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Prolotherapy: Applications, Mechanism of Action, Controversy and Evidence

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Prolotherapy: applications, mechanism of action, controversy and evidence.

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Abstract

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-inflammatories, 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 antibiotic in the postoperative period was detrimental to tendon healing. (Connizzo et al., 2014)
• Corticosteroids injections continue to be one of the most commonly used approaches in treating tendinopathy and other 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 matrix, 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) issued a national non-coverage decision desisted the request for PROLO coverage citing the lack of conclusive scientific evidence.
• In the last 15 years, a number of randomized controlled trials proved statistically and 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 the 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 low back pain; tendinopathy; rotator cuff injuries, and knee disorders.
• Pathophysiology factors: genetic component, repetitive stress, and individual patient characteristics.

• 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 osteoarthritis (Reeves & Hassanein, 2000), Osgood–Schlatter disease (Topol et al., 2011), lateral epicondylitis (Scarpone, Rabago, Zgierska, Argobas, & Snell, 2008), chronic low back pain (Yelland, Mar, Pirrozzo, Schoene, & Veroce, 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

Using 52 patients, a randomized controlled trial was conducted to determine the efficacy of PROLO for knee osteoarthritis. The patients were randomized to receive (a) PROLO, (b) saline sham, or (c) no treatment. The PROLO group received five consecutive PROLO injections of 4% dextrose into the knee joint space. The saline sham group received five consecutive injections of isotonic saline into the knee joint space. The control group did not receive any injections. The pain scores and knee function were recorded at baseline and at 1, 2, 4, and 6 months. The results showed that the PROLO group had significantly lower pain scores and improved knee function compared to the saline group and control group. (Rabago et al., 2013)

• Prolotherapy Clinical Reports

Prolotherapy Clinical Reports

<table>
<thead>
<tr>
<th>Condition</th>
<th>Prolotherapy Clinical Reports</th>
</tr>
</thead>
<tbody>
<tr>
<td>Knee osteoarthritis</td>
<td>Improved pain and function</td>
</tr>
<tr>
<td>Shoulder tendinopathy</td>
<td>Decreased pain</td>
</tr>
<tr>
<td>Ankle ligament laxity</td>
<td>Increased stability</td>
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</tbody>
</table>

Applicability to Clinical Practice

• Prolotherapy at a glance

What is prolotherapy?
Prolotherapy is an injection-based diagnostic and therapeutic technique used to treat musculoskeletal injuries by introducing hyperosmolar dextrose into the synovial space of a joint, tendon, or ligament to stimulate healing. It is a nonsurgical treatment that targets the underlying cause of pain and disability, rather than just treating the symptoms. (Yelland et al., 2013)

What is the mechanism of action?
Prolotherapy injections are thought to work by inducing a localized inflammatory response, which stimulates the body's natural healing processes. The hyperosmolar dextrose helps to draw fluids out of the joint or tendon, creating a localized inflammatory response. This response then triggers the body to heal and regenerate the damaged tissue. (Yelland et al., 2013)

What are the indications for using prolotherapy?
Prolotherapy is generally used for musculoskeletal pain of greater than 6 months' duration, postoperative pain, chronic pain due to ligament or tendon injuries, and pain due to chronic arthritis. It is also useful for treating chronic pain in the spine, shoulders, knees, and ankles. (Yelland et al., 2013)

What is the efficacy of prolotherapy?
Prolotherapy is considered to be effective for the treatment of chronic pain due to musculoskeletal injuries. It has been shown to provide relief for patients with chronic pain due to ligament or tendon injuries, chronic arthritis, and postoperative pain. It may be used as an alternative to surgical procedures or as a supplement to other treatments. (Yelland et al., 2013)

Is it safe?
Prolotherapy is generally considered to be safe, but as with any medical procedure, there is some risk. It is important to discuss the potential risks and benefits with a healthcare provider before deciding on this treatment. (Yelland et al., 2013)

Estimating the cost of treatment
A typical prolotherapy 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 when 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.

References


Floyd Dean, Franklin, Murphy, Javadi, & Carr, 2014


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