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Reviews

Platelet-Rich Plasma in the Treatment of Facet Mediated Low Back Pain: A Comprehensive Review

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Background

Facet-mediated pain is a major cause of low back pain and as a result, is a significant cause of morbidity, including disability and reduced functionality.

Setting

The present investigation involved a PubMed literature review between June 1, and 2021-January 1, 2022.

Methods

We systematically reviewed was carried Pubmed using the search terms “platelet-rich plasma”, “inflammatory mediators”, “facet arthropathy”, “axial back pain”, and “leukoreduction”. Data extraction and quality assessment were performed by 3 independent reviewers. Out of the studies analyzed 2 were retrospective, while 1 was a prospective study.

Results

PRP injections for facet mediated or modulated pain are an alternative to conventional pharmacotherapies and interventional injections/radiofrequency. There are limited numbers of studies in world literature at present.

Limitations

Small number of articles in the world literature and small numbers of patients in those published studies.

Conclusions

At present, there are limited studies in the literature; however, larger well-designed studies are warranted to precisely understand efficacy, potential side effects and best practice techniques for PRP injections for facet mediated or modulated pain.

INTRODUCTION

Back pain is one of the most prevalent problems worldwide with an estimated global prevalence of 7.5% and a US prevalence of 13.1%.[1] Approximately 25% of adults in the USA have reported back pain in the last 3 months.[2] Zygapophysial (facet) mediated pain accounts for 15-45% of low back pain with the incidence being as high as 52% inpatient over 65.[3] Patients with facet arthropathy present with

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morning stiffness, pain with use or loading of the joint (extension of the spine), and can also have radiating lumbar pain. Degenerated facets can also allow for spondylolisthesis, which is a contributor to discogenic pain. These facet joints are innervated by the medial branches of the dorsal rami. Prostaglandin E2 (PGE2) has been shown to be the key mediator of increased neuronal excitability and sensitization.[4] Current treatment modalities include diagnostic medial branch blocks along with intra-articular facet joint injections. If successful pain relief is obtained, the patient is a candidate for radiofrequency ablation of the medial branches. It is well established that radiofrequency ablation provides an improvement in pain scores; however, the long-term benefit and improvement in function are unclear with most studies following patients for less than 6 months.[5] Some prospective trials have been published which may suggest some role for PRP injection in the treatment of pain caused by facet joint arthropathy.

PROPOSED MECHANISM OF ACTION OF PLATELET-RICH PLASMA AND CURRENT BASIC SCIENCES KNOWLEDGE

Platelet-rich plasma consists of an increased concentration of platelets suspended in a small amount of plasma. These platelets are a source of various growth factors such as fibroblast growth factor (FGF), platelet-derived growth factor (PDGF), platelet-derived angiogenesis factor, transforming growth factor-beta TGF-β, PDGF, epidermal Growth factor, VEGF, hepatocyte GF, and IGF.[6] These concentrated growth factors initiate an inflammatory response which is thought to improve soft tissue healing, revascularization of grafts, and bone regeneration. In a healthy patient, the platelet concentration of blood is 150000-350000 per microliter. The ideal platelet concentration for PRP to be therapeutic is three to nine times greater than whole blood.[7,8] In articles published in 2015 and 2016, Cross et al and Simental-Mendía et al advocated for the use of leukocyte-depleted products as the inclusion of these cells can increase inflammation which may lead to increased pain and impaired outcomes. However, it is also suggested that leukocyte inclusion in PRP could produce greater GF concentrations while maintaining a similar safety profile compared to leukocyte-poor PRP.[9] More research is required regarding leukocyte inclusion effects on the clinical efficacy of platelet-rich plasma formulations.

Degranulation of the platelets upon exposure to collagen releases the growth factors. PDGF and TGF-β are involved in cellular remodeling and tissue repair, leading to increased cell-matrix synthesis and repair and cell proliferation.[10] Tohidnezhad et al. examined the impact of growth factors in a rheumatoid arthritis model. Platelet-released growth factor effect of inflammatory synoviocytes was measured using RT-PCR and ELISA to ascertain the expression of pro-inflammatory cytokines TNF-alpha, IL6, and IL1B. PRP injection reduced the expression of TNF-alpha and IL1B genes in vitro. In a 2018 study by Yang et al, both leukocyte-rich PRP and pure PRP showed reductions in osteoarthritis-related and autophagy-related gene expression in vitro. PRP upregulated anabolic and downregulated catabolic gene expression. In vivo studies in rat models however showed reduced cartilage degeneration without significant differences in markers of autophagy, implying chondroprotective effects of PRP are distinct from mechanisms regulating autophagy.[11]

AN OVERVIEW OF MUSCULOSKELETAL APPLICATIONS OF PRP

Although PRP has gained popularity as a conservative treatment option for certain musculoskeletal pathologies, the studies investigating its efficacy have been mixed in both quality and results.[12,13] The benefits of PRP injection for knee osteoarthritis in a patient after total knee arthroplasty were analyzed with a meta-analysis and no statistical clinical improvement was found; however, better pain scores were noted with the PRP injection.[14] A separate meta-analysis using patients after TKA concluded that patients had improved range of motion and pain intensity scores with PRP as compared to placebo.[15] A meta-analysis reviewed over 35 studies comparing the use of PRP to steroid plus local injections, autologous blood, dry needling, and other conservative therapies and they were unable to obtain a difference.[16]

Most intriguing is an article by Yung et al, whose examination of the repeat applications of PRP revealed a better duration of action with regard to pain reduction. In addition, it was found that when given in a confined space (joint cavity and intervertebral disc) and a solid form (PRP after activation), results were more consistent. As our understanding of biologics increases, so do the potential indications and more high-quality studies are required.[17]

ROLE OF PRP IN FACET JOINT DISEASE

Wu et al examined the role of PRP injections for facet joint syndrome in 2016 in patients who exhibited clinical signs as well as imaging showing facet arthropathy.[18] Patients were given autologous PRP injections using fluoroscopic guidance and pain scores were obtained immediately, 1 week, 1 month, 2 months, and 3-month post-injection. One week post-treatment, low back pain decreased significantly compared with prior to treatment both at rest and with flexion. The outcomes were assessed as “good” or “excellent” for 9 of the 19 total patients (47.37%) immediately after treatment, 14 patients (73.68%) at one week, 15 patients (78.95%) at one month, 15 patients (78.95%) at 2 months, and 15 patients (78.95%) at 3 months. Limitations of this study include small sample size, short follow-up period, and lack of appropriate control.

In a prospective randomized trial in 2017 by Wu et al, 46 patients were divided into two groups.[19] One of these groups (A) received an intra-articular injection with PRP and this other group (B) received an intra-articular injection with LA/corticosteroid. Patients were evaluated by pain visual analog scale (VAS) at rest and during flexion, and the Roland-Morris Disability Questionnaire, Oswestry

Table 1. Clinical studies utilizing platelet-rich plasma in facet-mediated pain states.

Study Details	Methods	Results	Conclusions
-Kirchner and Anitua, 2016 -Sample size=86 -Follow-up = 6 months -Observational retrospective pilot study	86 patients who simultaneously underwent one intradiscal, an intra-articular facet, and a transforaminal epidural injection of PRGF under fluoroscopy -Outcomes assessed with VAS	VAS decreased significantly at 1,3 and 6 months post-treatment. (P<0.05) VAS showed a statistically significant drop at 1, 3, and 6 months after the treatment (P < 0.0001) except for the pain reduction between the 3rd and 6th month whose signification was lower (P < 0.05)	•Positive study • Low-quality observational study. • Numerous confounding factors due to multiple interventions at once.
-Wu et al, 2016 -Sample size=19 -Follow-up=3 months -Prospective clinical evaluation	19 patients given intra-articular injections of PRP -Outcomes were assessed with VAS, ODI, and RMDQ	• 79% of the patients reported improvement with good or excellent at 3 month follow-up post-intervention • ODI and RMDQ were also significantly improved.	• Positive results in a study with a small number of patients • relatively short follow-up of 3 months
-Wu et al, 2017 -Sample size=46 -Follow-up=6 months -Prospective randomized trial	46 patients with lumbar facet syndrome were randomized to intra-articular injections of PRP versus LA/corticosteroid Outcomes were assessed with VAS, ODI, and RMDQ	• Back pain improved in both groups • At 3 months, back pain relief was superior in PRP injection group compared to steroid group • Functional status improvement was observed in both groups; however, degree of improvement was greater for PRP than for steroid group. • Highest improvement rate with over 50% pain relief in 81% was found at 3 and 6 months after treatment, in contrast to highest success rate in 85% of the patients in the steroid group after one month	• Positive study • There was significant improvement in both groups in short-term. However, improvement was long lasting for 6 months in PRP group • Limited with a small number of patients

Disability Index, and modified MacNab criteria immediately post-injection, 1 week, 1 month, 2 months, 3 months, and 6 months post-intervention. It was found that group B found patient satisfaction and objective success rate using the above parameters were the highest (80% and 85% respectively) after 1 month; however, at the 6-month mark, this decreased to 50% and 20% respectively. In group A, patient satisfaction and objective success rate increased over time implying that PRP may have higher long-term efficacy.

In a 2016 observational retrospective pilot study by Kirchner and Anitua eighty-six patients with low back pain and degenerative disc disease were enrolled and they received one intradiscal, one intra-articular facet, and one transforaminal epidural injection PRGF Eldoret.[20] It was found that pain was reduced from pre-procedure values from 8.4 ± 1.1 to 4 ± 2.6, 1.7 ± 2.3, and 0.8 ± 1.7 at 1, 3, and 6 months post-procedure respectively. As in the previous study performed by Wu et al, it was found that pain improvement was obtained in a gradual manner. Patients received 4ml PRGF Endoret into the nucleus pulposus, 2 ml into the peridural area, and 0.5 ml into the facet joint. Limitations of this study include lack of a control group, sole usage of careful clinical evaluation and lack of previous diagnostic injection for patient selection, lack of physical or functional outcome measures, and injection of all three areas at the same time and therefore being unable to dictate which of those three interventions provided the most relief. Table 1 outlines relevant clinical studies.

DISCUSSION

PRP has been used autogenously to decrease pain and enhance the healing process via many growth factors. PRP is a concentration of inflammatory mediators and growth factors that augment healing in injured tissues. Biologics including PRP is becoming a more accessible and reasonable option for patients who may fail treatments that are standard of care. The current evidence for use of biologics such as PRP is limited. There is a lack of well-designed RCTs with significant power regarding PRP for the treatment of facet joint syndrome. Of the studies that have been performed, there is a benefit of PRP injection; however, they have not had long term follow up or been compared to radiofrequency of medial branches in terms of symptomatic relief or functional capacity. PRP injections are also more expensive and less accessible than corticosteroids which are the current standard of care for joint degeneration. The clinical use of biologics for the treatment of facet joint syndrome can be further expanded by the publication of high-quality RCTs which demonstrate the long-term effects of both patient satisfaction and function improvement.

LIMITATIONS

The limitations of this study must be acknowledged. Many of the studies researched had small sample sizes, short follow-up periods, and lack appropriate controls. Other studies utilized careful clinical evaluation only and lacked previous diagnostic injections for patient selection.

Furthermore, they lacked physical or functional outcome measures and injected all three areas at the same time, therefore being unable to dictate which of those three interventions provided the most relief. The literature about platelet-rich plasma for facet-mediated low back pain is not very robust at this time. Further clinical trials must be employed to justify its use on a much wider scale.

CONCLUSION

Facet-mediated pain is a major cause of morbidity and a principal diagnosis when patients present with low back pain. Conventional pharmacotherapies and interval techniques have shown efficacy in recent decades. PRP injections for facet-mediated or modulated pain are an attractive alternative to conventional pharmacotherapies and interventional injections/radiofrequency. At present, there are limited studies in the literature; however, larger well-designed studies are warranted to precisely understand the efficacy, potential side effects, and best practice techniques for PRP injections for facet mediated or modulated pain.

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REFERENCES

1. Wu A, March L, Zheng X, et al. Global low back pain prevalence and years lived with disability from 1990 to 2017: Estimates from the Global Burden of Disease Study 2017. *Ann Transl Med*. 2020;8(6):299. doi:10.21037/atm.2020.02.175

2. Shmagel A, Foley R, Ibrahim H. Epidemiology of Chronic Low Back Pain in US Adults: Data From the 2009-2010 National Health and Nutrition Examination Survey. *Arthritis Care & Research*. 2016;68(11):1688-1694. doi:10.1002/acr.22890

3. Manchikanti L, Pampati V, Rivera J, Fellows B, Beyer C, Damron K. Role of facet joints in chronic low back pain in the elderly: a controlled comparative prevalence study. *Pain Pract*. 2001;1(4):332-337. doi:10.1046/j.1533-2500.2001.01034.x

4. Kras JV, Dong L, Winkelstein BA. The prostaglandin E2 receptor, EP2, is upregulated in the dorsal root ganglion after painful cervical facet joint injury in the rat. *Spine*. 2013;38(3):217-222. doi:10.1097/brs.0b013e3182685ba1

5. Centers for Disease Control and Prevention. Acute low back pain. Centers for Disease Control and Prevention. Published May 11, 2020. Accessed October 26, 2021. https://www.cdc.gov/acute-pain/low-back-pain/index.html

6. Kolber MJ, Purita J, Paulus C, Carreno JA, Hanney WJ. Platelet-Rich Plasma: Basic Science and Biological Effects. *Strength and Conditioning Journal*. 2018;40(5):77-94. doi:10.1519/ssc.0000000000000402

7. Alves R, Grimalt R. A Review of Platelet-Rich Plasma: History, Biology, Mechanism of Action, and Classification. *Skin Appendage Disord*. 2018;4(1):18-24. doi:10.1159/000477353

8. Appel TR, Pötzsch B, Müller J, von Lindern JJ, Bergé SJ, Reich RH. Comparison of three different preparations of platelet concentrates for growth factor enrichment. *Clinical Oral Implants Research*. 2002;13(5):522-528. doi:10.1034/j.1600-0501.2002.130512.x

9. Parrish WR, Roides B, Hwang J, Mafilios M, Story B, Bhattacharyya S. Normal platelet function in platelet concentrates requires non-platelet cells: a comparative in vitro evaluation of leucocyte-rich (type 1a) and leucocyte-poor (type 3b) platelet concentrates. *BMJ Open Sport Exerc Med*. 2016;2(1):e000071. doi:10.1136/bmjsem-2015-000071

10. Wang S, Chang Q, Lu J, Wang C. Growth factors and platelet-rich plasma: promising biological strategies for early intervertebral disc degeneration. *Int Orthop Springer Berlin Heidelberg*. 2015;39(5):927-934. doi:10.1007/s00264-014-2664-8

11. Yang F, Hu H, Yin W, et al. Autophagy is independent of the chondroprotection induced by platelet-rich plasma releasate. *Biomed Res Int Hindawi*. 2018;2018:1-11. doi:10.1155/2018/9726703

12. Mishra A, Harmon K, Woodall J, Vieira A. Sports medicine applications of platelet rich plasma. *Curr Pharm Biotechnol*. 2012;13(7):1185-1195. doi:10.2174/138920112800624283

13. Marx RE, Carlson ER, Eichstaedt RM, Schimmele SR, Strauss JE, Georgeff KR. Platelet-rich plasma: Growth factor enhancement for bone grafts. *Oral Surg Oral Med Oral Pathol Oral Radiol Endod*. 1998;85(6):638-646. doi:10.1016/s1079-2104(98)90029-4

14. Muchedzi TA, Roberts SB. A systematic review of the effects of platelet rich plasma on outcomes for patients with knee osteoarthritis and following total knee arthroplasty. *Surgeon*. 2018;16(4):250-258. doi:10.1016/j.surge.2017.08.004

15. Li F xin, Li Y, Qiao C wu, Zhu J, Chen J, Zhang P yi. Topical use of platelet-rich plasma can improve the clinical outcomes after total knee arthroplasty: a systematic review and meta-analysis of 1316 patients. *Int J Surg*. 2017;38:109-116. doi:10.1016/j.ijsu.2016.12.013

16. Franchini M, Cruciani M, Mengoli C, Marano G, Pupella S, Veropalumbo E, et al. Efficacy of platelet-rich plasma as conservative treatment in orthopaedics: a systematic review and meta-analysis. *Blood Transfus*. 2018;16:502-513.

17. Yung YL, Fu SC, Cheuk YC, et al. Optimisation of platelet concentrates therapy: Composition, localisation, and duration of action. *Asia-Pacific Journal of Sports Medicine, Arthroscopy, Rehabilitation and Technology*. 2017;7:27-36. doi:10.1016/j.asmart.2016.11.003

18. Wu J, Du Z, Lv Y, et al. A New Technique for the Treatment of Lumbar Facet Joint Syndrome Using Intra-articular Injection with Autologous Platelet Rich Plasma. *Pain Phys*. 2016;8;19(8;11):617-625. doi:10.36076/ppj/2016.19.617

19. Wu J, Zhou J, Liu C, et al. A Prospective Study Comparing Platelet-Rich Plasma and Local Anesthetic (LA)/Corticosteroid in Intra-Articular Injection for the Treatment of Lumbar Facet Joint Syndrome. *Pain Pract*. 2017;17(7):914-924. doi:10.1111/papr.12544

20. Kirchner F, Anitua E. Intradiscal and intra-articular facet infiltrations with plasma rich in growth factors reduce pain in patients with chronic low back pain. *J Craniovertebr Junction Spine*. 2016;7(4):250-256. doi:10.4103/0974-8237.193260