SYSTEMATIC REVIEW

Hypertonic Dextrose Injection (Prolotherapy) Effectiveness for Rotator Cuff Tendinopathy : A Systematic Review

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ABSTRACT

Introduction: Shoulder pain is the third most common musculoskeletal injury with a prevalence of 10:1000 person with the highest prevalence in the age group of 42-46 years old. The most common cause of shoulder pain is rotator cuff tendinopathy. Prolotherapy is an alternative injection-based therapy that using a fluid with high osmolarity like dextrose 20%. Prolotherapy already showed a promised outcome for musculoskeletal problems, but only a few pieces of research for rotator cuff tendinopathy. **Methods:** This study is a systematic review study using five best possible evidence. A systematic search was done to identify RCTs about prolotherapy hypertonic dextrose injection for patients with rotator cuff tendinopathy. **Results:** We select 5 out of 964 studies and found a wide variety of injection techniques, total of injection, control, follow-up periods, and measured outcome. Dextrose concentration that used was ranged from 12.5 – 25% and also with a single-site or multi-site and single injection or multi injection. For measured outcomes, there are VAS, SPADI, WORC, ROM, and ultrasound morphology. We also found 6 out of 272 patients develop a mild complication. This study also rated 2 out of 5 studies included as high risk of bias. **Conclusion:** Prolotherapy with hypertonic dextrose injection potentially beneficial for patients with rotator cuff tendinopathy. There is a significant improvement in pain, shoulder function, ROM, and ultrasound morphology. With some high risk of bias studies and a wide variety of injection techniques, further study is required to find factors that affecting hypertonic dextrose injection in rotator cuff tendinopathy.

Keywords: Hypertonic dextrose injection, Prolotherapy, Rotator cuff tendinopathy

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INTRODUCTION

The upper extremity is a part of the extremity which is quite widely used in daily activities. The activities themselves range from light activities such as writing to strenuous activities such as lifting or exercising. Injuries that can occur to the upper extremity due to the activities are such as injuries to the shoulder, elbow, arm, forearm, wrist, and hand. These injuries generally occur due to wrong movement or position, overuse, work factors, and trauma (1).

Shoulder pain is the third most common musculoskeletal disorder with a prevalence of 10 in 1,000 of all shoulder disorders, with its peak incidence at 42 – 46 years old (25 in 1,000 population) (2). In the age group of ≥ 60 years, 21% were found to have shoulder syndrome which is mostly caused by rotator cuff. However, the actual incidence rate is still difficult to predict because there are many asymptomatic cases (3,4).

The rotator cuff is a muscle group to maintain active stability of the glenohumeral joint as well as act as joint active range of motion (ROM). Rotator cuff tendinopathy is a term to describe an unspecific condition due to overuse and impaired tendon healing process that is characterized by pain and impaired shoulder function (5–7).

Rotator cuff tendinopathy is the leading cause of shoulder pain in all ages. Quite a few nonsurgical therapies have been performed, but the optimal procedure for this case is still being debated. In several systematic

reviews of randomized controlled trials of interventions for shoulder pain, there is little evidence to support the use of general therapy in the management of shoulder pain. Prolotherapy is an alternative and complementary injection therapy of choice for chronic musculoskeletal cases. Hyperosmolar dextrose is a common substrate used for injection (8).

Prolotherapy injection has shown promising effects in several cases like epicondylitis, , plantar fasciitis, hip adductor and achilles tendinopathy and osteoarthritis whereas studies for rotator cuff cases are still few in comparison with these cases (8–11).

This procedure is relatively easy to do, it shortens the rehabilitation period, and the percentage of success in the above cases raises the question of whether this prolotherapy can have a promising effect in cases of rotator cuff impingement. Therefore, we are interested in conducting a systematic review for the effectiveness of hypertonic dextrose injection (prolotherapy) on rotator cuff tendinopathy.

METHODS

We follow the PRISMA-P (Preferred Reposting Items for Systematic Review and Meta-analysis Protocols) 2015 checklist: recommended items to address in a systematic review protocol (12).

Search methods for identification of studies.

Potential studies were identified by searching the electronic database which is the Cochrane Central Register of Control Trials database, PubMed, Embase, CT.gov, CINAHL, and ICTRP with searching periods from their inception until October 2020. "prolotherapy" or "dextrose" and "rotator cuff" were used as the search keywords. The flow of literature search can be identified in fig 1.

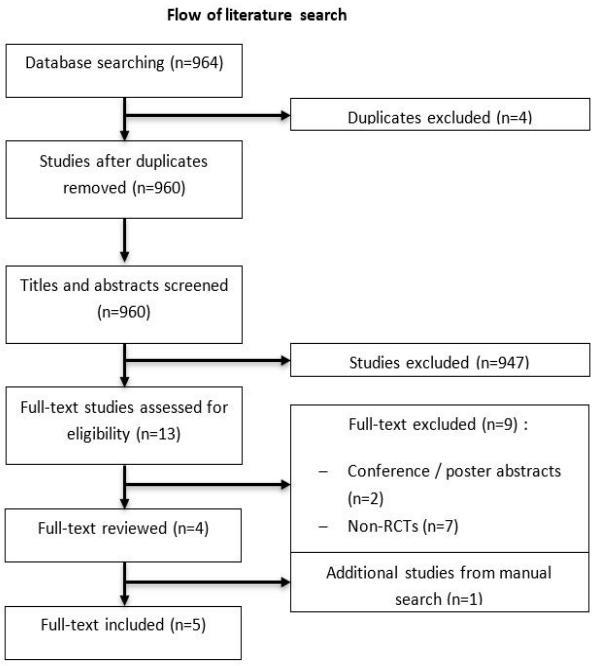

Fig 1.: Flow of Literature Search

Type of Studies

This systematic review included only randomized controlled trials (RCTs). There is no limitation on publication dates.

Type of intervention

Injection using dextrose 12.5% - 25% either using lidocaine 0.5% or not had to be administered to one group within the study with or without ultrasound-guided. Prolotherapy injection site had to include a tendon and/or muscle of rotator cuff with or without additional injection to the peri-articular ligament.

Eligibility Assessment and Data Extraction

Reviewers were performed database screened electronically for titles and abstracts, evaluates potentially relevant full texts, and assessed the eligibility of the full-text articles. For every eligible study, the extracted data were: study design, sample size, age, sex, intervention, control, follow-up, and outcome.

Risk of bias assessment

The risk of bias among all eligible studies was assessed using Risk of Bias visualization tool(13). Assessed risk of bias domains were as following: random sequence generation, allocation concealment, blinding of participants and personnel, blinding of outcome assessment, and incomplete outcome data.

Statistical Analysis

The analysis in this study using descriptive analysis for all eligible studies.

RESULTS

We identified 964 studies from all databases and exclude 4 studies due to duplications. After titles and abstracts screenings, we retrieved 13 studies to be assessed their eligibility. Of these, 9 were excluded for the following reasons: conference/poster abstracts (n=2) and non-randomized controlled trials (RCTs) studies (n=7). After assessing 4 studies, we add 1 more study from a manual search. Five full texts of RCTs were eligible for inclusion. Characteristics of the eligible studies for this systematic review are summarized in Table I.

Eligible studies

Bertrand et al. undertake a double-blind RCT of 73 outpatient with chronic shoulder pain (>3 months) and positive either calcific or non-calcific tendinosis, partial or full-thickness tear by ultrasound scanning. Participants were assigned into 3 different groups: (a) injection mixture of 25% dextrose, 0,1% lidocaine,

Table I. Summary of Eligible Study

Study (year)	Sample Size	Age (SD)	Sex (% female)	Intervention	Re-injection	Control	%Followup (cases - control)	Outcome
Bertrand et al. (2016)	73	53 (13)	37%	Injection Dextrose 25% / lidocaince 0.1% / saline (dextrose prolotherapy) into supraspinatus, infraspinatus, teres minor insertion, coracoid process, biceps long head, subscapularis insertion and inferior glenohumerah ligament with 1 mL solution at each primary sites. Other tender area along the enthesis and adjacent to the primary site were injected at 1 cm intervals, each with 0.5 mL of soulution. All participant will received two physical therapy sessions after each injection session	Injection given at 0, 1 and 2 months	Two control group injected with 0.1% lidocaine/saline at painful enthesis or superficial to painful enthesis (control 1 and control 2 respectively). All participant will receive two physical therapy sessions after each injection session.	6 months after the last injection or at 9 months of the study (100% - 98%)	**VAS: (at baseline and 9 months)** Prolotherapy : 7.3 ± 0.4 and 2.9 ± 0.6* Control 1 : 6.9 ± 0.5 and 1.8 ± 0.7 Control 2 : 6.9 ± 0.4 and 1.3 ± 0.6 **Ultrasound Shoulder Pathology Rating Scale** Prolotherapy : 4.0 ± 0.4 and 3.7 ± 0.5 Control 1 : 4.3 ± 0.5 and 3.7 ± 0.5 Control 2 : 4.3 ± 0.4 and 3.7 ± 0.4
Seven et al. (2017)	120	51 (12)	47%	Ultrasaound-guided prolotherapy solution injection (3.6mL of 25% dextrose and 0.4 mL lidocaine) was injected to the subacromial bursa and a maximum of 20 mL dextrose solution (18mL of 15% dextrose and 2 mL lidocaine) to supraspinatus, infraspinatus, teres minor insertions (tuberculum majus), pectoralis minor, coracobrachialis and biceps brachii insertions (coracoid process) and home exercise program (3 times a day after 3 days of injections)	Injection dropped if the pain score below 75% of baseline, received 6 rounds of injections, or deciding to withdraw	Detailed Physiotherapy program which consisted of 3 sessions per week for 12 weeks (@ 30 minutes per session)	At baseline, 3rd , 6th and 12th weels after the first injection and final follow up at minimum of 12 months (95% - 73%)	**VAS : (at baseline and 12 months, respectively)** Prolotherapy : 7.85 ± 1.29 and 0.89 ± 1,64* Control : 7.36 ± 1.38 and 3.77 ± 2.15 **WORC: (at baseline and 12 months, respectively)** Prolotherapy : 32.21 **± 17.49 and 90.37 ± 10.12*** Control : 37.77 ± 16.03 and 69.08 ± 16.70 **SPADI: (at baseline and 12 months, respectively)** Prolotherapy : 74.76 ± 18.54 and 7.66 ± 10.64* Control : 68.62 ± 20.4 and 34.94 ± 19.14 **ROM Flexion: (at baseline and 12 months, respectively)** Prolotherapy : 126.89 ± 40.89 and 176.57 ± 9.50* Control : 133.75 ± 34.84 and 166.36 ± 16.95 **ROM int.rot : (at baseline and 12 months, respectively)** Prolotherapy : 59.73 ± 26.03 and 68.77 ± 4.25* Control : 56.47 ± 15.56 and 66.02 ± 7.11 **ROM ext.rot : (at baseline and 12 months, respectively)** Prolotherapy : 77.19 ± 17.9 and 88.94 ± 4.09 Control : 79.31 ± 17.30 and 86.59 ± 9.69

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Table I. Summary of Eligible Study(CONT.)

Study (year)	Sample Size	Age (SD)	Sex (% female)	Intervention	Re-injection	Control	%Follow-up (cases - control)	Outcome
George et al. (2018)	12	5 9 (NR)	NR	Ultrasound-guided prolotherapy injection of 0.5 – 1 mL of mixture of 12.5% dextrose solution and 0.5% lignocaine in bacteriostatic water into hypoechoic area on ultrasound. Lignocain was infiltrated along the intended tract prior to injection. Physiotherapy conducted 2 weeks after injection	Single injection	No treatment described for control group	At week 12th after injection (100%-80%)	**DASH: (at baseline and 12 weeks, respectively)** Prolotherapy : 60.14 ± SD NR and 43.89 ± SD NR Control : 56.86 ± SD NR and 46.86 ± SD NR **DASH pain score : (at baseline and 12 weeks, respectively)** Prolotherapy : 3.29 ± SD NR and 1.86 ± SD NR Control : 3.20 ± SD NR and 2.40 ± SD NR **ROM abduction at week 12th** Prolotherapy : +20° ± SD NR* Control : -12° **± SD NR** (No significance difference in horizontal abduction, flexion, extension, int. rotation, ext. rotation and horizontal adduction ROM) **Ratio echogenicity** : Significant increase in echogenicity from baseline to 12th week
Cole et al. (2018)	36	48(6)	33%	Ultrasound-guided prolotherapy solution injection of 25% dextrose (1 mL of 50% dextrose and 1 mL of 1% lignocaine) into anechoic area of the supraspinatus tendon (multiple area depending on how many hypoechoic and anechoic area with no more than 0.5mL soulution being injected to each area). All patient advised to start home rehabilitation program at 2 week after injection	Single injection	Ultrasound-guided corticosteroid injection (1 mL of 40mg/mL methylprednisoline acretate and 1mL of 1% lignocaine) into subacromial bursa adjacent to the tendinopathic area of supraspinatus. All patient advised to start home rehabilitation program at 2 week after injection	At 6 week, 3 month and 6 month (88% - 84%)	**Likert Pain Score : (at baseline and 6 months, respectively)** Prolotherapy : 2.38 ± 0.22 and 2.12 ± 0.22 Control : 2.42 ± 0.2 and 1.92 ± 0.32 **Impingement Syndrome : (at baseline and 6 months, respectively)** Prolotherapy : 100% and 24% Control : 100% and 26% **Shoulder Strength Score :** No significance difference between prolotherapy and control group at ext. rotation, int. rotation, supraspinatus and lift off strength. **Shoulder ROM :** No difference between prolotherapy and control group at flexion, abduction, and ext. rotation ROM

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Table I. Summary of Eligible Study (CONT.)

Study (year)	Sample Size	Age (SD)	Sex (% female)	Intervention	Re-injection	Control	%Follow-up (cases - control)	Outcome
Lin et al (2019)	31	47(5.8)	39%	Ultrasound-guided prolotherapy solution injection of 5 mL of 20% hypertonic dextrose solution (4 mL of 50% dextrose and 1 mL normal saline) into supraspinatus tendon insertion site. All patient received rehabilitation specific for stenghtening and ROM exercises	Single injection	Ultrasound-guided normal saline injection at supraspinatus tendon insertion site	At baseline, 3rd week and 6th week (100%-100%)	**VAS : (at baseline and 6 week, respectively)** Prolotherapy : 5.56 ± 0.81 and 5.13 ± 0.72 Control : 5.33 ± 0.82 and 4.87 ± 0.64 **SPADI : (at baseline and 6 week, respectively)** Prolotherapy : 60.5 ± 7.87 and 61.56 ± 4.68 Control:65.0±2.78and60.0±4.9 **ROM Flexion: (at baseline and 6 week, respectively)** Prolotherapy : 157.15 ± 13.40 and 159.38 ± 7.50 Control : 156.21 ± 6.51 and 161.20 ± 159.38 **ROM abduction : (at baseline and 6 week, respectively)** Prolotherapy : 146.66 ± 13.96 and 148.69 ± 8.89 Control : 140.46 ± 13.35 and 145.93 ± 14.7 **ROM int.rot : (at baseline and 6 week, respectively)** Prolotherapy : 45.0 ± 8.17 and 45.0 ± 8.17 Control : 44.67 ± 7.32 and 44.67 ± 7.24 **ROM ext.rot : (at baseline and 6 week, respectively)** Prolotherapy : 57.50 ± 10.65 and 61.25 ± 8.27 Control : 60.0 ± 8.45 and 62.33 ± 4.17 **Ultrasound morphological measurements :** no significance difference for supraspinatus thickness, echogenicity mean and echogenicity ratio at baseline compared to 6th week post injection

Table I. Summary of eligible studies. VAS = Visual Analog Scale; SPADI = Shoulder Pain and Disability Index; Ext.rot = External Rotation; Int.rot = Internal Rotation, ROM = Range of Motion; SD = Standart Deviation; NR = Not Reported. *p<0.05 compared to control.

and saline into 9 entheses around shoulder gridle, (b) injection of 0.1% lidocaine and saline at painful entheses, or (c) superficial to painful entheses. Either study group or control group will receive two sessions of physical therapy after each injection session. The patients received reinjection at 1st and 2nd months after the first injection. All of the patients were evaluated at the 3rd and 9th months after the first injection for their Visual Analog Scale (VAS) as the primary outcome and Ultrasound Shoulder Pathology Rating Scale (USPRS) as the secondary outcome which evaluated supraspinatus tendinosis (calcific or non-calcific) and tear (partial or full-thickness). There is one case of adhesive capsulitis in the enthesis group that cause loss to follow-up. At final follow-up on 9th month after the first injection, there was a reduction of VAS 2.9 ± 0.6 vs 1.8 ± 0.7 vs 1.3 ± 0.6 from enthesis dextrose, enthesis saline, and superficial saline group, respectively. The significant reduction of VAS only occurred between enthesis dextrose and superficial saline group, not with enthesis saline group. For USPRS, there was no significant difference that was noted with a score of 3.7 ± 0.5 vs 3.7 ± 0.5 vs 3.7 ± 0.4

for enthesis dextrose, enthesis saline, superficial saline group at 9 months, respectively. Based on those findings, the author concludes that injection using a mixture of dextrose 25%/0.1% lidocaine/saline was superior for improvement in long-term pain (14).

Seven et al. undertake a prospective RCT of 120 patients to compare ultrasound-guided prolotherapy solution injection (3.6 mL of 25% dextrose and 0.4 mL lidocaine injected on subacromial bursa plus 18mL of 15% dextrose and 2 mL lidocaine at enthesis around the shoulder) with detailed physiotherapy and exercise program in patients with chronic rotator cuff injury. The injection was stopped if the pain score below 75% of baseline, already received 6 rounds of injections, or deciding to withdraw. The patients were evaluated for VAS scale, the Western Ontario Rotator Cuff Index (WORC), the Shoulder Pain and Disability Index (SPADI), and active ROM at baseline, 3rd week, 6th week, 12th week and 12th month. 19 patients were excluded (16 in control group and 3 in prolotherapy group) due to incomplete evaluation, adverse events, and dissatisfaction. This study found that prolotherapy had a significant difference in VAS score, WORC, SPADI, active ROM (flexion, abduction, and internal rotation) compared to control group ($p<0.05$). Only for active external rotation ROM that showed no significant difference. For clinical outcome, start from evaluation at the 6th and 12th week, there was a significant difference for prolotherapy. Furthermore, for shoulder ROM we can see a significant difference at one-year evaluation. Based on this finding, we conclude that prolotherapy has shown superiority in terms of reducing shoulder pain and improvement of ROM in long-term (15).

George et al. undertake a prospective randomized controlled trial of 12 patients to compared ultrasound-guided prolotherapy injection to control group (not reported about the treatment for control group). The solution is a mixture of 12.5% dextrose and 0.5% lignocaine in bacteriostatic water and injected into the hypoechoic area on ultrasound. Before injection, needling was performed at the area of tendinosis and physiotherapy then resumed again at 2 weeks post-injection. However, in the 12th week, there is one patient in the control group who did not include in the study due to the development of full-thickness tear. This study showed that prolotherapy gave a significant difference for sleep improvement compared to control ($p<0.05$). As for another DASH indicator like function and pain, this study found decreasing of pain score compared to control but no statistical difference. For ROM, there was a 20° improvement in abduction ROM with $p<0.05$. Moreover, there is a significant difference in echogenicity improvement of tendinosis from baseline to 12th week (16).

Cole et al. undertake a prospective, randomized, double-blinded clinical trial of 76 patients with a minimum of 3 months of symptomatic supraspinatus tendinopathy. This study compared ultrasound-guided prolotherapy solution of 25% dextrose (1 mL of 50% dextrose and 1 mL of 1% lignocaine) injection into hypoechoic or anechoic area of supraspinatus tendon to corticosteroid injection (1 mL of 40mg/mL methylprednisolone acetate and 1mL of 1% lignocaine) into subacromial bursa adjacent to the tendinopathic area of supraspinatus. This study only did a single injection to all patients. Either prolotherapy or control group was suggested to start a home rehabilitation program at the 2nd-week post-injection. The evaluation was conducted at the 3rd weeks, 3rd months, and 6th months after the first injection. There was a statistically significant improvement in the sign of impingement, pain triggered by overhead activities, frequency of pain at night, overall shoulder satisfaction, ultrasound morphology, forward flexion ROM and supraspinatus strength at 6th-month post-intervention compared to baseline in both groups. However, there were no significant differences between-group at 6 months of follow-up (17).

Lin et al. undertake a randomized double-blind placebo-controlled trial of 31 outpatients with chronic supraspinatus tendinopathy and shoulder pain for more than six months. The study group received one dose of an ultrasound-guided 20% dextrose solution (4 mL of 50% dextrose and 1 mL normal saline) injection at supraspinatus enthesis, whereas the control group received one dose of 5% normal saline through the same method. All patients only received a single injection. VAS scale, SPADI, active ROM (flexion, abduction, internal rotation and external rotation), and ultrasound morphological were recorded at baseline, 2-weeks, and 6-weeks after the first injection. There was no patient lost to follow-up. At the final follow-up, there was no significant difference in any measured outcome either VAS, SPADI, active ROM, or ultrasound morphological within or between groups (18).

Risk of Bias

All the studies rated as low-risk bias for random sequence generation domain, except George et al due to use odd and even number despite the fact still use random digit selection process. For allocation concealment domain, Bertrand et al. and Lin et al. were rated as low risk, Seven et al rated as unclear due to no explanation about the allocation of the participant and for George et al. and Cole et al. were rated as high risk due to using odd and even allocation and the different treatment for each group, respectively. Similar to the risk of allocation concealment domain, Bertrand et al. and Lin et al. also rated as low risk of blinding of participants and personnel, whereas the rest of the study rated as high risk due to the treatment and location for injection was different. All the studies were rated as low risk of blinding of outcome assessment, except George et al which remain unclear due to not mentioned either the

assessor was blinded or not. Seven et al and George et al were rated as high risk of incomplete outcome data due to high rate of loss to follow-up. Similar cases occurred in Cole et al. studies, but all patients who could not attend the follow-up submitted subjective scores via phone or e-mail. Summary and graph plot for risk of bias is presented in Fig 2 and Fig 3.

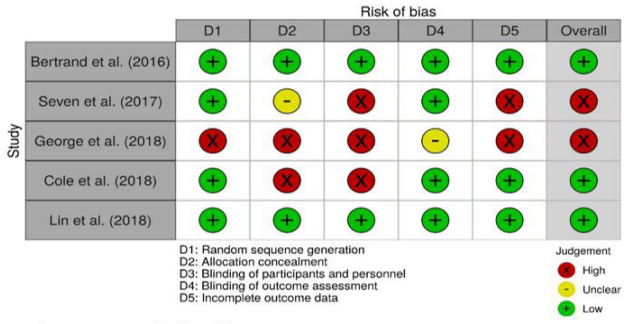

Fig 2: Summary of risk of bias

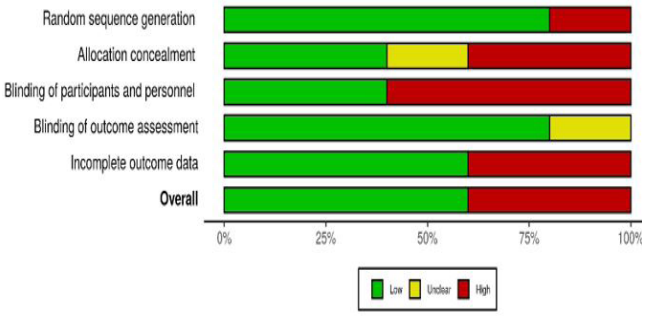

Fig 3: Graph of Risk of bias

DISCUSSION

The first thing we can clearly see from all eligible studies are a difference in the intervention (injection site), injection technique and total of injection. Multi-site injection in Bertrand et al. and George et al showed a better mean VAS score improvement than single-site injection. The mean VAS score improvements are 5.4, 6.69 and 0.43 for Bertrand et al, George et al, and Lin et al, respectively. The first two scores demonstrate clinically and statistically significant improvements with minimal clinically important difference (MCID) for VAS score is 1.4 points (19). Further research is necessary to find the effect of multi-site injection for pain improvement.

Seven et al, clearly found that there are significant active ROM improvement in long-term and this finding contrast with Cole et al that found no significant improvement in active ROM. This result may occur due to differences in injection site and total of injection. From this comparison, we could see that multi-site injection combined with multi injection will benefit active ROM. Meanwhile, Seven et al have high-risk of bias due to non-blinding trials and a high rate of loss to follow up. In this setting, we cannot conclude yet the benefit of multi-site and multi injection in long-term evaluation for chronic rotator cuff tendinopathy. However, George et al, using single-site and single-injection technique, found that there is a significant short-term improvement for active abduction ROM, but this study also rated with high-risk of bias.

Trebinjac et al and Lee et al in their retrospective uncontrolled study and retrospective case-control study, respectively, while using a similar technique (multi-site and multi injection) but without ultrasound-guided also found similar findings like Seven et al. They found statistically and clinically long-term VAS score and SPADI improvement (9,20). Due to those finding, another study is better to conducted to see the beneficial effect of multi-site and multi injection for pain and function improvements.

SPADI, DASH, and WORC scores are used to evaluated shoulder function. Lin et al did not find any significant statistical difference in SPADI, while Seven et al found it. Mean SPADI score improvement in prolotherapy injection at 6-weeks for Lin et al and Seven et al, respectively, are -1.1 point and 43.5 point. There is a worsening mean SPADI score in Lin et al study. MCID for SPADI is 8 – 13 point (21). Based on MCID point, Seven et al had clinically significant improvement for SPADI. DASH score was used by George et al to assess shoulder function clinically. With single-site and single-injection technique, George et al found significant improvement in DASH score, albeit only clinically not statistically. MCID for DASH score is 10.2 point (21) and DASH score improvement in George et al study was 16.25 point. Besides SPADI, seven et al also use WORC to assess shoulder function in patients who receive prolotherapy injection. The mean improvement WORC score in Seven et al study was 58,16 point with MCID for WORC is 11.7 point(22). This point showed significant improvement in the clinical setting and also Seven et al found it statistically significant ($p<0.05$).

Ultrasound morphology is also one of the outcomes measured to assess objectively prolotherapy efficacy for patients with chronic rotator cuff tendinopathy. Bertrand et al and Lin et al in their study did not found significant improvement on shoulder ultrasound either long-term or short-term, respectively. In contrast with those findings, George et al found a significant improvement in echogenicity ratio in the short-term, although we know that George et al study has a high risk of bias and Bertrand et al and Lin et al rated as low risk of bias. This bias can affect the result of the study either become better or worse. Therefore, future study also needed to find a better conclusion on which injection technique will give a better outcome in terms of ultrasound morphology.

Platelet-rich plasma (PRP) is a well-known therapy for rotator cuff tendinopathy. An RCT conducted by Rha et

al and Shams et al, showed that PRP had a superior effect in VAS score and SPADI compared to dry needling and corticosteroid injection, respectively (23,24). However, there still no trials to compared PRP and prolotherapy using hyperosmolar dextrose.

The limitation of this systematic review is the quality of the eligible study, as 2 out of 5 demonstrate an overall high risk of bias. Other than that, this review is also limited by heterogenicity in intervention technique, total of injection, dextrose concentration, and location of injection. The pathology for included criteria also widely varies from tendinosis to supraspinatus tear. All the included studies did not include complications in their outcome. Even though a few studies reported some complications, we do not know its significance clinically or statistically. This study unable to conduct a meta-analysis due to widely variable in dextrose intervention, control group, follow-up time, and outcome. Lastly, for now, this systematic review provides the best possible evidence about prolotherapy hypertonic dextrose injection although 2 out of 5 studies included rated as high risk of bias.

CONCLUSION

From this systematic review, we found a contrast result that prolotherapy hypertonic dextrose injection can significantly improve pain, function, and ROM in patient with rotator cuff tendinopathy. This result may occur due to a wide variety of intervention techniques, follow-up period, and control. This review also found that prolotherapy does not have a superior effect compared to saline enthesis and corticosteroid. Also, this study can not find which injection technique (multi-site or single site), and how much injection needed to have a beneficial effect for rotator cuff tendinopathy. Further study needed to know what factors that affecting prolotherapy hypertonic dextrose injection in rotator cuff impingement patients, either the beneficial effect or the complication.

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