

Hypertonic dextrose injection (prolotherapy) for knee osteoarthritis: Long term outcomes.

[Rabago D¹](#), [Mundt M²](#), [Zgierska A²](#), [Grettie J³](#).

Author information

Abstract

OBJECTIVE:

Knee osteoarthritis (OA) is a common, debilitating chronic disease. Prolotherapy is an injection therapy for chronic musculoskeletal pain. Recent 52-week randomized controlled and open label studies have reported improvement of knee OA-specific outcomes compared to baseline status, and blinded saline control injections and at-home exercise therapy ($p < 0.05$). However, long term effects of prolotherapy for knee OA are unknown. We therefore assessed long-term effects of prolotherapy on knee pain, function and stiffness among adults with knee OA.

DESIGN:

Post clinical-trial, open-label follow-up study.

SETTING:

Outpatient; adults with mild-to-severe knee OA completing a 52-week prolotherapy study were enrolled.

INTERVENTION AND OUTCOME MEASURES:

Participants received 3-5 monthly interventions and were assessed using the validated Western Ontario McMaster University Osteoarthritis Index, (WOMAC, 0-100 points), at baseline, 12, 26, 52 weeks, and 2.5 years.

RESULTS:

65 participants (58 ± 7.4 years old, 38 female) received 4.6 ± 0.69 injection sessions in the initial 17-week treatment period. They reported progressive improvement in WOMAC scores at all time points in excess of minimal clinical important improvement benchmarks during the initial 52-week study period, from 13.8 ± 17.4 points (23.6%) at 12 weeks, to 20.9 ± 2.8 points, ($p < 0.05$; 35.8% improvement) at 2.5 ± 0.6 years (range 1.6-3.5 years) in the current follow-up analysis. Among assessed covariates, none were predictive of improvement in the WOMAC score.

CONCLUSIONS:

Prolotherapy resulted in safe, significant, progressive improvement of knee pain, function and stiffness scores among most participants through a mean follow-up of 2.5 years and may be an appropriate therapy for patients with knee OA refractory to other conservative care.

2- Hyperosmolar dextrose injection for recalcitrant Osgood-Schlatter disease.

[Topol GA](#)¹, [Podesta LA](#), [Reeves KD](#), [Raya MF](#), [Fullerton BD](#), [Yeh HW](#).

Author information

Abstract

OBJECTIVE:

To examine the potential of dextrose injection versus lidocaine injection versus supervised usual care to reduce sport alteration and sport-related symptoms in adolescent athletes with Osgood-Schlatter disease.

PATIENTS AND METHODS:

Girls aged 9 to 15 and boys aged 10 to 17 were randomly assigned to either therapist-supervised usual care or double-blind injection of 1% lidocaine solution with or without 12.5% dextrose. Injections were administered monthly for 3 months. All subjects were then offered dextrose injections monthly as needed. Unaltered sport (Nirschl Pain Phase Scale < 4) and asymptomatic sport (Nirschl Pain Phase Scale = 0) were the threshold goals.

RESULTS:

Sixty-five knees in 54 athletes were treated. Compared with usual care at 3 months, unaltered sport was more common in both dextrose-treated (21 of 21 vs 13 of 22; $P = .001$) and lidocaine-treated (20 of 22 vs 13 of 22; $P = .034$) knees, and asymptomatic sport was more frequent in dextrose-treated knees than either lidocaine-treated (14 of 21 vs 5 of 22; $P = .006$) or usual-care-treated (14 of 21 vs 3 of 22; $P < .001$) knees. At 1 year, asymptomatic sport was more common in dextrose-treated knees than knees treated with only lidocaine (32 of 38 vs 6 of 13; $P = .024$) or only usual care (32 of 38 vs 2 of 14; $P < .0001$).

CONCLUSIONS:

Our results suggest superior symptom-reduction efficacy of injection therapy over usual care in the treatment of Osgood-Schlatter disease in adolescents. A significant component of the effect seems to be associated with the dextrose component of a dextrose/lidocaine solution. Dextrose injection over the apophysis and patellar tendon origin was safe and well tolerated and resulted in more rapid and frequent achievement of unaltered sport and asymptomatic sport than usual care.

Randomized, prospective, placebo-controlled double-blind study of dextrose prolotherapy for osteoarthritic thumb and finger (DIP, PIP, and trapeziometacarpal) joints: evidence of clinical efficacy.

[Reeves KD¹](#), [Hassanein K.](#)

Author information

Abstract

OBJECTIVES:

To determine the clinical benefit of dextrose prolotherapy (injection of growth factors or growth factor stimulators) in osteoarthritic finger joints.

DESIGN:

Prospective randomized double-blind placebo-controlled trial.

SETTINGS/LOCATION:

Outpatient physical medicine clinic.

SUBJECTS:

Six months of pain history was required in each joint studied as well as one of the following: grade 2 or 3 osteophyte, grade 2 or 3 joint narrowing, or grade 1 osteophyte plus grade 1 joint narrowing. Distal interphalangeal (DIP), proximal interphalangeal (PIP), and trapeziometacarpal (thumb CMC) joints were eligible. Thirteen patients (with seventy-four symptomatic osteoarthritic joints) received active treatment, and fourteen patients (with seventy-six symptomatic osteoarthritic joints) served as controls.

INTERVENTION:

One half milliliter (0.5 mL) of either 10% dextrose and 0.075% xylocaine in bacteriostatic water (active solution) or 0.075% xylocaine in bacteriostatic water (control solution) was injected on medial and lateral aspects of each affected joint. This was done at 0, 2, and 4 months with assessment at 6 months after first injection.

OUTCOME MEASURES:

One-hundred millimeter (100 mm) Visual Analogue Scale (VAS) for pain at rest, pain with joint movement and pain with grip, and goniometrically-measured joint flexion.

RESULTS:

Pain at rest and with grip improved more in the dextrose group but not significantly. Improvement in pain with movement of fingers improved significantly more in the dextrose group (42% versus 15% with a p value of .027). Flexion range of motion improved more in the dextrose group (p = .003). Side effects were minimal.

CONCLUSION:

Dextrose prolotherapy was clinically effective and safe in the treatment of pain with joint movement and range limitation in osteoarthritic finger joints.

Chronic neck pain: making the connection between capsular ligament laxity and cervical instability.

[Steilen D¹](#), [Hauser R¹](#), [Woldin B¹](#), [Sawyer S¹](#).

Author information

Abstract

The use of conventional modalities for chronic neck pain remains debatable, primarily because most treatments have had limited success. We conducted a review of the literature published up to December 2013 on the diagnostic and treatment modalities of disorders related to chronic neck pain and concluded that, despite providing temporary relief of symptoms, these treatments do not address the specific problems of healing and are not likely to offer long-term cures. The objectives of this narrative review are to provide an overview of chronic neck pain as it relates to cervical instability, to describe the anatomical features of the cervical spine and the impact of capsular ligament laxity, to discuss the disorders causing chronic neck pain and their current treatments, and lastly, to present prolotherapy as a viable treatment option that heals injured ligaments, restores stability to the spine, and resolves chronic neck pain. The capsular ligaments are the main stabilizing structures of the facet joints in the cervical spine and have been implicated as a major source of chronic neck pain. Chronic neck pain often reflects a state of instability in the cervical spine and is a symptom common to a number of conditions described herein, including disc herniation, cervical spondylosis, whiplash injury and whiplash associated disorder, postconcussion syndrome, vertebrobasilar insufficiency, and Barré-Liéou syndrome. When the capsular ligaments are injured, they become elongated and exhibit laxity, which causes excessive movement of the cervical vertebrae. In the upper cervical spine (C0-C2), this can cause a number of other symptoms including, but not limited to, nerve irritation and vertebrobasilar insufficiency with associated vertigo, tinnitus, dizziness, facial pain, arm pain, and migraine headaches. In the lower cervical spine (C3-C7), this can cause muscle spasms, crepitation, and/or paresthesia in addition to chronic neck pain. In either case, the presence of excessive motion between two adjacent cervical vertebrae and these associated symptoms is described as cervical instability. Therefore, we propose that in many cases of chronic neck pain, the cause may be underlying joint instability due to capsular ligament laxity. Currently, curative treatment options for this type of cervical instability are inconclusive and inadequate. Based on clinical studies and experience with patients who have visited our chronic pain clinic with complaints of chronic neck pain, we contend that prolotherapy offers a potentially curative treatment option for chronic neck pain related to capsular ligament laxity and underlying cervical instability.

KEYWORDS:

Atlanto-axial joint; Barré- Liéou syndrome; C1-C2 facet joint; capsular ligament laxity; cervical instability; cervical radiculopathy; chronic neck pain; facet joints; post-concussion syndrome; prolotherapy; spondylosis; vertebrobasilar insufficiency; whiplash.

Dextrose Prolotherapy Versus Control Injections in Painful Rotator Cuff Tendinopathy.

[Bertrand H¹](#), [Reeves KD²](#), [Bennett CJ³](#), [Bicknell S⁴](#), [Cheng AL⁵](#).

Author information

Abstract

OBJECTIVE:

To compare the effect of dextrose prolotherapy on pain levels and degenerative changes in painful rotator cuff tendinopathy against 2 potentially active control injection procedures.

DESIGN:

Randomized controlled trial, blinded to participants and evaluators.

SETTING:

Outpatient pain medicine practice.

PARTICIPANTS:

Persons (N=73) with chronic shoulder pain, examination findings of rotator cuff tendinopathy, and ultrasound-confirmed supraspinatus tendinosis/tear.

INTERVENTIONS:

Three monthly injections either (1) onto painful entheses with dextrose (Enthesis-Dextrose), (2) onto entheses with saline (Enthesis-Saline), or (3) above entheses with saline (Superficial-Saline). All solutions included 0.1% lidocaine. All participants received concurrent programmed physical therapy.

MAIN OUTCOME MEASURES:

Primary: participants achieving an improvement in maximal current shoulder pain ≥ 2.8 (twice the minimal clinically important difference for visual analog scale pain) or not. Secondary: improvement in the Ultrasound Shoulder Pathology Rating Scale (USPRS) and a 0-to-10 satisfaction score (10, completely satisfied).

RESULTS:

The 73 participants had moderate to severe shoulder pain (7.0 ± 2.0) for 7.6 ± 9.6 years. There were no baseline differences between groups. Blinding was effective. At 9-month follow-up, 59% of Enthesis-Dextrose participants maintained ≥ 2.8 improvement in pain compared with Enthesis-Saline (37%; $P=.088$) and Superficial-Saline (27%; $P=.017$). Enthesis-Dextrose participants' satisfaction was 6.7 ± 3.2 compared with Enthesis-Saline (4.7 ± 4.1 ; $P=.079$) and Superficial-Saline (3.9 ± 3.1 ; $P=.003$). USPRS findings were not different between groups ($P=.734$).

CONCLUSIONS:

In participants with painful rotator cuff tendinopathy who receive physical therapy, injection of hypertonic dextrose on painful entheses resulted in superior long-term pain improvement and patient satisfaction compared with blinded saline injection over painful entheses, with intermediate results for entheses injection with saline. These differences could not be attributed to a regenerative effect. Dextrose prolotherapy may improve on the standard care of painful rotator cuff tendinopathy for certain patients.

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Long-term effects of dextrose prolotherapy for anterior cruciate ligament laxity.

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Author information

Abstract

CONTEXT:

Use of dextrose prolotherapy. Prolotherapy is defined as injection that causes growth of normal cells or tissue.

OBJECTIVE:

Determine the 1 and 3 year efficacy of dextrose injection prolotherapy on anterior cruciate ligament (ACL) laxity. After year 1, determine patient tolerance of a stronger dextrose concentration (25% versus 10%).

DESIGN:

Prospective consecutive patient trial.

SETTING:

Outpatient physical medicine clinic.

PATIENTS OR OTHER PARTICIPANTS:

Eighteen patients with 6 months or more of knee pain plus ACL knee laxity. This laxity was defined by a KT1000 anterior displacement difference (ADD) of 2 mm or more.

INTERVENTION:

Intraarticular injection of 6-9 cc of 10% dextrose at months 0, 2, 4, 6, and 10. Injection with 6 cc of 25% dextrose at 12 months. Then, depending on patient preference, injection of either 10% or 25% dextrose every 2-4 months (based on patient preference) through 36 months.

MAIN OUTCOME MEASURES:

Visual analogue scale (VAS) for pain at rest, pain on level surfaces, pain on stairs, and swelling. Goniometric flexion range of motion, and KT1000-measured ADD were also measured. All measurements were obtained at 0, 6, 12 and 36 months.

RESULTS:

Two patients did not reach 6 month data collection, 1 of whom was diagnosed with disseminated cancer. The second was wheelchair-bound and found long-distance travel to the clinic problematic. Sixteen subjects were available for data analysis. KT1000 ADD, measurement indicated that 6 knees measured as normal (not loose) after 6 months, 9 measured as normal after 1 year (6 injections), and 10 measured as normal at 3 years. At the 3 year follow-up, pain at rest, pain with walking, and pain with stair use had improved by 45%, 43%, and 35% respectively. Individual paired t tests indicated subjective swelling improved 63% ($P = .017$), flexion range of motion improved by 10.5 degrees ($P = .002$), and KT1000 ADD improved by 71% ($P = .002$). Eleven out of 16 patients preferred 10% dextrose injection.

CONCLUSION:

In patients with symptomatic anterior cruciate ligament laxity, intermittent dextrose injection resulted in clinically and statistically significant improvement in ACL laxity, pain, swelling, and knee range of motion.

A Randomized Controlled Trial of Intra-Articular Prolotherapy Versus Steroid Injection for Sacroiliac Joint Pain

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Chang Mo Kim, MD, PhD, and Myung Ha Yoon, MD, PhD

Abstract

Objectives: Controversy exists regarding the efficacy of ligament prolotherapy in alleviating sacroiliac joint pain. The inconsistent success rates reported in previous studies may be attributed to variability in patient selection and techniques between studies. It was hypothesized that intra-articular prolotherapy for patients with a positive response to diagnostic block may mitigate the drawbacks of ligament prolotherapy. The purpose of this study was to evaluate the efficacy and long-term effectiveness of intra-articular prolotherapy in relieving sacroiliac joint pain, compared with intra-articular steroid injection.

Design: This was a prospective, randomized, controlled trial.

Settings/location: The study was conducted at an outpatient pain medicine clinic at Chonnam National University Hospital in Gwang-ju, Korea.

Subjects: The study included patients with sacroiliac joint pain, confirmed by $\geq 50\%$ improvement in response to local anesthetic block, lasting 3 months or longer, and who failed medical treatment.

Interventions: The treatment involved intra-articular dextrose water prolotherapy or triamcinolone acetonide injection using fluoroscopic guidance, with a biweekly schedule and maximum of three injections.

Outcome measures: Pain and disability scores were assessed at baseline, 2 weeks, and monthly after completion of treatment.

Results: The numbers of recruited patients were 23 and 25 for the prolotherapy and steroid groups, respectively. The pain and disability scores were significantly improved from baseline in both groups at the 2-week follow-up, with no significant difference between them. The cumulative incidence of $\geq 50\%$ pain relief at 15 months was 58.7% (95% confidence interval [CI] 37.9%–79.5%) in the prolotherapy group and 10.2% (95% CI 6.7%–27.1%) in the steroid group, as determined by Kaplan-Meier analysis; there was a statistically significant difference between the groups (log-rank $p < 0.005$).

Conclusions: Intra-articular prolotherapy provided significant relief of sacroiliac joint pain, and its effects lasted longer than those of steroid injections. Further studies are needed to confirm the safety of the procedure and to validate an appropriate injection protocol.

Introduction

CHRONIC LOW BACK PAIN is a disabling condition associated with significant economic, societal, and health impacts,¹ and its prevalence is reported to be increasing.² Although various etiologies exist, the sacroiliac (SI) joint is a major source of pain in up to 30% of patients complaining of low-back and buttock pain.³

To relieve SI joint pain, several techniques have been reported. Among them, intra-articular corticosteroid injection

can be helpful, but some patients gain only short-term benefits.^{4,5} Radiofrequency (RF) denervation of the SI joint can be an effective treatment, but the exact details of the joint's innervation are unclear, and reported success rates are inconsistent.^{6,7}

Prolotherapy may also be efficacious for SI joint pain,^{5,8} but questions regarding its benefits have also been raised.⁹ The inconsistent results of ligament prolotherapy may be explained by the variability in techniques and patient selection, as well as pain emanating from inaccessible ventral structures.^{3,8,10}

We hypothesized that diagnostic SI joint block may guide patient selection for prolotherapy. Thereafter, a modified intra-articular technique of prolotherapy may compensate for the weaknesses of the conventional periligamentous injection, thus improving the efficacy of prolotherapy in ameliorating SI joint pain. However, to date, there has been no published study examining the efficacy and benefits of sacroiliac intra-articular prolotherapy. The purposes of this study were to assess the efficacy of intra-articular prolotherapy in relieving SI joint pain, using dextrose water, and to evaluate the long-term effectiveness of this technique versus intra-articular steroid injections.

Materials and Methods

This study was approved by the institutional review board of Chonnam National University Hospital. Initial diagnosis was based on a history of pain lasting 2 months or longer in the buttock, groin, or thigh, regardless of associated lower extremity symptoms. Positive physical examination included tenderness over the area just below the posterior superior iliac spine, the Patrick test, or Gaenslen's test. Because these tests lack specificity,¹¹ a diagnostic local anesthetic intra-articular injection using 2.5 mL of 0.25% levobupivacaine was performed to confirm SI joint pain. A decrease in pain intensity of at least 50%, measured by the numeric rating scale (NRS, 0 = no pain, 10 = maximum pain), was deemed a positive response. Patients diagnosed with SI joint pain and who failed medical treatment for an additional 1 month were prospectively enrolled. Exclusion criteria were cancer, fractures, inflammatory arthritis, infection, unresolved litigation or workers' compensation claims, fibromyalgia, and pregnancy.

After informed consent was obtained, the patients were randomly assigned to receive intra-articular prolotherapy or intra-articular steroid injection according to a computer-generated randomization schedule. Patients and the outcome-measuring physicians were blinded to the treatment group throughout the study. The therapeutic injection was done by a different physician who was not otherwise involved in the study and not blinded to the treatment group. For the prolotherapy group, we injected 2.5 mL of 25% dextrose solution into the SI joint every other week and repeated this up to three times. The dextrose solution was prepared by diluting 50% dextrose water with 0.25% levobupivacaine. If a patient's symptoms were improved by more than 90% by NRS on the second or third visit, the next procedure was canceled. A similar treatment schedule was administered in the steroid group, but the injected drug was triamcinolone acetonide 40 mg (Triamcinolone,® Dong Kwang Pharm, Seoul, Korea) in 0.125% levobupivacaine 2.5 mL (Chirocaine,® Abbott Korea, Seoul, Korea). For managing postprocedure pain, an oral tramadol and acetaminophen combination tablet (Ultracet,® Janssen Korea Ltd, Seoul, Korea) and tizanidine hydrochloride were prescribed for 7 days to all patients. Analgesics being administered before the study were stopped prior to the first session and for the duration of the study. However, adequate medications were provided for patients with recurring severe SI joint pain.

SI joint intra-articular injection

SI joint injection was conducted using fluoroscopic guidance, as described below. Patients were positioned prone,

with the C-arm slightly tilted cephalad, to displace the posteroinferior portion of the SI joint inferiorly from the anterior aspect.¹² Then, the C-arm was orbited back and forth such that the medial joint line (the posterior portion of SI joint) and the edge of the sacrum are clearly identified.¹³ After the skin was draped and anesthetized slightly caudal to the most inferior aspect of the SI joint, a 22-gauge spinal needle was inserted into the joint. Then, the needle was advanced upward into the base of the joint while being checked for the depth of the tip on the lateral fluoroscopic view. After confirmation of the intra-articular position using an arthrogram, with 0.2–0.5 mL of contrast medium, the drug for diagnosis or therapy was injected. All procedures were performed in an outpatient setting by a specialist in interventional pain management certified by The Korean Pain Society; this specialist had over 5 years' experience as a pain physician (WMK).

Outcome measures

For assessment, a physician unaware of the patient's study group recorded the NRS for pain and the Oswestry disability index (ODI) before and 2 weeks after the completion of a series of treatment. The main outcome measure was the cumulative incidence of sustained pain relief, defined as maintenance of a 50% or more improvement in NRS from baseline, without analgesic medication, at the monthly follow-up session.

Sample size calculation

The sample size calculation was based on the main outcome measure. We assumed that the incidence of sustained pain relief of the prolotherapy group was approximately 0.65 and that of the steroid group was 0.35, according to the report of Chakraverty and Dias,⁵ in which the demographics of the populations and the standards used for the diagnosis of SI joint pain were relatively consistent with our pilot study. Thus, a sample size of 45 in each group was determined using Freedman's sample size table¹⁴ for detecting an improvement in survival rate of 0.3, over a baseline value of 0.35, to achieve a statistical power of 80% at a two-sided significance level of 0.05.

Interim analysis

To assess the efficacy of the two treatment methods, an interim analysis was conducted 12 months after starting the recruitment of the patients. From February 2008 to January 2009, 23 and 25 patients were recruited for the prolotherapy and steroid groups, respectively. The interim analysis revealed a significantly higher incidence of sustained pain relief in the prolotherapy group (log-rank $p < 0.005$). Thus, further recruitment of patients was terminated, but follow-ups were continued on the participating patients for an additional 3 months (Fig. 1).

Statistical analyses

Continuous variables were compared between groups using an unpaired *t*-test and are expressed as means \pm standard deviation. Categorical data were analyzed using Fisher exact test, and are reported as percentages. Within-group comparison of the NRS and ODI, before and after

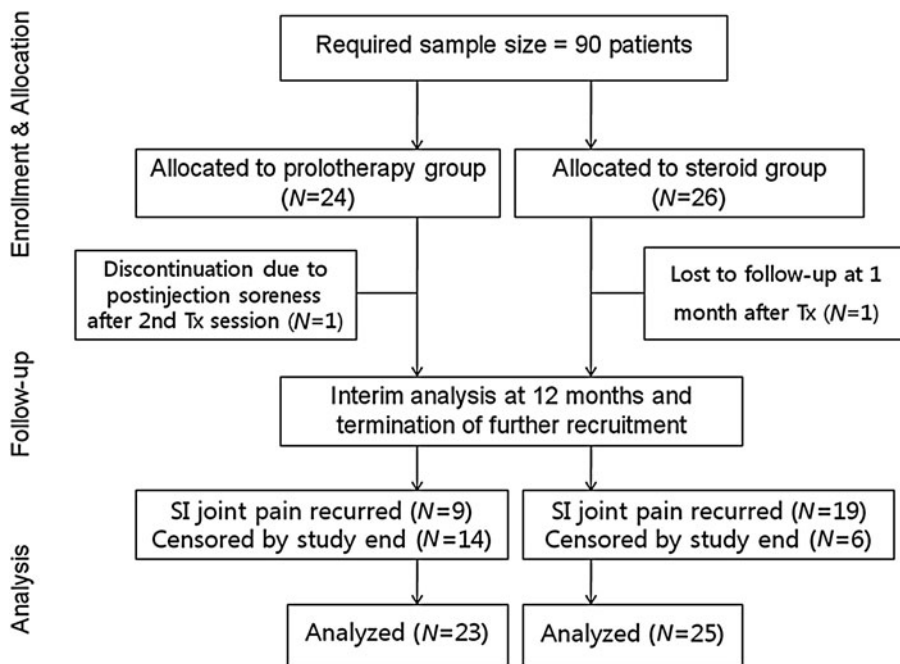


FIG. 1. Flow diagram of participants in the study. Tx, treatment; SI, sacroiliac.

treatment, were conducted using the paired *t* test. Kaplan-Meier survival analysis with the log-rank test was performed to compare the cumulative incidence of sustained pain relief between the two groups. All analyses were performed using SPSS software (version 17.0; SPSS Inc., Chicago, IL). *P* values of <0.05 were deemed to indicate statistical significance.

Results

Baseline demographics

A total of 50 patients enrolled; 24 were assigned to the prolotherapy group and 26 were to the steroid group. One (1) subject in the prolotherapy group refused further intervention after the second treatment session due to postinjection soreness lasting 7 days and received oral opioid analgesics to relieve her SI joint pain. The other 1 in the steroid group was lost to follow-up at 1 month after completion of treatment. Thus, the remaining 48 patients were followed until recurrence of SI joint pain or the end of the study.

The baseline demographic data of the two groups were comparable and are presented in Table 1. There was no significant difference in the duration of symptoms, pre-treatment medication, or baseline NRS and ODI between the groups. The number of injections in the steroid group was significantly lower than that in the prolotherapy group ($p < 0.01$). One (1) or two injections was sufficient to achieve pain relief $\geq 90\%$ from baseline for the 22 patients (88%) in the steroid group, whereas three injections were needed for the 16 patients (70%) in the prolotherapy group (Table 2).

Effectiveness at 2 weeks' follow-up

The NRS was significantly decreased from baseline in both groups at 2 weeks after the completion of the treatment series, from 6.3 ± 1.1 to 1.4 ± 1.1 for the prolotherapy group and from 6.7 ± 1.0 to 1.9 ± 0.9 for the steroid group ($p < 0.001$). At that time, all patients in both groups experienced $\geq 50\%$ reduction in pain. In addition, the ODI score

TABLE 1. DEMOGRAPHIC AND CLINICAL FEATURES OF STUDY PATIENTS

	Prolotherapy (n = 23)	Steroid (n = 25)
Age, mean (SD)	58.7 (13.0)	61.6 (15.2)
Gender, male/female (%)	7 (30)/16 (70)	7 (28)/18 (72)
Symptom duration, months (range)	40.1 (4–240)	44.0 (3–240)
Location, right/left/both (%)	9 (39)/6 (26)/8 (35)	9 (36)/6 (24)/10 (40)
Previous medication		
None (%)	4 (19)	6 (24)
NSAIDs (%)	14 (67)	13 (52)
Opioids (%)	3 (14)	6 (24)
Accompanying leg symptom		
Thigh pain (%)	12 (57)	11 (44)
Calf pain (%)	11 (52)	7 (28)
Pretreatment NRS (range)	6.3 (4–8)	6.7 (5–8)
Pretreatment ODI (SD)	33.9 (15.5)	35.7 (20.4)

SD, standard deviation; NSAIDs, nonsteroidal anti-inflammatory drugs; NRS, numeric rating scale; ODI, Oswestry disability index.

TABLE 2. SUMMARY OF OUTCOMES IN THE TWO GROUPS

	Prolotherapy (n = 23)	Steroid (n = 25)
NRS at 2 weeks		
Mean (SD)	1.4 (1.1)	1.9 (0.9)
% change from baseline	77.6 (16.8)	70.5 (16.8)
ODI at 2 weeks		
Mean (SD)	11.1 (10.0)	15.5 (10.7)
% change from baseline	67.9 (27.9)	58.8 (19.0)
Percent positive response (95% CI)		
6 months	63.6 (43.2–84.0)	27.2 (7.6–46.8)*
10 months	58.7 (37.9–79.5)	10.2 (6.7–27.1)*
15 months	58.7 (37.9–79.5)	10.2 (6.7–27.1)*
Median survival time,	NA ^a	
Mean (months, 95% CI)		3.0 (2.4–3.6)
Number of injections, mean (SD)	2.7 (1.1)	1.5 (0.8)*

* $p < 0.01$, versus prolotherapy group.

^aNot applicable, because above 50% of subjects in this group remained improved >50% from baseline at the time of the study end.

NRS, numeric rating scale; SD, standard deviation; CI, confidence interval; ODI, Oswestry disability index.

was significantly improved from the pretreatment value, 33.9 ± 15.5 to 11.1 ± 10.0 for the prolotherapy group and from 35.7 ± 20.4 to 15.5 ± 10.7 for the steroid groups ($p < 0.001$). There was no significant difference between the two groups with regard to the post-treatment NRS or ODI (Fig. 2). Transient aggravation of pain lasting several days was reported in some patients without significant difference between groups. None of the participants reported serious adverse event such as long-lasting exacerbation of pain, numbness or weakness, or signs of skin infection.

Long-term follow-up data

At 6 months after treatment, 63.6% of patients in the prolotherapy group remained 50% or more improved from baseline, whereas it was 27.2% in the steroid group (Table 2). The cumulative incidence of sustained pain relief at 15 months was 58.7% (95% confidence interval [CI] 37.9%–79.5%) in the prolotherapy group and 10.2% (95% CI 6.7%–27.1%) in the steroid group (Table 2); there was a significant difference between the two survival curves ($p < 0.005$; Fig. 3). No serious complication was reported during the follow-up period.

Discussion

In this study, intra-articular prolotherapy provided significant relief from SI joint pain, and its effect lasted longer than that of steroid injections. Key findings of this study are a patient-selection method for prolotherapy using a diagnostic SI joint block and the proliferant injection technique using a reproducible arthrogram.

Although various methods have been suggested to relieve SI joint pain, we suggest that intra-articular prolotherapy, as documented in this study, may have advantages over other techniques, such as periligamentous prolotherapy, RF denervation, and steroid injection. First, this method may reduce variability in patient selection and in the injection technique used in prolotherapy. In the systematic review of Yelland et al., there was no evidence that prolotherapy injections alone were more effective than control injections.¹⁵ However, these findings may be attributable to the lack of a specific diagnosis for patient selection and variations in the

proliferant injection technique. Cusi et al. pointed out the importance of patient selection and treatment protocol, noting that there was no evidence that the proliferation of soft tissue was analgesic *per se*.⁸ That is, the results of prolotherapy for SI joint pain are likely to vary, depending on the experience and skill of the practicing physician. Patient selection in this study was based on a specific procedure that has been suggested as the “gold standard” for diagnosing SI joint pain,¹⁶ and the injection method was not a blind technique, but a fluoroscopically guided, reproducible one, thus reducing variability in patient selection and injection technique. As a result, these advantages of the intra-articular prolotherapy technique may have led to the favorable results reported here.

Second, intra-articular prolotherapy may provide some beneficial effects on the ventral structures of the SI joint. Schwarzer et al.³ reported that ventral capsular pathology was shown to account for 69% of all computed tomography (CT) pathology in patients with positive responses to diagnostic block. However, these are inaccessible to ligament prolotherapy or RF denervation.

Finally, there is a need for a repeated needle puncture technique into multiple sites for ligament prolotherapy¹⁷ or RF denervation,⁶ in contrast to intra-articular prolotherapy, which uses theoretically a single injection for each session, thus minimizing patient discomfort during the procedure.

The rationale for prolotherapy is that it may produce dense fibrous tissue to strengthen the attachment of ligaments, tendons, joint capsules, and other fascial structures at their fibro-osseous junctions.¹⁸ Prolotherapy is the injection of an irritant proliferant solution into the abovementioned structures. However, the concept of intra-articular dextrose prolotherapy has also been reported. In a study by Hooper et al.,¹⁹ intra-articular zygapophysial joint prolotherapy using 0.5–1 mL of dextrose solution improved pain and function in patients with chronic whiplash. Reeves et al.^{20,21} reported that intra-articular dextrose prolotherapy resulted in clinically and statistically significant improvements in knee osteoarthritis, with or without anterior cruciate ligament laxity, at the 1- and 3-year follow-up. There was consideration that sacroiliac intra-articular prolotherapy might also work, based on the absent or rudimentary posterior

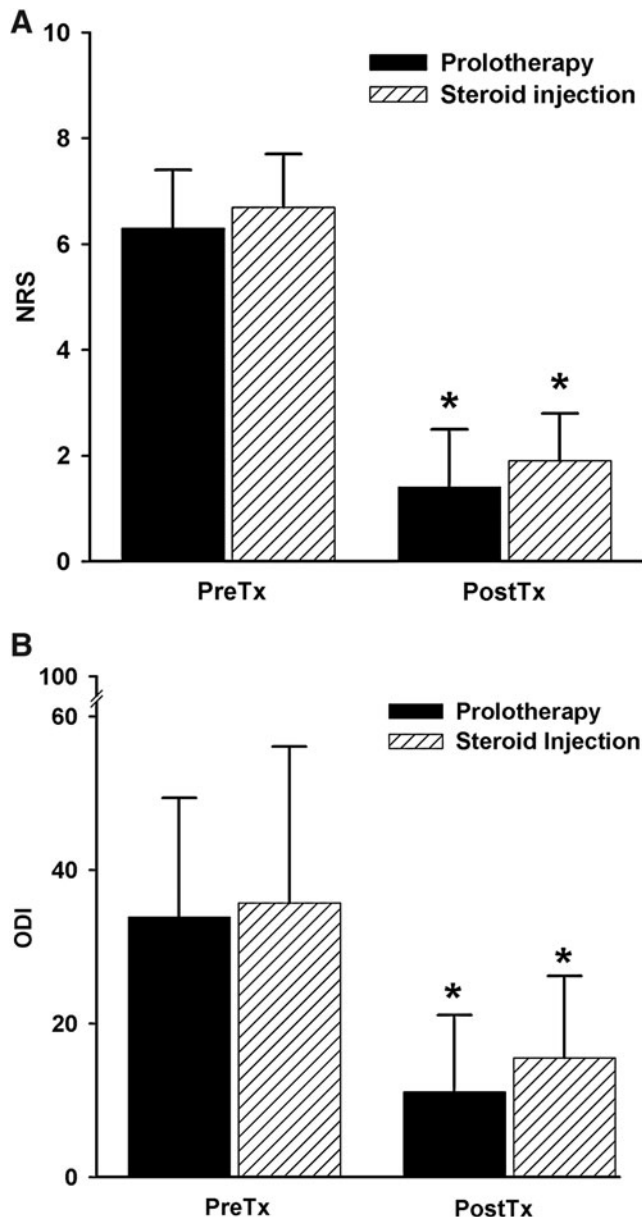


FIG. 2. Numeric rating scale (NRS) (A) and Oswestry disability index (ODI) (B) before and after intra-articular prolotherapy or steroid injection. Values are expressed as mean \pm standard deviation. PreTx, before treatment; PostTx, 2 weeks after treatment. * $p < 0.001$, versus before-treatment value.

capsule,²² which may allow spreading of the injected drug, allowing it to reach the dorsal SI ligamentous structures. Moreover, taking into account the significance of ventral capsular pathology,³ it was hypothesized that intra-articular prolotherapy would be more efficacious than a periligamentous injection.

The cumulative incidence of sustained pain relief in response to steroid injection in this study was 27.2% and 10.2% at 6 and 15 months, respectively, and the median duration of survival to recurrence of severe SI joint pain was 3 months, which is rather low or short, compared with other reports.^{23,24} The long-term effectiveness of SI joint

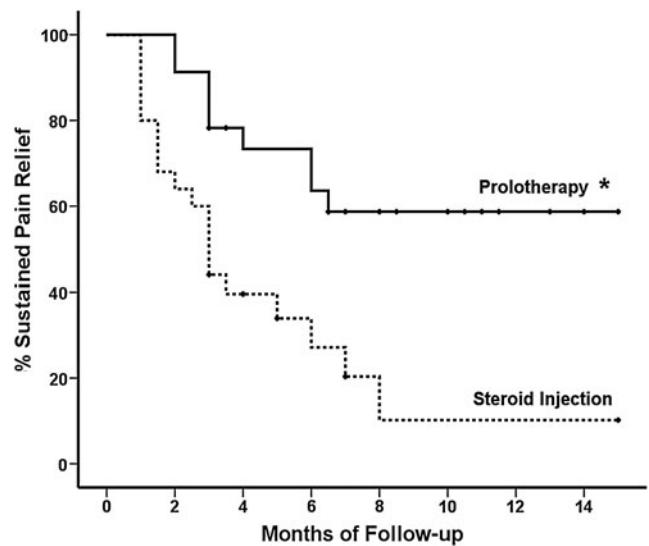


FIG. 3. Kaplan-Meier plot showing cumulative incidence of sustained 50% or greater relief of pain, which was significantly higher in the prolotherapy group compared with the steroid group, as analyzed by log-rank test. * $p < 0.005$, versus steroid injection group.

steroid injection has been reported, with the proportion of subjects with sustained pain relief at 6 months being 58%,²³ or the average duration of sufficient pain relief being 9.3 months.²⁴ However, the former was assessed in patients with spondyloarthropathy in which the inflammatory component could have been more important than the mechanical one, and the latter was determined by the time between injections, which may have overstated the duration of the response. Additionally, different definitions of a positive response to a diagnostic block can affect the sensitivity of the diagnostic block, which may in turn affect the success rate of the therapeutic injection. Diversity in the demographics of the study population and the duration of follow-up between studies may also explain the different results reported.

The results of this study indicated that intra-articular prolotherapy may be useful as a treatment modality for SI joint pain. However, this study also has some limitations. There was a need for more frequent intervention by intra-articular prolotherapy than by steroid injections to achieve pain relief of $\geq 90\%$ from baseline, indicating that the therapeutic effect of the former may appear later than the latter. However, from the viewpoint of long-term effectiveness, intra-articular prolotherapy may provide adequate pain relief with less frequent intervention than steroid injections. Further investigations are necessary to evaluate the long-term safety of repeated intra-articular injection of dextrose water and the adequacy of the volume and number of injections, although no patient here reported a serious adverse event.

Conclusions

Intra-articular prolotherapy with 5% dextrose water may be useful for the long-term relief of SI joint pain. Further studies are needed to confirm the safety of the procedure and to validate an appropriate injection protocol.

Acknowledgments

No financial support was provided for this study.

Disclosure Statement

No competing financial interests exist.

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