

# Prolotherapy Injection for Severe Knee Osteoarthritis

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## Abstract

Osteoarthritis (OA) is a progressive degenerative disease characterized by the abrasion of joint cartilage with the formation of new, irregular cartilage on the joint surface. Pain that occurs in osteoarthritis is induced by activities and relieved by rest. Degenerative processes, including age and genetics, have been associated with the development of osteoarthritis. Various problems emerge from knee OA patients, such as chronic pain, limitation in mobility, limitation in transferability, Activities of Daily Living (ADLs) dependency, limitation in social and leisure participation, and hence reduced Quality of Life (QoL). Prolotherapy stands for “proliferation therapy,” a regenerative medicine on interventional pain management in rehabilitation medicine. The primary purpose of prolotherapy injection is pain reduction and function improvement. Prolotherapy with hypertonic dextrose, as effective as hyaluronic acid or less effective than the Platelet-rich Plasma (PRP) and erythropoietin, has a beneficial effect in the short, medium, and long term<sup>5</sup>. In addition, no side effects or severe adverse reactions were reported in patients treated with hypertonic dextrose. This case reported a 77-year-old female having severe knee osteoarthritis for more than 5 (five) years and was relieved by prolotherapy injection.

**Keywords:** Knee osteoarthritis, prolotherapy, interventional pain management, functional activity, rehabilitation.

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## 1. Introduction

Knee osteoarthritis (OA) affects the elderly over 65 years of age, with a prevalence of 33.6% (12.4 million) in the United States, with women having a higher prevalence (42.1%) than men (31.2%). The incidence of OA will increase with increasing age and weight gain, especially in obese women. Strenuous physical activities, especially those that require fast and strong movement such as kneeling, squatting, and standing for a long time, and the presence of trauma to the knee joint can also be associated with symptoms of genu OA<sup>3</sup>. The prevalence of osteoarthritis increases sharply in women aged 40 years and men after 50 years. According to The Indonesian Basic Health Research by the Ministry of Health (Riskesdas), the prevalence of joint/rheumatic diseases, including OA, was 24.7%<sup>4</sup>.

The goals of OA treatment are to reduce pain, suppress the inflammatory process, improve joint function (ADL and mobilization), prevent joint changes, correct existing abnormalities, strengthen weak muscles, help patients to understand their disease, and provide psychological assistance<sup>4</sup>.

The recommended management for knee OA involves physical exercise, weight loss in patients, cane use, tibiofemoral bracing, anti-inflammatory drugs, and intra-articular injection for knee OA. Physical modalities that can benefit people with knee OA include hot and cold thermal modalities<sup>8</sup>. However, none of the available treatments modify the disease process, nor do they offer long-term effectiveness<sup>2</sup>.

Therefore, in recent years, there has been growing interest in regenerative treatments that have the potential to modify the disease. Although the precise mechanism of the prolotherapy effect is not fully understood, hypertonic solutions are believed to produce an inflammatory response through the recruitment of chemical mediators and growth factors that stimulate local healing of the injured intra- and extra-articular tissues. One hypothesis is that dextrose prolotherapy exerts its effect by stimulating fibroblast activity, vascular proliferation, collagen deposition, and cartilage growth<sup>1</sup>.

Reeves et al. reported that after 3 (three) sessions of prolotherapy at finger and knee OA, there was a significant improvement in the movement without pain ( $P = 0.027$ ) and flexion range of motion ( $P = 0.003$ ) in the experimental group compared to the control group—yet, pain at rest ( $P = 0.729$ ) and during walk showed non-significant improvement ( $P = 0.2$ )<sup>8</sup>.

Four trials were done on prolotherapy for musculoskeletal Low Back Pain (LBP). Each trial used a protocol involving injections to the ligamentous insertions of the L4-S1 spinous processes, sacrum, and ilium. Although outcome measures varied, a common measure was the number of participants showing >50% improvement in pain/disability scores at 6 (six) months<sup>8</sup>. Results showed that >77% of participants in the experimental group improved 50% or more on pain score ( $P = 0.001$ ).

Ongley et al. and Klein et al. compared the treatment effects of prolotherapy with injected steroids, spinal manipulation, and exercise. In the study by Ongley et al., 88% of the subjects in the experimental group reported 50% pain reduction, compared with 39% in the control group ( $P = 0.03$ ). Significant improvement of the

experimental group compared to the control group was also reported for LBP, disability, and pain grid scores ( $P = 0.001$ )<sup>8</sup>.

Klein et al. compared 2 (two) groups with more similar treatment protocols. Significant differences were reported between groups, where 77% of participants in the experimental group improved 50% or more on pain score or disability, compared with only 53% in the control group ( $P = 0.04$ ). Pain grid scores were also significantly better in the experimental group ( $P = 0.03$ ), although pain ( $P = 0.06$ ) and disability ( $P = 0.07$ ) scores individually trended toward significance compared to the control group<sup>8</sup>.

Robago et al. studied prolotherapy for knee OA. Participants in the experimental group received 3 (three) sessions of multiple dextrose injection 25%. Results confirmed an improvement in WOMAC scores for patients receiving dextrose prolotherapy ( $P < 0.05$ ) at 52 weeks compared to the control group that received saline and exercise. The score change was  $15.3 \pm 3.5$  versus  $7.6 \pm 3.4$ , and  $8.2 \pm 3.3$  points, respectively<sup>2</sup>. Hashemi et al. studied 100 patients with knee OA and reported improvement on KOOS pain subscale (from 44.6% to 68.8%) and function (from 43.2% to 71.5%) after 3 (three) months of prolotherapy<sup>2</sup>. Eroglu et al. reported an improvement of function on WOMAC scores from 30% to 35% after 2 (two) months of prolotherapy injection on 60 patients with knee OA grade I-III<sup>6</sup>.

## 2. Case

A 77-years-old female has complained of knee pain since 5 (five) years ago. It started at the right knee to the left knee. The pain was intermittent, dulled, localized, and not radiating with a VAS of 5/10. She has had a morning stiffness for < 15 minutes. The pain was aggravated by standing and walking for > 5 minutes, bending her knees, sitting to standing, carrying a heavy bag, and using stairs. The pain is relieved by lying and resting. She has had episodes of swelling at the knee induced by excessive activity. She also feels unsteady on her knees during walking. There is no tingling and numbness sensation.

### 2.1 Physical examination

The physical examination showed the following results. We found genu varum on both knees, and there was no sign of inflammation. Through palpation, we found tenderness at the suprapatellar area, prepatellar area, and crepitus on both knees. There were no signs of joint instability on both knees. There was atrophy on the quadriceps and hamstring muscle at both sites. We also found a patellofemoral joint disorder on both knees through a patellar grind test. From the other measurement, her upright Q-Angle was 23/25, MMT on lower extremity was 4 (pain) on both sites, and a full PROM on both knees. The WOMAC score was 27% (severe knee problem), and the KOOS score was 22 % (severe knee problem), Timed Up and Go (TUG test) was 20 seconds, and the Barthel Index was 14/20 (moderate dependent).



Figure 1. Genu varum bilateral deformity



Figure 2. Knee x-ray: Osteoarthritis tibiofemoral-femoropatellar dextra grade III and Osteoarthritis tibiofemoral-femoropatellar sinistra grade IV.

According to the physical examination and x-ray result, we diagnosed the patient with knee osteoarthritis grade III and IV.

## 2.2 Intervention

The patient got injection of prolotherapy dextrose 20% solution (5mL D40% + 5 mL NaCl 0.9%). We injected the solution with a lateral-patellar approach for articular injections (10mL) and peri-articular soft tissue injection involving peripatellar bursae, MCL, LCL, and pes anserinus (2mL each injection site) every 4 (four) weeks. We also recommended a home exercise program to strengthen lower extremity muscle, such as ergocycle and isotonic quadriceps-hamstring strength 3 (three) times per week.

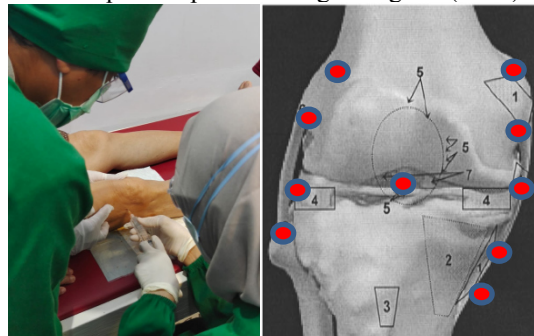


Figure 3. Intra-articular knee joint (anterior and lateral side) and extra-articular (patellar bursae, MCL, LCL, and pes anserinus).

## 2.3 Follow-up

She underwent prolotherapy at the PM&R department 4 (four) times. The pain scores reduced (VAS 5/10 to 2/10). The WOMAC and KOOS scores confirmed reduced morning stiffness, reduced pain when walking upstairs, and improved functional activity (WOMAC from 27% to 50% and KOOS 27% to 42%). The patient could do ADL more independently (Barthel index 14 to 18). There was an improvement of the TUG score but still above the average (TUG score from 20 to 15). She was able to participate in social activities.

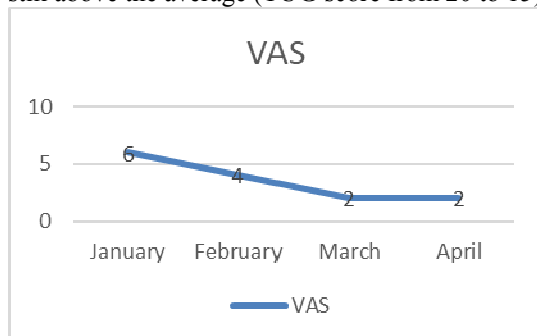


Figure 4. VAS progression from moderate pain to mild pain.

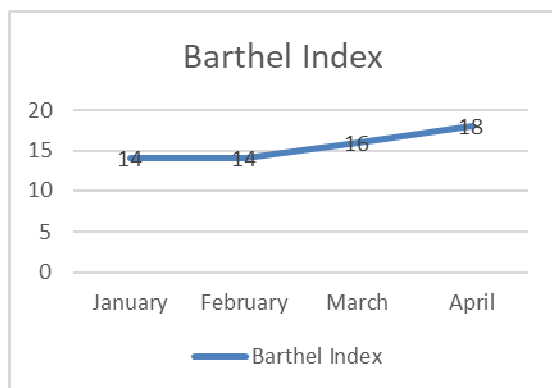


Figure 5. Barthel Index progression from moderate dependency to mild dependency.

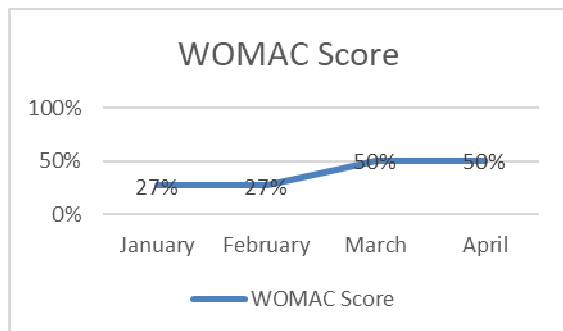


Figure 6. WOMAC score from a severe knee problem to a moderate knee problem.

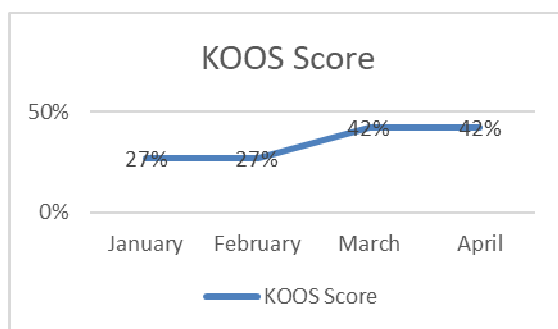
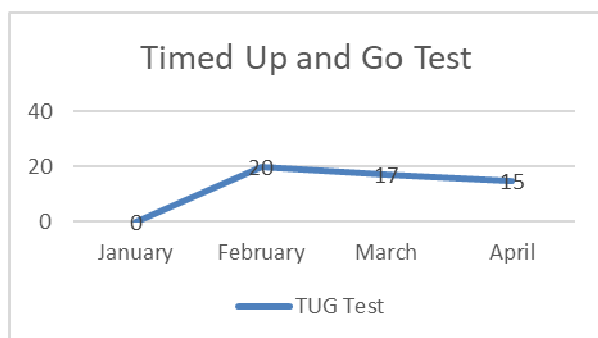


Figure 7. KOOS scores from a severe knee problem to a moderate knee problem.



Pic 8. TUG score improved from 20 to 15 seconds

### 3. DISCUSSION

Patient a 77-year-old female with grade III and IV knee OA that previously was subjected to surgery, still benefited from the prolotherapy injection. The findings indicated that dextrose prolotherapy effectively reduced pain and improved the function and quality of life of patients with knee OA<sup>5</sup>. The effectiveness of dextrose prolotherapy to reduce the pain and improve the functional status of patients with knee OA has been demonstrated in previous studies similar to the current data and systematic reviews<sup>7</sup>.

One study from Alketa T. Sert showed that the application of dextrose prolotherapy, saline injection, and the home exercise program resulted in a significant decrease in the WOMAC total and WOMAC-pain scores compared with the pre-treatment scores. The improvement in all three groups was higher than reported in other studies. However, the prolotherapy group reported significant improvements in the WOMAC scores at 6 (six) and 18 weeks compared to the control group and at 18 weeks compared to the saline group<sup>5</sup>.

Another study showed that prolotherapy would proliferate fibroblast, produce collagen type 1, and induce inflammatory factor to tissue regenerative. However, the research suggested a low concentration of dextrose solution, which was not expected to induce excessive inflammation and contribute to the matrix formation of tissue. The study also suggested using 10-25% dextrose solution for clinical purpose<sup>6</sup>.

Three studies compared hypertonic dextrose and saline solution plus lidocaine mixture. They reported that there was a statistically significant improvement in pain and function in both groups, with an effect in favor of the groups treated with Hypertonic Dextrose Prolotherapy (HDP)<sup>7</sup>.

Hashemi et al. compared the efficacy of HDP with HA intra-articular, reporting equal efficacy in reducing pain and improving function at 3-month follow-up<sup>7</sup>.

Hashemi et al. compared intra-articular infiltration with hypertonic dextrose with intra-articular ozone,

reporting equal efficacy in reducing pain and improving function at a 3-month follow-up<sup>7</sup>.

Rahimzadeh et al.. compared intra-articular infiltration of Hypertonic Dextrose with intra-articular PRP and observed statistically significant improvement of pain and function in both groups at 2 (two) and 6 (six) months; nevertheless, at 6-month follow-up, a better effect was observed in the PRP group<sup>7</sup>.

Rahimzadeh et al.. compared intra-articular infiltration with hypertonic dextrose with intra-articular infiltration with erythropoietin. They reported pain reduction in both groups at 3-month follow-up with a difference in favor of the erythropoietin group<sup>7</sup>.

Besides prolotherapy injections for knee OA, on physical medicine and rehabilitation division also able to provide physical modalities such as cryotherapy or short-wave diathermy which is highly recommended to support the functional improvement. Elly et al., study showed Knee OA patients who were given SWD and cryotherapy could improve VAS and WOMAC score. The VAS score was decrease to the patients had given SWD, average score from 4.4 to 2.4 with a significant value ( $p = 0.003$ ). WOMAC score also had reduced in patients who were given SWD, with an average before therapy of 24.6 to 15.2, with a significant value ( $p = 0.004$ ). Meanwhile, in Knee OA patients who were given cryotherapy, the results showed a decrease in VAS with an average of 5.467 to 2.867 after therapy, with a significant value ( $p: 0.003$ ). Likewise, the WOMAC results also showed an improvement in function with an average value of 35 to 23,867 after therapy with a significant value ( $p = 0.003$ )<sup>9</sup>.

#### 4. CONCLUSION

Prolotherapy or proliferation therapy using dextrose solution has reduced pain and improved functional activity in patients with knee OA as indicated by the improvement of VAS, WOMAC, and KOOS scores and TUG for severe knee OA.

#### 5. ACKNOWLEDGEMENT

There is no conflict of interest in this case report.

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