Prolotherapy in Primary Care Practice

David Rabago, MD*, Andrew Slattengren, DO, Aleksandra Zgierska, MD, PhD

KEYWORDS

- Prolotherapy • Injection therapy • Osteoarthritis
- Tendinopathy • Low back pain
- Chronic musculoskeletal pain

Prolotherapy is an injection-based complementary and alternative medical (CAM) therapy for chronic musculoskeletal pain. It has been used for approximately 100 years; however, its modern applications can be traced to the 1950s when the prolotherapy injection protocols were formalized by George Hackett,[1] a general surgeon in the United States, based on his clinical experience of more than 30 years. Prolotherapy techniques and injected solutions vary by condition, clinical severity, and practitioner preferences; a core principle is that a fairly small volume of an irritant or sclerosing solution is injected at sites on painful ligament and tendon insertions and in adjacent joint space over several treatment sessions.[1,2] Interest in prolotherapy among physicians and patients is high. It is becoming increasingly popular in the United States and internationally and is actively used in clinical practice.[3,4] A 1993 survey sent to osteopathic physicians estimated that 95 practitioners in the United States were estimated to have performed prolotherapy on approximately 450,000 patients. However, only 27% of surveys were returned; consequently, the true number of practitioners was probably dramatically underestimated.[5] No formal survey has been done since 1993. The current number of practitioners actively practicing prolotherapy is unknown but is probably several thousand in the United States based on attendance at continuing medical education (CME) conferences and physician listings on relevant Web sites. Prolotherapy has been assessed as a treatment for a wide variety of painful chronic musculoskeletal conditions that are refractory to ''standard-of care'' therapies. Although anecdotal clinical success guides the use of prolotherapy for many conditions, clinical trial literature supporting evidence-based

Grant Support: None.
Portions of this article were adapted from Rabago D, Best T, Beamsly M, Patterson J. A systematic review of prolotherapy for chronic musculoskeletal pain. Clin J Sports Med 2005;15(5):376–80; with permission.
Department of Family Medicine, University of Wisconsin School of Medicine and Public Health, 777 South Mills Street, Madison, WI 53715, USA
* Corresponding author.
E-mail address: David.rabago@fammed.wisc.edu (D. Rabago).

Prim Care Clin Office Pract 37 (2010) 65–80
doi:10.1016/j.pop.2009.09.013 **primarycare.theclinics.com**
0095-4543/10/$ – see front matter

decision-making for the use of prolotherapy exists for low back pain (LBP), several tendinopathies, and osteoarthritis (OA).

The name of prolotherapy has changed over time. Consistent with existing hypotheses and understanding of possible mechanisms of action, the name of this therapy has evolved. Nomenclature has reflected practitioners' perceptions of prolotherapy's therapeutic effects on tissue. Historically, this injection therapy was called sclerotherapy because early solutions were thought to be scar-forming. Prolotherapy is currently the most commonly used name and is based on the presumed "proliferative" effects on chronically injured tissue. It has also been called regenerative injection therapy (RIT),[2,6] and some contemporary authors name the therapy according to the injected solution.[7] The precise mechanism of action is not known.

The National Institute of Health identifies prolotherapy as a CAM therapy and has funded 2 ongoing clinical prolotherapy trials. The Centers for Medicare and Medicaid Services and Veteran's Administration have reviewed the prolotherapy literature for LBP and all musculoskeletal indications and determined existing evidence to be inconclusive. Neither recommends third-party compensation for prolotherapy. However, their review did not include the most recent clinically positive studies or reviews.[7–9] Private insurers are beginning to cover prolotherapy for selected indications and clinical circumstances; however, most patients pay "out-of-pocket."

PROLOTHERAPY TECHNIQUE

Although no formal practice guidelines have been published, prolotherapy treatment commonly consists of several injection sessions delivered every 2 to 6 weeks over several months. During an individual prolotherapy session, therapeutic solutions are injected at sites of painful and tender ligament and tendon insertions and in adjacent joint spaces. Injected solutions ("proliferants") have historically been hypothesized to cause local irritation, with subsequent inflammation and tissue healing, resulting in enlargement and strengthening of damaged ligamentous, tendon, and intra-articular structures.[10,11] These processes were thought to improve joint stability, biomechanics, and function, and ultimately, to decrease pain.[1,2]

MECHANISM OF ACTION

The mechanism of action for prolotherapy has not been clearly established and, until recently, received little attention. Supported by pilot-level evidence, the 3 most commonly used prolotherapy solutions have been hypothesized to act via different pathways: hypertonic dextrose by osmotic rupture of local cells, phenol-glycerine-glucose (P2G) by local cellular irritation, and morrhuate sodium by chemotactic attraction of inflammatory mediators[12] and sclerosing of pathologic neovascularity associated with tendinopathy.[13,14] The potential of prolotherapy to stimulate release of growth factors favoring soft tissue healing has also been suggested as a possible mechanism.[15,16]

In vitro and animal model data have not fully corroborated these hypotheses. An inflammatory response in a rat knee ligament model has been reported for each solution, although it was not significantly different from that caused by needle stick alone or saline injections.[17] However, animal model data suggest a significant biologic effect of morrhuate sodium and dextrose solutions compared with controls. Rabbit medial collateral ligaments injected with morrhuate sodium were significantly stronger (31%), larger (47%), and thicker (28%), and had a larger collagen fiber diameter (56%) than saline-injected controls[10]; increase in cell number, water content, ground substance amount, and various inflammatory cell types were hypothesized