Combined Effect of Prolotherapy and Personalized Physical Activity on Knee Osteoarthritis Progression, Impact on IL-1β, MMP-3 Biomarkers and Clinical Outcomes

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INFORMATION SHEET FOR PROSPECTIVE RESEARCH PARTICIPANTS

I, Muhammad Yusuf Hisam, as the principal investigator, together with Prof. Yunita Widyastuti, MD., Ph.D., and Prof. Ismail Setyopranoto, MD., Ph.D., will conduct a research study entitled:

"The Effectiveness of Prolotherapy Pain Management Combined with Personalized Physical Activity on the Reduction of Pain Scores, IL-1β and MMP-3 Biomarkers, and Quality of Life in Patients with Knee Osteoarthritis".

This study is funded by personal funds. The purpose of this study is to determine IL-1β and MMP-3 levels, clinical outcomes including pain (VAS and WOMAC), and quality of life in participants with knee osteoarthritis who receive prolotherapy pain management combined with personalized physical activity.

The research team invites you to participate in this study. A total of 76 subjects are required, with a participation period of approximately 4 weeks for each subject.

A. Voluntary Participation Participation in this study is entirely voluntary.

You are free to decide whether or not to participate without any coercion. If you agree to participate, you are also free to withdraw or change your decision at any time without any penalties. If you choose not to participate, your decision will be fully respected.

B. Research Procedures

If you agree to participate in this study, you will be asked to sign this informed consent form in duplicate: one copy for you and one for the research team.

The study consists of several stages over a defined time period. The first stage, conducted on day one, includes an interview, physical examination, pain score assessment, quality-of-life assessment, knee osteoarthritis evaluation, blood serum sampling for IL-1β and MMP-3 levels, and prolotherapy pain management in accordance with the applicable standard operating procedures (SOPs). Participants will then receive explanations regarding subsequent stages.

The research procedures include:

1. You will be interviewed regarding your identity and general health condition, followed by a structured interview about your current knee osteoarthritis condition.
2. You will undergo pre-test assessments including general physical examination and vital signs, grading of knee osteoarthritis using ultrasound, pain assessment, and blood serum collection to measure IL-1β and MMP-3 levels.
3. You will receive pain intervention therapy using prolotherapy according to SOPs.
4. You will receive instructions regarding whether to continue routine daily activities or to perform personalized physical activity according to SOPs, until the next prolotherapy pain management intervention at week 2 and week 4.
5. You will undergo short interviews and follow-up examinations periodically (two days after intervention and before subsequent prolotherapy sessions), focusing on pain assessment and improvement in knee function.
6. You will receive subsequent prolotherapy pain management interventions at week 2 and at the beginning of week 4 following the first prolotherapy session.
7. A post-test evaluation will be conducted after 4 weeks, including general physical examination and vital signs, grading of knee osteoarthritis using ultrasound, pain assessment, blood serum collection for IL-1β and MMP-3 analysis, and quality-of-life assessment.

C. Obligations of Research

Participants As a research participant, you are expected to follow the research procedures as described above. If any part is unclear, you are encouraged to ask the researchers for further explanation.

D. Risks, Side Effects, and Management

Risks: Participants may experience mild pain at the blood sampling site.

Side Effects:

1. Participants may experience allergic reactions following prolotherapy administration; appropriate anti-allergic management will be provided.
2. Participants may experience increased pain similar to pre-intervention levels; management will include analgesic therapy with paracetamol 500 mg every 8 hours and cold compresses applied to the knee treated with prolotherapy.

E. Benefits

Direct benefits for participants include free examinations for knee osteoarthritis grading using ultrasound, free blood serum analysis of IL-1β and MMP-3 to assess disease progression, and free clinical evaluation.

F. Confidentiality

All information related to participant identity and research results will be kept confidential and accessible only to the research team. Data will be recorded as part of the patient's medical record.

G. Compensation

Participants will receive refreshments during the study period and a souvenir gift in the form of a bowl or mug provided by the research team.

H. Costs

All costs related to the research will be fully covered by the researchers.

I. Additional Information

If you have any questions or require further clarification regarding this study, you may contact M. Yusuf Hisam, MD. at phone number +62 813-9250-0588.

You may also contact the Medical and Health Research Ethics Committee, Faculty of Medicine, Universitas Gadjah Mada, at the Ethics Committee Secretariat, Radiopoetro Building, 2nd Floor, West Wing, Farmako St., Sekip Utara, Yogyakarta 55128, telephone +62 274-588688 ext. 17225, mobile +62 811-266-6869, or by email at mhrec_fmugm@ugm.ac.id.

The research team thanks you for taking the time to read this information sheet. We wish you good health.

PARTICIPANT CONSENT FORM

STATEMENT OF CONSENT TO PARTICIPATE IN RESEARCH

I, the undersigned:

Name : ……..

Age : ……..

Address : ……..

Occupation : ……..

Hereby declare that I have received a full explanation, have been given the opportunity to ask questions, and that all my questions have been answered clearly. I fully understand the purpose and objectives of the research entitled:

"THE EFFECTIVENESS OF PROLOTHERAPY PAIN MANAGEMENT COMBINED WITH PERSONALIZED PHYSICAL ACTIVITY ON THE REDUCTION OF PAIN SCORES, IL-1β AND MMP-3 BIOMARKERS, AND QUALITY OF LIFE IN PATIENTS WITH KNEE OSTEOARTHRITIS".

I hereby state that I AGREE to participate in this study, willingly comply with all applicable procedures, and provide truthful information. This consent is given voluntarily and without any coercion.

Participant Name / Signature / Date

Participant Name	Signature	Date
Client ……	……	……..
Witness……	……	……..

Researcher Identity

Name : Muhammad Yusuf Hisam, MD.

Address : Ethics Committee Secretariat, Radiopoetro Building, 2nd Floor, West Wing, Farmako St., Sekip Utara, Yogyakarta

Phone : +62 813-9250-0588

Medical Supervisor

Name : ……..

Address : ……..

Phone : ……..