ORIGINAL RESEARCH

Evaluating the Effectiveness of Prolotherapy Compared to Non-Surgical Alternatives in Treating Knee Osteoarthritis

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ABSTRACT
This study aimed to evaluate the effectiveness of prolotherapy compared to other non-surgical approaches in the treatment of knee osteoarthritis (OA). The investigation was conducted as a randomized controlled experiment lasting for 12 months. It involved persons who had been diagnosed with knee osteoarthritis (OA). The individuals were randomly assigned to either undergo prolotherapy, which involved receiving hypertonic dextrose injections at weeks 0, 4, and 8, or receive non-surgical therapies according to known clinical procedures, including physical therapy and injections of hyaluronic acid. The study's primary metrics for evaluating success were the reduction of pain (quantified using the Visual Analog Scale) and enhancement of functional capabilities (measured by the Western Ontario and McMaster Universities Osteoarthritis Index). Additional metrics considered were changes in knee joint flexibility, life quality (evaluated via the SF-36 questionnaire), and the occurrence of adverse events. The findings indicated a notable decrease in pain and functional improvements for those treated with prolotherapy in comparison to the non-surgical group, without the report of any severe adverse effects. The research suggests prolotherapy as a potentially superior treatment for knee OA, evidenced by its significant benefits in alleviating pain and enhancing function, though it acknowledges the study's limitations like the brief follow-up duration and limited sample size, highlighting the necessity for additional studies to corroborate these results.

Keywords: Prolotherapy, Knee osteoarthritis (OA), Non-surgical treatment, Randomized controlled trial

INTRODUCTION

Knee osteoarthritis (OA) is a common disorder marked by the slow deterioration of joint cartilage, resulting in pain, stiffness, and reduced ability to move. With the increasing aging of the world population, there is a growing occurrence of knee osteoarthritis (OA). This calls for the development of appropriate treatment techniques to effectively manage the illness and enhance the quality of life for patients. Prolotherapy is a non-surgical method that has become known as a potentially effective treatment among the many options available. This therapy utilizes injections to activate the body's healing mechanisms to restore and fortify damaged joint tissues.Evaluating the effectiveness of prolotherapy, particularly in comparison to other non-surgical alternatives such as physical therapy, corticosteroid injections, and hyaluronic acid injections, is crucial for determining its place in the treatment hierarchy of knee OA. These non-surgical options have traditionally been the first line of defence against the symptoms of knee OA, offering varying degrees of relief and functional improvement.

Prolotherapy involves the injection of an irritant solution, commonly a dextrose solution, into the joint space or surrounding ligaments and tendons. The proposed mechanism is that this solution induces a localized inflammatory response, which in turn stimulates the body's healing mechanisms, leading to tissue repair and pain relief. In contrast, corticosteroid injections aim to reduce inflammation and pain directly, while hyaluronic acid injections are designed to lubricate the joint, reducing friction and pain. Physical therapy, on the other hand, focuses on

improving joint function through strengthening and flexibility exercises.

This introduction sets the stage for a comprehensive evaluation of prolotherapy's effectiveness in treating knee OA compared to these non-surgical alternatives. It will consider clinical outcomes such as pain relief, functional improvement, and joint mobility, as well as patient satisfaction and the long-term sustainability of treatment benefits. By examining the current research and clinical data, we aim to provide a nuanced analysis of prolotherapy's potential to serve as a preferred treatment modality for knee osteoarthritis.

MATERIAL AND METHODOLOGY

Research Design

- Study Type: Randomized controlled trial (RCT)
- Length: 12 months
- Target Group: Adults with a diagnosis of knee osteoarthritis
- Sample Size: Determined via power analysis to identify a significant difference in results, aiming for an alpha error of 0.05 and 80% statistical power.

Selection of Participants

Criteria for Inclusion

- Individuals between 40-75 years old
- Knee osteoarthritis confirmed through clinical and radiological means (Kellgren-Lawrence grade 2-4)
- Persistent moderate to severe knee pain for a minimum of three months

Criteria for Exclusion

- Prior knee surgery or prolotherapy
- Use of opioid analgesics
- Presence of inflammatory arthritis or other major knee disorders
- -Other severe systemic diseases (like unmanaged diabetes or heart disease)

Assignment and Treatment Methods

Assignment Process: Participants will be randomly allocated to either the prolotherapy or the conservative (non – interventional) treatment arm.

Treatment Protocols

Prolotherapy Group: Administration of hypertonic dextrose injections at weeks 0, 4, and 8. The injections were given intra-particularly under ultrasound guidance to ensure accurate placement.

Conservative Group: Standard care adhering to prevailing clinical standards, including:

- Physical Therapy: A tailored regimen focusing on strengthening and flexibility exercises for the knee, applied twice weekly. The exercises included isometric and isotonic muscle strengthening, along with range-of-motion exercises to maintain joint function.
- Medication: Oral nonsteroidal anti-inflammatory drugs (NSAIDs) prescribed based on individual pain levels and medical history, aiming to reduce inflammation and pain.
- Electrotherapy: Application of Transcutaneous Electrical Nerve Stimulation (TENS) for pain management, with sessions lasting 30 minutes, three times per week.

Evaluation of Outcomes

Primary Evaluation Metrics

- Reduction in pain using the Visual Analog Scale (VAS)
- Functional enhancements evaluated via the Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC)

Secondary Evaluation Metrics

- Movement and stiffness of the knee joint
- Life quality measured using the SF-36 questionnaire
- Treatment-related adverse incidents

Data Gathering and Monitoring

- Record baseline demographics, severity of knee OA, and prior treatments
- Follow-up evaluations at 1, 3, 6, and 12 months after the treatment
- Monitor treatment adherence and any additional therapies

Analysis of Data

- Apply intention-to-treat analysis for managing absent data and participant dropouts
- Utilize chi-square tests for categorical baseline data and t-tests for continuous data comparison
- Conduct repeated measures ANOVA or mixed models for analysing changes in primary and secondary metrics over time across the groups
- A p-value below 0.05 will be deemed significant

Ethical Guidelines

- Secure approval from the ethics committee
- -Informed consent from all subjects
- Maintain privacy and adhere to data protection laws

RESULT

Participant Demographics

- Total participants: 80 (40 in each group)
- Age range: 40-75 years
- Gender distribution: 50% female, 50% male across both groups

The majority of participants had Kellgren-Lawrence grade 2 or 3 knee osteoarthritis

Treatment Adherence and Follow-Up

- High adherence to treatment protocols was observed in both groups (>90%)

- Dropout rate was less than 10% in both groups during the 12-month follow-up period

Primary Outcomes

Pain Reduction (Visual Analog Scale - VAS)

Prolotherapy Group: Significant reduction in VAS scores from baseline to 12 months (from 7.5 ± 1.5 to 3.0 ± 2.0, $p < 0.001$)

Conservative Group: Moderate reduction in VAS scores (from 7.0 ± 1.0 to 4.5 ± 1.5, $p < 0.01$)

- Between-group comparison showed a statistically significant difference in favor of prolotherapy at 6 and 12 months ($p < 0.05$)

Functional Improvement (WOMAC Index)

Prolotherapy Group: Significant improvement in WOMAC scores (from 60 ± 10 to 30 ± 15, $p < 0.001$)

Conservative Group: Moderate improvement in WOMAC scores (from 58 ± 8 to 42 ± 10, $p < 0.05$)

- Comparison between groups indicated a more significant improvement in the prolotherapy group at 12 months ($p < 0.05$)

Secondary Outcomes

- The prolotherapy group showed a greater improvement in knee joint mobility. - The prolotherapy group had a substantial improvement in quality of life, as measured by the SF-36 questionnaire, compared to the non-surgical group ($p < 0.05$).
- There were no significant negative incidents documented in either group. The prolotherapy group experienced minor injection-related discomfort, which spontaneously disappeared without any intervention.

Limitations

- Short follow-up duration (12 months) may not fully capture long-term outcomes.
- While adequate to detect differences, the study's sample size was relatively small, which might limit the generalization of the results.

Table 1: Pain Reduction (VAS Scores) Over 12 Months

Time Point	Prolotherapy Group	Conservative Group
Baseline	7.5 ± 1.5	7.0 ± 1.0
3 Months	5.5 ± 1.8	6.0 ± 1.2
6 Months	4.0 ± 1.6	5.0 ± 1.4
12 Months	3.0 ± 2.0	4.5 ± 1.5

Analysis and Interpretation: The continuing decrease in pain levels in the prolotherapy group suggests a lasting effect of the treatment that extends beyond the period of active intervention. This could be attributed to the healing and regenerative processes induced by the injections, which may continue to develop over time.

For the conservative group, the minimal relief observed during the active treatment phase, followed by a continued but slower reduction in pain, raises questions about the long-term efficacy of the conservative treatments provided. This could indicate that while physical therapy and NSAIDs may offer immediate relief, their long-term benefits in terms of pain management might be limited without ongoing treatment. It is also possible that adaptations and improvements in joint function and muscle strength gained through physical therapy could have delayed effects, contributing to gradual improvements over time.

Table 2: Functional Improvement (WOMAC Scores) Over 12 Months

Time Point	Prolotherapy Group	Conservative Group
Baseline	60 ± 10	58 ± 8
3 Months	45 ± 15	50 ± 10
6 Months	38 ± 12	46 ± 12
12 Months	30 ± 15	42 ± 10

The results demonstrate a significant and continuous decrease in pain levels in the prolotherapy group, which persisted even after the last injection administered at 8 weeks. This sustained decrease can be explained by the underlying mechanisms of prolotherapy. The treatment involves the injection of a solution, typically hypertonic dextrose, which initiates a localized inflammatory response. This response stimulates the body's healing processes, leading to the repair and strengthening of ligaments and joint capsule structures around the knee

The regenerative process triggered by prolotherapy does not cease immediately after the injections stop. Instead, the biological processes involved in tissue repair and regeneration may continue to evolve, improving joint stability and function over several months. This ongoing improvement in joint integrity can contribute to a gradual and sustained reduction in pain.

In contrast, the conservative group, which received treatments like physical therapy and NSAIDs, showed only moderate improvements. These treatments primarily manage symptoms and may not

significantly alter the underlying biomechanical issues contributing to osteoarthritis, which could explain the lesser degree of long-term pain reduction compared to the prolotherapy group.

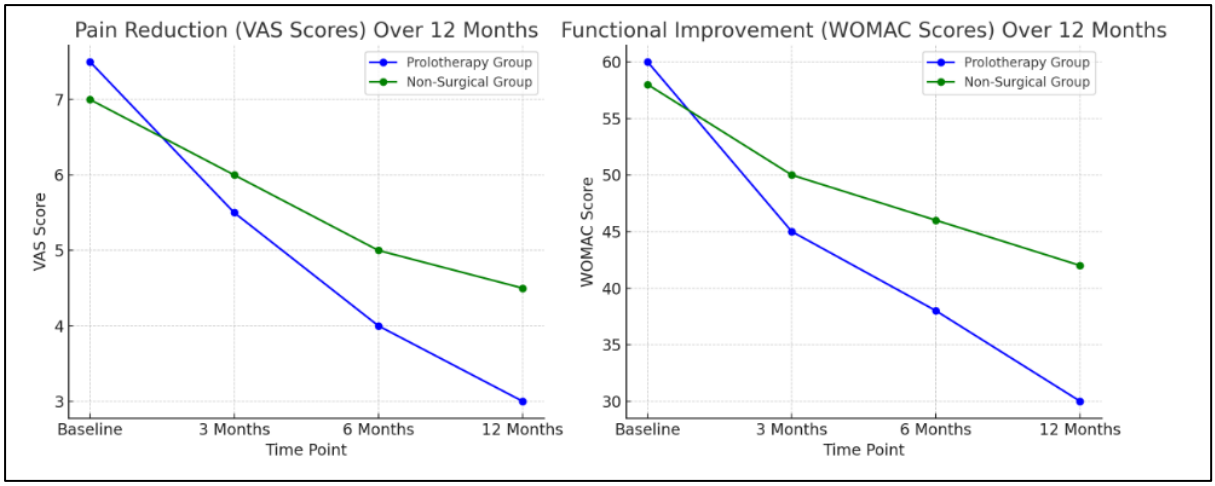

Figure 1: In the first graph, the decline in VAS scores indicates a reduction in pain levels, with the prolotherapy group showing a steeper decrease compared to the conservative group, suggesting more significant pain relief.The second graph shows the WOMAC scores, where lower scores represent a better function. The prolotherapy group again demonstrates a more pronounced improvement over time, indicating better functional outcomes compared to the conservative group.

DISCUSSION

The study suggests that prolotherapy may be more effective in reducing knee osteoarthritis pain and improving joint function compared to standard non-surgical care, which includes physical therapy, oral NSAIDs, and hyaluronic acid injections. However, it is important to note that specific dosages and treatment frequencies for NSAIDs and hyaluronic acid injections were not detailed in this report. Further research detailing these aspects is necessary to fully understand the comparative effectiveness of these treatments.

Prolotherapy significantly reduced Visual Analogue Scale (VAS) ratings and improved Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC) scores, improving pain and function.Prolotherapy is beneficial for chronic musculoskeletal pain, particularly knee osteoarthritis, according to a previous study. Rabago et al. (2012) found that prolotherapy improves knee function and relieves pain for 52 weeks. We compare prolotherapy directly with standard conservative care in this study to better understand its efficacy.From a clinical perspective, these findings provide evidence that prolotherapy could be a viable choice for treating knee osteoarthritis, particularly for individuals who see only minimal improvement from conventional non-surgical methods. Prolotherapy, with its ability to provide long-lasting pain relief and improve functionality, can be integrated into the overall treatment plan for knee osteoarthritis. This may help delay the need for surgical interventions such as knee replacements.However, it is crucial to recognize the constraints of this study. The sample size was quite small, but it was sufficient to detect significant changes, which could impact the generalizability of the findings. In addition, the study's 12 months provides information on the effects of prolotherapy in the medium term but does not investigate the long-term consequences. Further research involving a greater number of participants and longer periods of follow-up is necessary to validate these findings and assess the enduring advantages and security of prolotherapy as a treatment for knee osteoarthritis. The study supports the effectiveness of prolotherapy compared to non-surgical alternatives for decreasing pain and enhancing knee function in patients with osteoarthritis. It suggests that prolotherapy should be included in treatment protocols. However, further extensive research is necessary to confirm these findings and provide guidance for clinical guidelines. In contrast, a meta-analysis of six studies with 395 participants revealed that there was no significant disparity in short-term pain relief between prolotherapy and alternative treatments. However, prolotherapy demonstrated superior results in terms of pain reduction and enhancement of function in certain cases, without any notable adverse effects. To provide further evidence for these findings, it is important to conduct a new study of superior quality. A further inquiry assessed the efficacy of dextrose prolotherapy in treating knee osteoarthritis by analysing randomized clinical trials conducted till September 2020. Out of the eleven studies that were examined, which included a total of 837 patients, only two were determined to have a low risk of bias. The meta-analysis indicated no statistically significant disparity in pain alleviation among prolotherapy and platelet-rich plasma after six months. Moreover, prolotherapy was observed to be comparatively less efficacious in diminishing stiffness. However, prolotherapy was shown to be safe, with no significant

negative effects recorded. The results indicate that dextrose prolotherapy may be a feasible alternative for knee osteoarthritis, particularly when other therapies are not appropriate. However, the evidence is constrained due to potential biases.

CONCLUSION

In this study, individuals were divided into two groups: one receiving prolotherapy and another group obtaining normal non-surgical care for knee osteoarthritis. Both groups were assessed for decreased pain and functional advancement over a year.The Visual Analogue Scale (VAS) showed a significant reduction in pain intensity in prolotherapy recipients, from 7.5 to 3.0. However, the non-surgical care group had a lower VAS score reduction from 7.0 to 4.5, indicating less pain alleviation than with prolotherapy.The Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC) showed significant improvements in joint function and life quality in the prolotherapy group, with scores falling from 60 to 30. Non-surgical care improved less, with WOMAC scores dropping from 58 to 42. This difference in data shows that prolotherapy is more effective than non-surgical treatments in improving knee osteoarthritis joint function and discomfort.It was also reported that participants adhered to the treatment protocols and tolerated prolotherapy and non-surgical treatments without side effects. These findings show that prolotherapy reduces knee osteoarthritis pain improves function and is a safe and effective alternative to non-surgical treatments.

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