



**CO-ADMINISTRATION OF UMBILICAL CORD
MESENCHYMAL STEM CELL SECRETOME AND INTRA-
ARTICULAR DEXTROSE PROLOTHERAPY IN KNEE
OSTEOARTHRITIS WITH JOINT EFFUSION: A CASE REPORT**

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ABSTRACT

Introduction

Knee osteoarthritis affects 7.8 million people in Indonesia. Since 1990, the number of osteoarthritis cases in Indonesia has more than doubled. A proportion of patients derive inadequate benefit from pharmacological therapy and from conventional intra-articular injections. Umbilical cord mesenchymal stem cell (UC-MSC) secretome and dextrose prolotherapy are two injectable modalities with distinct mechanisms of action, yet their concurrent administration has never been reported, still less in a knee complicated by joint effusion.

Case Presentation

A 49-year-old woman with right knee pain of one year's duration, a body mass index of 33.8 kg/m², radiographic features consistent with Kellgren–Lawrence grade 1, and an effusion demonstrated on

(VAS) score was 6/10 and the Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC) score 57/96. Previous therapy comprising nonsteroidal anti-inflammatory drugs, hyaluronic acid, and intra-articular corticosteroid had conferred no meaningful improvement. The patient underwent three ultrasound-guided sessions at three-week intervals, each consisting of synovial fluid aspiration when an effusion was present, followed by injection of 1.5 mL UC-MSC secretome and 2 mL of 20% dextrose intra-articularly, and 2 mL of 12.5% dextrose peri-articularly.

Results

At week six, the VAS score had fallen to 1/10 and the WOMAC score to 3/96, both exceeding the minimal clinically important difference. The volume of aspirated fluid decreased from 8 mL to 3 mL, and at the week-six assessment the effusion was no longer demonstrable on ultrasonography. The patient regained the ability to stand for prolonged periods without pain and to perform prayer in the standard posture, including sitting with maximal knee flexion. Adverse effects were confined to mild injection-site pain.

Conclusion

Co-administration of UC-MSC secretome and dextrose prolotherapy in knee osteoarthritis with effusion was accompanied by substantial improvement in pain and function and by resolution of the effusion within six weeks, without significant adverse effects. As a single case report, causality cannot be established and the contribution of each individual modality cannot be disentangled.

Keywords: umbilical cord mesenchymal stem cell secretome; dextrose prolotherapy; knee osteoarthritis; joint effusion; case report

ultrasonography. The
visual analogue scale

INTRODUCTION

Knee osteoarthritis affects 7.8 million people in Indonesia. Since 1990, the number of osteoarthritis cases in Indonesia has more than doubled.¹ A proportion of patients derive inadequate benefit from pharmacological therapy and from conventional intra-articular injections, giving rise to a need for alternative modalities.

Umbilical cord mesenchymal stem cell secretome acts through paracrine signalling mediated by bioactive constituents and, in preclinical studies, exhibits anti-inflammatory properties and inhibits degradation of the articular cartilage matrix.^{2,3} In humans, UC-MSC secretome has been reported to improve pain and function and to reduce matrix metalloproteinase-3 (MMP-3) concentrations.⁴ Dextrose prolotherapy, by contrast, has long been in clinical use and has demonstrated clinical benefit in several randomised trials,^{5,6} although its mechanism of action remains under investigation.⁷

The two modalities rest upon distinct mechanisms of action and are theoretically complementary. To the best of our knowledge, however, their concurrent administration has not previously been reported — still less in a knee complicated by effusion, a condition that has in fact constituted an exclusion criterion in the existing UC-MSC secretome trial.⁴ We report a single case in order to describe the clinical course and outcomes under these circumstances.

CASE PRESENTATION

Patient Information

A 49-year-old woman presented to the pain clinic with right knee pain that had begun one year earlier. The pain was insidious in onset and was aggravated by walking and by prolonged standing, such that her activities of daily living became restricted. Over the preceding several months she had increasingly conducted her activities in a seated position in order to alleviate her symptoms. This limitation obliged her to perform prayer while seated on a chair, as she was able neither to stand for prolonged periods nor to flex the knee maximally when sitting between the two

prostrations. The pain diminished after cold compression or immersion of the knee in cold water. She also reported morning stiffness of the right knee lasting less than 30 minutes, which improved gradually with activity. There were no complaints referable to other joints, and no fever, weight loss, or other systemic symptoms.

The patient had previously received regular treatment from an orthopaedic surgeon, comprising nonsteroidal anti-inflammatory drugs, hyaluronic acid, and intra-articular corticosteroid. In her own assessment, none of these modalities conferred clinically meaningful improvement. Nonsteroidal anti-inflammatory drugs were discontinued on her own initiative because of epigastric pain, accompanied by a perceived increase in body weight during the period of use. She had also adopted non-pharmacological measures comprising intermittent fasting, use of a knee brace, and light physical exercise; ideal body weight was nevertheless never attained and her weight in fact increased.

Four years earlier the patient had fallen from a motorcycle; no surgical intervention was undertaken and no subsequent symptoms ensued. There was no history of systemic disease, drug allergy, or a family history of similar complaints. She habitually ascended and descended stairs frequently in the course of her daily activities.

Clinical Findings

Body weight was 76 kg and height 150 cm, yielding a body mass index of 33.8 kg/m², corresponding to class I obesity. The right knee exhibited mild swelling, tenderness, and crepitus, without erythema or warmth on palpation. The VAS score was 6/10 and the WOMAC score 57/96.

Timeline

Date	Event
June 2025	Radiography of the right knee: minimal joint space narrowing without osteophytes, consistent with Kellgren–Lawrence grade 1
25 June 2026	Baseline clinical assessment: VAS 6/10, WOMAC 57/96 Ultrasonography: intra-articular effusion Aspiration of 8 mL of clear yellow fluid

	Injection of UC-MSC secretome and dextrose
16 July 2026	Clinical assessment: VAS 2/10, WOMAC 13/96 Ultrasonography: effusion reduced Aspiration of 3 mL of clear yellow fluid Injection of UC-MSC secretome and dextrose Repeat radiography: no change in radiographic grade
6 August 2026	Clinical assessment: VAS 1/10, WOMAC 3/96 Ultrasonography: no effusion detected Aspiration not performed Injection of UC-MSC secretome and dextrose

Diagnostic Assessment

Weight-bearing anteroposterior and lateral radiographs of the right knee, obtained one year before the intervention, demonstrated minimal joint space narrowing without osteophytes and no abnormality of the femorotibial articular surfaces or of the periarticular soft tissues. On the basis of this description, the radiographic appearance was classified as grade 1 of the Kellgren–Lawrence classification (Figures 1A and 2A). Musculoskeletal ultrasonography of the right knee demonstrated an intra-articular effusion.

A diagnosis of Kellgren–Lawrence grade 1 osteoarthritis of the right knee with joint effusion was established according to the 1990 American College of Rheumatology clinical criteria, as recommended by the Indonesian Rheumatology Association.⁸ The patient fulfilled four of the six clinical criteria — morning stiffness of less than 30 minutes, crepitus, bony tenderness, and absence of palpable warmth — whereas the minimum requirement is three criteria. Inflammatory arthritis was considered in the differential diagnosis but was rendered unlikely by the absence of involvement of other joints, of systemic symptoms, and of signs of acute inflammation on physical examination.



Figure 1. Weight-bearing anteroposterior radiographs of the right knee. (A) June 2025, one year before the intervention: minimal joint space narrowing without osteophytes, consistent with Kellgren–Lawrence grade 1. (B) 16 July 2026, after the second session: no change in radiographic grade.



Figure 2. Lateral radiographs of the right knee. (A) June 2025. (B) 16 July 2026. At neither time point were patellar osteophytes or alterations of the femorotibial articular surfaces observed.

Therapeutic Intervention

After the available treatment options had been discussed together with their benefits and limitations, the patient elected combined ultrasound-guided injection of UC-MSC secretome and dextrose prolotherapy, and provided written consent for the procedure and for publication of this case report in anonymised form.

The secretome used was manufactured by Stem Cell and Cancer Research Indonesia, batch number 7D260490150, and originated from a facility certified for Good Manufacturing Practice by the Indonesian National Agency of Drug and Food Control (Badan Pengawas Obat dan Makanan).

The prolotherapy solutions were prepared from 40% dextrose. The intra-articular preparation was made from 2 mL of 40% dextrose mixed with 2 mL of 2% lidocaine, yielding a 20% dextrose solution with a final lidocaine concentration of 1%. The peri-articular preparation was made from 4 mL of 40% dextrose mixed with 2 mL of 2% lidocaine and 6 mL of physiological saline, yielding an approximately 12.5% dextrose solution with a final lidocaine concentration of 0.33%. This method of diluting concentrated dextrose with lidocaine and saline accords with the protocols employed in previous randomised prolotherapy trials.^{5,15}

Three treatment sessions were performed at three-week intervals, in keeping with the interval range customary in dextrose prolotherapy, namely one to four weeks.¹² Each session commenced with ultrasonographic examination both to assess the effusion and to guide the procedure, followed by aspiration of synovial fluid when an effusion was present, and thereafter by intra-articular injection of 1.5 mL UC-MSC secretome and 2 mL of 20% dextrose, together with 2 mL of 12.5% dextrose administered to the medial and lateral collateral ligaments. At the third session no effusion was present and aspiration was therefore not performed, while the composition and volume of the injectate remained unchanged. All procedures were performed under ultrasound guidance by the same anaesthesiologist.

The patient was advised to limit strenuous physical activity, and paracetamol 500 mg was provided as rescue analgesia should pain arise. Use of the knee brace, intermittent fasting, and light

physical exercise were continued as before. No change was made to the intervention during the observation period.

Follow-up and Outcomes

Clinical assessments were performed by the same general practitioner at weeks one, three, and six, independently of the operator who performed the procedures. The week-three and week-six assessments were carried out before the subsequent treatment session was administered.

Parameter	Week 1	Week 3	Week 6
VAS	6/10	2/10	1/10
WOMAC	57/96	13/96	3/96
Effusion (ultrasonography)	present	reduced	absent
Aspirated volume	8 mL	3 mL	not aspirated

The VAS score fell by 5 points and the WOMAC score by 54 points over the six-week observation period. The greater part of this reduction — 4 of the 5 VAS points and 44 of the 54 WOMAC points — had already occurred before the second treatment session was administered.

The fluid aspirated at the first two sessions was yellowish and clear. At the week-six assessment, ultrasonography no longer demonstrated an effusion and aspiration was accordingly not performed. Radiographs repeated at week three using identical projections and weight-bearing conditions showed no change in radiographic grade (Figures 1B and 2B). The patient's body weight had decreased by approximately 3 kg, as recorded at the week-six assessment.

At the week-six evaluation the patient was able to stand for prolonged periods without pain and to perform prayer in the standard posture, including sitting with maximal knee flexion between the two prostrations. The paracetamol provided as rescue analgesia was reported never to have been taken during the observation period. Post-procedural complaints were confined to mild injection-site pain that resolved spontaneously; no signs of infection, haemarthrosis, or other adverse effects were encountered.

Upon completion of the three-session course, the patient was deemed not to require further attendance at the pain clinic and was advised to continue a medical rehabilitation programme for the maintenance of joint function.

DISCUSSION

Clinical Outcomes

The reduction of 5 points in the VAS score and of 54 points in the WOMAC score in this case exceeded the minimal clinically important difference, namely a reduction of at least 30% for chronic pain⁴ and of approximately 12 points for the WOMAC score.^{5,9} This improvement was accompanied by functional recovery that was meaningful to the patient, namely restoration of the ability to stand for prolonged periods without pain and to perform prayer in the standard posture, including sitting with maximal knee flexion. The volume of aspirated fluid decreased from 8 mL to 3 mL at the second session, and at the week-six assessment the effusion was no longer demonstrable on ultrasonography.

The magnitude of this improvement is comparable to that reported in a previous study of UC-MSC secretome, which documented significant reductions in VAS and WOMAC scores,⁴ and to that reported in studies of dextrose prolotherapy demonstrating improvement in pain and function up to week 52.⁵ Resolution of the effusion at the week-six assessment constitutes an examiner-observable outcome that is independent of patient report and therefore adds information beyond the two scores. Conversely, radiographs repeated at week three showed no change in radiographic grade, indicating that the improvement observed was symptomatic and functional rather than a structural change within the joint. The procedures proceeded without significant adverse effects, in keeping with the safety profile reported for both modalities.

Mechanistic Basis of the Two Modalities

UC-MSC secretome contains soluble factors and extracellular vesicles that act in paracrine fashion. In preclinical studies, its administration suppressed matrix-degrading enzymes such as the MMPs and ADAMTSs, increased their inhibitors, and enhanced the synthesis of type II collagen

and aggrecan.^{2,3} In humans, administration of UC-MSC secretome was accompanied by a fall in MMP-3 concentrations and a rise in TGF- β 1, indicating diminished matrix catabolism and augmented tissue-repair signalling.⁴

Dextrose prolotherapy acts through a different pathway. The mechanism proposed hitherto is stimulation of local tissue-repair processes through the release of growth factors.⁷ In humans, intra-articular dextrose administration has been accompanied by a fall in urinary uCTX-II concentrations, denoting reduced type II collagen degradation,⁹ and by changes in synovial fluid neuropeptides, namely a fall in NPY concordant with the reduction in pain.¹⁰ At the peri-articular level, injections were directed at the medial and lateral collateral ligaments as the supporting structures of the joint.

The two modalities therefore address different facets of osteoarthritis pathology. The secretome is directed principally at the control of matrix catabolism, whereas dextrose prolotherapy is directed at the stimulation of tissue repair and joint stability. Their combination is theoretically complementary, and there is precedent for combining dextrose with other modalities within a single treatment session, which has been reported to yield superior results to monotherapy.^{11,12} Nevertheless, the interaction between secretome and hypertonic dextrose has never been investigated directly, whether at the laboratory or at the clinical level.

Causality Assessment

The improvement observed in this case may have arisen from several sources. The first is the two injected substances, whether individually or in combination. The second is aspiration of synovial fluid, which in controlled trials has been shown to confer improvement in its own right, even in the absence of the injection of an active substance.¹⁰ The third is the act of injection itself, given that even intra-articular saline yields improvement exceeding the clinically meaningful threshold for almost all outcomes.¹³ The fourth is the weight loss of approximately 3 kg during the observation period, weight reduction being a cornerstone of knee osteoarthritis management with a measurable relationship to the WOMAC score.⁸ The fifth is the natural history of the disease, given that osteoarthritic pain may fluctuate. The sixth is the mild radiographic grade, since structural

damage that is not yet advanced affords greater scope for symptomatic improvement than do more severe grades.

These possibilities cannot be disentangled from one another. All three modalities were administered within the same session at very short intervals, whereas a single case report affords no comparator group in which the situation without any one of them might be observed. The pattern of improvement, the greater part of which occurred before the second session, likewise favours no single explanation, since all modalities had been administered together at the first session. Nor can resolution of the effusion at week six be attributed to any one modality, given that aspiration had been performed at both preceding sessions.

The evidentiary standing of the two substances also warrants consideration in interpreting these findings. UC-MSD secretome has never been evaluated against placebo in knee osteoarthritis; the available trials respectively lacked a control group and employed an active substance as comparator.^{4,14} For dextrose prolotherapy, the results of trials against saline remain heterogeneous — superiority has been reported at long-term follow-up,⁵ whereas within the first eight weeks no significant difference was demonstrated.¹⁵

Strengths and Limitations

This report possesses several strengths. All procedures were performed under ultrasound guidance by the same operator, the volume of aspirated fluid was recorded at both sessions, and the interval between sessions was held uniform. Outcome assessment was undertaken by a physician not involved in the injection procedures, and by the same individual at all three assessment time points. The secretome product used carried a batch number and Good Manufacturing Practice certification and is therefore traceable. The paracetamol provided as rescue analgesia was reported never to have been taken, so that the outcomes were not confounded by analgesic use.

The limitations are more numerous. This report compares the patient's condition only before and after the intervention, without a comparator group; causality therefore cannot be established and the contribution of each modality cannot be disentangled. Assessment was not blinded, as the assessor formed part of the treating team. The baseline radiographs were obtained one year before the intervention, so that the radiographic grade at the time of the procedure was not directly

verified, although repeat radiography at week three showed no change. Joint range of motion was not measured in degrees, either at baseline or at final assessment, so that the improvement in knee flexion reported by the patient rests upon her capacity to assume the prayer positions rather than upon goniometric measurement.

Tissue-level changes were not assessed, as these were not among the target outcomes of this case report. The outcomes reported are confined to symptoms, function, and ultrasonographic findings. The effusion was assessed qualitatively by ultrasonography and by the volume of fluid successfully aspirated; semi-quantitative assessment such as measurement of suprapatellar recess depth was not undertaken. Observation is reported to week six, at which point the treatment course was completed and the patient was transferred to medical rehabilitation services; the durability of the effect and long-term safety therefore could not be assessed.

CONCLUSION

Co-administration of UC-MSC secretome and intra-articular dextrose prolotherapy in knee osteoarthritis with effusion was accompanied by substantial improvement in pain and function and by resolution of the effusion within a six-week observation period, without significant adverse effects. The patient regained the ability to stand for prolonged periods and to undertake activities that had previously been restricted. As a single case report without a comparator, causality cannot be established and the contribution of each individual modality cannot be disentangled. This report describes the clinical course in a condition that has hitherto been excluded from studies of UC-MSC secretome, and is intended to serve as a basis for further, more rigorously controlled observation.

PATIENT PERSPECTIVE

The patient reported that her knee pain had diminished substantially after undergoing the course of treatment. In her account, the two most palpable changes were the restoration of her ability to stand and of her ability to flex the knee. Previously she had been unable to stand for

prolonged periods, whereas at the final observation she was able to conduct activities in a standing position for prolonged periods without experiencing pain.

Before the intervention, the patient performed prayer while seated on a chair because she was able neither to stand for prolonged periods nor to flex the knee when sitting between the two prostrations. After the intervention, she was able to resume prayer in the standard posture, including sitting with the knee fully flexed. The patient judged the outcome of this treatment to be good and was willing to continue the planned course of treatment.

DECLARATIONS

Patient Consent

The patient provided written consent for the procedures performed and for the publication of this case report together with her clinical data in anonymised form. A copy of the consent form is available upon request.

Conflict of Interest

The authors declare that they have no conflict of interest.

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REFERENCES

1. Butarbutar JC, Basuki P, Sungono V, Riantho A, Fidiastianto K. Burden of osteoarthritis in Indonesia: a Global Burden of Disease (GBD) study 2019. *Narra J.* 2024;4(2):e884.
2. Suteja RC, Harianto JE, Hendrawan G, Angelina V, Wijaya Putra IGNP. In vitro and in vivo potential of human stem cell-derived conditioned medium (secretome) and exosomes as a novel treatment for osteoarthritis: a systematic review of experimental studies. *Clin Orthop Surg.* 2025;17(5):797-814.

3. D'Arrigo D, Roffi A, Cucchiaroni M, Moretti M, Candrian C, Filardo G. Secretome and extracellular vesicles as new biological therapies for knee osteoarthritis: a systematic review. *J Clin Med*. 2019;8(11):1867.
4. Partan RU, Putra KM, Kusuma NF, Darma S, Reagan M, Muthia P, et al. Umbilical cord mesenchymal stem cell secretome improves clinical outcomes and changes biomarkers in knee osteoarthritis. *J Clin Med*. 2023;12(22):7138.
5. Rabago D, Patterson JJ, Mundt M, Kijowski R, Grettie J, Segal NA, et al. Dextrose prolotherapy for knee osteoarthritis: a randomized controlled trial. *Ann Fam Med*. 2013;11(3):229-37.
6. Sit RWS, Chung VCH, Reeves KD, Rabago D, Chan KKW, Chan DCC, et al. Hypertonic dextrose injections (prolotherapy) in the treatment of symptomatic knee osteoarthritis: a systematic review and meta-analysis. *Sci Rep*. 2016;6:25247.
7. Huang K, Cai H. Hypertonic dextrose prolotherapy in osteoarthritis: mechanisms, efficacy, and future research directions. *Front Endocrinol (Lausanne)*. 2025;16:1602727.
8. Perhimpunan Reumatologi Indonesia [Indonesian Rheumatology Association]. Rekomendasi diagnosis dan pengelolaan osteoarthritis [Recommendations for the diagnosis and management of osteoarthritis]. Jakarta: Perhimpunan Reumatologi Indonesia; 2023. Indonesian.
9. Waluyo Y, Budu, Bukhari A, Adnan E, Haryadi RD, Idris I, et al. Changes in levels of cartilage oligomeric proteinase and urinary C-terminal telopeptide of type II collagen in subjects with knee osteoarthritis after dextrose prolotherapy: a randomized controlled trial. *J Rehabil Med*. 2021;53:jrm00196.
10. Topol GA, Pestalardo IG, Reeves KD, Elias F, Steinmetz NJ, Cheng AL, et al. Dextrose prolotherapy for symptomatic grade IV knee osteoarthritis: a pilot study of early and longer-term analgesia and pain-specific cytokine concentrations. *Clin Pract*. 2022;12(6):926-38.
11. Fu Y, Du Y, Li J, Xi Y, Ji W, Li T. Demonstrating the effectiveness of intra-articular prolotherapy combined with peri-articular perineural injection in knee osteoarthritis: a randomized controlled trial. *J Orthop Surg Res*. 2024;19:279.

12. Hsieh RL, Lee WC. Effects of intra-articular coinjections of hyaluronic acid and hypertonic dextrose on knee osteoarthritis: a prospective, randomized, double-blind trial. *Arch Phys Med Rehabil.* 2022;103:1505-14.
13. Previtali D, Merli G, Di Laura Frattura G, Candrian C, Zaffagnini S, Filardo G. The long-lasting effects of "placebo injections" in knee osteoarthritis: a meta-analysis. *Cartilage.* 2021;13(1 Suppl):185S-196S.
14. Soetjahjo B, Herunefi U, Ermawan R, Saputra RD, Adriansyah D. Allogenic umbilical cord mesenchymal secretome for knee osteoarthritis: a clinical efficacy, imaging and safety study. *Int J Hematol Oncol Stem Cell Res.* 2026;20(1):38-46.
15. Teymouri A, Birang N, Fakheri M, Nasiri A. Comparison of the efficacy of ultrasound-guided dextrose 25% hypertonic prolotherapy and intra-articular normal saline injection on pain, functional limitation, and range of motion in patients with knee osteoarthritis: a randomized controlled trial. *BMC Musculoskelet Disord.* 2025;26:313.