e-ISSN: 0975-1556, p-ISSN:2820-2643

Available online on www.ijpcr.com

International Journal of Pharmaceutical and Clinical Research 2023; 15 (12); 1331-1336

Original Research Article

Dextrose Prolotherapy in Osteoarthritis of Knee Joint

Vaibhav Bhadbhade[1], Anand B Jabshetty[2]

[1]Assistant Professor, Department of Orthopaedics, BRIMS, Bidar, Karnataka
[2]Professor and HOD, Department of Orthopaedics, BRIMS, Bidar, Karnataka

Received: 25-09-2023 / Revised: 02-10-2023 / Accepted: 05-10-2023
Corresponding author: Dr. Vaibhav Bhadbhade
Conflict of interest: Nil

Abstract:

Introduction: Osteoarthritis (OA) of knee joint is a chronic, progressive, and joint disabling disease, often resulting in a poor quality of life. Knee osteoarthritis often results in joint pain, stiffness, and decreased function. The Agency for Healthcare Research and Quality has called for the development of new therapies to prevent and treat knee osteoarthritis. These include hypertonic dextrose prolotherapy, ozone, botulinum toxin, platelet-rich plasma, and hyaluronic acid.

Materials and Methods: This prospective study enrolled patients from orthopaedic OPD who were given intra-articular hypertonic dextrose solution which was blinded by normal saline, at BRIMS Teaching Hospital, Bidar , Karnataka. Injections were given at 0, 4, and 8 weeks with additional session at 16 weeks. The primary outcome measure was change in knee-related quality-of-life as assessed by the composite score of Western Ontario McMaster University Osteoarthritis Index (WOMAC)

Results: Of the 205 participants considered for inclusion in the study, 76 met eligibility criteria and were enrolled and divided into 2 groups containing 38 participants each. The study participants had a mean age of 63.2 years, 71% were female, 21% were overweight, and 46% were obese. Mean duration of knee pain was 8.9 years.

Conclusion: According to our results, dextrose prolotherapy appears to be more effective for pain reduction and function improvement. More studies and better methodological quality are needed to establish a better level of evidence on the efficacy and safety of using dextrose prolotherapy in patients with knee OA.

Keywords: Prolotherapy, hypertonic dextrose, osteoarthritis of knee joint.

Introduction

Osteoarthritis (OA) of knee joint is a chronic, progressive, and joint disabling disease, often resulting in a poor quality of life. It is common in the adult population with a lifetime risk of symptomatic knee osteoarthritis of 45%[1]. Knee osteoarthritis often results in joint pain, stiffness, and decreased function[2]. Sources of pain include intra-articular and supportive extra-articular structures[3]. Contrary to previous belief that OA was simply a degenerative joint disease, on-going research has shown that the pathogenesis of OA is much more complex than just a degenerative process[4].

At present, available treatments are focused mainly on symptom relief and improvement of joint disabilities rather than modifying the disease progression. There is on-going research on various disease-modifying treatments that regulate cartilage catabolism and anabolism, inflammation control, and remodeling of sub-chondral bone[5]. The Agency for Healthcare Research and Quality has called for the development of new therapies to prevent and treat knee osteoarthritis[6]. These include hypertonic dextrose prolotherapy, ozone, botulinum toxin, platelet-rich plasma, and hyaluronic acid[7]. Dextrose is low-cost and widely-available in the clinical setting. Intuitively, dextrose prolotherapy appears to be a promising alternative injection-based therapeutic procedure for managing chronic painful musculoskeletal conditions. Modern applications of prolotherapy date back to the 1950s, with increased interest by physicians and patients in the 1990s.

A core principle is the injection of small volumes of an irritant solution at multiple painful ligament and tendon insertions and in adjacent joint spaces over several treatment sessions[8]. This incites body's healing response. (figure 1)

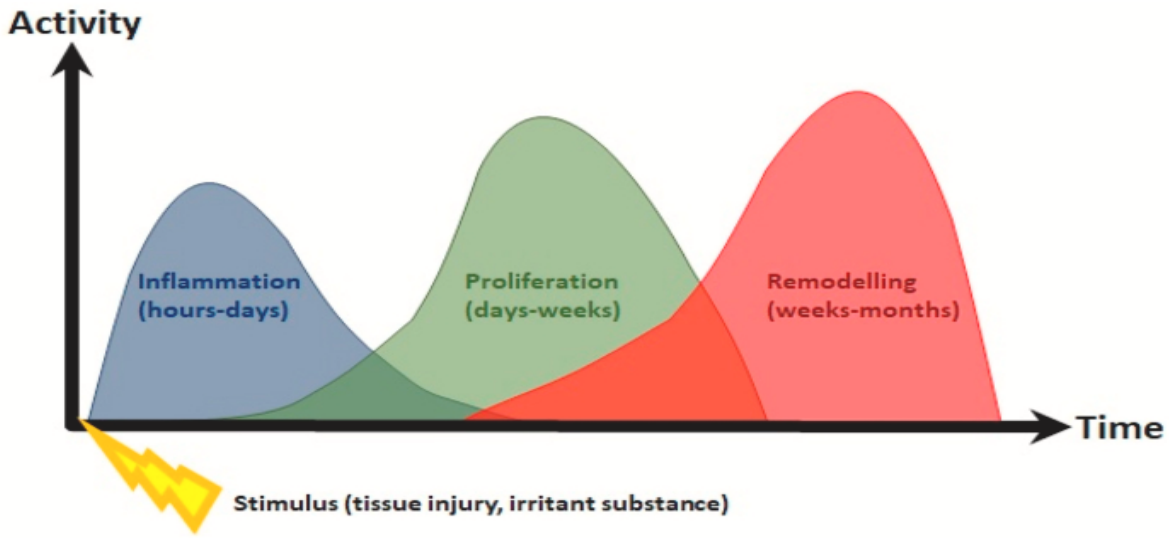

Figure 1: Relationship of prolotherapy to the tissue injury timeline

Despite the various guidelines recommending against dextrose prolotherapy, randomized trials of prolotherapy continued to emerge in recent years with a growing body of literature review, especially in 2016 and 2017. These reviews suggested positive benefits of using prolotherapy for various functional domains of OA[9].

Materials and Methods

This prospective study enrolled patients from orthopaedic outpatient department who were given intra-articular hypertonic dextrose solution which was blinded by normal saline, at BRIMS Teaching Hospital, Bidar, Karnataka, India and outcome was assessed for 52 weeks (Sept 2023).

Inclusion Criteria

1. Symptomatic knee joint pain patients other than traumatic cause, and diagnosis of knee osteoarthritis based on clinical criteria (American College of Rheumatology), identification of knee osteoarthritis by a radiologist on present knee radiograph;
2. Age criteria are 45-75 years.

Exclusion Criteria

1. 1.Patients with grade 4 osteoarthritis, septic knee arthritis, ligaments injury around knee were excluded;
2. Pregnancy, diabetes, anticoagulation therapy, history of total knee replacement, prior knee prolotherapy, any other knee injection within 3 months.

Injection Regime: Injections were given at 0, 4, and 8 weeks with additional session at 16 weeks. Before the procedures the dextrose and saline syringes were blinded using an opaque paper sleeve.

Participants were offered an optional single stat 200-mg ibuprofen tablet 30 minutes before injection. The injector examined the knee, marked infero-medial entry point, placed anesthetic skin wheals of 1% lidocaine, and performed intra-articular injections according to a protocol, ie in a 10-mL syringe: 5 ml 50% dextrose + 5 ml 2% lidocaine. The 6-mL intra-articular injection was then delivered using an inferomedial approach . Ultrasound guidance was not used. After the injection, participants were offered 500mg acetaminophen tablets to use as needed for up to 1 week. They were discouraged from using Nonsteroidal anti-inflammatory drugs (NSAIDs) and from starting new therapies for their osteoarthritis during the study period. Patients were advised on relative knee rest for 2 to 3 days with progressive resumption of routine activity over 1 month. The primary outcome measure was change in knee-related quality-of-life as assessed by the composite score of Western Ontario McMaster University Osteoarthritis Index (WOMAC), a validated questionnaire evaluating osteoarthritis severity using pain, stiffness, and function subscales[10].

The WOMAC composite score, constructed as the weighted average of the 3 subscale scores, ranges from 0 (worst) to 100 (best) knee-related quality-of-life[11]. Secondary outcomes included the knee pain scale (KPS)[12] , a validated questionnaire assessing knee pain frequency (0 to 4 ordinal scale) and severity (0 to 5 ordinal scale), with higher values indicating worse symptoms. KPS data were collected separately for each treated knee and for untreated knees. The WOMAC and KPS scores were collected in person and before any procedure at baseline, 4, 8, and 16 weeks, and by telephone at 52 weeks. Tertiary outcomes for injection participants included,

1. Ratings of procedure-related pain severity, using a 1 to 7 ordinal scale, obtained immediately after and 2 days after each injection session;

2. Daily logs of opioid medication use (yes/no) during the 7 days after each injection.

Treatment satisfaction was assessed among all participants at 52 weeks with the question, "Would you recommend the therapy you received in this study to others with knee osteoarthritis like yours? (Yes/no)." All participants were able to make brief qualitative comments about their experiences. Demographics, self-reported weight and height, and severity of knee osteoarthritis seen on knee radiographs were collected at baseline to characterize the sample and to evaluate as covariates for statistical analysis. Attendance at injection sessions was tracked. Blinding of the injector and injection participants was assessed at each injection session by asking each to identify the participant's group assignment using the items "dextrose," "saline," or "don't know."

Adverse Outcomes

Overall, there were no serious adverse events reported apart from self-limiting post-injection pain and bruises.

Results

Of the 205 participants considered for inclusion in the study, 76 met eligibility criteria and were enrolled and divided into 2 groups containing 38 participants each (figure 2).

All participants completed the baseline questionnaire and were included in the intention-to-treat analysis.

Participants adhered to the protocol of 4 planned injections except for 1 participant that missed the last injection. Two participants in the Normal Saline group were lost to follow-up.

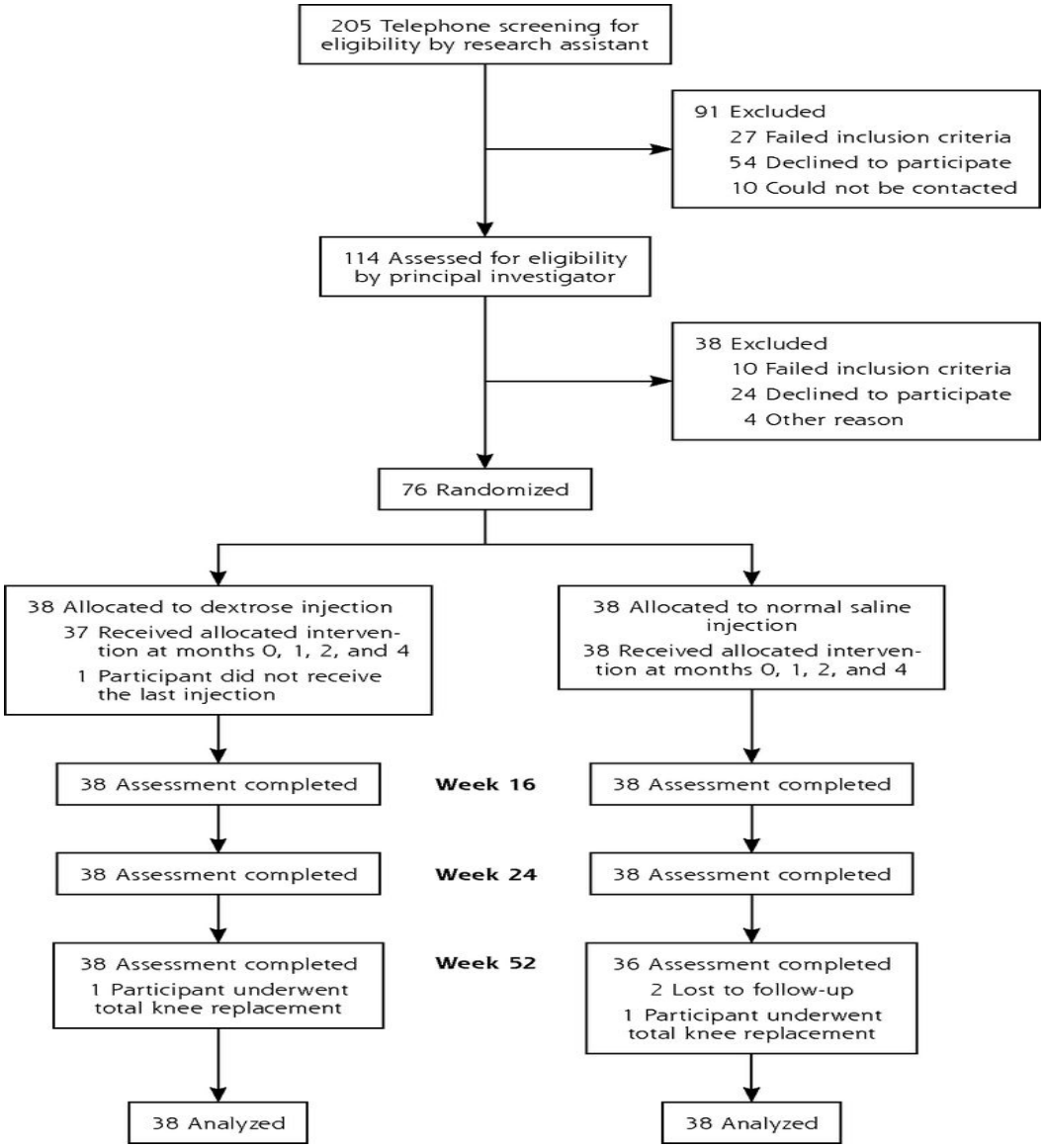

Figure 2: Study flowchart

The study participants had a mean age of 63.2 years, 71% were female, 21% were overweight, and 46% were obese. Mean duration of knee pain was 8.9 years.

In our primary linear mixed models analysis, all outcomes demonstrated a positive trend favoring the dextrose prolotherapy group over the Normal Saline group. The WOMAC pain score at 52 weeks showed a difference-in-difference estimate of −10.34 (95% CI, −19.20 to −1.49, P = 0.022). The improvement was confirmed by the overall trend of −8.26 (95% CI, −14.83 to −1.69, P = 0.014). Similar favorable effect was shown on the difference-in-difference estimate on WOMAC function score of −9.55 (95% CI, −17.72 to −1.39, P = 0.022), the WOMAC composite score of −9.65 (95% CI, −17.77 to −1.53, P = 0.020), knee pain scale (KPS) of −10.98 (95% CI, −21.36 to −0.61, P = 0.038)(fig 3).

In terms of treatment satisfaction, 94.7% in the dextrose prolotherapy group and 91.7% in the Normal Saline group reported that they would recommend the treatment to others (P = 0.670).

The within-group improvements in the WOMAC composite scores of the dextrose prolotherapy group and in the Normal Saline groups were 20.9 and 9.4, respectively.

One participant in each group underwent a total knee replacement between 26 and 52 weeks.

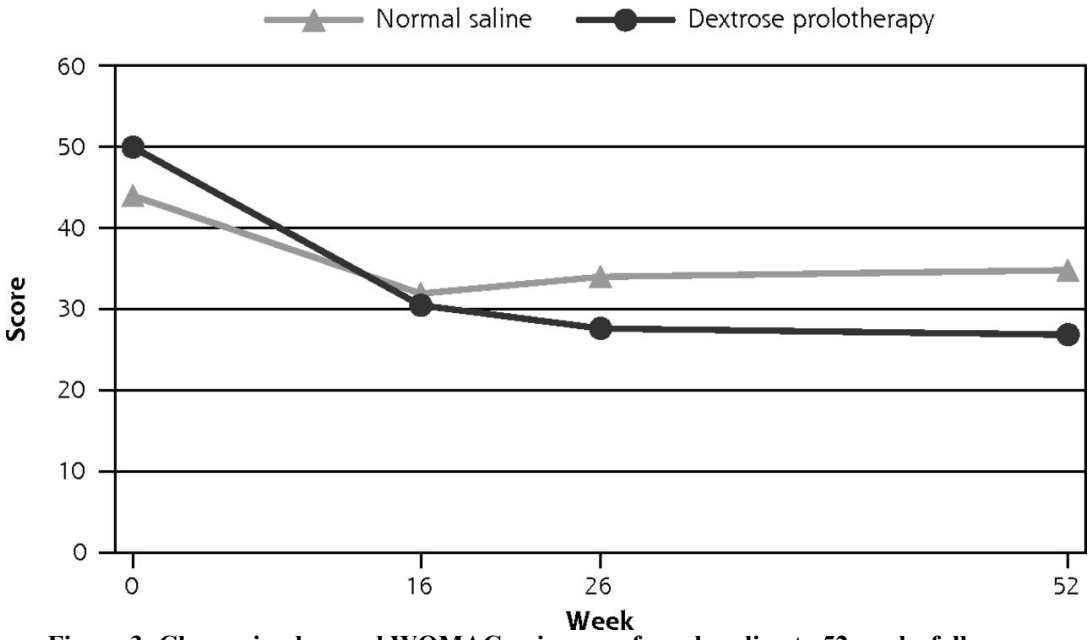

Figure 3: Change in observed WOMAC pain score from baseline to 52 weeks follow up.

Discussion

Our main objective was to evaluate the efficacy and safety of prolotherapy with dextrose in patients with osteoarthritis of knee joint. Clinical studies have reported favorable effects of hypertonic dextrose for knee OA treatment. Case series studies[13,14,15] show that dextrose prolotherapy application in patients with knee OA promotes pain reduction and improves function during approximately 12 months or longer without generating adverse events; nevertheless, the absence control groups limits the strength of these findings. Participants in that study were slightly more symptomatic at baseline but reported similar overall effects at 52 weeks on WOMAC and KPS outcome measures; uninjected contralateral knees also showed significant improvement, suggesting that dextrose prolotherapy for more symptomatic knee osteoarthritis may also result in improvement of the un-injected side, likely through reduction in compensatory mechanisms[16]. The mechanism of action for dextrose is unclear. Hypertonic dextrose has been hypothesized to stimulate healing of chronically injured extra- and intra-articular tissue[17]; animal model studies reported increased inflammatory markers[18] and significantly enlarged cross-sectional area in medial collateral ligaments[19]. The potential of prolotherapy to stimulate release of growth factors favoring soft tissue healing[20] and a positive neural effect[21] have also been suggested. In addition to dextrose-specific effects, needle trauma and volume expansion of local tissue may also produce tissue-level effects[22].

These findings suggest that dextrose prolotherapy may improve upon standard care of knee osteoarthritis for certain patients. Its use in clinical practice is relatively uncomplicated; prolotherapy is performed in the outpatient setting without ultrasound guidance using inexpensive solutions. For responders, whether prolotherapy results in sustained effect past 52 weeks, disease

modification, or delayed definitive care, such as knee replacement, is not known. Clinical experience suggests that repeated sessions and tune-up sessions after 52 weeks improve outcomes and do not pose additional risk. Prolotherapy for knee osteoarthritis has not been compared with other current therapy, including intra-articular corticosteroid and hyaluronic acid injections. Prolotherapy performed by a trained doctor resulted in safe, significant, and sustained improvements on validated, quality-of-life, pain, function, and stiffness measures compared with blinded (saline injections). Prolotherapy may be an appropriate therapy for patients with knee osteoarthritis refractory to conservative care.

Conclusion

According to our results, dextrose prolotherapy appears to be more effective for pain reduction and function improvement. The beneficial effects of dextrose prolotherapy were observed in the short, medium and long term, reporting duration of the effect up to 1-year follow-up.

Nevertheless, these results should be interpreted with reservation, given the low methodological quality and high risk of bias of the studies included, which limits the evidence provided and does not allow solid conclusions; so our findings do not indicate that dextrose prolotherapy is a therapeutic agent of first choice for the treatment of knee OA, but it can be considered as an alternative or adjuvant treatment.

More studies and better methodological quality are needed to establish a better level of evidence on the efficacy and safety of using dextrose prolotherapy in patients with knee OA.

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