2017

Prolotherapy: Applications, Mechanism of Action, Controversy and Evidence

Boris M. Davydov
University of North Dakota

Follow this and additional works at: https://commons.und.edu/pas-grad-posters

Part of the Alternative and Complementary Medicine Commons, and the Musculoskeletal System Commons

Recommended Citation
https://commons.und.edu/pas-grad-posters/36

This Poster is brought to you for free and open access by the Department of Physician Studies at UND Scholarly Commons. It has been accepted for inclusion in Physician Assistant Scholarly Project Posters by an authorized administrator of UND Scholarly Commons. For more information, please contact zeinebyousif@library.und.edu.
Prolotherapy: applications, mechanism of action, controversy and evidence.

Merriam-Webster defines prolotherapy (PROLO) as "an alternative therapy for treating musculoskeletal pain that involves injection of irritant substance (as dextrose) into a ligament or tendon to promote the growth of new tissue". (2017) Experimental research and multiple clinical trials have generated evidence suggesting that PROLO is effective at treating a variety of musculoskeletal conditions, including tendinopathies, joint instability and ligament laxity. PROLO may also hold a potential to delay or avoid joint replacement and rotator cuff surgeries. Further research is needed to demonstrate the therapeutic effect of PROLO unequivocally.

Introduction

• The traditional approach to treating acute tendon injuries and chronic tendinopathy is with anti-inflammatory, such as NSAIDs, even though histopathological, biochemical and molecular studies of damaged tendons have not been able to demonstrate classical inflammatory processes or components. In addition to that, at least one study found that the early administration of bupivacain in the postoperative period was detrimental to tendon healing. (Connizzo et al., 2014)

• Corticosteroid injections continue to be one of the most commonly used approaches in treating tendinopathy and other MSK soft tissue pathology. This treatment is deemed to be very effective and provides relatively fast and often long lasting pain relief. The cytotoxic side effect of corticosteroids includes: degradation of fibroblasts, collagen degradation, collagen repair, and deterioration of mechanical properties of tendons. (Floyd Dean, Franklin, Murphy, Javadi, & Carr, 2014)

• Surgical intervention.

Statement of the Problem

• At the present time, PROLO is classified as an alternative and/or complementary therapy. Therefore, it is not on the list of services that are covered by commercial healthcare insurance carriers.

• In 1999, the Centers of Medicare and Medicaid Services (CMS) (CMS) recommended non-conclusive decision due to lack of PROLO coverage citing the lack of conclusive scientific evidence.

• In the last 15 years, a number of randomized controlled trials performed statistically significant evidence in support of PROLO. The studies were published in a variety of established and recognized medical periodicals.

• Will those new pieces of evidence turn out to be sufficient, compelling and significant enough to sway position the medical establishment and the insurance carriers hold regarding PROLO?

Merriam-Webster defines prolotherapy (PROLO) as “an alternative therapy for treating musculoskeletal pain that involves injection of irritant substance (as dextrose) into a ligament or tendon to promote the growth of new tissue”. (2017) Experimental research and multiple clinical trials have generated evidence suggesting that PROLO is effective at treating a variety of musculoskeletal conditions, including tendinopathies, joint instability and ligament laxity. PROLO may also hold a potential to delay or avoid joint replacement and rotator cuff surgeries. Further research is needed to demonstrate the therapeutic effect of PROLO unequivocally.

Introduction

• The traditional approach to treating acute tendon injuries and chronic tendinopathy is with anti-inflammatory, such as NSAIDs, even though histopathological, biochemical and molecular studies of damaged tendons have not been able to demonstrate classical inflammatory processes or components. In addition to that, at least one study found that the early administration of bupivacain in the postoperative period was detrimental to tendon healing. (Connizzo et al., 2014)

• Corticosteroid injections continue to be one of the most commonly used approaches in treating tendinopathy and other MSK soft tissue pathology. This treatment is deemed to be very effective and provides relatively fast and often long lasting pain relief. The cytotoxic side effect of corticosteroids includes: degradation of fibroblasts, collagen degradation, collagen repair, and deterioration of mechanical properties of tendons. (Floyd Dean, Franklin, Murphy, Javadi, & Carr, 2014)

• Surgical intervention.

Statement of the Problem

• At the present time, PROLO is classified as an alternative and/or complementary therapy. Therefore, it is not on the list of services that are covered by commercial healthcare insurance carriers.

• In 1999, the Centers of Medicare and Medicaid Services (CMS) (CMS) recommended non-conclusive decision due to lack of PROLO coverage citing the lack of conclusive scientific evidence.

• In the last 15 years, a number of randomized controlled trials performed statistically significant evidence in support of PROLO. The studies were published in a variety of established and recognized medical periodicals.

• Will those new pieces of evidence turn out to be sufficient, compelling and significant enough to sway position the medical establishment and the insurance carriers hold regarding PROLO?

Research Questions

• What are the common MSK disorders that can potentially be treated with PROLO?

• What is the proposed mechanism of action behind?

• What clinical studies are available in support of effectiveness and efficacy of PROLO?

• What are the existing alternatives to PROLO and how do they compare with it?

Literature Review

The information used for this project was retrieved from peer reviewed periodicals that can be located at: PubMed, SPORT Discus and Cochrane. The data regarding the epidemiology and pathogenesis was collected from the Centers for Disease Control and Prevention and the Congressional Budget Office. The policies of the following healthcare insurers were reviewed regarding the coverage of PROLO: Aetna, United Healthgroup, and Blue Cross/Blue Shield. The national non-coverage decision of the Centers of Medicare and Medicaid Services regarding PROLO was utilized for this project.

• MSK conditions are the single most common reason for patients visiting their physician. (CDC)

• MSK conditions identified as amenable to PROLO: injured or torn ligaments and tendons; chronic MSK pain, including back pain; tendinopathy; rotator cuff injuries, and knee disorders.

• Pathophysiology factors: genetic component, repetitive micro trauma, no evidence for inflammatory processes or components.

• Proposed intrinsic regeneration elements: growth factors, cytokines and neuropeptides. (Riley, 2004)

• Proposed mechanism of action of PROLO – trigger of inflammatory reaction: recruitment of granulocytes, monocytes, macrophages and other inflammatory mediators. Polypeptide growth factors attract fibroblasts which deposit new collagen fibers at the site of PROLO therapy. (Freeman et al., 2011) Having been injected with hyperosmolar dextrose solutions, the cell becomes dehydrated and releases lipids from cell membrane that produce growth factors. (Reeves, 2015)

• At the present time, there is level I and/or level II evidence demonstrating efficacy of PROLO for treating the following conditions: knee (Rabago et al., 2013) and hand osteoarthrosis (Reeves & Hassanein, 2000), Osgood- Schlatter disease (Topol et al., 2011), lateral epicondylitis (Scarpone, Rabago, Zgierska, Arbogast, & Snell, 2008), chronic low back pain (Yelland, Mar, Pirozzo, Schoene, & Vercuo, 2004), anterior cruciate ligament laxity (Reeves & Hassanein, 2003), and rotator cuff tendinopathy (Bertrand et al., 2016).

Discussion

• Contemporary Research

Since the mid 1980s, research on PROLO effects has accelerated and the number and methodological quality of studies assessing PROLO have increased dramatically.

PROLO for knee osteoarthritis: a randomized controlled trial

Trial parameters: Number of patients: 93; duration of the trial: 52 weeks; PROLO injections performed at 1.5, 9, 13.17 weeks; Western Ontario McMaster University Osteoarthritis Index (WOMAC) was used as primary outcome measure in evaluating results (WOMAC is scored on a range of 0 to 100 points, with higher scores indicating better knee-related quality of life)


• PROLO for knee osteoarthrosis: a randomized controlled trial

Trial parameters: Number of patients: 93; duration of the trial: 52 weeks; PROLO injections performed at 1.5, 9, 13.17 weeks; Western Ontario McMaster University Osteoarthritis Index (WOMAC) was used as primary outcome measure in evaluating results (WOMAC is scored on a range of 0 to 100 points, with higher scores indicating better knee-related quality of life).

Figure 2: Change in WOMAC composite scores over 52 weeks (a standard error. Prolotherapy confidence intervals indicate significance of change in dextrose scores compared with change in scores of both saline (P<0.05) and exercise (P<0.05) groups. Adapted from Rabago, D., Patterson, J. J., Mundt, M., Kijowski, R., Greihsa, J., Segal, N. A., & Zgierska, A. (2013). Dextrose Prolotherapy for Knee Osteoarthritis: A Randomized Controlled Trial. Annals of Family Medicine, 11(3), 259-267. http://doi.org/10.1370/afm.1564

RESULTS: At the end of the tracking period, week 52, there was a statistically significant improvement on the WOMAC score among the participants who received dextrose PROLO injections. The score improved by more than 15 points, which corresponded to 24% compared with the baseline score. These changes exceed the minimal clinical important difference (MCID) on the WOMAC for the knee osteoarthrosis, which is set at 12 points.

Applicability to Clinical Practice

• Prolotherapy at a glance

What is it?

Prolotherapy is an injection-based complementary and alternative medicine (CAM) therapy for treating musculoskeletal pain that involves injection of an irritant substance (as dextrose) into a ligament or tendon to promote growth of new tissue.

What is it made of?

Prolotherapy is a mixture of a variety of substances that are varied depending on the specific conditions of the patient. Common ingredients include saline, local anesthetics, platelet-rich plasma, pentosan polysulfate sodium, dextrose, and calcium ammonium lactate among others.

What conditions do people get it for?

Prolotherapy is generally used for musculoskeletal pain of greater than 3 months, and it is contraindicated in acute trauma, active infection, or when there is no definitive improvement after 3-6 months of conservative therapy. Common conditions include knee osteoarthritis, knee ligament tears, chronic rotator cuff tendinopathies, chronic low back pain, and chronic ankle pain.

Does it hurt?

No one loves getting a shot, though prolotherapy injections typically hurt less than most orthopedic injections. The dextrose component can help minimize discomfort and pain.

• Estimated cost of treatment

A typical PROLO protocol consists of 4 to 6 sessions, each separated by intervals of 4 to 6 weeks. At the present time, most insurers do not cover PROLO, and patients pay out-of-pocket. The average cost of PROLO treatment ranges from $1,125 for wrist/foot/hand disorders to $2,500 for back pain. (Hauser, Baird 2010)

• PROLO coverage by insurance

The number of random controlled studies that explore the potential of PROLO continues to grow. Every single one of them has produced positive results supporting PROLO with additional studies needed to establish an unequivocal efficacy. However, most of these studies are self-funded and receive no financial support from any pharmaceutical or medical corporation. Therefore, it will likely take more time for the cumulative solid scientific evidence to reach a point where the insurance policy makers no longer be able to ignore the PROLO potential. Major healthcare insurers, such as Aetna, United Healthgroup, and Blue Cross/Blue Shield, find the available data insufficient or have not recognized it, thus making PROLO inaccessible for most of the patients.

Acknowledgements

I would like to thank Doctor Lawrence Biel for his guidance in completing this scholarly project. I would also like to thank my family and the faculty at UND PA program for their support and encouragement throughout this endeavor.