The Influence of Naproxen on Biological Factors in Leukocyte-Rich Platelet-Rich Plasma- A Prospective Comparative Study AVOID FOR ONE WEEK PRIOR TO PRP

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Purpose

To quantify and compare normative catabolic and anabolic factor concentrations in leukocyte-rich platelet-rich plasma (LR-PRP) at various time points, including baseline, 1 week after initiating <u>naproxen</u> use, and after a 1-week washout period.

Methods

Asymptomatic healthy donors aged between 18 and 70 years were recruited (average age, 36.6 years; range, 25-64 years). Subjects were excluded from the study if they were actively taking any prescribed medications or nonsteroidal anti-inflammatory drugs (NSAIDs) or if they had any of the following at present or previously: blood or immunosuppression disorders, cancer, osteonecrosis, rheumatoid arthritis, avascular necrosis, NSAID intolerance, gastrointestinal or peptic ulcer disease, or kidney dysfunction. The anabolic factors vascular endothelial growth factor, fibroblast growth factor 2, platelet-derived growth factor AB (PDGF-AB), and platelet-derived growth factor AA (PDGF-AA) and the catabolic factors interleukin (IL) 1 β , IL-6, IL-8, and tumor necrosis factor α in LR-PRP were measured. Peripheral blood was drawn at 3 time points: baseline, after 1 week of naproxen use, and after a 1-week washout period.

Results

The <u>angiogenic factors</u> PDGF-AA (44% decrease in median) and PDGF-AB (47% decrease) significantly declined from baseline (P < .05) after 1 week of naproxen use. There was a significant recovery (P < .05) of PDGF-AA (94% increase) and

PDGF-AB (153% increase) levels after the 1-week washout period, with a return to baseline levels. The catabolic factor IL-6 also had a significant decline from baseline (77% decrease in median, P < .05) after 1 week of naproxen use. After a 1-week washout period, the IL-6 level was similar to the baseline level (130% increase, P < .05).

Conclusions

Naproxen use diminished several biological factors in LR-PRP; however, a 1-week washout period was sufficient for the recovery of PDGF-AA, PDGF-AB, and IL-6 to return to baseline levels. Tumor necrosis factor α , IL-1 β , IL-8, vascular endothelial growth factor, and <u>fibroblast growth factor 2</u> did not show differences between the 3 time points of data collection. Discontinuing NSAIDs for a minimum of 1 week before LR-PRP treatment may improve certain biological factor levels.

Level of Evidence

Level II, prospective comparative study.

Section snippets

Donor Enrollment and Study Design

After institutional review board approval (Vail Health Institutional Review Board, protocol 2017-07), asymptomatic healthy donors aged between 18 and 70 years were recruited through flyers posted in our clinic and hospital; interested applicants were screened and enrolled in the study. Previously established STROBE (Strengthening the Reporting of Observational Studies in Epidemiology) guidelines for the design and implementation of cohort or group studies were followed.¹³ Subjects were excluded

Donor Demographic Characteristics

A total of 19 healthy volunteers were enrolled in the study. Of these volunteers, 3 had their samples clot and declined participation with a repeated blood draw during the first week of the study. A total of 16 participants (8 women and 8 men), with a mean age of 36.6 years (range, 25-64 years), met the inclusion criteria and voluntarily participated in the study to its completion. The average height of the study participants was 1.74 m (range, 1.52-1.9 m). The average weight was 75.7 kg

Discussion

The most important finding of this study was that after 1 week of naproxen use in healthy donors, the anabolic factors PDGF-AA and PDGF-AB, as well as the catabolic factor IL-6, showed diminished levels in LR-PRP. After a 1-week washout period, PDGF-AA, PDGF-AB, and IL-6 had returned to baseline levels. Previous studies have examined the effects of naproxen on growth factors and found that VEGF and PDGF, as well as other anabolic factors, were impaired.13, 14 It is interesting that we did not

Conclusions

Naproxen use diminished several biological factors in LR-PRP; however, a 1-week washout period was sufficient for the recovery of PDGF-AA, PDGF-AB, and IL-6 to return to baseline levels. TNF- α , IL-1 β , IL-8, VEGF, and FGF-2 did not show differences between the 3 time points of data collection. Discontinuing NSAIDs for a minimum of 1 week before LR-PRP treatment may improve certain biological factor levels.

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2023, Physical Medicine and Rehabilitation Clinics of North America *Citation Excerpt :*

Generally, there does not seem to be major drug-to-drug interactions with orthobiologics but nonsteroid anti-inflammatory drugs (NSAIDs) or antiplatelet medications could affect the therapeutic effects of biological strategies and even affect healing postprocedure, such as after bone marrow harvesting.1,14,33 NSAIDs, such as aspirin and naproxen, have also shown to interfere in the growth factor release given their direct inhibition of cyclooxygenase (COX) pathway and can impair platelet function.34–36 Although there is no literature correlating growth factor release and efficacy of PRP treatment in vivo, studies may provide good reason to recommend holding NSAIDs and aspirin for 7 days before PRP, and use of other analgesics such as acetaminophen for postinjection pain control, if the benefits outweigh the risks.34

 The Efficacy of Platelet-Rich Plasma for Improving Pain and Function in Lateral Epicondylitis: A Systematic Review and Meta-analysis with Risk-of-Bias Assessment

2021, Arthroscopy - Journal of Arthroscopic and Related Surgery *Citation Excerpt :*

Mishra et al.18 created a PRP classification nearly a decade ago based on leukocyte content, use of activation, and platelet concentration, yet this system is seldom used within published level 1 RCTs. Additional factors such as recent NSAID usage,76,77 time from completion of PRP preparation to injection,78 and choice of activating compound79 have all been shown to influence PRP content, and any clinical trial that does not control for such variables is at high risk of confounded results. Murray et al.72 used Delphi techniques to generate a comprehensive 23-statement checklist for PRP studies to help standardize future trials, but current studies typically do not report even a small fraction of the items on that list.

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S-HA-NPs have already demonstrated anti-angiogenic properties as they affect the proliferative capacity of endothelial cells (Fig. 9b). Previous studies revealed that NAP might affect the expression of VEGF [63], a growth factor that plays a key role in angiogenesis [64]. NSAIDs' inhibitory effect on angiogenic factors are cell-, dose- and, time-dependent.

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2020, Operative Techniques in Sports Medicine *Citation Excerpt :*

The application of PRP for the treatment of skeletal muscle has been widely investigated, while very limited data exist on PPP treatment for skeletal muscle repair and regeneration. PRP and PPP also contain deleterious cytokines, such as TGF- β 1, that can cause fibrosis and inhibit native skeletal muscle regeneration.15,111 Recent efforts have focused on the customization of PRP and PPP to inhibit/reduce biological factors associated with SASP and fibrosis for local administration.12,15,16

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Journal of Shoulder and Elbow Surgery, Volume 24, Issue 12, 2015, pp. 1852-1859

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The Role of Platelet-Rich Plasma in Cartilage Pathology: An Updated Systematic Review of the Basic Science Evidence

Arthroscopy: The Journal of Arthroscopic & Related Surgery, Volume 35, Issue 3, 2019, pp. 961-976.e3

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Tissue and Cell, Volume 52, 2018, pp. 17-27