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(RESEARCH ARTICLE)

A comparative analysis of autologous conditioned serum (ACS) & platelet-rich plasma (PRP) in early osteoarthrosis of knee

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Abstract

Osteoarthrosis represents a failure of the diarthrodial, synovial lined joint. Among the elderly, knee osteoarthrosis is the most frequent cause of chronic disability. The prevalence of osteoarthrosis is rising in the Indian population because of the increased life span. Platelet rich plasma (PRP) is defined as a volume of plasma with a platelet concentration more than that in the peripheral blood. Many basic, preclinical and even clinical case studies and trails report PRP's efficacy to improve musculoskeletal conditions including osteoarthrosis. Autologous conditioned serum (ACS) is an autologous blood product eNRIched with interleukin-1 receptor antagonist (il-1ra), a naturally occurring inhibitor of interleukin-1 (il-1). Our study on ACS & platelet rich plasma has thrown up an exciting choice of treatment modality in knee osteoarthrosis, and it has proved efficient in observation period of two years.

Keywords: Autologous Conditioned Serum (ACS); Platelet-Rich Plasma (PRP); Osteoarthrosis Knee; Intra-Articular Injections

1 Introduction

Osteoarthrosis is a chronic degenerative disorder of synovial lined joints resulting in progressive softening and disintegration of articular cartilage accompanied by the new growth of bone at the joint margins, subchondral cyst formation, and subchondral sclerosis, mild synovitis, and capsular fibrosis. Treatment with intra-articular injection which includes steroids, viscosupplements and blood-derived products are considered to have a key role in managing of osteoarthrosis knee conservatively (1,2). While steroids and viscosupplements have proven short-term efficacy in early osteoarthrosis; orthobiologics are gaining increased attention for treating oa (3). The aim of this study was to compare autologous conditioned serum and platelet-rich plasma to each other in treating osteoarthrosis.

Aim of this study

Our aim is to compare the effectiveness of platelet rich plasma and autologous conditioned serum in reducing stiffness, relieving pain, and improving functional status in patients with early osteoarthrosis knee.

1.1 Autologous Conditioned Serum

- Autologous conditioned serum (ACS) is an autologous blood product eNRIched with interleukin-1 receptor antagonist (il-1ra), a naturally occurring inhibitor of interleukin-1 (IL-1) (4)
- ACS is administered locally to treat certain pathologic conditions where il-1 is an important agent.
- Study participants treated with ACS have improved pain scale and performance., however, these results are preliminary.

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- With the assistance of innovative and tested technology, a regenerative & anti inflammatory serum is obtained from the patients own blood. The same is injected into the affected area. The body's regenerative capacity is activated by ACS.
- ACS was first used clinically in 1997 (5)
- The focus of ACS is on the assembly of positive interleukins & growth factors. These are crucial in intervening with the pain cascade, stopping it and subsequently triggering the regeneration process (6)

1.2 Platelet Rich Plasma (PRP)

It is defined as a volume of plasma with a platelet concentration higher than that in the peripheral blood. Many trials and case studies report the efficacy of PRP to improve musculoskeletal conditions including osteoarthrosis (6).

2 Review of literature

Khosbin et al., in a systematic review with the quantitative synthesis in 2013, concluded that intraarticular PRP injections might have benefits in the treatment of adult patients with mild to moderate osteoarthrosis (7). The study also reported an increased incidence of non-specific adverse events among patients treated with platelet-rich plasma. Kalbkhani et al. (8) in 2014 studied the effect of PRP in experimentally induced oa in rabbits knee joint concluded that the PRP group had near-normal joint structure at 16-week post-op interval, and hence PRP could potentially be used for the treatment of osteoarthrosis. Giuseppe filardo, (9) in 2010, studied platelet-rich plasma intraarticular knee injections for the treatment of degenerative cartilage lesions, and osteoarthrosis concluded that treatment with PRP could reduce pain and improve knee function and quality of life with short term efficacy. Kon et al. (10) trial - the effectiveness of PRP injections were compared to hyaluronic acid (ha) intra-articular injection therapy. The primary outcomes of pain reduction function improvements were measured through the international knee document committee (ikdc) and visual analogue scale (eq-vas) coring system. Evaluation of the ikdc score in the PRP group showed a steady increase from (baseline) to 62.7 and 64.0 at 2 and 6 months follow up, respectively.

Objectives

To evaluate the role of autologous platelet rich plasma (PRP) and autologous conditioned serum in treating patients presenting with early osteoarthrosis knee and analyze whether which could be a cost-effective disease-modifying the measure.

3 Material and methods

Patients attending the outpatient department of orthopaedics at NRI medical college and orthocare ,vijayawada with complaints of bilateral knee pain were screened, and those diagnosed as bilateral knee osteoarthrosis (upto grade3) were chosen for the study.

The patients, classified either grade 0 to 3 on the kellgren-lawrence (kl) grading scale were included in the study after prior well informed written consent.

Study of 12 ACS and 18 PRP
Total 24 cases (30 knees)
Period 24 months
Started august 2019 till july 2021
Follow-up at 3,6,12,18&24 months.
20 female and 4 male
06 bilateral knees
Obesity or over weight in all women.
Bmi was more than 30 in all women.
Men had bmi between 28 to 32.
Age 45to75years
All women were below 60 years and men were over 60to75 years .
PRP done in NRIgh
ACS done at orthocare, vijayawada.
Clinical results of this was evaluated using the western ontario and mcmaster universities arthritis index (WOMAC) questionnaire knee society score (KSS) and visual analogue scale (vas) at 3,6,12,18&24 months

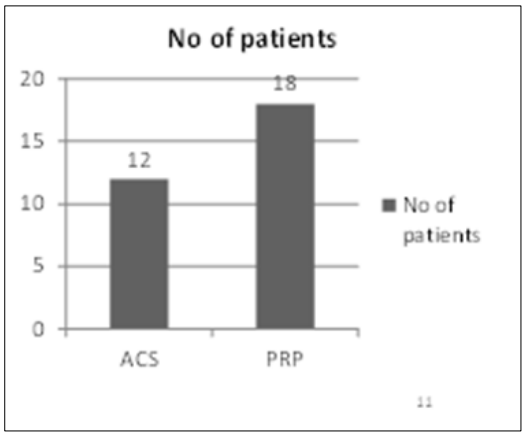

Figure 1 Materials & Methods

- Place of study :
  Orthopaedic department opd of NRI medical college (PRP)
  Orthocare clinic, vijayawada (ACS)
- Period: august 2019 to July 2021
- Follow up at 3, 6, 12, 18 & 24 months.
- Number of patients; 24
- Number of knees: 30

3.1 Inclusion criteria

- KL Score G1 To G3.
- Varus Angle of <10˚
- Uni compartmental OA.
- Patients Younger Than 35 Years.
- Patients who gave consent for the study.
- Platelet Count (Minimum 2 Lakhs Per Microliter)
- ESR & CRP in Normal Limits
- Haemoglobin >10 Gm%

3.2 Exclusion criteria

- Previous intraarticular steroid or ha injections
- Previous knee surgeries
- Active urine infection or diabetics with uncontrolled blood sugars, active skin lesions in and around the site of injection .
- Platelet dysfunction syndrome.
- Critical thrombocytopenia (<105 /ml).
- Hypofibrinogenemia.
- Septicemia.
- Coagulopathies.
- Presence of tumors or metastasis.
- Active infection.
- Pregnancy or breast-feeding.
- Immune deficiencies.
- Patients with vascular injuries.

3.3 Selection criteria for ACS /PRP

Random Selection, Bilateral Cases were treated with PRP only.

3.4 Procedure

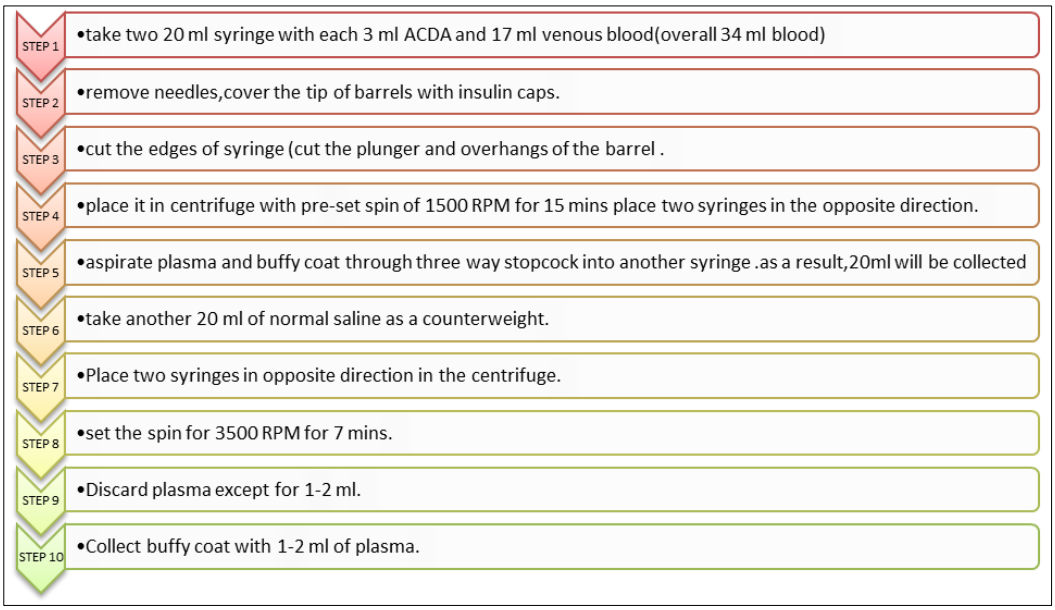

Figure 2 Steps of making PRP

Figure 3 PRP - Preparation Images

ACS - Prep Images

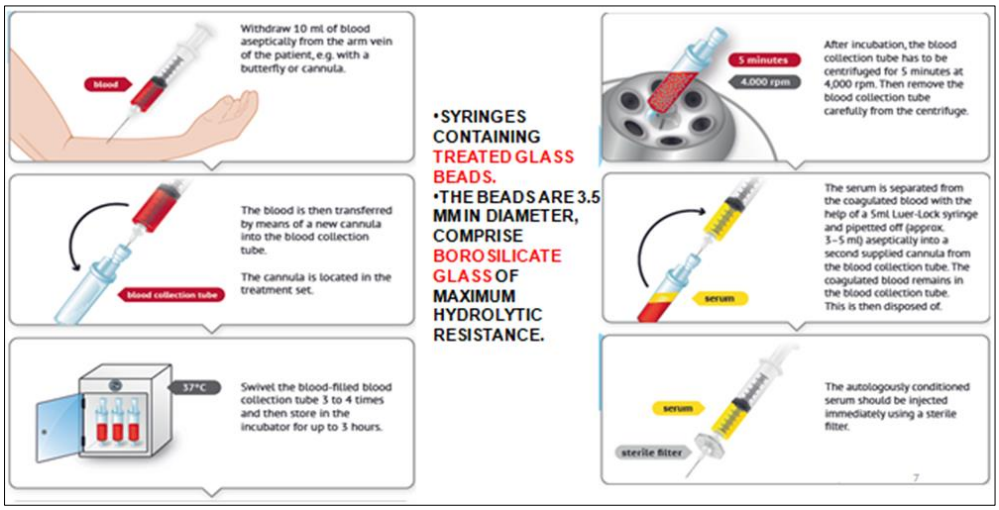

Figure 4 Steps of making ACS diagrammatic

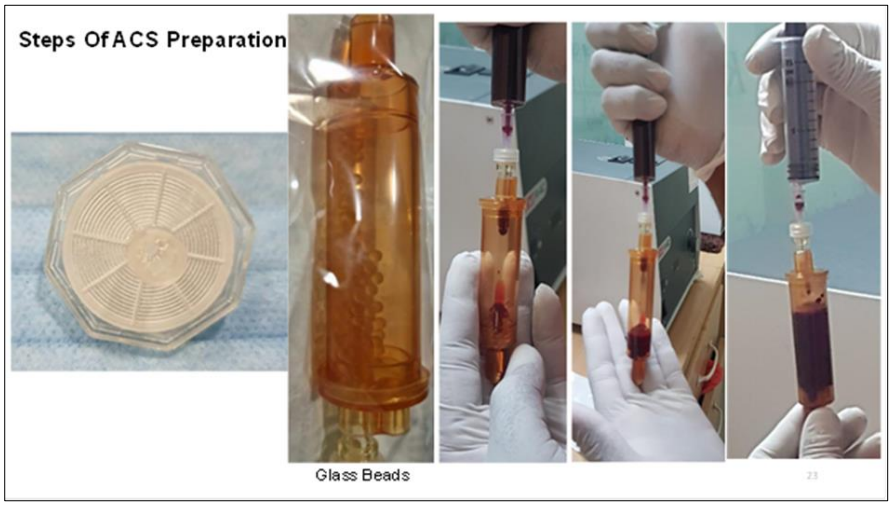

Figure 5 Steps of ACS preparation

Figure 6 Incubator & Injection

Injection interval for ACS is 10 days , whereas for PRP it is 2 weeks.

Post injection protocols-

Ice packs are applied for 2 days

Paracetamol SOS for pain.

Knee strengthening exercises

Weight reduction in over weight or obese patients.

Gels to use locally without massage 48 hours after injection.

Advised to avoid strenuous activities like running, jogging, long distance walking, jumping etc....

Advised to do swimming or cycling.

No n saids

No oral steroids

POST INJECTION SCORES

	ACS – GROUP 1					PRP – GROUP 2				
DURATION IN MONTHS	3 Mon	6 Mon	12 Mon	18 Mon	24 Mon	3 Mon	6 Mon	12 Mon	18 Mon	24 Mon
WOMAC	0-5	0-5	0	0	40-50	5-10	0-5	0	15-20	45-50
KSS – CLINICAL SCORE	75	75	75	75	25-30	60	65	75	20-25	25-30
KSS - FUNCTIONAL SCORE	70	70	80	80	50-60	60	70	80	35-40	30
VAS	2/10	2/10	0/10	0/10	6/10	3/10	3/10	1/10	4/10	8/10

Figure 7 scores after injection

	ACS (GROUP-1)	PRP (GROUP-2)
Good Results	10 (83.3%)	12 (66.6%)
Fair Results	2 (16.7%)	6 (33.3%)

Figure 8 Results

4 Results

10 out 12 Knees who got ACS treatment done had an excellent outcome. 10 cases had same relief till 24months ie end of the study. 2 cases didn't come back for physical assessment. but these 2 cases were analyzed by phone. Despite having good outcome with less pain, they were not happy with it as they could not go for marathons or long walks.

12 out 18 knees who were treated with PRP had an excellent pain relief and improved range of mobility of knee and they didn't require analgesics or topical application of pain relief gels during this period of 21 months.

6 remaining cases had relief of pain just for 15 months as they were involved in walking and gaming activities, pain reappeared. These 6 cases had to revisit us with pain and they were advised 2nd round of PRP.

The main reason we found in getting the pain back was the body weight and strenuous activities within which these patients were involved.

4.1 Complications

Transient synovitis – 01 aseptic effusion - 01 both in post injection with PRP managed with medication.

4.2 Statistical analysis

Done - Z test of 2 proportions: test of difference between the two proportions was done.

Z Value (Calculated): 1.02 P Value Is 0.30 used Medcalc 20.013 Trial Version.

5 Discussion

Given the limited data available on the composition of ACS, the mechanisms through which ACS produces clinical improvement, the duration of its effect and the subsequent changes in cytokine levels after repeated injections are still unknown. Although previous clinical data are encouraging and confirm the safety and clinical efficacy of this procedure, given the constraints of current studies, there should be additional trials to further confirm efficacy for the employment of ACS in early osteoarthritis.

Osteoarthrosis is a disorder of synovial joints caused mainly by the uncoupling of balance between cartilage regeneration and degeneration due to focal loss of hyaline cartilage leading to proliferation of cells and the formation of new bone and remodeling of joint surfaces, osteoarthrosis is a dynamic repair process of synovial joints that may be triggered by a wide variety of causes (11,12)

The use of biological agents, including PRP and mesenchymal stem cells (MSCS) in orthopaedics, has increased exponentially over the previous years because of its autologous nature, lack of side-effects, and supposed effectiveness.

Platelet-rich plasma is an autologous blood product with platelet concentrations much more than the normal (13)

tissue repair is a complex process comprising chemotaxis, cell proliferation, angiogenesis, and matrix formation. Platelets play a crucial role in all of these functions by releasing growth factors.

High concentrations of proteins such as platelet-derived growth factor (PDGF), endothelial cell growth factor, vascular endothelial growth factor (VEGF), and the fibroblast growth factor (FGF) have led to the conclusion that PRP may be useful in conditions requiring tissue healing. Conversely, transforming growth factor (TGF-β1), present in PRP, has an inhibitory effect and can lead to non-predictable results (14,15).

Preparation of PRP may end up in four products:

- Pure PRP (P-PRP) with a relatively low content of leucocytes. This can be injected as a liquid or a gel.
- Leucocyte-rich PRP (L-PRP) includes a higher concentration of platelets than P-PRP. Similarly to P-PRP, it can be used as an activated gel or in a liquid form to be injected intra-articular.
- Pure platelet-rich fibrin (P-PRF). This is obtained by double-spinning centrifugation without adding any anticoagulants. Platelet-rich fibrin scaffold is stiffer than the conventional PRP, takes the form of a gel and can be used for wound healing.

- Leucocyte- and platelet-rich fibrin (L-PRF), which is a leucocyte-rich gel which is non-injectable and is applied locally.

Platelets are regarded as the primary mediators of hemostasis (16,17). They contain alpha granules eNRIched with growth factors. Platelets even have anti-bacterial and fungicidal agents, which provoke the synthesis of interleukins and chemokine's. When platelets get activated, they release growth factors. Among them, important ones are transforming growth factor-beta family (TGF-BETA), insulin-like growth factor (IGF), platelet- derived growth factor (PDGF), and fibroblast growth factor (FGF), etc. Calcium chloride acts as an activator releasing these growth factors, eventually promoting healing (18,19)

PRP also has anti-inflammatory actions. The inflammatory cascade generated by cyclooxygenase family can be inhibited by anti-inflammatory mediators present in PRP. PRP has an influence on all structures of joint (20). Chemotactic assays have revealed that the PRP stimulated the differentiation of type-ii collagen, secretion of prostaglandins along with the migration of corticospongious bone cells (21).

6 Conclusion

hypothesis is ACS contains extra substances like interleukin-1 receptor antagonist (IL-1RA), inhibitor of interleukin-1 (il-1) helps in reducing the inflammation,PRP don't have these substances and post injection was more painful for 1-2 days. However sample size is not big enough but with modest sample size our study is in line with international studies. ACS proved to be more superior to PRP in this analysis. This is because of the presence of good molecules like TGF – transforming growth factor, TIMP 1&2 – tissue inhibitor of metalloproteinases IRAP – interleukin receptor antagonist protein, a2m – alpha 2 macroglobulin.this explains the anti-inflammatory properties. Pain can be dramatically reduced with ACS. Fast-acting while providing long-lasting relief, Chondrogenic properties. We found both ACS and PRP are definitely good alternatives for patients with early unicompartmental oa knee without pain killers.

Compliance with ethical standards

Disclosure of conflict of interest

No conflict of interest

Statement of informed consent

Informed consent was obtained from all individual participants included in the study.

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