American Association of Orthopaedic Medicine Position Statement

Prolotherapy for the Treatment of Back Pain

This pronouncement was written for the American Association of Orthopaedic Medicine by Robert G. Klein, M.D., Jeffrey Patterson, D.O., Bjorn Eek, M.D. and David Zeiger, D.O.

Summary

It is the position of the American Association of Orthopaedic Medicine that prolotherapy is a safe efficacious therapy for the treatment of selected cases of low back pain and other chronic myofascial pain syndromes. This is based upon basic science data showing the effects of prolotherapy in animal models, clinical studies, a lengthy history of clinical use and efficacy, and increasingly widespread acceptance within the medical community. While we recognize that further basic science and clinical studies need to be done and are currently in process, we believe that prolotherapy is a safe, cost effective and efficacious therapy that can provide pain relief and return of function for many patients.

Introduction

Prolotherapy is an injection therapy used to treat chronic ligament, joint capsule, fascial and tendinous injuries of the low back. The goal of this treatment is to stimulate proliferation of collagen at fibro-osseous junctions to promote non-surgical soft tissue repair and to relieve pain. [1] Animal studies by Liu and others have shown proliferation of collagen with strengthening of ligaments with prolotherapy.[2] Further animal research is currently underway at the University of Wisconsin Medical School. Prolotherapy is commonly used in veterinary medicine.

The mechanism of action of ligament proliferation was supported by a pilot study in human volunteers that demonstrated an average increase of 65% in cross-sectional diameter of posterior sacroiliac ligaments 3 months after treatment. Computerized measurements of range of lumbar motion before and after treatment have also demonstrated improvements in motion that are consistent with soft tissue healing. [3, 4]

Scientific Evidence

There have now been 5 randomized clinical trials (RCT'S) of prolotherapy [5-9]for chronic low back pain; their methodology has varied considerably. Two of the trials [6, 7]used similar protocols with well defined injection sites, using dextrose-glycerine-phenol-xylocaine as the solution injected, and 6 weekly injection treatments of 20-30mL each. Both trials used multiple standardized and validated outcome measures to capture changes in pain, disability, and function over a minimum of 6 months, and both trials reported statistically significant improvements in pain and disability in the treatment groups.

The 3 other trials differed considerably. The study by Mathews et al [9] enrolled only 22 patients (16 treatment and 6 controls) and was unlikely to have the statistical power needed to detect a reasonable difference between treatment and placebo. The study by Dechow et al [8] had only 3 weekly injection treatments of 10mL each (total volume 30mL vs. 120-180mL in the two successful trials) of dextrose-glycerine-phenol solution. In addition, the authors attempted to inject all low back ligaments from only 2 injection sites rather than lifting and reinserting the needle at multiple sites as is commonly practiced. This technical difference may have impacted where the solution was injected. Patient selection was also an impediment in this trial, and the authors concluded that: "Many patients were not considered ideal candidates for sclerosing injections by the operator at the time of the treatment for a variety of reasons relating to technical difficulties, deconditioning, patients relying on invalidity benefit, excessive psychological stress, etc. even though they technically fulfilled the inclusion criteria. Therefore, the group of patients recruited into our study was likely to respond poorly to any single intervention in keeping with the relatively poor prognosis in the group of patients today in the UK."

The most recent study by Yelland from Australia [5] used a 20% dextrose solution that was injected at only 20% of the usual sites and did not include facet joint capsules included in the 2 positive RCT's. Not surprisingly, the study failed to show an advantage of plain dextrose, which is a weak prolotherapy solution, compared to a placebo injection of saline. Despite the shortcomings of this study the results obtained in terms of pain relief and increased function are quite striking. In both the group of prolotherapy patients (mean duration of pain was 14.8 years) and in the saline injection group (mean duration was 13.8 years), there was a statistically significant decrease in pain and disability scores at both 12 and 24 months' follow-up. In fact, just a fraction less than half of the patients in the prolotherapy group (46%) achieved a greater than 50% reduction of pain and 42% achieved a greater than 50% reduction in disability score. The authors stated that "participants exhibited marked and sustained improvements in their pain and disability, even with saline injections and normal activity." It should be appreciated that the bleeding and tissue disruption associated with needling and saline injections also has a mild proliferant effect so in fact there was no true placebo treatment. There may also be neurological effects of prolotherapy in relieving pain. The authors also admitted that "this trial's success rates in reducing pain and improving disability are at least as good as those reported for spinal cord stimulation, surgery or multidisciplinary treatment for patients with low back pain of shorter duration."

Although there is disagreement among the studies regarding the use of prolotherapy for chronic low back pain, this situation is hardly unique to this specific injection treatment. A recent systematic review of the literature by Nelemans in Spine ([10]attached) demonstrates how little evidence there is for the efficacy of a variety of commonly utilized and reimbursed low back treatments including facet injections, trigger point injections, and epidural injections. One of the prolotherapy trials discussed above [6]was included in this review and ranked fourth out of twenty-one randomized trials in terms of study design and is mentioned as the only one with significant follow-up. This study was

one of the few that they cited as showing definite statistical efficacy when compared to a control treatment using placebo saline injections.

The literature also indicates that prolotherapy appears to be very safe. None of the clinical trials have reported any serious adverse events with this treatment. In addition, a survey of adverse events related to prolotherapy reported that a group of almost 100 physicians had collectively almost 500,000 patients with this treatment approach and experienced only 66 complications, none of which were life-threatening. This is supported by the low number of serious or adverse reactions documented in the Florida review.

Although additional studies regarding the use of prolotherapy for chronic low back pain are necessary to address methodological issues of the previous trials, the same is true for all other low back treatment approaches, many of which are commonly utilized and covered by insurers with less documentation than prolotherapy. The reality is that despite the enormous impact of low back pain to our society there are no clearly effective treatments for chronic back pain, at least not in the sense that they are supported by multiple, high-quality randomized clinical trials using multiple validated outcome measures and an appropriate follow-up period. Nevertheless, patients continue to receive care for their chronic low back pain and insurers routinely pay for such care despite a lack of convincing efficacy for all chronic low back pain treatments. In fact, because of multiple pain generators that may come into play in low back pain, it is quite likely that multiple therapies will be necessary in any one patient or group of patients.

Recommendations

Prolotherapy should be considered a valid treatment option in a selected group of chronic low back pain patients. As such, it should not be held to a higher standard than other treatments with the same lack of efficacy that are nevertheless covered by insurers, such as epidural injections, steroid injections, and IDET, not to mention surgery for cases in which instability or progressive neurological deficit is absent. The goal of providing access only to the highest quality of treatments supported by the scientific literature is laudable. However, if insurers were to adopt a universal policy of denying payment for chronic low back pain treatments based on lack of definitive evidence, no one with chronic back pain would be able to obtain any treatment. Since this is clearly unacceptable, an alternative is to provide coverage for those treatments that are biologically plausible, supported in the literature by a number of cohort and randomized clinical trials, and have a reasonable safety profile.

Prolotherpy should be performed by well trained providers utilizing selected solutions and techniques. A number of different solutions are used in prolotherapy. The most common ingredients in these solutions are hyperosmolar dextrose and/or glycerine, combined with local anesthetics such as lidocaine or marcaine. A more detailed description of prolotherapy is available in the appended position paper by the Florida Academy of Pain Management and the review in Musculoskeletal Medicine that is also appended.

Conclusions

Vert Mooney, M.D., a prominent orthopedic surgeon and former chairman of orthopedics at the University of California, San Diego, wrote a recent editorial in The Spine Journal concerning prolotherapy ([11], see attached). He concluded that "this fringe treatment (prolotherapy) is no longer at the periphery and seems to be at the frontier of a justifiable, rational treatment with a significant potential to avoid destructive procedures."

We therefore urge the California Technical Assessment Forum to provide coverage for prolotherapy for chronic low back pain.

References

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Appendices

1. Klein, R. and B. Eek, *Prolotherapy: an alternative way of managing low back pain.* J of musculoskeletal Med, 1997: p. 45-49.
2. Nelemans, P. and et.al., *Injection therapy for subacute and chronic benign low back pain.* Spine, 2001. **26**(5): p. 501-15.
3. Mooney, V., *Prolotherapy at the fringe of medical care, or is it at the frontier?* Spine, 2003. **3**(4): p. 253-4.
4. The Florida Academy of Pain Medicine (FAPM), Position Paper on Regenerative Injection Therapy (RIT): Effectiveness and Appropriate Usage. May, 2001.