

Knee OA 2013 (Dextrose vs Saline vs In-Home Exercise

- Rabago D, Patterson JJ, Mundt M, Kijowski R, Grettie J, Segal NA, Zgierska A **Dextrose prolotherapy for knee osteoarthritis: a randomized controlled trial.** Ann Fam Med. 2013 May-Jun;11(3):229-37.

[Commentary by K. Dean Reeves, M.D. www.DrReeves.com]

One level I study considered was published in the Annals of Family Medicine in 2013. This was a well designed randomized controlled study double blinded between dextrose injection and saline injection and also with a random assignment to in-home exercise. There is a free PDF of the whole article at <http://www.annfammed.org/content/11/3/229.full?sid=cf599129-aa40-4ec3-8776-4ef8b83034fe>

Here is a news article on the paper which is easy reading

<http://www.medicaldaily.com/articles/15890/20130524/sugar-water-injections-knee-pain-arthritic-knees-prolotherapy.htm>

Here is the abstract (and the following two slides will summarize)...

PURPOSE

Knee osteoarthritis is a common, debilitating chronic disease. Prolotherapy is an injection therapy for chronic musculoskeletal pain. We conducted a 3-arm, blinded (injector, assessor, injection group participants), randomized controlled trial to assess the efficacy of prolotherapy for knee osteoarthritis.

METHODS

Ninety adults with at least 3 months of painful knee osteoarthritis were randomized to blinded injection (dextrose prolotherapy or saline) or at-home exercise. Extra- and intra-articular injections were done at 1, 5, and 9 weeks with as-needed additional treatments at weeks 13 and 17. Exercise participants received an exercise manual and in-person instruction. Outcome measures included a composite score on the Western Ontario McMaster University Osteoarthritis Index (WOMAC; 100 points); knee pain scale (KPS; individual knee), post-procedure opioid medication use, and participant satisfaction. Intention-to-treat analysis using analysis of variance was used.

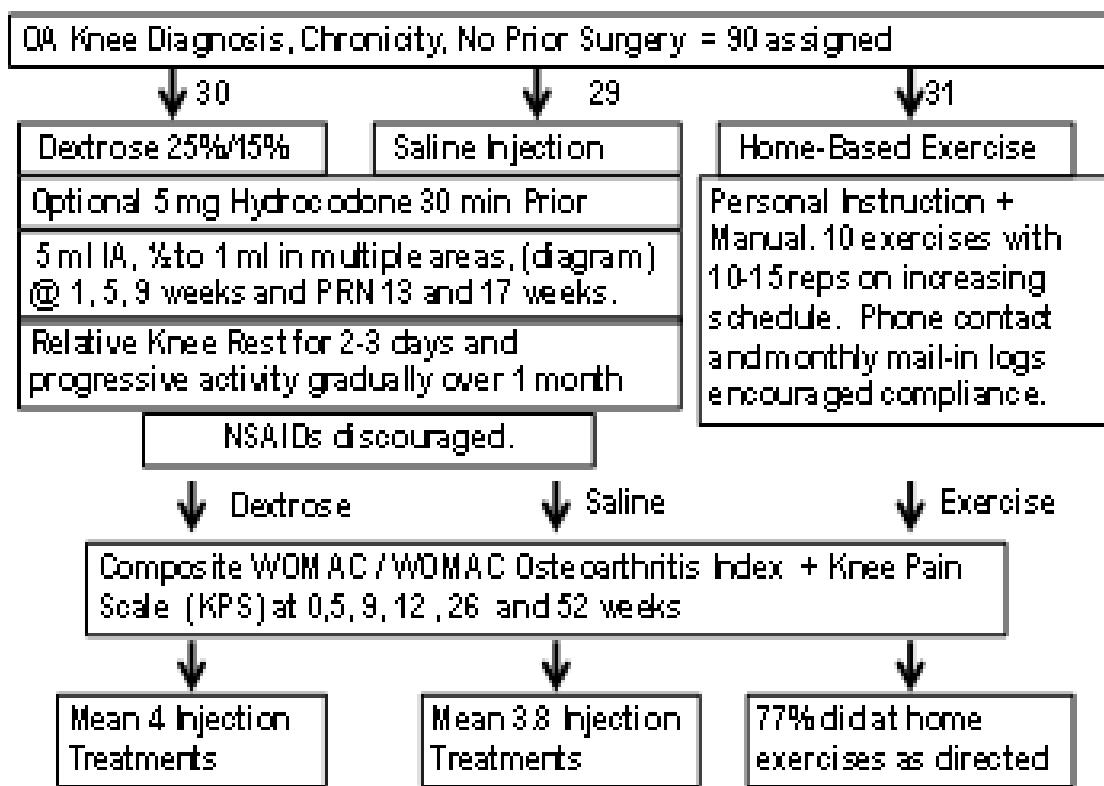
RESULTS

No baseline differences existed between groups. All groups reported improved composite WOMAC scores compared with baseline status ($P <.01$) at 52 weeks. Adjusted for sex, age, and body mass index, WOMAC scores for patients receiving dextrose prolotherapy improved more ($P <.05$) at 52 weeks than did scores for patients receiving saline and exercise (score change: 15.3 ± 3.5 vs 7.6 ± 3.4 , and 8.2 ± 3.3 points, respectively) and exceeded the WOMAC-based minimal clinically important difference. Individual knee pain scores also improved more in the prolotherapy group ($P = .05$). Use of prescribed postprocedure opioid medication resulted in rapid diminution of injection-related pain. Satisfaction with prolotherapy was high. There were no adverse events.

CONCLUSIONS

Prolotherapy resulted in clinically meaningful sustained improvement of pain, function, and stiffness scores for knee osteoarthritis compared with blinded saline injections and at-home exercises.

General Method 2013 Knee RCT



Subject were randomly assigned to either at-home exercise or blinded injection of either dextrose prolotherapy or saline injection. Injections were both extra and intraarticular. Next subjects either received dextrose injection or a home-based program exercise program.

Those that received injection were given the option of receiving a single pain pill prior to injection. Then they were injected with either dextrose or saline in a method described in the next slide. Injections were given 3 times at weekly intervals than then as needed with relative rest for 2-3 days afterward. Those assigned randomly to home-based exercise were given a manual with 10 exercises, which were demonstrated in person. They then were contacted intermittently for encouragement and to answer questions about the exercises. Monthly mail in logs were utilized through the first 6 months to encourage and document compliance further.

Subjects were informed that this was standard of care treatment and that they would likely be candidates for a follow-up study that would involve dextrose injection to further encourage compliance with exercises.

Those that received dextrose injection received 6.5 ml of 25% dextrose in the knee via a knee-bent approach without ultrasound guidance and 15% dextrose into collateral ligaments in each side. This was given every 4 weeks up to 4 treatments)

The primary measuring tool was the WOMAC (Western Ontario and McMaster Universities Osteoarthritis Index) which has 24 items with 5 points each. Five items are for pain, 2 are for stiffness and 17 are function related.

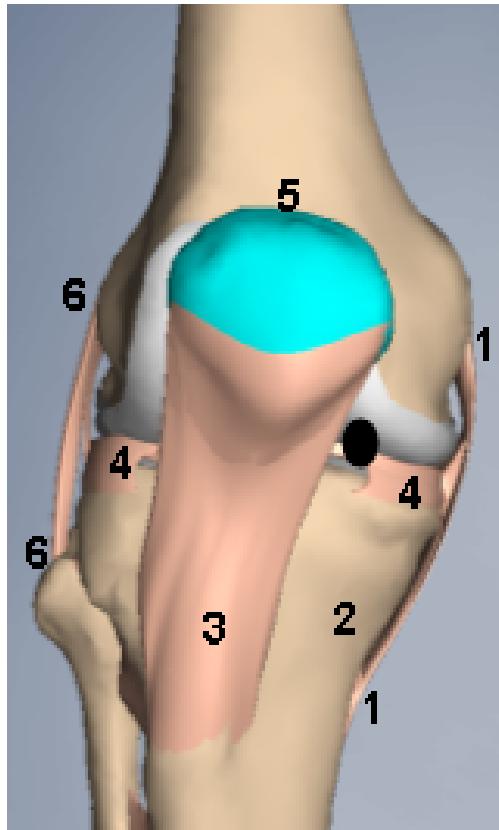
A Knee pain scale was also used.

For simplicity we will consider the WOMAC results, since the results from the two main scales parallel each other.

INJECTION METHOD

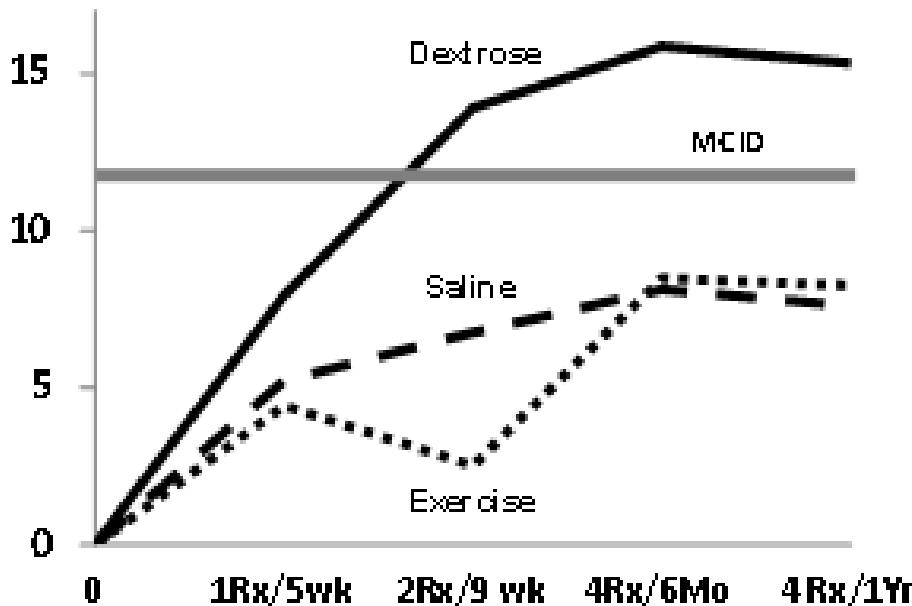
6 ml of 25% dextrose was injected in the knee via an infero medial approach. (Solid circle) 15% dextrose was then injected in 0.5 ml aliquots in up to 3 areas using skin slide and redirection with each of up to 15 separate sites for a maximum of 22.5 ml. Areas emphasized included

- 1: Medial collateral ligament origin and insertion.
- 2: Pes anserine attachment.
- 3: Tibial tuberosity/patellar ligament insertion.
- 4: Medial and lateral coronary ligaments.
- 5: Superior patella at quads insertion, medial patella at retinacular attachments, and inferior patella and patellar ligament origin, and
- 6: Lateral collateral ligament origin and insertion



This study involved much more injections at one time than the previous single injection study earlier. This is a depiction of areas of injection. This would be expected to address more mechanical structures of importance outside the knee and potentially nerve structures as well since many of the injections were of superficial structures which would be the equivalent of perineural subsutaneous injection. Overall, this study involved contact with deep structure with intention of repair and would be considered prolotherapy.

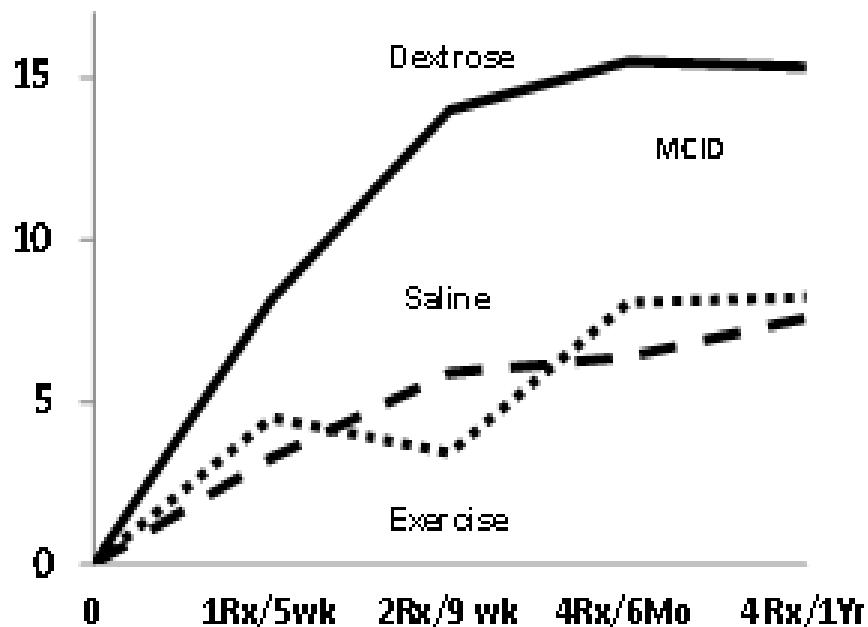
WOMAC IMPROVEMENT OVER TIME Significant Difference by 2 Rx



This graph shows changes over 1 year in the well-accepted WOMAC score. The improvement in the dextrose group was 24%, and the improvement in excess of 15 exceeds the level that clearly indicates a clinically significant improvement (MCID = minimal clinically important difference). The solid black line represents the results in knees treated with dextrose. The dash line is the saline group result and the dotted line is the exercise group result.

Note that exercise is the standard of care. However the standard of care is not necessarily effective care. This study suggests that dextrose prolotherapy may improve upon standard care of knee osteoarthritis for certain patients. This is not a large study but reinforces results in other studies to be summarized below.

WOMAC PAIN IMPROVEMENT OVER TIME Significant Difference by 2 Rx



This graph shows changes over 1 year in the pain subscale of the WOMAC. The important thing to notice is that pain improvements were clearly diverging in the dextrose treated subjects even after only 1 treatment. It is also important to notice that the improvement was measured at 5 weeks which is too early for useful repair to occur. This suggests that there is an effect of dextrose other than repair. This would likely be an effect via decreasing nerve sensitivity in the region. (See information on perineural injection seen above)

2013 Knee RCT Strengths/Weaknesses

REC	2013 Knee OA Crossover (Rabago et al)	
Good Size	Moderate to somewhat small size	
Sig Clinically	Yes.	
Sig Statistically	Yes.	
Adequate F-UP	Yes	
Data Capture	Yes	
Accepted Tool	Excellent tool choice	
Simple	No. Multiple area of injection.	
Inexpensive	Yes in materials. Moderate in terms of time	
Min invasive	Yes in terms of surgery. Moderate in # injections	
Grade	Ia-	

This is a summary of the strengths of this study, with size somewhat small, and complexity of injection amount the only observed limitations. The key is that this and the following study both indicate that dextrose injection is better than standard of care exercise. This study suggests another mechanism of dextrose other than repair alone, given speed of improvement in pain. However, as there were still significant numbers of partial responders, it also suggests that not all pain sources in the knee were treated by this method.