Functional outcome from sacroiliac joint prolotherapy in patients with sacroiliac joint instability

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ABSTRACT

Objectives: Examine the effectiveness of sacroiliac (SI) joint prolotherapy for SI joint instability, and characterize the patients most likely to benefit from this treatment.
Design: Retrospective cohort study.
Setting: Department of Veterans Affairs outpatient physical medicine clinic.
Interventions: Patients referred for low back pain and diagnosed with SI joint instability received a series of three SI joint prolotherapy injections (15% dextrose in lidocaine) at approximately a one-month interval. The outcome of those completing treatment was retrospectively examined, and characteristics were compared between those with at least a minimum clinically important improvement and those without improvement.
Main outcome measures: Patients completed the Oswestry Disability Index (ODI) before treatment was initiated, immediately preceding each prolotherapy injection, and at 3–4 month follow-up.
Results: Of 103 treated patients returning for post-treatment follow-up at a median of 117 days, 24 (23%) showed a minimum clinically important improvement despite a median of 2 years with low back pain and a mean (± SD) pre-intervention ODI of 54 ± 15 points. Much of the improvement was evident after the initial prolotherapy injection, and a 15-point improvement in ODI prior to the second prolotherapy injection had a sensitivity of 92% and specificity of 80% for determining which patients would improve.
Conclusions: A satisfactory proportion of patients with symptomatic SI joint instability as an etiology of low back pain can have clinically meaningful functional gains with prolotherapy treatment. The patients who are not likely to improve with prolotherapy are generally evident by lack of improvement following the initial pro-lotherapy injection.

1. Introduction

Chronic low back pain has considerable economic, social and individual health consequences. While various underlying etiologies are known to exist, the sacroiliac (SI) joint is now recognized as a primary source of low back pain in up to 15% of the population.[1] The pathophysiology of pain related to the SI joint is often thought to be due to mechanical dysfunction, although this has not gone without question.[2] Nonetheless, recent treatment trials directed at increasing SI joint stability with prolotherapy have suggested this might be an effective treatment for this condition.[3,4]

Prolotherapy has been used for approximately 100 years, but its modern applications can be traced to Hackett[5] in the 1950s who coined the term from the word "proles", which means "growth" or "offspring" in Latin under the premise that it induces increased growth of

connective tissue from a local inflammatory response setting off the wound healing cascade. It has subsequently been recognized that the tissue response from prolotherapy may also be evoked through stimulating the release of various tissue growth factors,[6,7] Recent animal studies have demonstrated increased cross-sectional area of connective tissue,[8-11] and increased load to rupture and increased tissue strength[9-11] after 10–20% dextrose injections. Furthermore, biopsies of the posterior sacroiliac ligaments of human subjects before and 3 months after prolotherapy with a solution of 1.25% phenol, 12.5% glucose and 12.5% glycerine in lidocaine showed increased collagen and size of the collagen fibers.[12]

A recent review of the use of prolotherapy in chronic low back pain[13] concluded that there is conflicting evidence regarding its efficacy but noted that the conclusions were confounded by clinical heterogeneity. We are aware of only two clinical trials focusing on the

effectiveness of prolotherapy specifically for SI joint pain. Cusi and coworkers[3] reported on prolotherapy treatment (18% dextrose, 3 injections at 6 week intervals) of 25 patients who were clinically diagnosed with SI joint pain that had been unresponsive to an exercise program. Each continued to receive physical therapy during treatment. Favorable clinical outcomes, based upon functional questionnaires, were reported. In another clinical trial, Kim and colleagues[4] randomized 48 patients with SI joint pain, confirmed by diagnostic block, to prolotherapy (25% dextrose, 2–3 injections at 2 week intervals) or corticosteroid injections (1–2 injections at 2 week intervals). The prolotherapy group demonstrated significantly better outcomes than the steroid group in terms of incidence of ≥50% reduction in pain rating at 6 and 15 months post-treatment.

Thus, the limited research supporting prolotherapy for SI joint instability provides rational for further exploration of this treatment approach. The present work examines the outcome from a large cohort of patients in order to provide additional insight into the potential effectiveness of the treatment and to characterize the patients who are most likely to benefit from the treatment.

2. Methods

The present work is a retrospective cohort study of patients treated with SI joint prolotherapy for SI joint instability by the first author between December 2010 and April 2017. Patients were United States Veterans who had been referred to an outpatient physical medicine clinic for low back symptoms. Data were collected retrospectively by chart review on all patients receiving SI joint prolotherapy during this time period. The research was approved by the VA Northern California Health Care System Institutional Review Board with waiver of consent.

The possibility of SI joint instability was considered in patients with pain symptoms involving the low back and buttock and emanating from an area immediately inferomedial to the posterior superior iliac spine,[14] with or without referred pain into the hip, groin and leg. The supporting examination used a modification of the diagnostic algorithm of Laslett and colleagues[15] with focus on local tenderness over the involved SI joint and lack of SI joint motion with the standing SI mobility (Gillet) test.[16,17] In one small study, pain originating from immediately inferomedial to the posterior superior iliac spine was found to have 100% sensitivity and specificity in identifying patients with SI joint dysfunction.[14] The standing SI mobility test has been shown to have 93% specificity for identifying SI joint hypomobility[18] and has a small false positive rate of 13–16% in populations without low back pain[16,17,19] SI joint arthritis was ruled out with radiological examination when it was a consideration.

When the diagnosis of SI joint instability was uncertain, patients underwent a fluoroscopically-guided diagnostic injection with lidocaine and triamcinolone acetonide, or the initial prolotherapy injection was considered to serve a dual treatment and diagnostic purpose. In general, only those with at least transient reduction in symptoms after an injection continued the prolotherapy injection series. Prolotherapy injections were largely performed with fluoroscopic guidance in the early stages of the analysis period, but as fluoroscopy access became increasingly challenging, most of the prolotherapy injections were performed in the clinic without guidance from any imaging technique. The treating physician had previously verified his successful needle placement with his imaging-free injection technique.

The fluoroscopically-guided injections were performed with the patient in the prone position and pelvis on a pillow. The lower portion of the anterior and posterior SI joint lines were aligned with a contralateral oblique fluoroscopy angle.[20] From the skin location within this plane and overlying the lower third of the joint line, a 22G 90 mm spinal needle was directed to the lower third of the joint using aseptic technique after locally anesthetizing the area. Position in the SI joint was verified by medial and lateral deflection of the needle hub and observation of a characteristic bend of the needle while the tip
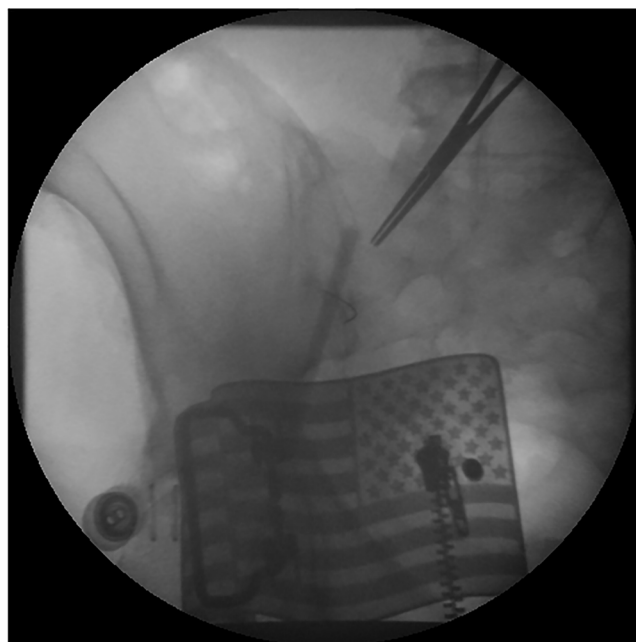

Fig. 1. Fluoroscopic view showing alignment of the anterior and posterior joint lines of the lower portion of the left SI joint and characteristic bend of the needle positioned in the joint during lateral deflection with an aluminum rod. The patient's belt buckle and pants and a hemostat, which had been used as a pointer, were inadvertently not removed from the field.

remained stationary (Fig. 1). For the imaging-free technique, the needle was inserted approximately 3 cm caudal and one-third of the distance towards the midline from the posterior superior iliac spine. The needle was inserted obliquely and the tip was then walked medially or laterally if necessary until it could be felt passing through dense ligamentous tissue and slipping into the joint.

Prolotherapy treatment involved a series of three injections at approximately one month intervals. Post-treatment follow-up was requested at 3–4 months following the third prolotherapy injection. Prolotherapy injections used a mixture of 7 ml of 1% lidocaine and 3 ml of 50% dextrose (15% dextrose solution), with the solution being injected directly into the involved SI joint. Patients were requested to stop non-steroidal anti-inflammatory drugs for a day before and for a few days after each injection.

The Oswestry Disability Index (ODI)[21] was used as the outcome measure, and was completed by patients at each clinic visit and prior to diagnostic and prolotherapy injections. For data analysis, the "pre-intervention" ODI was defined as the average of the ODI at the initial clinic visit and prior to the initial prolotherapy injection, if these were separate visits, or the average of the ODI at the initial clinic visit and prior to a diagnostic injection if performed. Based on prior work of others,[22–25] a minimum clinically important improvement for the ODI of 15 points was selected. Patients with a reduction in ODI of 15 points or more were considered to have improved, and those with no change or an increase in the ODI were considered to have not improved.

Characteristics of the group that improved and the group that did not improve were compared. Continuous data were analyzed with the unpaired *t*-test when the data passed the D'Agostino-Pearson normality test and the Mann Whitney test when the data were determined to be skewed. Categorical data were analyzed with the Fisher's exact test. ODI data across time were examined with one-way repeated-measures ANOVA and Tukey posttests when following a normal distribution and the Friedman test when skewed. A paired *t*-test was used to compare ODI scores for those who completed the ODI twice before receiving a diagnostic or prolotherapy injection. Statistical significance was set at $P < .05$.

Table 1
Comparison of characteristics of patients with presumed sacroiliac (SI) joint instability who improved ≥15 points on the Oswestry Disability Index (ODI) with those who did not improve or worsened on the ODI following SI joint prolotherapy. Data are reported as mean ± SD, median and interquartile range (if skewed) or a percentage.

Characteristic	Improved (n = 24)	Not Improved (n = 50)	P value
Age (years)	59 ± 13	52 ± 15	< 0.05
Sex (% men)	83.3	82.0	> .99
Body mass index (kg/m^2)	29.5 ± 4.9	30.2 ± 6.7	0.63
Duration of low back pain (years)	2 (0.3–20)	13 (4–19)	0.03
Abrupt onset of low back pain (%)	25.0	58.0	0.01
Clicking, popping or grinding present (%)	53.3	51.4	> .99
Evidence of lumbar disc disease (%)	75.0	66.0	0.59
Other chronic pain diagnosis (%)	29.2	50.0	0.13
Mental health diagnosis (%)	45.8	62.0	0.22
Service connected diagnosis (%)	25.0	40.0	0.30
Prior physical therapy for low back pain (%)	52.9	79.5	0.06
Prior low back steroid injection (%)	4.2	20.0	0.09
Prior lumbar surgery (%)	8.3	8.0	> .99
Unilateral symptoms (%)	62.5	60.0	> .99
Pre-intervention ODI (score)	54 ± 15	42 ± 11	< 0.001

3. Results

During the study period, 139 patients completed the prolotherapy injection series. Of this group, 36 patients did not return for the post-treatment follow-up visit, so complete ODI data were available for 103 patients. Considering these 103 patients, there were 56 who completed the ODI twice before receiving a diagnostic or prolotherapy injection, and their ODI scores across a median interval of 37 days were stable (p = .15) at 48 and 46 points.

Of the 103 patients with full ODI data through the post-treatment follow-up, 24 (23%) showed an improvement of at least 15 points on the ODI at the follow-up visit compared with the pre-intervention value. There were 50 patients that did not improve (ODI was unchanged or worsened), and an additional 29 patients had an improvement in ODI score of less than 15 points. Characteristics of the groups that improved and did not improve are compared in Table 1. Compared with the group that did not improve, the group that showed improvement was older (p < .05), had a shorter history of low back pain (p = .03), was less likely to have had an abrupt onset of symptoms (p = .01), and had higher pre-intervention ODI scores (p < .001).

The time profile of ODI scores for the 103 patients with full ODI data through the post-treatment follow-up showed a significant change (p < .001) across time. Post tests revealed improvements from pre-intervention scores to prior to the third prolotherapy injection (p < .01) and at post-prolotherapy follow-up (p < .05). However, the mean (± SD) improvement at post-prolotherapy follow-up a median of 110 days after the third prolotherapy injection was only 4 ± 17 points.

Changes in ODI scores across time for the group that improved and the group that did not improve are shown in Fig. 2. The group that improved had a significant change (p < .001) in ODI score across time. Post tests revealed an improvement from pre-intervention to before the second prolotherapy injection (p < .001) a mean (± SD) of 14 ± 15 points, and additional improvement between the second and third prolotherapy injections (p < .05). At the post-treatment follow-up, a median of 117 days following the third prolotherapy injection, the ODI had improved (p < .001) a mean (± SD) of 29 ± 11 points from the pre-intervention score. This improvement in ODI score was due to a 1–2 point improvement in each of the ten ODI domains. For the group that did not improve, ODI scores were stable across the treatment period, and then worsened (p < .01) at the post-treatment follow-up compared with each prior time point.

Among the group that improved, 12 (50%) of the 24 patients showed at least a 15-point improvement in ODI score prior to the second prolotherapy injection. Among the group that did not improve,
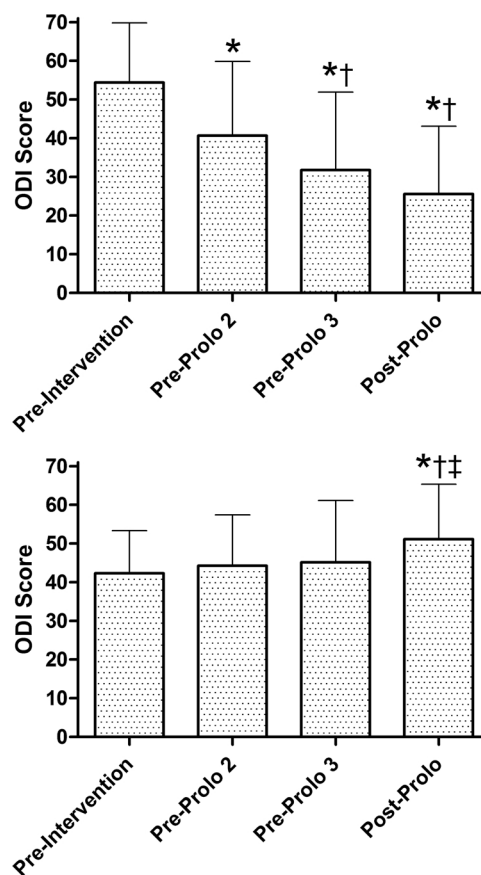

Fig. 2. Oswestry Disability Index (ODI) scores prior to intervention (pre-intervention), prior to the second (pre-prolo 2) and third (pre-prolo 3) prolotherapy injections, and at follow-up after SI joint prolotherapy treatment in patients with presumed SI joint instability. The top graph displays those patients with an overall improvement of at least 15 points, and the bottom graph displays the patients who showed no change or worsening of ODI score. Brackets represent 1 SD. * p < 0.05 compared with pre-intervention; † p < 0.05 compared with pre-prolo 2, ‡ p < 0.05 compared with pre-prolo 3.

less patients (1 of 50 or 2%, p < .0001) had at least a 15-point improvement in ODI score prior to the second prolotherapy injection. As a result, a 15-point improvement in ODI score prior to the second prolotherapy injection had a sensitivity of 92%, specificity of 80%, positive

Table 2

Comparison of treatment variables for those improving ≥15 points on the Oswestry Disability Index (ODI) and those who did not improve or worsened on the ODI. Data are reported as a percentage or median and interquartile range since skewed.

Variable	Improved (n = 24)	Not Improved (n = 50)	P value
Received diagnostic injection (%)	58.3	56.0	> .99
First prolotherapy injection was fluoroscopic guided (%)	70.8	44.0	< 0.05
Second prolotherapy injection was fluoroscopic guided (%)	66.7	44.0	0.08
Third prolotherapy injection was fluoroscopic guided (%)	66.7	42.0	0.08
Interval between first two prolotherapy injections (days)	32 (28–35)	35 (28–49)	0.27
Interval between last two prolotherapy injections (days)	28 (28–40)	31 (28–35)	0.82
Interval between last prolotherapy injection and follow-up (days)	117 (92–125)	103 (90–126)	0.72

predictive value of 50%, and negative predictive value of 98% for the likelihood of improvement at post-treatment follow-up.

Details on treatment variables for the group that improved and the group that did not improve are shown in Table 2. Groups did not differ in terms of the percentage receiving a diagnostic injection prior to the prolotherapy treatment, or with regard to the intervals between prolotherapy injections and the follow-up visit. However, the group that improved had a higher proportion (p < .05) of the initial prolotherapy injections performed with fluoroscopic guidance than those not improving. Also noted was that those who improved were seen for initial evaluation an average of 7 months earlier within the study period than those who did not improve.

Given that a sizeable number of patients (36 of 139) did not return for the post-treatment follow-up visit, an examination of this group is warranted. This group was found to have no overall time effect (p = .13) for ODI scores. There was 1 (3%) of 36 patients who showed an improvement of at least 15 points prior to the second prolotherapy injection.

4. Discussion

The key findings of this work are that (1) a noteworthy proportion of patients with presumed SI joint instability as an etiology of low back pain can have clinically meaningful functional gains with prolotherapy treatment despite having severe disability from low back pain for a long period of time and other complicating medical issues, and (2) most patients who are unlikely to improve are distinguished by a lack of improvement following the initial prolotherapy injection.

Of the study group of 103 patients with full ODI data through the post-treatment follow-up, 23% experienced a minimum clinically important improvement in ODI score (at least 15 points) at the follow-up visit a median of 117 days following the third prolotherapy injection compared with the pre-intervention score. In fact, the ODI score had improved a mean of 29 points in this group. On initial consideration of this response rate, it may appear to be unsatisfactory. Furthermore, when considering the group that did not return for the follow-up visit, it is likely that an even lower proportion of 139 patients completing the prolotherapy injection series experienced a minimum clinically important improvement (possibly as low as 17%). On the other hand, in the context of this patient population with severe baseline disability,[21] extended duration of low back pain, common presence of other chronic pain diagnoses, and high frequency of mental health diagnoses, this response rate seems satisfactory from a relatively low risk and inexpensive intervention.

Those patients receiving a minimum clinically important improvement differed from the group that did not improve or worsened with treatment in that the former were older, had experience a shorter duration of low back pain, and had higher baseline ODI scores. While interesting, it is not reasonable to utilize these characteristics to determine who should be offered prolotherapy treatment. However, a clinically-valuable distinction between groups was that those who ultimately had a minimum clinically important improvement were much

more likely to show such improvement when seen a median of 32 days after the first prolotherapy injection and prior to the second injection. In other words, many patients who were likely to improve from prolotherapy were evident by improvement early in the treatment, and those who did not respond early were highly unlikely to ultimately improve.

Two addition characteristics of the patient groups that were examined deserve comment. Nearly half (47%) of the 103 patients completing the study had a history of abrupt onset of low back symptoms. We also found that the presence of clicking, popping or grinding in the low back was more likely than not (53%) in this patient group, although the history of these symptoms was not a distinguishing characteristic for outcome from prolotherapy treatment. However, a history of abrupt onset of low back pain distinguished those who were more unlikely to improve with prolotherapy treatment. We might speculate that such history would be consistent with a more extensive injury that would be less likely to respond to treatment.

Some limitations of this work are acknowledged. Of course, as a retrospective cohort study, there was no comparison group receiving sham injections. Thus, a placebo effect in some patients cannot be excluded. Without a control group, we also cannot be certain that ODI scores would not have changed over time without intervention, although the pre-intervention ODI scores showed stability across a median interval of 37 days among the subset of patients in which two ODI scores were obtained before receiving a diagnostic or prolotherapy injection. We also recognize that greater diagnostic confirmation of SI joint instability than utilized in this study would be warranted in a formal treatment trial, and so it is possible that some of the patients did not have SI joint instability as an etiology of their symptoms. It is also possible that optimal prolotherapy treatment for SI joint instability is not limited to intra-articular injections, and involves a different dextrose concentration and solution volume than was used in this study, though there is not adequate science to clarify. A more extended follow-up period would also be optimal. Another study limitation is that the ODI was the only outcome measure that was obtained. It is quite likely that medical issues other than SI joint instability contributed to disability in this patient population, and therefore may have attenuated the extent of improvements that were observed from treatment. Inclusion of other outcome measures should be considered in future work. Finally, it was noted that the group that improved with prolotherapy was more likely to have received the initial prolotherapy injection with fluoroscopic guidance compared with the group that did not improve. This effect was associated with a greater proportion of the group that did not improve being treated during a time in which fluoroscopy was being used less for prolotherapy injections. The fact that there was no statistical difference between groups in the use of fluoroscopic guidance for the last two prolotherapy injections suggests that the use of fluoroscopy was not a key issue in determining outcome, but our lack of confirmation of proper needle placement for a high percentage of the prolotherapy injections could be considered a study limitation.

From this work, we conclude that a satisfactory proportion of

patients with presumed SI joint instability as an etiology of low back pain can have clinically meaningful functional gains with prolotherapy treatment even if they have severe disability and have had low back pain for an extended period of time. Many patients who are likely to improve from prolotherapy are evident early in the treatment, and most patients who are unlikely to improve are distinguished by a lack of improvement that is evident following the initial prolotherapy injection.

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Competing interests

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