Approved by Lokman Hekim University Non-Interventional Clinical Research Ethics Committee
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Study Protocol based on CONSORT Statement
(Consolidated Standards of Reporting Trials)

Investigating of Difference Between Center-based Physical Therapy and Home-based Physical Therapy After Platelet Rich Plasm Injection in Women with Knee Osteoarthritis

Introduction

Scientific background and explanation of rationale.

Osteoarthritis (OA) of the knee is a chronic disease characterized by pain, reduced range of motion, instability and effusion in the joint. The weakness of the quadriceps as well as the hip muscles are commonly seem symptoms (1). Although the primary effects of the disease occur in articular cartilage; osteophytes, subchondral sclerosis, and cyst formation are concomitant complications to cartilage degradation (2). Progressive deterioration of the joint and chronic pain limit to perform knee functions, which result with a decline in quality of life in knee OA patients.

Physical therapy applications, exercise therapy, pharmacological treatments and intra-articular injections are considered as effective methods to relieve the symptoms of knee OA patients (3). Recently, Platelet-rich Plasma (PRP) treatment has received much attention for its use in the treatment of knee OA (4, 5). It has been showed that PRP injection would reduce pain and improve knee functions in patients with knee OA in the available literature, but some studies are underpowered or unblinded, thus the findings have low reliability. A number of systematic reviews and meta-analyses' evidence have not been exactly comprehensive and are even sometimes controversial (6-9). Because previous studies differed in the concentrations of leucocytes used for the preparation (11) of PRP, dosage schedules, and so on. Moreover, no study has investigated the effect of PRP in comparison with that of a placebo injection in the same patient with bilateral knee OA. It is of interest to examine the effect of PRP in the same patient with bilateral OA.

After PRP injection, patients with knee OA are recommended to exercise.(16). it is thought that home exercises combined with PRP treatment may be an effective approach in the treatment of knee OA, but the importance of performing exercise program under the supervision of a

physiotherapist is emphasized (16). Isokinetic training under the supervision of a physiotherapist had significant effects on pain, function and muscle strength in OA patients after PRP injection (17). However, the combination of PRP injection and exercise therapy under the guidance of a physiotherapist has yet to be established.

Specific objectives or hypotheses

The purpose of this study was to compare the effectiveness of supervised physiotherapy and home exercises after PRP injection in patients with knee OA. We hypothesized that the supervised physiotherapy program would be more effective in decreasing pain and improving muscle strength, physical function, and quality of life than home exercises following PRP injection in patients with knee OA.

Methods

Description of trial design (such as parallel, factorial) including allocation ratio

This will be a randomized allocation ratio 1:1, controlled study conducted in the Hacettepe University, Turkey.

Eligibility criteria for participants.

Inclusion Criteria:
- PRP injection due to knee OA,
- The PRP injection is given at least three days ago,
- 45- 70 years old
- Grade 2-3 according to Kellgren Lawrence osteoarthritis classification

Exclusion Criteria:
- Being male
- Have a neurologic, oncologic and/or rheumatologic disease

- Having any intra-articular application and / or physiotherapy and rehabilitation in the last 6 months,
- Have any other orthopedic problems involving the lower extremities
- having cognitive problem

Methodology of the study

Patients who underwent PRP injection for knee OA were included in the study. It will be noted that PRP injection to the patients is done by the same physician using the same PRP kit by the same method at the Hacettepe University Faculty of Medicine Department of Orthopaedics and Traumatology.

Outcome Measures

Participants and Methods

A randomized control clinic study design was used for the present study. A sample size calculation was conducted using G*power (v3.1.9.2, Heinrich-Heine-University, Dusseldorf, Germany). An estimated more than 2-point pain level changes on VAS between pre- and posttreatments for repeated measures analysis, a power of 0.80, a α of 0.05 and a total sample size of 28 knee OA patients need to be included in the present study.

Pain Measurement

Visual Analog Scale was used to assess the subjects' pain during rest and activity. A 10 cm line was driven and subjects was wanted to mark the point (0; no pain, 10; worst imaginable pain) as representing the pain during rest and activity (18).

Muscle Strength Measurement

Quadriceps, hamstring muscles and the hip stability isometric test (HipSIT) strength were measured with a hand-held digital dynamometer (Lafayette Instrument Company, Lafayette□). Each subject was verbally informed before the test in order to ensure correct movement and subjects were asked to perform submaximal contraction against the evaluator's hand before testing (19). ''Break test'' technique was performed for the strength measurement. According to this technique, the evaluator gradually overcomes the muscle strength and stops when the joint gives way (20). The quadriceps muscle strength was measured in a sitting position (Hip 90° flexion, knee extended) with hands crossed across the chest. The hand-held dynamometer was positioned on the anterior surface of the lower leg proximal to the ankle during test (21) . Hamstring muscle group measurement was carried out on prone position (Hip neutral position, knee flexion 90°). The hand-held dynamometer was positioned on the posterior surface of the lower leg proximal to the ankle during test (21) . The HipSIT evaluates the abductor, external rotator and extensor muscles of the hip together. This test was performed in a side-lying position (Hips 45° flexion, knees 90° flexion, heels in contact with the limb tested superior to opposing limb as 20° abduction). The hand-held dynamometer was placed on laterally positioned 5 cm above the knee joint interline during test (22). Each measurement for each muscle was performed 3 times at 30 sec intervals and the higher value was recorded. There was also a minute interval between muscle groups measurements.

Functional Performance Measurement

A 30-sec chair stand test and stair climb test were used to assess physical performance. The subjects were asked to stand up from a chair (height: □43cm) and sit down in 30 sec with their arms folded across the chest during the 30-sec chair stand test. The number of the repetitions were recorded (23). The subjects were asked to ascend and descend 10 steps (step height 20 cm) at a safe and comfortable pace during the stair climb test. The time (sec) of stair ascend and descend were recorded separately (24).

Functional Status

The Western Ontario and McMaster Universities (WOMAC) index is a disease specific self-administered test for OA to assess functions of the affected joints. It consists of 24 questions

(three subscale; pain (5 questions), stiffness (2 questions) and daily activities (17 questions) (25).

Interventions

Each subject was informed about knee OA and daily activities that negatively affect the knee OA. They were also asked to use cold press 3 times (10-15 min) a day for 6 weeks. Supervised physiotherapy group performed exercises 3 times a week for 6 weeks under supervision of a physiotherapist after the first evaluation. The subjects in home exercise group were taught exercises and they were informed to do exercises 3 times a week for 6 weeks. Home exercise group was telephoned to motivate them to do exercise or to find out if they have any problem about the exercises once a week for 6 weeks. The exercise programs for each group consisted of these parts: warm up, strengthening, balance and cool down period (Appendix 1). The standard exercises were performed by all of the subjects in each group in order to standardize the exercise procedure. We used OMNI Resistance Exercise Scale for perceived effort to standardize elastic-band (Thera-Band; The Hygenic Corporation, Akron, OH) resistance among subjects (26). Subjects were asked to do 3 repetitions for each exercise starting with lowest resistance elastic band, and the resistance of the elastic band was increased until it reached 5 on the 11-point scale to determine the appropriate elastic band. Second measurements were performed at the end of 6 weeks, the day of routine doctor control for PRP injection. All assessments were performed by the same physiotherapist.

Statistical Analysis

A two-way repeated-measures analysis was initially used to investigate differences in the primary outcome variable (muscle strength) between the supervised physiotherapy group and home exercise group over 6- week period; followed by secondary outcomes measures (VAS, WOMAC). In the occurrence of significant main or interaction effects, a Bonferroni post hoc correction was used to assess significant findings between the groups at specific assessment time points. Statistical analysis was performed using SPSS software (version 22.0). The significance level was set at an alpha of 0.05.

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