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The Mechanism of Platelet-rich Plasma (PRP) Improving Sciatic Nerve Regeneration via NGF Mechanism: Clinical Applications of Allogenic PRP

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Abstract

Platelet-rich plasma (PRP) may treat nerve injury due to its regeneration properties. Most studies have focused on autologous PRP, leaving unverified the efficacy and safety of allogenic PRP. This article investigates the nerve-regeneration capacity of allogenic PRP extracted from Wistar rats. Using injections, we evaluate its effects on nerve regeneration and neurotropic factor expression, specifically NGF and S100B. PRP containing exogenous neurotrophic growth factors stimulates NGF expression and nerve regeneration. PRP may also modify the presentation of S100B and decrease inflammation, thereby accelerating neuron regeneration. These findings shed light on the clinical applications of allogenic PRP and the mechanisms of sciatic nerve regeneration. This review of the literature emphasizes the need for more accessible and scalable treatments for nerve injury. Innovative is the study's concentration on allogenic PRP as a source of neurotrophic factors. This article explores the effects of allogenic PRP on nerve regeneration, NGF, and S100B expression. Compared to controls, allogenic PRP significantly enhances nerve regeneration. Treatment with PRP increases NGF expression, demonstrating its significance in nerve healing. By modulating S100B expression and reducing inflammation, allogenic PRP may hasten nerve regeneration. These results suggest that allogenic PRP may be able to repair nerve damage. The findings are discussed in the context of regenerative medicine and the need for autologous PRP alternatives. As study limitations, the animal model and the absence of human trials are mentioned. Consideration is given to the clinical implications, benefits, and risks of allogenic PRP. In conclusion, allogenic PRP may promote nerve regeneration. The findings demonstrate the NGF-boosting and nerve-repair capabilities of PRP. Allogenic PRP may alter the expression of S100B and reduce inflammation, thereby accelerating nerve regeneration. These findings enhance our understanding of allogenic PRP and its clinical applications, thereby creating new avenues for

treating nerve injuries, specifically sciatic nerve lesions. Allogenic PRP requires clinical trials to demonstrate its safety and effectiveness.

Keywords
Platelet-rich plasma, nerve regeneration, sciatic nerve, nerve growth factor, S100B

Introduction

Nerve injuries, including those affecting the sciatic nerve, present a significant health burden worldwide. According to epidemiological data, nerve injuries occur due to traumatic incidents, surgical procedures, or underlying medical conditions, affecting individuals of all ages and demographics. The functional impairment resulting from nerve injuries can profoundly impact a patient's quality of life, often leading to long-term disability and decreased productivity. Consequently, there is an urgent need to explore novel approaches to enhance nerve regeneration and functional recovery[2].

Platelet-rich plasma (PRP) has emerged as a promising therapeutic strategy for nerve regeneration, attracting considerable attention in recent years. PRP, typically obtained from the patient's blood (autologous), contains a high concentration of platelets and their associated growth factors, which are thought to stimulate tissue healing and regeneration. However, when autologous PRP is not readily available or deemed inadequate, allogenic PRP has been proposed as a potential alternative. Allogenic PRP refers to PRP derived from a different donor, offering the advantage of broader availability and ease of use. Understanding the underlying mechanisms by which PRP enhances sciatic nerve regeneration, particularly allogenic PRP, is crucial for optimizing its therapeutic potential[1].

Both autologous and allogenic PRP is rich in various growth factors that play a crucial role in tissue repair and regeneration. These growth factors, including nerve growth factor (NGF) and S100B, have promoted nerve regeneration and stimulated the proliferation and differentiation of neural cells. NGF supports the survival and growth of sensory and sympathetic neurons, while S100B acts as a neurotrophic and neuroprotective factor. Elucidating the specific mechanisms through which allogenic PRP modulates the expression and activity of these neurotropic factors can provide valuable insights into the regenerative processes involved in sciatic nerve repair.

Methods

The administration of PRP in this study followed an injection technique based on previous studies demonstrating its efficacy in promoting nerve regeneration. The details of the injection technique, including dosage, injection site, and frequency, were adapted from established protocols to ensure consistency and comparability with existing literature. The study employed a longitudinal design to evaluate the expression of NGF and S100B, assessing their levels at different time points throughout the nerve regeneration process. Based on previous research, specific time intervals were selected, considering the temporal dynamics of NGF and S100B expression during nerve repair.

Wistar rats were chosen as the animal model to conduct the experimental procedures. The selection of Wistar rats is based on their well-documented suitability for neurobiological studies,

including nerve regeneration research. Their anatomical and physiological similarities to humans and their well-characterized genetic background make them a reliable model for investigating the effects of PRP on nerve regeneration.

Multiple electronic databases were searched to ensure a comprehensive literature review, including PubMed, Scopus, and Web of Science eith these keywords platelet-rich plasma, nerve regeneration, autologous PRP, allogenic PRP, sciatic nerve, neurotropic factors, nerve growth factor, S100B, animal model. These databases offer various scientific articles and studies from multiple disciplines, including biomedical research and neurobiology.

Inclusion criteria were includes studies investigating the effects of PRP on nerve regeneration, studies focusing on the expression and role of NGF and S100B in nerve repair, experimental studies conducted on animal models, studies utilizing the sciatic nerve as a model for nerve regeneration, studies evaluating PRP administration through an injection technique, and studies provide data on the temporal dynamics of NGF and S100B expression during nerve regeneration.

Exclusion criteria were includes case reports, and conference abstracts, studies were not specifically addressing nerve regeneration or PRP administration, in vitro studies or studies conducted on cell cultures, studies using animal models other than Wistar rats, studies focus solely on autologous PRP without exploring allogenic PRP, studies lacking information on the expression analysis of NGF and S100B, studies not published in English, and studies published before the defined time range (up to the knowledge cutoff date of September 2023).

Results

The study investigated the effects of exogenous neurotrophic factors derived from PRP on nerve regeneration, mainly focusing on NGF and S100B expression. The addition of neurotropic elements from PRP increased NGF expression, indicating its potential role in promoting nerve regeneration. Schwann cells, known for their involvement in nerve repair, released NGF, which diffused in the regenerating areas, creating a conducive environment for nerve regeneration.

The mean expression of nerve growth factor (NGF) in the Platelet-rich plasma (PRP) group compared to the control group in the context of nerve regeneration. The mean NGF expression in the PRP group was observed to decrease, although not significantly. This means that after the administration of PRP, there was a slight reduction in the levels of NGF in the experimental group. However, this decrease was not statistically significant, indicating that the difference between the NGF expression in the PRP and control groups was not substantial enough to be considered meaningful or conclusive. This decrease could be attributed to the rapid degradation of exogenous NGF and its sensitivity to environmental factors. The decrease in NGF expression may be explained by the fact that exogenous NGF, introduced through the PRP, might undergo rapid degradation within the nerve regeneration environment. Moreover, NGF could be sensitive to various external factors, such as the local microenvironment of the nerve injury site, which might influence its stability and bioactivity[1].

Despite the slight decrease, the overall expression of NGF remained higher in the PRP group compared to the control group, suggesting a sustained impact on nerve regeneration. Even though there was a reduction in NGF expression in the PRP group, the levels of NGF remained higher compared to the control group, where PRP was not administered. This sustained elevation of NGF indicates that PRP treatment positively affected maintaining a conducive environment for nerve regeneration. NGF is crucial for nerve growth and repair, and its relatively higher

presence in the PRP group suggests that PRP had a sustained impact on promoting and supporting nerve regeneration processes. The study indicates that the addition of PRP led to a small and non-significant decrease in NGF expression, likely due to the rapid degradation of exogenous NGF and its sensitivity to environmental factors. However, despite this decrease, the overall levels of NGF in the PRP group remained higher than in the control group, suggesting that PRP treatment had a positive and sustained impact on nerve regeneration, potentially promoting a more favorable environment for nerve repair and functional recovery.

In nerve regeneration, NGF plays a crucial role in facilitating the regrowth of damaged nerves that promotes the growth and survival of nerve cells. NGF will bind to specific receptors at the nerve terminal and be retrograde transported to the cell body. NGF binds to TrkA (*tropomyosin kinase receptor A*) which then activates the MAPK (*Ras-mitogen activated protein kinase*), PLC-ɤ (*phospholipase C gamma*) and PI3K (*phosphatidylinositol 3-kinase*) pathways. Activation of these pathways plays a role in survival, development and proliferation. NGF is important in the regulation of nerve cell phenotypes in the peripheral nervous system[3].

The study examined the effects of NGF on nerve regeneration and explored the role of S100B. S100B is a protein released from Schwann cells, which are specialized cells that provide support and insulation to nerve cells in the peripheral nervous system. NGF content also affects proliferation and migration of schwann cells so that the administration of PRP containing NGF can have an effect on the concentration of S100B[7]. In addition, schwann cells play an important role in axon growth, so they can be used as a marker of nerve regeneration by looking at S100B expression[9]. In the case of acute peripheral nerve injury, S100B is released in the injured area[4]. It is involved in the immune reaction and inflammatory response that follows such an injury. In nerve regeneration, the role of S100B at low concentrations can stimulate neurite outgrowth, neuron survival, collateral sprouting and synaptogenesis for synaptic plasticity[5,6,8].

When S100B is released, it activates a receptor called RAGE (Receptor for Advanced Glycation End) on infiltrating macrophages (a type of immune cell) and activates Schwann cells. This activation initiates an immune response, producing pro-inflammatory cytokines (molecules involved in inflammation) and the recruitment of macrophages. Pro-inflammatory cytokines are signaling molecules that promote inflammation in the body. They are involved in various immune and inflammatory processes, such as recruiting immune cells to the site of injury or infection, increasing blood flow to the area, and activating other immune cells. Some examples of pro-inflammatory cytokines include interleukin-1 (IL-1), interleukin-6 (IL-6), and tumor necrosis factor-alpha (TNF-alpha)[4]. In addition, S100B-RAGE affects schwann cell migration during the repair process of injured peripheral nerves by inducing thioredoxin protein interaction and activating p38 MAPK, CREB and NF-□B. S100B stimulates neuronal cell survival and differentiation through the involvement of RAGE[4].

In the specific context of nerve regeneration after acute peripheral nerve injury, producing pro-inflammatory cytokines is part of the inflammatory response. While inflammation is typically seen as a protective response to injury or infection, excessive or prolonged inflammation can hinder regeneration. This is because chronic inflammation can cause tissue damage and inhibit the growth of new nerve cells. The study discovered that the addition of PRP influenced the expression of S100B. PRP is a substance derived from a patient's blood that contains a higher concentration of platelets rich in growth factors and other beneficial proteins. The exact mechanism by which PRP influenced S100B expression is not fully understood and requires further investigation.

However, the findings suggest that PRP has the potential to modulate the immune response by attenuating the inflammatory reaction triggered by S100B. This modulation of the immune response can create a more favorable environment for nerve regeneration to occur. In summary, this study examined the effects of NGF and S100B on nerve regeneration after acute peripheral nerve injury. The findings indicate that PRP may influence the expression of S100B, potentially regulating the immune response and promoting a conducive environment for nerve regeneration. Further research is needed to understand better the precise mechanism involved.

Conclusion

This study provides insights into how PRP, specifically allogenic PRP, improves sciatic nerve regeneration. Adding exogenous neurotrophic factors derived from PRP increased NGF expression, promoting a conducive environment for nerve repair. Moreover, PRP appeared to modulate S100B expression, potentially attenuating the inflammatory response and accelerating the nerve regeneration process. These findings contribute to understanding the clinical applications of allogenic PRP and its role in promoting nerve regeneration.

Novelty

While autologous PRP has been extensively studied for its regenerative potential, exploring allogenic PRP as an alternative therapy for nerve regeneration is relatively novel. Allogenic PRP offers the advantage of being readily available. It can be used in situations where autologous PRP is not feasible, such as in cases of severe trauma or insufficient platelet concentration. Investigating the effects of allogenic PRP on sciatic nerve regeneration can provide valuable insights into its efficacy and broaden the therapeutic options for patients.

Urgency and Aim of the Study

Given the increasing prevalence of nerve injuries and the potential of PRP as a therapeutic intervention, it is imperative to investigate the mechanisms underlying the regenerative effects of allogenic PRP on sciatic nerve repair. This study addresses this knowledge gap by exploring the role of neurotropic factors, particularly NGF and S100B, in nerve regeneration facilitated by allogenic PRP. Understanding how allogenic PRP influences the expression and function of these factors will not only contribute to our understanding of nerve regeneration mechanisms and provide critical insights for developing improved therapeutic approaches for patients with nerve injuries.

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