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

Muhammad Yusuf Hisam

Doctoral Program in Medical and Health Sciences

Faculty of Medicine, Public Health, and Nursing

Gadjah Mada University

Yogyakarta

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STUDY PROTOCOL

SUMMARY OF THE STUDY PROTOCOL

To be filled by investigator

BACKGROUND INFORMATION / RATIONALE

Knee Osteoarthritis (OA) is a degenerative joint disease with a treatment target focused on pain reduction, improved clinical outcomes, and changes in biomarkers associated with OA. Prolotherapy has emerged as an effective intervention, showing significant improvement in symptoms like pain and joint function compared to other treatments for knee OA. Additionally, the effectiveness of personalized physical activity has been established in improving clinical outcomes, although it has been less significant when compared to other intervention therapies. Combining prolotherapy with personalized physical activity is expected to provide enhanced efficacy and more meaningful outcomes, particularly when measuring biomarkers such as IL-1β and MMP-3, which are considered significant in the progression of knee OA.

OBJECTIVES

The primary objective of this study is to evaluate the levels of IL-1β and MMP-3, clinical outcomes such as pain (VAS and WOMAC), and quality of life in participants with knee osteoarthritis (OA) undergoing a pain management intervention involving prolotherapy combined with personalized physical activity. This study aims to determine whether this combined therapy offers a more effective, cost-effective alternative compared to prolotherapy alone, with a focus on affordability and widespread availability.

STUDY DESIGN / METHODS

Study Type: Randomized Controlled Trial (RCT)
Study Design: Pre- and post-test design

Participants will be randomly assigned to one of the two intervention arms:

- Arm 1: Prolotherapy Alone
- Arm 2: Prolotherapy + Personalized Physical Activity

The study will assess the impact of the interventions on pain reduction, functional improvement, and biomarker changes associated with knee OA.

INCLUSION CRITERIA

1. Participants aged ≥ 18 years
2. BMI between 18.5 and ≤ 29.9 kg/m²
3. Participants diagnosed with primary knee osteoarthritis confirmed by ultrasound
4. Participants who are cooperative and have signed the informed consent form

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EXCLUSION CRITERIA

1. Participants with a history of knee arthritis or trauma
2. Participants with knee osteoarthritis complicated by trauma, fractures, ankylosing spondylitis, or septic arthritis
3. Participants with comorbidities that significantly affect quality of life (e.g., cancer, heart failure, chronic kidney disease, stroke)
4. Participants currently consuming NSAIDs or steroids within the past week
5. Participants who have received intra-articular steroid injections within the last 2 months
6. Participants using injectable or hormonal contraception

DATA ANALYSIS PLAN

- Kappa test for inter-rater reliability
- Univariate analysis to examine individual variables
- Bivariate analysis:
    - Independent T-test
    - Paired T-test
    - Wilcoxon test
    - Chi-Square test
    - Spearman and Pearson correlation tests
- ANCOVA for adjusting for potential confounders

ANTICIPATED OUTCOMES

- Low risk of allergic reactions or complications
- Pain reduction in participants
- Improved functional outcomes
- Enhanced quality of life in Knee OA patients

RISK AND BENEFIT

Risk:

- The study may present risks such as side effects or complications, including allergic reactions or infection at the injection sites. These risks will be mitigated as much as possible through medical monitoring and preventative measures.

Benefit:

- The study aims to discover alternative, cost-effective, and widely accessible complementary therapies for Knee OA. It is anticipated that prolotherapy combined with physical activity will provide significant pain relief, improve joint function, and enhance the overall quality of life for participants. The findings could lead to the development of affordable treatment options for Knee OA patients.

ETHICAL CONSIDERATIONS

The study has been designed with full ethical consideration, and all measures will be taken to prevent deviations from ethical standards. Informed consent will be obtained from all participants, ensuring their understanding of the study and their voluntary participation. Fairness in the administration of interventions will be closely monitored throughout the study. Ethical approval for this trial will be sought from the relevant Institutional Review Board (IRB) prior to participant recruitment. This study already approved by Medical and Health Research Ethics Committee (MHREC) with reference number KE/FK/1000/EC/2024.