

**Evidence-Based Practice Group Answers to Clinical
Questions**

**“Prolotherapy as Treatment for Chronic Knee
Pain”**

A Rapid Systematic Review

By

WorkSafeBC Evidence-Based Practice Group

***Dr. Craig Martin
Manager, Clinical Services
Chair, Evidence-Based Practice Group***

November 2017

About this report

Prolotherapy as Treatment for Chronic Knee Pain

Published: November 2017

About the Evidence-Based Practice Group

The Evidence-Based Practice Group was established to address the many medical and policy issues that WorkSafeBC officers deal with on a regular basis. Members apply established techniques of critical appraisal and evidence-based review of topics solicited from both WorkSafeBC staff and other interested parties such as surgeons, medical specialists, and rehabilitation providers.

Suggested Citation

WorkSafeBC Evidence-Based Practice Group, Martin CW. Prolotherapy as Treatment for Chronic Knee Pain. Richmond, BC: WorksafeBC Evidence-Based Practice Group; November 2017.

Contact Information

Evidence-Based Practice Group
WorkSafeBC
PO Box 5350 Stn Terminal
Vancouver BC V6B 5L5

Email • craig.martin@worksafebc.com
Phone • 604 279-7417
Toll-free • 1 888 967-5377 ext 7417

Objective

To determine whether there is any evidence to support the efficacy and/or effectiveness of Prolotherapy as treatment for chronic knee pain.

Methods

- A comprehensive systematic literature search was conducted on November 28, 2017
- The literature search was conducted on commercial medical literature databases, including Cochrane Database of Systematic Reviews® (from 2005 to November 22, 2017), ACP Journal Club® (from 1991 to November 2017), UK York University Database of Abstracts of Reviews of Effects® (1st Quarter 2016), Cochrane Central Register of Controlled Trials® (November 2017), UK NHS Health Technology Assessment® (4th Quarter 2016), UK NHS Economic Evaluation Database® (1st Quarter 2016), BIOSIS Previews® (from 1969 to 2008), Embase® (from 1974 to 2017 November 27), Medline Epub Ahead of Print®, Medline In-Process & Other Non-Indexed Citations®, Medline Daily Update® and Medline® (from 1946 to Present), that are available through the Ovid® platform.
- The search was done by employing combinations of keywords, as follows:
 1. ((ligament **ADJ** sclerotherapy) **OR** (regenerative **ADJ** injection **ADJ** therapy) **OR** (nonsurgical **ADJ** ligament **ADJ** reconstruction) **OR** (proliferation **ADJ** therapy) **OR** prolotherapy) **AND** (chronic **ADJ** knee **ADJ** pain)
 - No published study was identified through this search
 2. ((ligament **ADJ** sclerotherapy) **OR** (regenerative **ADJ** injection **ADJ** therapy) **OR** (nonsurgical **ADJ** ligament **ADJ** reconstruction) **OR** (proliferation **ADJ** therapy) **OR** prolotherapy) **AND** (knee **ADJ** pain)
 - Twenty four⁽¹⁻²⁴⁾ published studies were identified through this search
- No limitations, such as on the language and/or date of publication, were employed in any of these searches.

Results

- Examination of the titles and abstracts of the 24⁽¹⁻²⁴⁾ published studies identified show that none of the studies were relevant to the objective of this systematic review.

Summary

- At present, there is no published study investigating the efficacy and/or effectiveness of prolotherapy as treatment for knee pain or chronic knee pain.

References

1. Carey P.M. Pop goes the marine. *Clinical. Journal of Sport Medicine*. Conference: 24th Annual Meeting of the American Medical Society for Sports Medicine, AMSSM 2015. Hollywood, FL United States. Conference Publication: (var.pagings). 25 (2) (pp e41), 2015. Date of Publication: March 2015.
2. Centeno C.J.; Schultz, J., and Freeman, M. Sclerotherapy of Baker's cyst with imaging confirmation of resolution. *Pain. Physician*. 11 (2) (pp 257-261), 2008. Date of Publication: March/April 2008.
3. Chang E.H.; Onishi, K.; Zhao, X., and Takemoto, R. Ultrasound guided neural prolotherapy for treatment of iliotibial band friction syndrome at the knee: A case report. PM. and R. Conference: 2014 Annual Assembly of the American Academy of Physical Medicine and Rehabilitation. San Diego, CA United States. Conference Publication: (var.pagings). 6 (9 SUPPL. 1) (pp S263-S264), 2014. Date of Publication: September 2014.
4. Chen S.-H.; Kuan T.-S.; Kao M.-J.; Wu W.-T., and Chou L.-W. Clinical effectiveness in severe knee osteoarthritis after intra-articular platelet-rich plasma therapy in association with hyaluronic acid injection: Three case reports. *Clinical. Interventions in Aging*. 11 (pp 1213-1219), 2016. Date of Publication: 08 Sep 2016.
5. Dumais, R.; Benoit, C.; Dumais, A.; Babin, L.; Bordage, R.; de Arcos, C.; Allard, J., and Belanger, M. Effect of Regenerative Injection Therapy on Function and Pain in Patients with Knee Osteoarthritis: A Randomized Crossover Study. *Pain. Medicine (United States)*. 13 (8) (pp 990-999), 2012. Date of Publication: August 2012.
6. Fleming, S.; Rabago, D. P.; Mundt, M. P., and Fleming, M. F. CAM therapies among primary care patients using opioid therapy for chronic pain. *BMC. Complementary & Alternative Medicine*. 7:15, 2007 May 16.
7. Hashemi S.M.; Madadi, F.; Razavi, S.; Nikooseresht, M.; Kiyabi F.H., and Nasiripour, S. Intra-articular hyaluronic acid injections Vs. dextrose prolotherapy in the treatment of osteoarthritic knee pain. [Persian]. *Tehran. University Medical Journal*. 70 (2) (pp 119-125), 2012. Date of Publication: May 2012.
8. Hauser R.A. and Orlofsky, A. Regenerative injection therapy with whole bone marrow aspirate for degenerative joint disease: A case series. *Clinical. Medicine Insights: Arthritis and Musculoskeletal Disorders*. 6 (no pagination), 2013. Date of Publication: 04 Sep 2013.
9. Hauser R.A. and Sprague I.S. Outcomes of prolotherapy in chondromalacia patella patients: Improvements in pain level and function. *Clinical. Medicine Insights: Arthritis and Musculoskeletal Disorders*. 7 (pp 13-20), 2014. Date of Publication: 14 Feb 2014.
10. Helena P.-R.D.; Mariana G.-S.; Eloina A.-D.A., and Carmina G.-T. Effects of prolotherapy on patients with primary knee osteoarthritis: A prospective uncontrolled clinical trial. PM. and R. Conference: 8th World Congress of the International Society of Physical and Rehabilitation Medicine, ISPRM 2014. Cancun Mexico. Conference Publication: (var.pagings). 6 (8 SUPPL. 2) (pp S166), 2014. Date of Publication: August 2014.
11. Palmer, Jonathan S.; Monk, Paul A.; Hopewell Sally; Bayliss, Lee E.; Jackson William; Beard, David J., and Price, Andrew J. Surgical interventions for early structural knee osteoarthritis [Protocol]. *Cochrane*. 2016; (3).
12. Rabago, D.; Mundt, M.; Zgierska, A., and Grettie, J. Hypertonic dextrose injection

- (prolotherapy) for knee osteoarthritis: Long term outcomes. *Complementary. Therapies in Medicine*. 23(3):388-95, 2015 Jun.
13. Rabago, D. and Nourani, B. Prolotherapy for Osteoarthritis and Tendinopathy: a Descriptive Review. *Current. Rheumatology Reports*. 19 (6) (no pagination), 2017. Article Number: 34. Date of Publication: 01 Jun 2017.
 14. Rabago, D.; Patterson J.J.; Mundt, M.; Kijowski, R.; Grettie, J.; Segal N.A., and Zgierska, A. Dextrose prolotherapy for knee osteoarthritis: a randomized controlled trial. *Annals. of family medicine*. 11 (3) (pp 229-237), 2013. Date of Publication: 01 May 2013.
 15. Rabago, D.; Patterson, J. J.; Mundt, M.; Zgierska, A.; Fortney, L.; Grettie, J., and Kijowski, R. Dextrose and morrhuate sodium injections (prolotherapy) for knee osteoarthritis: a prospective open-label trial. *Journal. of Alternative & Complementary Medicine*. 20(5):383-91, 2014 May.
 16. Rabago, D.; Zgierska, A.; Fortney, L.; Kijowski, R.; Mundt, M.; Ryan, M.; Grettie, J., and Patterson, J. J. Hypertonic dextrose injections (prolotherapy) for knee osteoarthritis: results of a single-arm uncontrolled study with 1-year follow-up. *Journal. of Alternative & Complementary Medicine*. 18(4):408-14, 2012 Apr.
 17. Rabago D.P.; Miller D.J.; Zgierska A.E.; Mundt, M.; Kijowski R.X.; Jessica, B., and Patterson J.J. Dextrose prolotherapy for knee osteoarthritis: Results of a randomized controlled trial. *Osteoarthritis. and Cartilage. Conference: 2011 Osteoarthritis Research Society International World Congress, OARSI. San Diego, CA United States. Conference Publication: (var.pagings)*. 19 (pp S142-S143), 2011. Date of Publication: September 2011.
 18. Reeves, K. D. Hassanein KM. Long-term effects of dextrose prolotherapy for anterior cruciate ligament laxity. *Alternative. therapies in health and medicine*. 9(3):58-62, 2003 May-Jun.
 19. Rezasoltani, Z.; Taheri, M.; Mofrad M.K., and Mohajerani S.A. Periarticular dextrose prolotherapy instead of intra-articular injection for pain and functional improvement in knee osteoarthritis. *Journal. of Pain Research*. 10 (pp 1179-1187), 2017. Date of Publication: 17 May 2017.
 20. Sert A.T.; Ozcan, E., and Esmaeilzadeh, S. Effects of dextrose prolotherapy in the treatment of patients with knee osteoarthritis: A randomized controlled trial. *PM. and R. Conference: 2016 Annual Assembly of the American Academy of Physical Medicine and Rehabilitation, AAPM and R 2016. United States*. 8 (9 Supplement) (pp S286), 2016. Date of Publication: September 2016.
 21. Slattengren A.H.; Christensen, T.; Prasad, S., and Jones, K. Prolotherapy: A nontraditional approach to knee osteoarthritis. *Journal. of Family Practice*. 63 (4) (pp 206-208), 2014. Date of Publication: April 2014.
 22. Uthman, I.; Raynauld J.-P., and Haraoui, B. Intra-articular therapy in osteoarthritis. *Postgraduate. Medical Journal*. 79 (934) (pp 449-453), 2003. Date of Publication: 01 Aug 2003.
 23. VA Technology Assessment Program (VATAP). Prolotherapy for musculoskeletal pain (Structured abstract). *Health. Technology Assessment Database*. 2016 Issue 4, John Wiley & Sons, Ltd. Chichester, UK. Division: ST.
 24. Van Leuven, L.; Benes, L.; Fortney, L.; Slattengren, A.; Nourani, B.; Grettie, J., and Rabago, D. Qualitative aspects of treatment with hypertonic dextrose injection (prolotherapy) for

knee osteoarthritis in a multi-method study. Journal. of Alternative and Complementary Medicine. Conference: International Congress on Integrative Medicine and Health, ICIMH 2016. United States. 22 (6) (pp A63-A64), 2016. Date of Publication: 2016.

Appendix 1

WorkSafeBC - Evidence-Based Practice Group Levels of Evidence

(adapted from 1,2,3,4)

1	Evidence from at least 1 properly randomized controlled trial (RCT) or systematic review of RCTs.
2	Evidence from well-designed controlled trials without randomization or systematic reviews of observational studies.
3	Evidence from well-designed cohort or case-control analytic studies, preferably from more than 1 centre or research group.
4	Evidence from comparisons between times or places with or without the intervention. Dramatic results in uncontrolled
5	Opinions of respected authorities, based on clinical experience, descriptive studies or reports of expert committees.

References

1. Canadian Task Force on the Periodic Health Examination: The periodic health examination. CMAJ. 1979;121:1193-1254.
2. Houston TP, Elster AB, Davis RM et al. The US Preventive Services Task Force Guide to Clinical Preventive Services, Second Edition. AMA Council on Scientific Affairs. American Journal of Preventive Medicine. May 1998;14(4):374-376.
3. Scottish Intercollegiate Guidelines Network (2001). SIGN 50: a guideline developers' handbook. SIGN. Edinburgh.
4. Canadian Task Force on Preventive Health Care. New grades for recommendations from the Canadian Task Force on Preventive Health Care. CMAJ. Aug 5, 2003;169(3):207-208.