Intra-Articular Platelet-Rich Plasma Combined With Hyaluronic Acid Injection (Synvisc) for Knee Osteoarthritis Is Superior to Platelet-Rich Plasma or Hyaluronic Acid Alone in Improving Function

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Purpose

To evaluate the effectiveness and explore the therapeutic mechanisms of platelet-rich plasma (PRP) combined with hyaluronic acid (HA) as a treatment for knee osteoarthritis (KOA).

Methods

In total, 122 knees were randomly divided into HA (34 knees), PRP (40 knees), and PRP+HA (48 knees) groups. Platelet densities in whole blood and PRP were examined using Wright–Giemsa staining. Visual analogue scale, Lequesne, Western Ontario and McMaster Universities Osteoarthritis Index, Lysholm scores, and postoperative complications were evaluated. High-frequency color Doppler imaging was used to observe the synovium and cartilage. Enzyme-linked immunosorbent assays were used to quantify interleukin-1β, tumor necrosis factor-α, matrix metalloproteinase-3, and tissue inhibitor of metalloproteinase-1 levels in synovial fluid.

Results

The platelet density in PRP was 5.13-times that in whole blood ($P = .002$). At 24 months, pain and function scores in the PRP+HA group were better than those in the HA-alone and PRP-alone groups ($P_{pain} = .000$; $P_{function} = .000$). At 6 and 12 months, synovial hyperplasia in the PRP and PRP+HA groups was improved ($P < .05$). After 6 and 12 months, the synovial peak systolic velocity, synovial end-diastolic velocity, systolic/diastolic ratio, and resistance index were improved in the PRP+HA group ($P < .05$). Complications were greatest in the PRP group ($P = .008$). After 6 and 12 months, interleukin-1β, tumor necrosis factor-α, matrix metalloproteinase-3, and tissue inhibitor of metalloproteinase-1 in the PRP and PRP+HA groups decreased ($P < .05$), with more apparent inhibition in the PRP+HA group ($P < .05$).

Conclusions

PRP combined with HA is more effective than PRP or HA alone at inhibiting synovial inflammation and can effectively improve pain and function

and reduce adverse reactions. Its mechanism involves changes in the synovium and cytokine content.

Level of Evidence

Level II, Prospective cohort study.

Section snippets

Patient Selection

The study protocol was approved by the Ethics Committee and was publicly accessible before enrollment of the first patient. We performed the study in accordance with the ethical standards outlined in the 2013 revision of 1975 Declaration of Helsinki, and we report the results according to the 2010 Consolidated Standards of Reporting Trials statement. The potential benefits and risks of PRP injection and follow-up were explained to each study patient. All patients provided written informed

Results

In total, 122 knees (78 patients, with 44 patients receiving a bilateral injections) were randomly divided into 3 groups. The follow-up ended on October 1, 2019. The study included 23 male patients and 55 female patients ranging in age from 42 to 79 years with a body mass index between 22.0 and 25.0. Overall, 46 left knees and 76 right knees had a Kellgren–Lawrence grade of II-III, and the duration of joint pain was less than 1 year. Due to additional procedures, 98 knees were excluded from the

Discussion

This study demonstrated that PRP combined with HA improved local synovial hyperplasia and blood flow and better inhibited nonbacterial inflammation of the synovium than HA or PRP alone. Furthermore, the combination treatment effectively improved pain and function scores and reduced the incidence of adverse reactions. PRP combined with HA and PRP alone partially reduced the level of inflammatory factors (IFs) and MMPs in the synovial fluid, reflecting the potential therapeutic mechanism of the 2

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References (65)

- J. Lin *et al.*
  Isofraxidin inhibits interleukin-1β induced inflammatory response in human osteoarthritis chondrocytes
  Int Immunopharmacol
  (2018)
- M.L. Louis *et al.*
  Growth factors levels determine efficacy of platelets rich plasma injection in knee osteoarthritis: A randomized double blind noninferiority trial compared with viscosupplementation
  Arthroscopy
  (2018)
- P. Niemeyer *et al.*
  Open-wedge osteotomy using an internal plate fixator in patients with medial-compartment gonarthritis and varus malalignment: 3-year results with regard to preoperative arthroscopic and radiographic findings
  Arthroscopy
  (2010)
- W.H. Jung *et al.*
  Second-look arthroscopic assessment of cartilage regeneration after medial opening-wedge high tibial osteotomy
  Arthroscopy
  (2014)
- W.M. Oo *et al.*
  Superb microvascular imaging in low-grade inflammation of knee osteoarthritis compared with power Doppler: Clinical, radiographic and MRI relationship
  Ultrasound Med Biol
  (2020)
- A. Sarmanova *et al.*
  Synovial changes detected by ultrasound in people with knee osteoarthritis—a meta-analysis of observational studies
  Osteoarthritis Cartilage
  (2016)
- F.W. Roemer *et al.*

Whole joint MRI assessment of surgical cartilage repair of the knee: cartilage repair osteoarthritis knee score (CROAKS)
Osteoarthritis Cartilage
(2014)

- S. Maschek *et al.*
  Rates and sensitivity of knee cartilage thickness loss in specific central reading radiographic strata from the osteoarthritis initiative
  Osteoarthritis Cartilage
  (2014)
- R.E. Marx
  Platelet-rich plasma: evidence to support its use
  J Oral Maxillofac Surg
  (2004)
- K.Y. Lin *et al.*
  Intra-articular injection of platelet-rich plasma is superior to hyaluronic acid or saline solution in the treatment of mild to moderate knee osteoarthritis: A randomized, double-blind, triple-parallel, placebo-controlled clinical trial
  Arthroscopy
  (2019)