CLINICAL EVALUATION OF HYALURONIC ACID AND PLATELET RICH FIBRIN INJECTION EFFICACY IN INTERDENTAL PAPILLA RECONSTRUCTION

Study Protocol with Statistical Analysis Plan

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Scientific Background

Loss of the interdental papilla is a frequent aesthetic concern, particularly in the anterior region where even minor deficiencies create visible black triangles. These deficiencies contribute to plaque accumulation, food impaction, and phonetic disturbances, in addition to compromising smile harmony. Earlier attempts to reconstruct missing papillae through surgery often yielded unpredictable outcomes, largely due to the delicate blood supply of the papillary region. As a result, attention has shifted toward non-surgical injectable biomaterials designed to restore soft-tissue volume with minimal invasiveness.

Hyaluronic acid (HA) dermal fillers have become widely used in aesthetic and periodontal therapy due to their biocompatibility, hydrophilicity, and ability to stimulate wound healing. Clinical studies have consistently reported partial or complete closure of black triangles following repeated HA injections. Injectable platelet-rich fibrin (i-PRF), prepared via low-speed centrifugation, represents an autologous alternative that provides a fibrin scaffold enriched in platelets and leukocytes. Its gradual release of growth factors promotes angiogenesis, fibroblast proliferation, and extracellular matrix formation.

Despite increasing interest, direct comparisons between these two materials are scarce, and previous trials have not used a split-mouth design to minimize interpatient variability. This study directly compares HA and i-PRF administered under identical intraoral conditions. We hypothesized that both would yield significant improvement in papilla fill without clinically meaningful differences between them.

Study design

This randomized split-mouth clinical trial included 13 systemically healthy adults with a total of 65 papilla deficiencies in the aesthetic zone. The study was approved by the Altınbaş University Ethics Committee. All participants provided written informed consent.

Inclusion criteria required ≥2 papillae classified as Papilla Presence Index (PPI) class 2 or 3, probing depths ≤3 mm, and plaque and bleeding scores below 15%. Exclusion criteria included PPI class 4, diastema, active periodontal disease, smoking, pregnancy, systemic conditions influencing healing, anticoagulant use, and previous surgical papilla reconstruction.

For each participant, one side was randomly assigned HA and the contralateral side i-PRF. The clinical examiner underwent intra-examiner calibration until repeated measurements were consistent within ±1 mm. Outcome assessments were performed by a blinded examiner.

For i-PRF sites, 10–20 mL of venous blood was collected into plastic tubes and centrifuged at 700 rpm for 3 minutes. The upper orange plasma layer was aspirated and transferred to 1-mL insulin syringes. Injections were delivered within 5 minutes to ensure liquid consistency before polymerization.

All treatments were performed with buccal infiltration anesthesia. HA or i-PRF (0.1–0.2 mL) was injected from the buccal aspect, 2–3 mm apical to the papilla tip, at a 45° angle. A single

puncture per session was used to minimize trauma. Slight blanching indicated correct placement. Each papilla received three injections at baseline, week 3, and week 6.

Participants avoided mechanical oral hygiene for 24 hours and interdental brushes for one week, replacing them with 0.12% chlorhexidine rinses. Modified Bass brushing resumed the following day.

Standardized photographs were obtained using a custom photograph standardization device (PSD), enabling consistent image acquisition. Black triangle height (BTH), width (BTW), area (BTA), and papilla height (PH) were measured at baseline, 1 month, and 3 months using ImageJ. PPI was recorded visually. Radiographs were taken to measure the distance between the interdental bone crest and contact point (IBC–ICP). Keratinized tissue thickness (KTT) was measured at baseline.

Pain was assessed after each injection using a VAS scale from 0 (none) to 10 (worst). Aesthetic satisfaction was rated at each visit using a VAS scale from 0 (not satisfied) to 10 (highly satisfied).

Statistical Analysis Plan

The data were analysed using the Statistical Package for the Social Sciences (SPSS) version 26.0. The normality of distribution for the numerical variables related to the patients and the evaluated interdental papilla sites was assessed based on skewness and kurtosis values. Normality of continuous data will be assessed using the Shapiro–Wilk test and visual inspection of Q–Q plots. A reference range of ±1.96 was adopted as the criterion for normal distribution (Kalaycı, 2005).

For each material, changes over time from baseline to follow-up will be analysed using repeated-measures ANOVA when assumptions are met, or the Friedman test in the case of non-parametric or ordinal data. Post-hoc pairwise comparisons between time points will include Bonferroni adjustments. Since the study design is split-mouth, inter-group comparisons between HA and i-PRF at each time point, as well as comparisons of change scores, will use paired t-tests for normally distributed variables and Wilcoxon signed-rank tests otherwise. PPI, being ordinal, will be evaluated with non-parametric paired procedures. Subgroup analyses will be performed separately for maxillary and mandibular papillae using similar paired or repeated-measures methods. Patient-reported VAS outcomes will be analysed using repeated-measures methods for within-group changes and paired testing for between-group differences.

Comparisons of KTT and IBC-ICP measurements across jaw localizations and treatment groups, as well as intergroup analyses of clinical outcome variables, were performed using the One-Way ANOVA test. Intragroup comparisons of variables measured at different time points were conducted using the Repeated Measures ANOVA. Where applicable, Post Hoc tests were employed to further investigate significant intergroup differences.

Additionally, to evaluate the relationship between KTT and IBC-ICP measurements and the percentage changes in clinical parameters, the Spearman correlation test was used. In interpreting the correlation coefficients, a range of 0.00–0.30 was considered low, 0.30–0.70 moderate, and 0.70–1.00 high. A significance level of $p < 0.05$ and $p < 0.01$ was adopted for all statistical analyses.