

Cover Letter – Protocol Registration and Results System (PRS)

Date: Dec.13.2025

To:

Protocol Registration and Results System (PRS) Review Team

Subject: Protocol Registration Submission

Dear PRS Review Team,

We respectfully submit the study protocol entitled “**Application of Growth Factors Derived from Platelets to Accelerate Healing and Reduce Post-extraction Complications in Diabetic Individuals**” for registration in the Protocol Registration and Results System (PRS).

This protocol describes a **randomized, double-blinded, split-mouth clinical trial** that will be conducted at King Abdulaziz University Dental Hospital. The study is designed to evaluate the effect of **Advanced Platelet-Rich Fibrin (A-PRF)** on post-extraction soft tissue healing in patients with diabetes mellitus, a population known to exhibit impaired wound healing and increased susceptibility to postoperative complications.

The study will enroll adult diabetic patients requiring bilateral extraction of the same tooth type. One extraction socket will be randomly assigned to receive A-PRF, while the contralateral socket will serve as a control. Healing will be assessed using **digital intraoral scanning at predefined time points**, along with patient-reported outcome measures. The split-mouth design has been selected to minimize inter-individual variability and improve internal validity.

The protocol has been developed in accordance with ethical and methodological standards for human clinical research. Ethical approval has been obtained from the Institutional Review Board of King Abdulaziz University Dental Hospital, and the study will be conducted in compliance with the Declaration of Helsinki. Written informed consent will be obtained from all participants before enrollment. At the time of registration, no participants have been enrolled, and no data have been collected.

This registration is being submitted to ensure **transparency, methodological rigor, and prospective documentation** of the study design and planned analyses. We confirm that the information provided in the PRS submission accurately reflects the study protocol and that study results will be reported in accordance with PRS requirements upon completion.

Thank you for your review and consideration of this protocol registration. Please do not hesitate to contact us if you require any additional information or clarification.

Sincerely,

Dr. Amal Ghazi Jamjoom

Principal Investigator

King Abdulaziz University Dental Hospital

Jeddah, Saudi Arabia

Email: [your institutional email]

On behalf of the study team:

Ziyad Alsefri; Osamah Shindi; Amal Jamjoom

**Application of Growth Factors Derived from Platelets to Accelerate Healing and Reduce
Post-Extraction Complications in Diabetic Individuals**

Authors

Abstract

Introduction

Diabetes Mellitus (DM) represents a significant global public health challenge, with a particularly high prevalence in Saudi Arabia. The increasing incidence of DM has raised concerns regarding optimal management strategies for surgical procedures such as dental extractions. Diabetic individuals frequently experience impaired postoperative healing due to compromised tissue repair mechanisms and increased susceptibility to infection. Conventional management approaches may be insufficient, highlighting the need for biologically driven adjunctive therapies.

Objective

This study aims to evaluate the clinical effectiveness of Advanced Platelet-Rich Fibrin (A-PRF) in enhancing soft-tissue healing and reducing post-extraction complications in diabetic patients.

Methods

A randomized, double-blinded, split-mouth clinical trial will be conducted at King Abdulaziz University Dental Hospital. Diabetic patients requiring bilateral extraction of the same tooth type will be enrolled. One extraction socket will be randomly assigned to receive A-PRF, while the contralateral socket will serve as the control. Healing will be assessed using digital intraoral scanning at baseline, 1 week, and 3 weeks post-extraction. Statistical analysis will be performed using paired-comparative tests, with a significance level of $p < 0.05$.

Expected Outcomes

The application of A-PRF is expected to enhance soft tissue healing and reduce postoperative complications in diabetic individuals.

Conclusion

This study is expected to provide clinical evidence supporting the use of A-PRF as a biologically based adjunctive approach to improve post-extraction healing outcomes in diabetic patients.

Introduction

Diabetes Mellitus (DM) is a global public health problem, with an especially high prevalence in Saudi Arabia. The rising incidence of DM has increased concerns regarding the management of diabetic patients undergoing surgical procedures, including tooth extractions. Diabetic individuals often exhibit impaired postoperative healing characterized by delayed tissue repair,

prolonged inflammation, and an increased risk of infection. Conventional treatment strategies may not adequately address these challenges, necessitating the exploration of novel regenerative approaches.

Platelet-derived growth factors, particularly Advanced Platelet-Rich Fibrin (A-PRF), have recently gained attention as potential promoters of wound healing and tissue regeneration. A-PRF is a biologically active autologous scaffold that aligns with the physiological principles of wound healing by providing a sustained release of key growth factors such as platelet-derived growth factor (PDGF), transforming growth factor- β (TGF- β), and vascular endothelial growth factor (VEGF). These growth factors are essential for cellular migration, angiogenesis, and extracellular matrix remodeling.

In diabetic patients, chronic hyperglycemia, prolonged inflammation, microvascular dysfunction, and impaired collagen synthesis contribute to delayed wound healing. The theoretical premise of A-PRF is that it may enhance the natural healing cascade in diabetic individuals by compensating for impaired biological responses. However, despite promising biological rationale and preliminary clinical evidence, there remains limited high-quality clinical data evaluating the effectiveness of A-PRF in post-extraction socket healing in diabetic patients.

Therefore, this study will aim to evaluate the effectiveness of A-PRF in enhancing soft tissue healing and reducing post-extraction complications in diabetic individuals using a split-mouth randomized clinical trial design. The findings are expected to contribute to evidence-based clinical protocols and improve standards of care for diabetic patients undergoing dental extractions at King Abdulaziz University Dental Hospital.

Research Question

Does the application of growth factors derived from platelets accelerate healing and reduce post-extraction complications in diabetic individuals?

Research Hypotheses

Null Hypothesis (H0):

The application of platelet-derived growth factors will not enhance healing or reduce post-extraction complications in diabetic individuals.

Alternative Hypothesis (H1):

The application of platelet-derived growth factors will accelerate healing and reduce post-extraction complications in diabetic individuals.

Objectives

Using a split-mouth design, this study will evaluate soft tissue closure of extraction sockets by comparing sites treated with A-PRF to sites without A-PRF application at King Abdulaziz University Dental Hospital.

Significance of the Study

1. This research is expected to demonstrate the potential of A-PRF to enhance postoperative healing and improve the quality of life in diabetic patients undergoing dental extractions.
2. The findings may contribute to the development of improved, biologically based treatment protocols for diabetic patients in dental practice.

Literature Review

Diabetes Mellitus (DM) is a complex chronic disease affecting millions worldwide, with a notably elevated prevalence in Saudi Arabia. The increasing incidence of DM has been attributed to lifestyle changes, urbanization, and genetic predisposition. Microvascular complications such as retinopathy, nephropathy, and neuropathy significantly increase morbidity and mortality among diabetic patients.

In oral health, diabetes is associated with delayed wound healing, increased susceptibility to infection, periodontal disease, and tooth loss. The healing of extraction sockets normally progresses through distinct stages, including clot formation, inflammation, proliferation, and remodeling. However, in diabetic individuals, chronic hyperglycemia disrupts these processes by impairing angiogenesis, inflammatory regulation, collagen synthesis, and bone formation.

Platelet-rich fibrin (PRF) has emerged as a regenerative biomaterial capable of enhancing wound healing through sustained growth factor release. Advanced PRF (A-PRF), produced using low-speed centrifugation protocols, retains higher concentrations of platelets and leukocytes within a fibrin matrix. This biological scaffold is expected to improve cellular migration, angiogenesis, and tissue regeneration, making it particularly relevant for diabetic patients with compromised healing capacity.

Despite promising biological mechanisms, there remains limited clinical evidence evaluating the specific role of A-PRF in post-extraction socket healing in diabetic patients, highlighting the need for well-designed randomized clinical trials.

Materials and Methods

Study Design and Ethics

This double-blinded, randomized controlled clinical trial will be conducted at King Abdulaziz University Dental Hospital. Ethical approval has been obtained from the Institutional Review Board, and the study will be conducted in accordance with the Declaration of Helsinki (2013). Written informed consent will be obtained from all participants prior to enrollment.

Sample and Study Population

The sample size has been calculated using G*Power software with an alpha level of 0.05, 80% power, and a medium effect size of 0.5. Diabetic patients aged 18 years or older requiring bilateral extraction of the same tooth type will be recruited. Patients with systemic conditions other than diabetes, bleeding disorders, pregnancy, lactation, or tobacco use will be excluded.

A split-mouth design will be employed, with one extraction site randomly assigned to receive A-PRF and the contralateral site serving as a control. Randomization will be performed using a computer-generated sequence. Patients and outcome assessors will remain blinded throughout the study.

Clinical Procedure

All extractions will be performed using a standardized atraumatic technique by a single calibrated operator. After extraction, venous blood will be collected to prepare A-PRF using a low-speed centrifugation protocol. The A-PRF membrane will be placed into the assigned socket, while control sockets will receive no adjunctive material. All sites will be sutured using standardized suture material.

Outcome Measures

Healing will be assessed quantitatively using digital intraoral scanning at baseline, 1 week, and 3 weeks post-extraction. Patient-reported outcomes, including pain, swelling, and satisfaction, will be collected using validated questionnaires at specified follow-up intervals.

Statistical Analysis

Data will be analyzed using Stata software (Version 16). Normality will be assessed using the Shapiro–Wilk test. Paired statistical tests will be used to compare healing outcomes between A-PRF-treated and control sites, with significance set at $p < 0.05$.