeated.

In this fashion, all potential nociceptors on the course of medial branches or dorsal rami and lateral branches are investigated from its periphery to the origin. Consequently, a differential diagnosis of pain arising from vertebral and paravertebral structures innervated by medial branches or dorsal rami and lateral branches can be made (Figures 1 and 2).

Manipulation under local anesthesia may be performed at any stage after local anesthesia has taken effect and the musculature sufficiently relaxed.96
Pain from the upper cervical synovial joints presents a diagnostic and a therapeutic challenge. Because pain patterns overlap, it is usually a diagnosis of exclusion. Intra-articular atlanto-axial and atlanto-occipital joint injections of 3% phenol have secured a long-lasting therapeutic effect in selected patients. Also a good therapeutic effect with intraarticular injections of 25% dextrose to the same joints and mid-cervical synovial joints, were reported to relieve persistent pain after RF and capsular injection failure. Because of the possible serious complications, all intraarticular injections of the axial Synovial joints including AA, AO, ZJ, costovertebral, and intervertebral discs should be performed only under fluoroscopic guidance by an experienced practitioner.

Painful connective tissue proximal to enthesis are commonly injected at the following sites: spinous processes, occipital bone at inferior and superior nuchal lines, mastoid processes, posterior tubercles of transverse processes, posterior tubercles and angles of the ribs, proximal and distal portions of the clavicle, superomedial margin and spine of the scapula, sternum and xiphoid, capsular ligaments of cervical, thoracic and lumbar ZJs, and costotransverse joints, posterior sacroiliac, intersosseus and sacrotuberous ligaments and occasionally SI joint. Tendon insertions to the medial and lateral aspects of the iliac crests.

Figure 2  Schematic drawing demonstrating sites of origins and tendon insertions (enthesis) of the vertebral and paravertebral and peripheral musculature in the cervical, thoracic and lumbar regions and partly upper and lower extremities. Clinically significant painful enthesopathies are common at these locations defined by dots. Dots also represent most common locations of needle insertions and infiltration during RIT (please note: not all of the locations must be treated in each patient). Modified from Sinelnicov’s Atlas of Anatomy (vol 1), Meiditsina Moskow, 1972. Modified and prepared for publication by Tracey Slaughter. (Color version of figure is available online.)

Complications

Complications do occur with RIT but statistically, they are rare. The most recent statistical data are from a survey of 450 physicians performing prolotherapy. A hundred twenty respondents revealed that 495,000 patients received injections. Twenty-nine instances of pneumothorax have been reported, 2 of them requiring chest tube placement. Twenty-four nonlife threatening allergic reactions were also reported. Stipulating that each patient had at least 3 visits and during each visit receives at least 10 injections; the occurrence of pneumothorax requiring chest tube is 1 per 247,500 injections. Self-limited pneumothoraces is 1 per 18,333 and allergic reaction is 1 per 20,625 injections.

In the 1960s, five cases of postinjectional arachnoiditis were reported. Two of them were fatal. One was a direct sequence of arachnoiditis; another was a sequence of incompetent shunt and persistent hydrocephalus with increased intracranial pressure. Of the three other cases, the first, with mild paraparesis, recovered after a ventriculojugular shunt. The second recovered spontaneously with a mild neurological deficit. Three cases of intrathecal injections have not been reported in the literature because of medico-legal issues. Two of them resulted in paraplegia. The first occurred after injection at the thoracic level, the second after a lumbar injection. A third case was performed by an untrained person who injected zinc sulfate solution at the cranio-cervical level resulting in immediate onset of severe neurologic deficit, quadriplegia and subsequent hydrocephalus.

One case of self-limiting sterile meningitis after lumbosacral sclerosing injections was reported in 1994. Adjacent endplate fractures associated with intraarticular dextrose injections was recently reported. Postspinal puncture headaches have been reported after lumbosacral injections. Two such cases occurred in the first author’s practice during the past 14 years. Patients recovered after 1 week with bed rest and fluids. Overall, pneumothorax is the most common reported complication. Injections of anterior synovial joints, such as sternoclavicular, costosternal and interchondral, may also result in pneumothorax in the same subset of patients.

Solutions for injections

The most common solutions are dextrose-based. To achieve a 12.5% concentration, dilution is made with local anesthetic in 1:3 proportions, ie, 1 mL of 50% dextrose mixed with 3 mL of 1% lidocaine. A 1:2 proportion, ie, 1 mL of 50% dextrose with 2 mL of 1% lidocaine, will equal 16.5%
dextrose. Further, a 1:1 dilution makes a 25% dextrose solution.

For intraarticular injections, a 25% dextrose solution is commonly utilized though a recent double-blind study suggests that 10% dextrose solution may be equally effective.\textsuperscript{103}

If dextrose proves ineffective, progression to a stronger solution such as sodium morrhuate up to full strength has been described. A 5% sodium morrhuate is a mixture of sodium salts of saturated and unsaturated fatty acids of cod liver oil and 2% benzyl alcohol, which acts as a local anesthetic and a preservative. Note that benzyl alcohol chemically is very similar to phenol.

Dextrose/phenol/glycerin solution consists of 25% dextrose, 2.5% phenol and 25% glycerin and is referred to as DPG, a.k.a. P2G. It is diluted in concentrations of 1:2, 1:1 or 2:3 with a local anesthetic before injection.

Diluted 6% phenol in glycerin solution is advocated by Wilkinson for injections at donor harvest sites of iliac crests for neurolytic and proliferative responses.\textsuperscript{67}

**Conclusion**

Chronic spinal pain is common and an expensive problem in the United States. Prolotherapy is one of the interventional techniques utilized in managing spinal pain. Present evidence with inclusion of systematic reviews, randomized and nonrandomized evidence indicates effectiveness of RIT in painful spinal conditions with enthesopathies.

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