Content available at: https://www.ipinnovative.com/open-access-journals

IP International Journal of Orthopaedic Rheumatology

Journal homepage: www.ijor.org

Editorial

Platelet-rich plasma for treatment of rheumatoid arthritis

Ashim Gupta[1,2,3,4,5,*], **Manish Khanna**[4,5,6]

[1]*Regenerative Orthopaedics, Noida, Uttar Pradesh, India*
[2]*Future Biologics, Lawrenceville, GA, USA*
[3]*BioIntegrate, Lawrenceville, GA, USA*
[4]*South Texas Orthopaedic Research Institute (STORI Inc.), Laredo, TX, USA*
[5]*Indian Stem Cell Study Group (ISCSG) Association, Lucknow, Uttar Pradesh, India*
[6]*Dept. of Orthopaedics, Autonomous State Medical College, Ayodhya, Uttar Pradesh, India*

ARTICLE INFO

Article history:
Received 20-09-2022
Accepted 09-11-2022
Available online 23-01-2023

Keywords:
Rheumatoid arthritis
clinical trials
Plateletrich plasma
PRP

ABSTRACT

Rheumatoid Arthritis (RA) is a chronic, inflammatory, autoimmune ailment which involves joint pathogenesis, bone and cartilage irregularities, together with systemic comorbidities, impacting over 75 million people worldwide. At present there is no remedy for RA and the existing treatment modalities utilized have shortcomings and side effects. Recently, there has been an increased interest in use of biologics, such as platelet-rich plasma (PRP), for regenerative medicine applications, including for musculoskeletal ailments. This prompted consideration of use of PRP in patients suffering with RA. In this editorial, we highlighted the safety and efficacy of PRP to treat RA based on recently published clinical studies. These studies, despite preliminary, demonstrated that use of PRP is safe and laid the foundation for multi-center prospective open-label non-randomized trials and double-blinded randomized controlled trials with larger sample size to further evaluate the efficacy of PRP to alleviate symptoms of RA for potential clinical usage.

1. Introduction

Rheumatoid Arthritis (RA) is a chronic, inflammatory, autoimmune ailment which involves joint pathogenesis, bone and cartilage irregularities, together with systemic comorbidities, impacting over 75 million people worldwide.[1,2] Typical signs of RA entail pain, stiffness and swelling which are often followed by gradual debility and joint disfunction.[3] Currently, there is no remedy for RA. Successful modalities frequently commence with the use of corticosteroids, which halt the disease process while controlling symptoms, till disease modifying antirheumatic drugs (DMARDs), for example, methotrexate, begin to take effect. Patients devoid of a satisfactory response to non-biological DMARDs, either switch or supplement with other synthetic DMARDs and/or with one of various increasingly available biological DMARDs, including TNF-α inhibitors, Anti-B/T cell and IL-6R therapies.[4–6] Even though not common, these treatments can have serious side effects, including infections, hematologic, renal and hepatic dysfunction, bone marrow suppression, etc.[7,8] Additionally, long-term use of DMARDs may result in drug resistance, leading to inefficient therapeutic outcomes. Therefore, need for safe and effective alternatives is necessary for those who respond poorly to current treatment modalities.

Over the last decade, there has been an increased interest in use of biologics, including Platelet-rich plasma (PRP) for regenerative medicine applications,

* *Corresponding author*.
E-mail address: ashim6786@gmail.com (A. Gupta).

https://doi.org/10.18231/j.ijor.2022.011

especially in musculoskeletal medicine.[9] This has prompted consideration of its use in patients suffering with RA, despite limited knowledge and insufficient studies related to its efficacy in patients suffering with RA. The goal of this editorial is to highlight the safety and efficacy of PRP to treat and/or mitigate symptoms in patients suffering with RA based on recently published clinical studies.

2. PRP and Rheumatoid Arthritis

A case series by Badsha et al.,[10] presented their clinical experience for treatment with PRP of four patients suffering with RA who had insufficient response and continual pain and inflammation after intra-articular injection of steroids. The PRP utilized was activated (through calcium chloride), leukocyte-poor PRP with two times the concentration of platelets compared to whole blood in a volume of 2-4mL. The Visual Analog Pain Scale (VAS), clinical examination, and Disease Activity Score using 28 joints (DAS 28) were documented. No adverse effects were reported in any patient. Regardless of the past and ongoing therapies and duration of RA, all patients demonstrated improvement in the VAS and DAS 28 at 4 and 8 weeks post-injection. An improvement in joint inflammation (showed decrease in synovial hypertrophy and effusion) was also observed in some patients on ultrasound examination. These results were sustained for up to 1 year. The results from this study demonstrated that administration of PRP is safe and have potential in patients suffering with RA who failed to respond to more established treatment modalities. This study, despite preliminary, should be applauded, being one of the first to evaluate the safety and efficacy of PRP for treatment of RA along with justifying the need for further prospective open-label non-randomized and randomized controlled trials with appropriate sample size to establish safety and efficacy of PRP to treat patients suffering with RA.

In another case series by Shively et al.,[11] the authors presented three clinical cases in which PRP was utilized to treat RA in patients seeking a new treatment to mitigate pain and improve range of motion (ROM), particularly in certain joints of the hand. The PRP utilized was activated and a volume of 7mL PRP was mixed with 1mL lidocaine for administration. Of this volume, 0.5mL intra-articular and 1.5mL peri-articular dose was administered in each affected joint. The patients were evaluated via clinical examination. The severity of RA was assessed via Patient Activity Scale II (PAS II) at day of injection, and at 1, 3 and 6 months post-injection. All three included patients had an established diagnosis of RA affecting the proximal interphalangeal and metacarpophalangeal joints of the hand. Over the duration of this study, i.e., 6 months, 2/3 patients reported a 20% pain reduction compared to the initial visit and a 30% improvement in the overall well-being. 1 patient reported a 50% reduction in pain compared to the initial visit and a 50% improvement in the overall well-being. All patients demonstrated functional improvement, reduction in long-term pain and inflammation. Similar to aforementioned study by Badsha et al., no adverse effects were reported in any patients and these results were independent of the past and ongoing therapies as well as the duration of the disease. One of the limitations of this study was not determining platelet concentration compared to whole blood prior to injection. In addition, like aforementioned study, this study also had a small sample size. In spite of this, it emphasizes that administration of PRP is safe and potentially beneficial in patients with RA primarily affecting the joints of the hand. This study also lays the foundation for prospective clinical trials for further evaluating the efficacy of PRP in treating RA patients including ones with affected hand joints.

An open-label parallel randomized controlled trial by Saif et al.[12] evaluated the therapeutic effect of intra-articular PRP versus steroid in patients suffering with RA and their impact on inflammatory cytokines interleukin 1β (IL-1β), tumor necrosis factor α (TNF-α), local joint inflammation, disease activity and quality of life (QL). This study included 60 patients with 30 in PRP group who received 3 intra-articular injections at a monthly interval and 30 in steroid group who received single intra-articular injection. These patients were subjected to clinical, laboratory, serum IL-1β and TNF-α evaluations at baseline and at 3 and 6 months post-injections. Patients in both groups demonstrated improvements in their scores of evaluating tools at 3 months post-injection and this improvement was continued in the PRP group up to 6 months follow-up. On the other hand, the improvements lasted only 3 months in the steroid group. The results from this study, in accordance with both aforementioned case series, demonstrated that administration of PRP is safe and effective in treating patients suffering with RA. This can be attributed to PRP's ability to down regulate the expression of inflammatory cytokines, such as IL-1β and TNF-α. However, more prospective studies with higher sample size are warranted to further establish efficacy of PRP to treat RA. Future studies should also focus on furthering our understanding of the mechanism of action of PRP in patients suffering with RA. Additionally, there is a need to standardize the type and dose (platelet count, concentration compared to whole blood and injection volume) of PRP to ensure that future studies can be replicated and repeated.

3. Conclusion

In conclusion, these studies, despite preliminary, demonstrated that use of PRP is safe and laid the foundation for multi-center high powered prospective open-label non-randomized trials and double-blinded randomized controlled trials to further establish the efficacy to alleviate symptoms of RA for potential clinical usage. As of September 30, 2022, there is only 1 ongoing (or

Table 1: Ongoing clinical trials registered on ClinicalTrials.gov till September 30, 2022 utilizing Platelet-rich Plasma for treatment of Rheumatoid Arthritis.

Study Identifier	Study Phase; Estimated Enrollment (N)	Primary Outcome Measure(s)	Recruitment Status	Country
NCT04264494	Not applicable; N=100	1. Visual analogue scale (VAS). [Time Frame: Change from baseline to 6 months post injection.]: the pain severity determined by the patients on scale of 0(no pain) to 10 (Agonizing pain) 2. Inflammatory mediators. [Time Frame: Change from baseline to 6 months post injection.]: By means of ELISA (IL 1 beta and TNF alpha 3. Health assessment questionnaire disability index. (HAQ-DI) [Time Frame: Change from baseline to 6 months post injection]: Is a patient reported outcome which is usually self-administered by the patient and scales range from 0 (no difficulty) to 3 (unable to do)	Unknown	Egypt

status unknown) clinical trial registered on clinicaltrials.gov (search terms: "Rheumatoid Arthritis" and "platelet-rich plasma" or "PRP"). This is summarized in Table 1.

4. Author Contributions

A.G. conceptualized the manuscript and wrote the initial manuscript draft. A.G. and M.K. reviewed and edited the manuscript. All authors have read and agreed to the published version of the manuscript.

5. Conflicts of Interest

None

6. Source of Funding

None.

Acknowledgements

None.

References

1. Mcinnes IB, Schett G. The pathogenesis of rheumatoid arthritis. *N Engl J Med*. 2011;365(23):2205–19.
2. Mcinnes IB, Schett G. Cytokines in the pathogenesis of rheumatoid arthritis. *Nat Rev Immunol*. 2007;7(6):429–42.
3. Sun L, Akiyama K, Zhang H, Yamaza T, Hou Y, Zhao S, et al. Mesenchymal stem cell transplantation reverses multiorgan dysfunction in systemic lupus erythematosus mice and humans. *Stem Cells*. 2009;27(6):1421–32.
4. Schett G, Emery P, Tanaka Y, Burmester G, Pisetsky DS, Naredo E, et al. Tapering biologic and conventional DMARD therapy in rheumatoid arthritis: current evidence and future directions. *Ann Rheum Dis*. 2016;75(8):1428–37.
5. Wilsdon TD, Hill CL. Managing the drug treatment of rheumatoid arthritis. *Aust Prescr*. 2017;40(2):51–8.
6. Smolen JS, Aletaha D, Barton A, Burmester GR, Emery P, Firestein GS, et al. Rheumatoid arthritis. *Nat Rev Dis Primers*. 2018;4:18001. doi:10.1038/nrdp.2018.1.
7. Bongartz T, Sutton AJ, Sweeting MJ, Buchan I, Matteson EL, Montori V, et al. Anti-TNF antibody therapy in rheumatoid arthritis and the risk of serious infections and malignancies: systematic review and metaanalysis of rare harmful effects in randomized controlled trials. *JAMA*. 2006;295(19):2275–85.
8. Salliot C, Gossec L, Ruyssen-Witrand A, Luc M, Duclos M, Guignard S, et al. Infections during tumour necrosis factor-alpha blocker therapy for rheumatic diseases in daily practice: a systematic retrospective study of 709 patients. *Rheumatology*. 2007;46(2):327–34.
9. Gupta A, Jeyaraman M, Maffulli N. Common Medications Which Should Be Stopped Prior to Platelet-Rich Plasma Injection. *Biomedicines*. 2022;10(9):2134. doi:10.3390/biomedicines10092134.
10. Badsha H, Harifi G, Murrell WD. Platelet Rich Plasma for Treatment of Rheumatoid Arthritis: Case Series and Review of Literature. *Case Rep Rheumatol*. 2020;p. 8761485. doi:10.1155/2020/8761485.
11. Shively D, Amin N. Platelet-Rich Plasma for Rheumatoid Arthritis: A Case Series. *Cureus*. 2021;13(11):e19629. doi:10.7759/cureus.19629.
12. Saif DS, Hegazy NH, Zahran ES. Evaluating the Efficacy of Intra-articular Injections of Platelet Rich Plasma (PRP) in Rheumatoid Arthritis Patients and its Impact on Inflammatory Cytokines, Disease Activity and Quality of Life. *Curr Rheumatol Rev*. 2021;17(2):232–41.

Author biography

Ashim Gupta, Founder and CEO https://orcid.org/0000-0003-1224-2755

Manish Khanna, HOD https://orcid.org/0000-0002-2890-869X

Cite this article: Gupta A, Khanna M. Platelet-rich plasma for treatment of rheumatoid arthritis. *IP Int J Orthop Rheumatol* 2022;8(2):44-46.