Prolotherapy: Can it help your patient?

Prolotherapy appears to be effective for Achilles tendinopathy and knee osteoarthritis, but has limited efficacy for low back pain. Find out when—and whether—to consider this option.

Over the past several years, prolotherapy has been gaining support as an option for patients with tendinopathies and painful osteoarthritic conditions. Yet the technique lacks both a consistent definition and an abundance of evidence.

Because the prefix “prolo” is thought to refer to proliferation or regeneration, some physicians prefer the term “sclerotherapy” when injecting sclerosing agents. Others point out that “prolotherapy” refers to the proliferation of tissue that the injections provoke, which has never been proven. We believe that the material injected should dictate the term used to describe it—dextrose prolotherapy (DPT) or platelet-rich plasma therapy (PRP), for example.

In this update, we focus on DPT—the injection of a solution containing hypertonic dextrose into ligaments, tendons, and joints to promote healing. You’ll find an overview of the proposed mechanism of action and a description of the technique (see “How DPT works” on page 765), as well as a look at the evidence of its effectiveness for a variety of musculoskeletal conditions in the text and TABLE that follow. Our review is limited by the dearth of large, definitive studies, and consists mainly of anecdotal evidence, case reports, and other low-quality studies.

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Considering DPT—

for which patients?

Even for conditions for which the evidence of its efficacy is unequivocal, DPT is only one part of a comprehensive treatment plan. Functional assessment and correction of any weaknesses, inflexibilities, and/or training errors are also essential.

There are a number of other considerations, as well. For one thing, DPT is rarely covered by health insurance and is often considered only after conservative treatment has failed. What’s more, it is not suited to every patient.

**Absolute contraindications** include acute infections at the injection site, such as cellulitis, abscess, or septic arthritis. Relative contraindications include acute gout flare and acute fracture near the site.

When DPT is a viable alternative, keep in mind that the procedure should only be done by a physician experienced in the techn-
And that ultrasound guidance should be used to ensure precise anatomical delivery (FIGURE 1). Consent must be obtained and documented, and universal precautions observed.

Read on to find out whether to consider DPT for particular patients.

**Achilles tendinopathy: DPT decreases pain, improves function (SOR A)**

Non-insertional Achilles tendinopathy can be treated with prolotherapy to decrease pain and tendon thickness (FIGURE 2). A small, single blind randomized trial compared the effectiveness of eccentric exercise (ie, contractions performed to lengthen the muscle), DPT alone, and a combination of DPT and exercise for patients with chronic Achilles tendinopathy.\(^{10}\)

The investigators found greater improvement in the Victorian Institute of Sport Assessment-Achilles (VISA-A) score at 12 months with the combined therapy (41.1 on a 0-100 scale) vs either eccentric exercise (23.7) or DPT (27.5) alone. The increase from baseline was greater for those who received combination therapy at 6 weeks (+11.7) compared with the eccentric-only group.\(^{10}\) Adding DPT (injected into the tender points of the subcutaneous tissues adjacent to the Achilles tendon) to eccentric exercise resulted in a more rapid and sustained improvement in pain, function, and stiffness.

In an earlier observational study, researchers achieved improvement in pain scores using a different DPT technique.\(^{22}\) Here, patients with chronic Achilles tendinosis received ultrasound-guided intratendinous dextrose injections every 6 weeks until symptoms resolved. Pain scores, calculated using a visual analogue scale (VAS), showed a mean reduction at rest (88%), during normal daily activities (84%), and during physical activity (78%). The mean number of treatment sessions was 4, and the mean time to achieve results was 30 weeks.\(^{22}\)

**Knee osteoarthritis: Pain level and movement improve (SOR A)**

In a study of patients with knee osteoarthritis (OA) and pain lasting 6 months or more, participants received bimonthly injections of either DPT with lidocaine or lidocaine alone. At 12 months, only those in the DPT group had achieved significant improvement in VAS pain score (44%), self-reported swelling (63%), and knee flexion (14%).\(^{11}\)

A more recent study randomized 90 adults with painful knee OA of at least 3 months’ duration to blinded injection (either DPT or saline) or at-home exercise.\(^{9}\) The injections involved both intra- and extra-articular techniques, performed monthly for a total of 3 to 5 injections. At 52 weeks, the DPT group had improved scores on the Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC) by 15.3 points compared with the saline group (7.6 points) and the exercise-only group (8.2 points).

Half of those receiving DPT improved by 12 or more points, compared with less than a third of those receiving saline and a quar...
Finger OA. One small randomized study tested the efficacy of DPT in patients with symptomatic finger OA affecting the distal or proximal interphalangeal joint or the trapeziometacarpal (thumb) joint. Participants received either DPT with xylocaine or xylocaine alone. Injections were done on the medial and lateral aspects of the affected joints at baseline, 2, and 4 months. Pain (VAS score) during active finger movement improved by 45% in the DPT group vs 15% in the group treated with xylocaine alone. After 6 months, those in the xylocaine-only group received the DPT protocol, and their pain reduction scores rose, on average, from 18% to 54%.

Low back pain: Little help for chronic condition (SOR A)

Early studies of DPT for the treatment of low back pain had conflicting results. In 2004, the largest (N=110) and most rigorous study of DPT for chronic non-specific low back pain found no significant improvement.

Participants received either DPT or normal saline injections into tender lumbopelvic ligaments every 2 weeks for a total of 6 treatments. They were then randomized to either core and low back strengthening exercises or normal activity for 6 months. At 12 months, VAS pain and disability scores significantly decreased from baseline in all the groups, with a decline ranging from 26% to 44% for pain and 30% to 44% for disability. However, at no point were there significant differences between injection groups or activity groups.

A 2007 Cochrane review found insufficient evidence to support the use of DPT alone for the treatment of non-specific low back pain but suggested that, as an adjunct, it may improve pain and disability scores. And in 2011, a Cochrane review confirmed that there was insufficient evidence for the use of DPT in sub-acute and chronic low back pain. Other studies on the use of DPT for specific low back conditions, including sacroiliac joint pain, coccydynia, and degenerative disc disease, have shown trends toward improvement in pain scores and disability, but only one of these was a randomized controlled trial (RCT).

Lateral epicondylitis: More effective than saline (SOR B)

A single RCT compared DPT to placebo in patients with 6 months of moderate to severe lateral epicondylitis who had failed conservative treatment. Patients received 3 injections of either hypertonic dextrose or saline tendon insertions every 4 weeks, with needle touching bone at the supracondylar ridge, lateral epicondyle, and annular ligament. Patients randomly assigned to DPT experienced significant pain relief from baseline to 16 weeks, with a Likert score decline from...
To avoid inhibiting the desired inflammatory response to prolotherapy, nonsteroidal anti-inflammatory drugs should not be used to treat post-injection pain.

Osgood-Schlatter: DPT improves pain relief (SOR B)
In one of the few studies of prolotherapy for adolescents, patients with recalcitrant Osgood-Schlatter disease were randomized to either structured physical therapy or 3 monthly injections of lidocaine, with or without dextrose, over the apophysis and patellar tendon origin. Injections began at the most distal point of tenderness and were repeated at 1 cm intervals for a total of 3 to 4 midline injections. The proximal injections were deep to the patellar tendon, on the tibia above the tiberosity.

Pain scores, measured by the Nirschl Pain Phase Scale (0-7), improved significantly more in the DPT group (3.9) compared with either the lidocaine group (2.4) or the exercise group (1.2). Dextrose-treated knees were significantly more likely than knees treated with lidocaine (14 of 21 vs 5 of 22) to be asymptomatic with sport activity. After 3 months, patients in the lidocaine and exercise groups who had not responded adequately were given the option of receiving DPT; those who underwent the 3-month DPT protocol achieved the same level of improvement as the initial DPT group.

When considering or recommending DPT for an adolescent with Osgood-Schlatter disease, however, it is particularly important that he or she be referred to a physician with expertise in prolotherapy.

Plantar fasciosis: A possibility when conservative treatment fails (SOR B)
An early case series showed that DPT effectively improved pain at rest and during activity in patients with chronic plantar fasciosis refractory to conservative care. A small RCT recently compared PRP with DPT in such patients.

Pain, disability, and activity limitation were measured by the Foot Functional Index. The PRP group improved by 29.7%, 26.6%, and 28% in pain, disability, and activity limitation, respectively, vs improvements of 17%, 14.5%, and 12.4% in the DPT group. Although there was a trend for PRP to be superior, the results were not statistically significant. This suggests that DPT may be an additional treatment option for patients with plantar fasciosis when conservative treatment fails.

Chondromalacia patella: Not enough is known (SOR C)
One study showed that DPT improved self-reported pain and function scores in patients with chronic knee pain secondary to chondromalacia patella. However, the study had no control group and no standardized injected solution; rather, the solution was tailored for each individual. Thus, there is insufficient data to make recommendations regarding the effectiveness of DPT in treating chondromalacia patella or other causes of patellofemoral pain syndrome.

What to tell patients about recovery and adverse effects
Injection of dextrose into ligaments, tendons, and joints carries the theoretical risks of light-headedness, allergic reaction, infection, and structural damage. However, there have been no reports of serious or significant adverse events associated with DPT when used for peripheral joint indications.

The most common risks of DPT are needle trauma-induced pain, mild bleeding, and bruising. A sense of fullness, stiffness, and occasional numbness at the site at the time of injection are common, benign, and typically self-limiting. If post-procedure numbness continues, the patient should follow up in 48 to 72 hours to rule out nerve damage.

Post-injection pain flare during the first 72 hours may occur. In a study of prolotherapy for knee OA pain, 10% to 20% of patients experienced such flares. Most patients respond well to acetaminophen and experience resolution of pain within a week. Nonsteroidal anti-inflammatory drugs should not be used to treat post-procedure pain because they may interfere with the local inflammatory response needed for healing. Regular activities can be resumed immediately after an injection into a large joint, such as the knee, or after full sensation and proprioception re-
Ballistic weight bearing and full strength activity should be limited for 48 hours after an injection into a non-weight-bearing tendon and for 5 to 7 days for a weight-bearing tendon.