Comparison of the Regenerative Effects of Platelet-Rich Fibrin and Plasma Rich in Growth Factors on Injured Peripheral Nerve: An Experimental Study

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Purpose: The aim of this study was to investigate the effects of platelet-rich fibrin (PRF) and plasma rich in growth factors (PRGF) on peripheral nerve injury in the early period of healing.

Material and Methods: Thirty Wistar albino rats were used in this study. Rats were divided into control (C), damaged (D), PRF, and PRGF groups. The left sciatic nerves of each group were identified as group C. Crush-type injury was performed on the right sciatic nerves of the D, PRF, and PRGF groups. In the PRF and PRGF groups, blood 2 mL was obtained to prepare the PRF and PRGF and the biomaterials were applied to the injured nerve area. After 8 weeks, functional, electrophysiologic, and stereological evaluations were performed.

Results: For the electrophysiologic evaluation, the latency and amplitude values in the D, PRF, and PRGF groups were significantly lower than those in the C group ($P > .05$). According to the sciatic functional index result, there were significant differences between groups D and PRF and between groups D and PRGF ($P = .000$). For the stereological evaluations, although no significant difference was observed between the PRGF and C groups ($P > .05$), a significant difference was observed among the D, PRF, and PRGF groups for myelinated axon number. There were significant differences between groups D and PRF and between groups D and PRGF for axon area ($P = .021$ and .001, respectively). No significant difference was observed among the D, PRF, and PRGF groups for myelin sheath thickness and ratio of axon area to myelin sheath thickness ($P > .05$).

Conclusions: The results of this study suggest that PRGF increases nerve regeneration in the early period of healing and that the limited early action of PRF should be re-evaluated in the late period.

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Peripheral nerve injury is a frequently encountered clinical problem in maxillofacial surgery practice and can occur as a result of trauma, iatrogenic damage, and pathologic conditions.[1,2] The axon, nerve fiber, fascicles, and ultimately all structures of the nerve can be affected depending on the severity of the

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injury.[3] Although peripheral nerve injuries are not life threatening, they create a heavy social burden by causing long-term functional loss, esthetic problems, psychological distress, and high economic costs.[4,5] The management of nerve injury is challenging because of the limited regenerative capacity and complex structure of the nervous tissue.[6] Many different treatment protocols, such as microsurgery, grafts, tissue adhesives, pharmacologic agents, hyperbaric oxygen therapy, immunosuppressants, steroids, stem cells, and lasers, have been used to improve the repair and regenerative process after nerve injury.[2,7] However, in most of these methods, healing of the nerve can result in poor regenerative capacity, abnormal reinnervation, and end-organ atrophy.[8]

During the past 30 years, progressive cellular and molecular developments have led to a better understanding of the regenerative processes being carried out by a complex signaling network containing many bioactive molecules such as cytokines and chemokines.[9] A successful regenerative process depends on the coordination of signals originating from these bioactive molecules and the translation of these signals into several cellular events related to regeneration.[10] The success of peripheral nerve regeneration is strongly associated with the interaction between cellular elements and chemical mediators that organize the regenerative process.[7,8]

Platelet concentrates, which transform thrombocytes into thrombocyte-rich biomaterials with various centrifugation protocols, have gained popularity as an innovative regenerative approach.[11,12] There is increasing literature about the positive effects of bioactive molecules and the fibrin matrix of platelet concentrates on nerve regeneration.[13-17] In the early 2000s Choukroun et al[18] developed a second-generation platelet concentrate known as platelet-rich fibrin (PRF). The biological capacity of PRF is based on the fibrin architecture and growth factors, which have mitogenic and chemotactic properties.[19] Various clinical and experimental studies have reported on the positive effects of PRF on wound and bone healing.[20-23] However, limited studies have described the effects of PRF on nerve regeneration.[2,4,24,25] Plasma rich in growth factors (PRGF) is a plasma-based platelet concentrate that was introduced by Anitua[26] in 1999. This biomaterial does not contain leukocytes and PRGF is believed to provide an optimal biological benefit because of the presence of a platelet concentration that is moderately increased compared with that in normal blood levels.[12] Several studies have been conducted with PRGF and positive results on the efficacy of this biomaterial have been reported in many fields of medicine,[27-29] but a limited number of studies have reported on the effect of PRGF on nerve regeneration.[17,30]

No definitive protocol that provides optimal treatment of peripheral nerve injuries has been reported. Thus, there is a growing need for new protocols to overcome this clinical problem. The aim of this study was to investigate the effects of PRF and PRGF on peripheral nerve regeneration in the early healing period and to compare these 2 biomaterials in their regenerative capacity.

Materials and Methods

This study was carried out at the Animal Research Center of Ondokuz Mayis University (Samsun, Turkey) and was approved by the institutional review board and local ethics committee on animal experiments (protocol number 68489742-604.01.03-E.64724). Care was taken to ensure that the regulations of the ethics committee were met for all subjects. In this study, 30 healthy female Wistar albino rats weighing 200 to 250 g were used. The rats were randomly divided into control (C), damaged (D), PRF, and PRGF groups (Fig 1).

SURGICAL PROTOCOL

Animals were anesthetized by intraperitoneal administration of ketamine 50 mg/kg (Ketalar; Pfizer, Istanbul, Turkey) and xylazine 8 mg/kg (Rompun; Bayer, Istanbul, Turkey). After induction of anesthesia, the right medial thigh region was shaved. Antisepsis of the region was provided with povidone-iodine solution (Poviiodex; Kimpur, Istanbul, Turkey). After performing local anesthesia with articaine solution containing 1:200,000 epinephrine (Ultracain-DS; Hoechst Marion Roussel, Istanbul, Turkey), a longitudinal cutaneous incision of approximately 1.5 cm was made on the back of the thigh. Then, the right sciatic nerve was exposed and freed from the

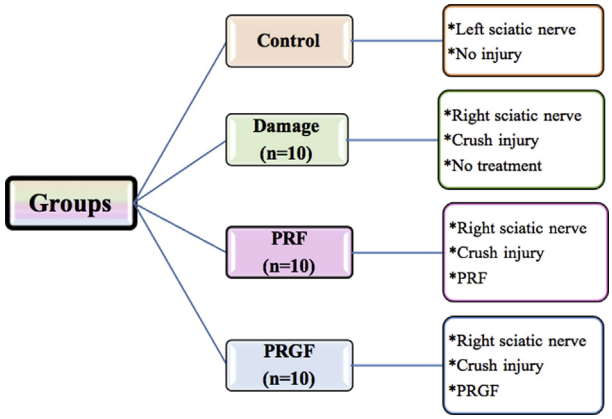

FIGURE 1. Experimental design. Abbreviations: PRF, platelet-rich fibrin; PRGF, plasma rich in growth factors.

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