Evidence-Based Practice Group
Answers to Clinical Questions

Efficacy/Effectiveness of Prolotherapy in Treating Wrist Sprain/Strain or Repetitive Strain Injury (RSI)

A Rapid Systematic Review

Prepared by	Dr. Craig Martin Manager Medical Services, Evidence-Based Practice Group
Date	March 2024

WorkSafeBC

About this report

Efficacy/Effectiveness of Prolotherapy in Treating Wrist Sprain/Strain or Repetitive Strain Injury (RSI)

Published: March 2024

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. Efficacy/Effectiveness of Prolotherapy in Treating Wrist Sprain/Strain Repetitive Strain Injury (RSI). Richmond, BC: WorkSafeBC Evidence-Based Practice Group; March 2024.

Contact information

Address	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

View other systematic reviews by the EBPG online at: http://worksafebc.com/evidence

Objectives

- To determine whether there is any evidence to support the efficacy/effectiveness of prolotherapy in treating (wrist) sprain/strain/repetitive strain injury (RSI).

Methods

- A systematic and comprehensive literature search was conducted on March 6, 2024.
- The search was done on commercial medical literature databases, including Cochrane Database of Systematic Reviews (2005 to February 28, 2024), ACP Journal Club (1991 to February 2024), UK York University Database of Abstracts of Reviews of Effects (1st Quarter 2016), Cochrane Clinical Answers (February 2024), Cochrane Central Register of Controlled Trials (January 2024), UK NHS Health Technology Assessment (4th Quarter 2016), UK NHS Economic Evaluation Database (1st Quarter 2016), BIOSIS Previews (1969 to 2008), Embase (1974 to 2024 Week 09), Medline and Epub Ahead of Print, Medline In-Process, In-Data-Review & Other Non-Indexed Citations, Medline Daily and Medline (1946 to March 05, 2024), Joanna Briggs Institute Evidence Based Practice Database (Current to February 28, 2024), that are available through Ovid platform.
- Combination of keywords were employed in this search. These keywords included:
    1. (repetitive strain injury) **AND** wrist **AND** prolotherapy
    2. (repetitive strain injury) **AND** prolotherapy
    3. (sprain **OR** strain) **AND** wrist **AND** prolotherapy
    4. (sprain **OR** strain) **AND** prolotherapy
- No limitation, such as on the language and year of publication, was implemented in this search.
- Manual search, on the references of the articles that were retrieved in full, was also done.

Results

- Search results:
    - No published study on the application of prolotherapy in treating RSI, on the wrist or other part of the extremities, was identified from search #1 and #2.
    - One([1]) published study was identified from search #3 while search #4 identified further thirty-four([2-35]) published studies. Hence, overall, thirty-five([1-35]) studies were identified in this systematic review.
    - Upon examination on the titles and abstracts of these thirty-five([1-35]) studies, five([1,4,16,27,28]) studies were thought to be relevant and were retrieved in full for further appraisal. No further study was identified from manual searches.
    - Of these five([1,4,16,27,28]) studies that were retrieved in full, one([1]) study was a case report (level of evidence 4. Appendix 1) on tendinosis and two([27,28]) studies were an expert review (level of evidence 5. Appendix 1) and did not provide any relevant data. Hence, these three([1,27,28]) studies will not be discussed further.
- In a case report (level of evidence 4. Appendix 1), Ada and Yavus([4]) reported on the application of prolotherapy to treat medial collateral ligament (MCL) in a rugby player. A 21-year-old male rugby player sustained stress trauma to the knee valgus. He had severe pain over the medial side of his right knee and a swollen knee joint. His pain dramatically increased with any weight bearing and, on physical examination, notable tenderness was observed over the MCL. Magnetic resonance imaging (MRI) showed a grade 2 sprain of the MCL, subchondral bone marrow edema, and contusion at the

corner of the lateral tibial plateau. with prolotherapy and home-based exercise. The patient received three prolotherapy treatments for three weeks at 1-week intervals. A total of 4 - 5 mL of solution consisting of 15% dextrose and 0.2% lidocaine were used per injection session. After the first injection, isometric and active range of motion (ROM) exercises—3 sets of 8 repetitions, up to 3 times daily—were given as an initial exercise program. The patient reached 1200 ROM on the 5th day post-injection and started progressive resistance training and was able to walk without knee pain at the 10th day post-injection. By day 21 post-injection, the patient was pain free with a full active ROM. *It should be noted that it was unclear why this patient was selected and reported; further, there was a potential of effect of exercise co-intervention.*

- In an abstract only form, Kajbaf et al[16] presented the application of prolotherapy in treating chronic medial collateral ligament (MCL) sprain. A 40-year-old male, with past medical history of post-traumatic stress disorder and two arthroscopic meniscal surgeries, presented with chronic left knee pain that began 15 years ago after a military injury. Physical examination revealed point tenderness of the MCL and pain with valgus stress testing. The patient was then offered prolotherapy injections as a treatment option. Four, monthly, 2cc injections, that were composed of 1cc 50% hypertonic dextrose and 1cc normal saline to the MCL, was applied in this patient. The patient reported exponentially improving pain relief after each injection, with near resolution after completion of the series (*it was not clear how pain was measured, and no functional effect was reported*). *It should be noted that it was clear why this patient was selected to be reported and it was not clear whether there were any other treatment modalities implemented in this patient*.

Summary

- At present, there was no study reporting the application of prolotherapy in treating RSI on the wrist or any other parts of the extremities.
- At present, there was no published study reporting the application of prolotherapy in treating sprain/strain on the wrist.
- At present, there is some evidence, in the form of two, low level (level of evidence 4. Appendix 1) low quality (due to potential selection bias as well as potential effect of co-intervention), case report on the effectiveness of prolotherapy in treating knee sprains (acute or chronic). Based on these two case reports, it should be noted on the variability of the reported prolotherapy protocols.

References

1. Tseng V, Ibrahim V, Yokel N.R. Prolotherapy for dequervain's tenosynovitis/tendonosis: A case report. PM and R. Conference: 2012 American Academy of Physical Medicine and Rehabilitation, AAPM&R Annual Assembly. Atlanta, GA United States. Conference Publication: (var.pagings). 4(10 SUPPL. 1) (pp S275), 2012. Date of Publication: October 2012.
2. Clinical Effectiveness of Hypertonic Dextrose Prolotherapy in Chronic Ankle Instability: a Randomized Clinical Trial. 2020. [No additional source data available.].
3. Efficacy of Injection Therapy for Lateral Epicondylosis. 2011. [No additional source data available.].
4. Ada A.M., Yavuz F. Treatment of a medial collateral ligament sprain using prolotherapy: a case study. Alternative therapies in health and medicine. 21(4) (pp 68-71), 2015. Date of Publication: 01 Jul 2015.
5. Albano A.W., Nelson V. Approaching Foot and Ankle Injuries in the Ambulatory Setting. Primary Care - Clinics in Office Practice. 47(1) (pp 133-145), 2020. Date of Publication: March 2020.
6. Almeida MO, Silva NG Brenda, Andriolo RB, Atallah AN, Peccin MS. Conservative interventions for treating exercise-related musculotendinous, ligamentous and osseous groin pain [Systematic Review]. Cochrane 2013; (6).
7. Borg-Stein J, Zaremski J.L., Hanford M.A. New Concepts in the Assessment and Treatment of Regional Musculoskeletal Pain and Sports Injury. PM and R. 1(8) (pp 744-754), 2009. Date of Publication: August 2009.
8. 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.
9. Castle CD, Dunderdale CM, Patzkowski JC, Carius BM. Platelet-Rich Plasma Improves Strength and Speed of Recovery in an Active-Duty Soldier with Isolated Injury to the Lateral Collateral Ligament of the Knee: A Case Report. The Medical journal / US Army Medical Center of Excellence. . 1(Per 23-4/5/6):17-9, 2023 Apr-Jun.
10. Chen T, Xu Y, Xu W *et al*. Hypertonic glucose inhibits growth and attenuates virulence factors of multidrug-resistant Pseudomonas aeruginosa. BMC Microbiology. 20(1) (no pagination), 2020. Article Number: 203. Date of Publication: 09 Jul 2020.
11. Dagenais S, Mayer J, Wooley J.R., Haldeman S, Hite M. Acute toxicity evaluation of proliferol: A dose-escalating, placebo-controlled study in rats. International Journal of Toxicology. 26(5) (pp 451-463), 2007. Date of Publication: September 2007.
12. De Luigi A.J., Tow S, Flowers R, Gordon A.H. Special Populations in Orthobiologics: Athletic, Elderly, and Pediatrics Populations. Physical Medicine and Rehabilitation Clinics of North America. 34(1) (pp 199-237), 2023. Date of Publication: February 2023.
13. Gustas C.N., Lee K.S. Multimodality Imaging of the Painful Elbow: Current Imaging Concepts and Image-Guided Treatments for the Injured Thrower's Elbow. Radiologic Clinics of North America. 54(5) (pp 817-839), 2016. Date of Publication: 01 Sep 2016.
14. Istomin D.A., Banit O.V., Istomin A.H. Mathematical modeling of changes in lumbosacral region of the spine-pelvis kinematic chain in iliolumbar ligament syndrome. New Armenian Medical Journal. 12(3) (pp 59-66), 2018. Date of Publication: 2018.
15. Jensen KT [Author], Rabago DP [Author, Reprint Author, E-mail: david.rabago@fammed.wisc.edu], Best TM [Author], Patterson JJ [Author], Vanderby RJr [Author]. Early inflammatory response of knee ligaments to prolotherapy in a rat model. Journal of Orthopaedic Research. 26(6):816-23, JUN 2008.
16. Kajbaf J, Robinson M.R., Pham A. Prolotherapy for chronic medial collateral ligament sprain. PM and R. Conference: American Academy of Physical Medicine and Rehabilitation Annual

Meeting , AAPM and R 2019. San Antonio, TX United States. 11(Supplement 2) (pp S214), 2019. Date of Publication: November 2019.
17. Khanna M, Walker M, Amiras D, Rosenfeld P. Image-Guided Intervention of the Postoperative Foot and Ankle after Ligament and Tendon Repair. Seminars in Musculoskeletal Radiology. 20(1) (pp 116-129), 2016. Date of Publication: 01 Feb 2016.
18. Kim T.-H., Jo G.-Y., Kim W, Do H.-K. Complex regional pain syndrome type II caused by iatrogenic lateral dorsal cutaneous nerve injury: A case report. Medicine (United States). 100(49) (no pagination), 2021. Article Number: e28108. Date of Publication: 10 Dec 2021.
19. Lagattuta L.M., Salandra C, Papaioannou P, Hicks C, Tanveer R. Chronic ankle instability due to split tear of peroneus longus. PM and R. Conference: Annual Assembly of the American Academy of Physical Medicine and Rehabilitation, AAPM and R 2021. Virtual. 13(pp S78), 2021. Date of Publication: 2021.
20. Lee K.S., Rabago D, Kobayashi H, Vanderby R, Rosas H, Wilson J. Treatment of chronic lateral epicondylosis using hyperosmolar dextrose solution: Can acoustoelastography monitor tissue healing?. Skeletal Radiology. Conference: 2011 Annual Meeting of the Society of Skeletal Radiology. Scottsdale, AZ United States. Conference Publication: (var.pagings). 40(4) (pp 501), 2011. Date of Publication: April 2011.
21. Malanga G, Nakamura R. The role of regenerative medicine in the treatment of sports injuries. Physical Medicine and Rehabilitation Clinics of North America. 25(4) (pp 881-895), 2014. Date of Publication: 2014.
22. McCarthy E, Hegazi T.M., Zoga A.C. *et al*. Ultrasound-guided Interventions for Core and Hip Injuries in Athletes. Radiologic Clinics of North America. 54(5) (pp 875-892), 2016. Date of Publication: 01 Sep 2016.
23. Mofrad M.K., Rezasoltani Z, Dadarkhah A, Panah S.H., Tabatabaee S.M., Azarakhsh A. Neurofascial Dextrose Prolotherapy for Managing Chronic Ankle Ligament Injury. Anesthesiology and Pain Medicine. 12(1) (no pagination), 2022. Article Number: e118317. Date of Publication: Feb 2022.
24. Ozcakar L, Ricci V, Chang K.-V., Mezian K, Kara M. Musculoskeletal ultrasonography: Ninety-nine reasons for physiatrists. Medical Ultrasonography. 24(2) (pp 137-139), 2022. Date of Publication: 2022.
25. Patel D.N., Strauss E.J. Alternative therapeutic modalities in sports medicine. Bulletin of the Hospital for Joint Diseases. 73(2) (pp 122-127), 2015. Date of Publication: June 2015.
26. Pellarin M, Youmbi C.T., Lotchuang J *et al*. From Protocol to Definitive Study - The State of Randomized Controlled Trial Evidence in Sports Medicine Research: A Systematic Review and Survey Study. Clinical Journal of Sport Medicine. 33(3) (pp E44-E70), 2023. Date of Publication: 01 May 2023.
27. Prabhakar G, Kanawade V, Ghali A.N., Dutta A.K., Brady C.I., Morrey B.F. Medial Elbow Pain Syndrome: Current Treatment Strategies. Orthopedics. 46(2) (pp E81-E88), 2023. Date of Publication: March 2023.
28. Reeves K.D. Prolotherapy: Present and future applications in soft-tissue pain and disability. Physical Medicine and Rehabilitation Clinics of North America. 6(4) (pp 917-926), 1995. Date of Publication: 1995.
29. Sharma G.S., Jayakar R. Prolotherapy for the treatment of interspinous ligament injury: A case report. PM and R. Conference: 2017 Annual Assembly of the American Academy of Physical Medicine and Rehabilitation, AAPM and R 2017. Denver, CO United States. 9(9 Supplement 1) (pp S274-S275), 2017. Date of Publication: September 2017.
30. Singh J.R., Bartolozzi A, Roza R. Platelet rich plasma therapy in an athlete with adductor longus tendon tear: A case report. PM and R. Conference: 71st Annual Assembly of the American Academy of Physical Medicine and Rehabilitation. Seattle, WA United States. Conference Publication: (var.pagings). 2(9 SUPPL. 1) (pp S88), 2010. Date of Publication: September 2010.

31. Sit R.W.S., Wu R.W.K., Ling S.K.K. *et al*. A protocol for a randomized clinical trial assessing the efficacy of hypertonic dextrose injection (prolotherapy) in chronic ankle instability. Trials. 23(1) (no pagination), 2022. Article Number: 1063. Date of Publication: December 2022.
32. Stewart Z.E., Lee K. Lower extremity ultrasound-guided interventions: tendon, ligament, and plantar fascia. Skeletal Radiology. 52(5) (pp 991-1003), 2023. Date of Publication: May 2023.
33. Tiwari M, Bhargava R. Platelet rich plasma therapy: A comparative effective therapy with promising results in plantar fasciitis. Journal of Clinical Orthopaedics and Trauma. 4(1) (pp 31-35), 2013. Date of Publication: March 2013.
34. Tseng V, Ibrahim V, Yokel N.R. Prolotherapy for dequervain's tenosynovitis/tendonosis: A case report. PM and R. Conference: 2012 American Academy of Physical Medicine and Rehabilitation, AAPM&R Annual Assembly. Atlanta, GA United States. Conference Publication: (var.pagings). 4(10 SUPPL. 1) (pp S275), 2012. Date of Publication: October 2012.
35. Westerbeck E.M., Strakowski J. Sternocleidomastoid muscle snapping after a rock-climbing fall: A case report. PM and R. Conference: American Academy of Physical Medicine and Rehabilitation Annual Meeting , AAPM and R 2019. San Antonio, TX United States. 11(Supplement 2) (pp S17), 2019. Date of Publication: November 2019.

Appendix 1

WorkSafeBC — Evidence-Based Practice Group levels of evidence (adapted from 1-6)

1	Experimental, randomized controlled trial (RCT), systematic review RTCs with or without meta-analysis.
2	Evidence from controlled trials without randomization (quasi-experimental studies) or systematic reviews of observational studies.
3	Evidence from 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 experiments.
5	Opinions of respected authorities, based on clinical experience, descriptive studies or reports of expert committees based on scientific evidence.

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.
5. (2014). Canadian task force on preventive health care procedure manual. Downloaded from https://canadiantaskforce.ca/methods/ in May 12, 2022.
6. (2021). US Preventive Services Task Force. Procedure Manual. Downloaded from https://www.uspreventiveservicestaskforce.org/uspstf/about-uspstf/methods-and-processes/procedure-manual , in May 12 2022.