Cover Letter 01-18-2026

Protocol Registration and Results System (PRS)

Title of Study:
Platelet-Derived Growth Factors to Enhance Healing and Reduce Post-Extraction Complications in Smokers

Dear PRS Review Team,

We are pleased to submit the study protocol entitled **"Application of Growth Factors Derived from Platelets to Accelerate Healing and Reduce Post-Extraction Complications in Smokers: A Randomized Clinical Trial"** for registration in the **Protocol Registration and Results System (PRS)**.

This submission presents a **prospective, randomized, split-mouth clinical trial protocol** to be conducted at the Faculty of Dentistry, King Abdulaziz University, Jeddah, Saudi Arabia. The study aims to evaluate the effectiveness of **Advanced Platelet-Rich Fibrin (A-PRF)** in enhancing soft-tissue healing following tooth extraction in smokers, a population known to be at increased risk of delayed wound healing and postoperative complications.

The manuscript has been prepared **exclusively as a protocol**, written entirely in the **future tense**, and **does not include any results, discussion, or conclusions**. The document ends with a clearly defined **statistical analysis plan**, in full compliance with PRS and clinical trial registration requirements. Ethical approval for this study has been obtained from the Research Ethics Committee of the Faculty of Dentistry, King Abdulaziz University, and all study procedures will be conducted in accordance with the principles of the Declaration of Helsinki.

Registration of this protocol will enhance research transparency, support reproducibility, and contribute valuable evidence toward improving postoperative care strategies for smokers undergoing dental extractions.

Thank you for your time and consideration of our submission. Please do not hesitate to contact us should further information or clarification be required.

Sincerely,

Dr. Amal Ghazi Jamjoom
Department of Periodontics
Faculty of Dentistry
King Abdulaziz University
Jeddah, Saudi Arabia

Platelet-Derived Growth Factors to Enhance Healing and Reduce Post-Extraction Complications in Smokers (Study Protocol)

Abstract

Smoking is a well-established risk factor for impaired wound healing following dental extractions due to its vasoconstrictive, hypoxic, and immunosuppressive effects. These alterations increase the risk of postoperative complications, including delayed soft-tissue healing, infection, and alveolar osteitis. Advanced Platelet-Rich Fibrin (A-PRF) is an autologous biomaterial rich in growth factors that promotes angiogenesis, collagen synthesis, and tissue regeneration. This study protocol describes a randomized, split-mouth clinical trial to evaluate the effectiveness of A-PRF in enhancing soft-tissue healing and reducing post-extraction complications in smokers. Adult smokers requiring bilateral simple tooth extractions will be recruited from King Abdulaziz University Dental Hospital. One extraction socket will receive A-PRF, while the contralateral socket will heal naturally and serve as the control. Soft tissue healing will be assessed using standardized digital intraoral scans at baseline, 7 days, and 14 days post-extraction. Patient-reported outcomes related to pain and interference with daily activities will also be collected. The findings of this study are expected to contribute to evidence-based strategies for improving postoperative healing outcomes in smokers.

Keywords

Advanced Platelet-Rich Fibrin; Smoking; Tooth Extraction; Wound Healing; Growth Factors

1. Introduction

Wound healing following oral surgical procedures is a complex biological process involving hemostasis, inflammation, proliferation, and tissue remodeling. These phases require adequate blood supply, oxygenation, immune competence, and cellular activity to proceed normally. Smoking has been shown to significantly disrupt these mechanisms, resulting in delayed and compromised wound healing. Nicotine-induced vasoconstriction, carbon monoxide–related hypoxia, and smoking-associated immune suppression collectively impair clot formation, fibroblast function, collagen synthesis, and angiogenesis. Consequently, smokers are at a higher risk of postoperative complications such as delayed healing, infection, and alveolar osteitis following tooth extraction.

Advanced Platelet-Rich Fibrin (A-PRF) is a second-generation platelet concentrate obtained from autologous blood without the use of anticoagulants. It acts as a biological scaffold that gradually releases key growth factors, including platelet-derived growth factor, transforming growth factor-beta, and vascular endothelial growth factor, over an extended period. These properties support neovascularization, fibroblast migration, epithelialization, and soft tissue regeneration. Due to its autologous nature and sustained biological activity, A-PRF represents a promising adjunctive therapy for enhancing healing in patients with compromised regenerative capacity, such as smokers.

While the benefits of platelet-rich fibrin have been demonstrated in healthy populations, evidence regarding its effectiveness in smokers remains limited. Given the increased prevalence of smoking-related oral surgical complications, there is a clinical need to investigate regenerative strategies that may mitigate the negative effects of tobacco use. This study protocol outlines a randomized, split-mouth clinical trial designed to evaluate the effect of A-PRF on soft tissue healing following tooth extraction in smokers.

2. Materials and Methods

2.1 Study Design

This study will be designed as a randomized, controlled clinical trial with a split-mouth design. Each participant will require bilateral simple tooth extractions and will serve as their own control. One extraction socket will be randomly allocated to receive A-PRF, while the contralateral socket will heal naturally.

2.2 Study Setting

The study will be conducted at the Faculty of Dentistry and University Dental Hospital, King Abdulaziz University, Jeddah, Saudi Arabia.

2.3 Study Population

Participants will include adult smokers aged 18 years or older who require bilateral simple tooth extractions. Eligible participants must be active cigarette smokers consuming at least 10 cigarettes per day.

2.4 Inclusion and Exclusion Criteria

Inclusion criteria will include adults aged 18 years or older, active cigarette smokers, and patients requiring bilateral simple extractions. Exclusion criteria will include patients with systemic diseases affecting healing, bleeding disorders, pregnancy or lactation, and use of tobacco products other than conventional cigarettes.

2.5 Randomization and Allocation

Randomization will be performed using a sealed-envelope technique. One extraction site will be randomly assigned to receive A-PRF, while the contralateral site will serve as the control. Allocation concealment will be maintained until the time of intervention.

2.6 Intervention

Advanced Platelet-Rich Fibrin will be prepared immediately before extraction using autologous venous blood centrifuged at 2700 rpm for 13 minutes. The resulting fibrin clot will be compressed, placed into the designated extraction socket, and stabilized with figure-of-eight sutures. Control sites will receive suturing only.

2.7 Outcome Assessment

Soft tissue healing will be assessed by measuring the socket area using digital intraoral scanning at baseline, 7 days, and 14 days post-extraction. Patient-reported outcomes will be

collected using an electronic questionnaire assessing pain intensity and interference with daily activities.

2.8 Statistical Analysis

Descriptive statistics will be used to summarize the data. Normality will be assessed using the Shapiro–Wilk test. Due to the split-mouth design and expected non-normal distribution, comparisons between intervention and control sites will be performed using the Wilcoxon signed-rank test. A p-value < 0.05 will be considered statistically significant.