DOI: 10.7860/JCDR/2023/61906.18249

Research Protocol

Dentistry Section

Effect of Injectable Platelet-Rich Fibrin and Micro-Osteoperforation on Accelerated Orthodontic Tooth Movement: Protocol for a Split-Mouth Randomised Clinical Trial

KUSHAL TAORI[1], PRIYANKA NIRANJANE[2]

ABSTRACT

Introduction: Orthodontic treatment is often perceived as time-consuming by patients. Various techniques have been developed to accelerate treatment and reduce its duration, but there is limited literature supporting their efficacy and advantages. This study aims to compare the effectiveness and acceptability of two methods in accelerating orthodontic tooth movement, providing valuable insights for clinicians.

Need for the study/Rationale: Injectable Platelet-Rich Fibrin (i-PRF) and Micro-Osteoperforation (MOP) are two modalities known to accelerate tooth movement. i-PRF is a chemical modality, while MOP is a minimally invasive mechanical procedure. Both stimulate osteoclastic inflammatory cytokines, facilitating rapid tooth movement. However, there is limited evidence comparing the efficacy of these two methods. By comparing the mechanical i.e. MOP and chemical i.e. i-PRF modes of accelerated orthodontics, this planned protocol will study to determine the most feasible treatment modality based on objective patient outcomes, rate of tooth movement, and advantages/disadvantages.

Aim: To evaluate and compare the effects of i-PRF and MOP on accelerated orthodontic movement in a young adult population.

Materials and Methods: This split-mouth prospective randomised study will involve 10 participants selected from the departmental Out Patient Department (OPD) based on inclusion and exclusion criteria. Informed consent will be obtained. The participants will be divided into two groups:

Group A: Undergoing MOP

Group B: Undergoing i-PRF

Group allocation (left or right side) will be randomised. The rate of maxillary canine retraction will be measured after intervention in both study groups.

Expected results: Both i-PRF and MOP are expected to accelerate orthodontic tooth movement, with MOP being more effective in this regard.

Keywords: Accelerated tooth movement, Canine retraction, Osteoclastic inflammatory cytokines

INTRODUCTION

Prolonged orthodontic treatment continues to be a major concern for clinicians and patients. Standard orthodontic treatment with fixed appliances typically takes more than 18 months, which can be further prolonged depending on tooth misalignment severity, treatment complexity, and various clinician and patient factors [1]. Such long treatment duration can lead to challenges and unfavourable outcomes, including halitosis, mucosal discomfort, increased risk of caries, root resorption, as well as gingival and periodontal diseases. Additionally, patient satisfaction and compliance may be negatively affected. Therefore, there is a growing interest in reversing the treatment time in orthodontics. Various treatment modalities have been developed to address this issue. One common approach is surgical intervention, such as corticotomy and Periodontally Accelerated Osteogenic Orthodontics (PAOO). However, these invasive procedures carry risks of postoperative bleeding, infections, pain, and negative impacts on patients [2].

Minimally invasive procedures like MOP offer advantages by being less invasive and minimising side effects. MOP involves minimal perforation of the cortical bone using tools like the PROPEL device or miniscrews, without raising a flap (flapless bone puncturing) [3]. Teixeira and associates introduced this procedure and hypothesised that limited cortical bone perforations are sufficient to trigger the Regional Acceleratory Phenomenon (RAP), thereby accelerating tooth movement [4,5]. MOP stimulates inflammatory markers in the alveolar bone, leading to increased osteoclastic resorptive activity and accelerated tooth movement [6].

Another treatment modality for accelerated tooth movement involves using biological autogenous promoters like platelet concentrates, including Platelet Rich Plasma (PRP) and Platelet Rich Fibrin (PRF). PRF, a second-generation concentrate without anticoagulants, has advantages over PRP, the first-generation platelet concentrate, such as lower risk of infections, bleeding, and longer duration of action [7,8]. As there is limited literature and evidence regarding the effects of Platelet Rich Fibrin (PRF) in accelerated orthodontics and its impact on optimal force application, this study will primarily focus on the derivative of PRF, known as Injectable Platelet-Rich Fibrin (i-PRF). i-PRF is a second-generation platelet concentrate developed by Dr. Joseph Choukroun. Unlike PRP, i-PRF does not contain added anticoagulants during the spinning process, which can interfere with its regenerative properties [9]. A study has shown that i-PRF significantly affects osteoblastic behavior by influencing proliferation, migration, and differentiation, leading to increased cellular activity, accelerated bone turnover, and healing [10]. It also stimulates the expression of inflammatory cytokines, which increase clastic activity and promote faster tooth movement [7].

Hence the planned research protocol will study to evaluate and compare the effect of MOP and i-PRF on accelerating tooth movement and also genderwise comparison of these modalities.

REVIEW OF LITERATURE

A standard orthodontic treatment using fixed appliances typically takes more than 18 months, with the duration depending on factors such as the severity of malaligned teeth, treatment complexity,

and clinician and patient variables [11]. A study by Alikhani M et al. aimed to evaluate the effect of MOP on tooth movement rate and expression of inflammatory markers. The results showed that MOP significantly increased the rate of tooth movement by 2-3 times, accompanied by a significant increase in inflammatory markers [3]. Another study by Aboalnaga AA et al. included a split-mouth clinical trial to investigate the effect of MOP on orthodontic tooth movement (OTM). This study found that the mean rate of canine retraction in control and MOP sides was 0.99±0.3 mm/month [4]. Zeitounlouian TS et al. examined the effectiveness of i-PRF in accelerating maxillary canine retraction [8]. The results showed that the average rates of canine retraction were higher in the i-PRF group. However, the rate of canine retraction following i-PRF was not significantly greater in the experimental group compared to the control sides, except in the second month (T2).

MATERIALS AND METHODS

This split-mouth prospective double-blinded randomised clinical trial will be conducted in the Department of Orthodontics and Dentofacial Orthopaedics Sharad Pawar Dental College, Sawangi (Meghe), Wardha, Maharashtra, India. All procedures involving patients will comply with the ethical standards of the Institutional Ethics committee, as well as the 1964 Helsinki statement and its subsequent revisions or equivalent ethical standards. The Institutional Ethics Committee meeting held on 31-01-2022 has approved the proposed research (Ref.No. DMIMS(DU)/IEC/2022/746). The study trial has been registered in the clinical trial registry of India (CTRI/2022/12/048404).

The study sample will be selected from patients visiting the departmental outpatient department (OPD), based on the following inclusion and exclusion criteria:

Inclusion criteria: Patients aged 15-30 years with Class 2 Division 1 malocclusion (ANB angle from 5-7 degrees) [11] and bimaxillary protrusion requiring extraction of maxillary first premolars and the patients with average growth pattern (Frankfort-Mandibular Plane Angle [FMA] from 20-30 degrees) [12], patients with no systemic conditions or diseases, those with fully erupted maxillary canines, healthy periodontal parameters, with no clinical attachment loss or probing pocket depth greater than 2-3 mm and the ones indicated for fixed orthodontic therapy will be included in the study.

Exclusion criteria: The patients with a horizontal or vertical growth pattern, those with developmental and congenital syndromes or with systemic diseases such as clotting disorders or conditions like pregnancy or on anticoagulant therapy, those above the age of 30 years and patients with deleterious habits such as smoking, those undergoing removal or myofunctional orthodontic treatment, those on medication that decreases Oral Transmucosal (OTM) like Non-Steroidal Anti-Inflammatory Drugs (NSAIDs) like ibuprofen, aspirin, aceclofenac, diclofenac, bisphosphonates, or hormonal replacement therapies will be excluded from the study.

After taking informed consent from the selected patients, complete case history and study records will be collected from both groups.

Sample size calculation: To determine the sample size for the study, the rate of canine retraction will be considered. The sample size will be calculated using the following formula for the difference between two means:

$$N=\frac{(Z\alpha+Z\beta)^2(\sigma1+\sigma2/1)^2}{\Delta^2}$$

Where:

$Z\alpha$ is the level of significance at 5% (0.05). $Z\beta$ is the power of the test (80% = 0.8). σ_1 is the standard deviation of the distance travelled by the maxillary canine in the control group at two weeks. σ_2 is the standard deviation of the distance travelled by the maxillary canine in the experimental group at two weeks. K=1 (as only two groups are being compared). Δ is the difference between the two means.

The study by Abdelhameed AN and Refai WMM [5] was used as a reference for the above calculations.

Planned Procedure

Based on the split-mouth study design, each patient will be divided into two groups: Group A (undergoing MOP) and Group B (undergoing i-PRF). The allocation will be randomised to either the left or right side. Randomisation will be performed in a 1:1 ratio, and allocation concealment will be ensured using the centralised online randomisation service “sealed envelope” with a web front-end.

Pre-radiographic records (to evaluate canine root and estimate centre of resistance based on root length) and impression records will be taken before the start of orthodontic treatment. The orthodontic treatment will begin with fixed therapy using MBT (McLaughlin, Bennett, Trevisi) 0.022 brackets for initial levelling and alignment in patients with Class 2 Division 1 malocclusion or bimaxillary protrusion.

After initial alignment of the dentition, miniscrews i.e. Temporary Anchorage Devices (TAD) will be placed bilaterally between the maxillary second premolar and first molar, 5-6 mm from the alveolar crest, to avoid anchorage loss and ensure accurate results. After the alignment and placement of TADs, the patient will be referred to the Department of Oral Surgery for the extraction of the planned first premolars on both sides. Canine distalisation will be conducted using calibrated 150 g Nickel-Titanium (Ni-Ti) closed-coil springs, which will be connected with the miniscrews to a hook in front of the canine bracket [13].

Preparation and Application of Injectable Platelet Rich Fibrin (i-PRF) Injection

A venous blood sample of 20 ml will be obtained from the patient’s brachial vein in the cubital fossa using an IV cannula and a 20 ml disposable syringe. The blood will be collected in a dry sterile glass tube without any anticoagulant [9]. The centrifugation protocol will involve one cycle at 700-800 rounds per minute (rpm) for 3-4 minutes at room temperature. The yellowish-orange top supernatant portion of the tube will be collected to obtain 3-4 ml of i-PRF using a 27-gauge needle [8].

The i-PRF will be immediately injected intraligamentally into the distobuccal and distopalatal sides of the canine to be retracted (1.5 mL on each side), as well as on the buccal and palatal mucosa of the extraction site (1 ml on buccal submucosa and 0.5 mL on palatal side, equidistant from the maxillary canine and second premolar). Before the injection, a topical anaesthesia spray (2% lignocaine) will be applied to control pricking pain [8].

Frequency of Injections

- T0: First week of treatment post-extraction of the first premolar
- T1: Fourth week of treatment
- T2: Eighth week of treatment
- T3: Twelfth week of treatment

MOP Intervention Protocol

On the contralateral side, the MOP intervention will be performed post-extraction under local infiltrative anaesthesia (2% lignocaine). The MOPs will be performed distal to the canine and before retraction. Six small MOPs will be performed in the extraction space at equal distances from the canine and second premolar. Each perforation will be 1.5-1.8 mm wide and 3-8 mm in depth, using a Propel device in the attached gingiva [3]. No pain or prophylactic antibiotic coverage will be prescribed.

Frequency of MOP:

- T0: First week of treatment post-extraction of the first premolar
- T1: Fourth week of treatment
- T2: Eighth week of treatment
- T3: Twelfth week of treatment.

Measuring Distalisation Rate (Data Collection)

All measurements will be taken on dental casts obtained from putty or alginate impressions on study models poured in dental stone at four time points:

- T0: First week of treatment post-extraction
- T1: Fourth week of treatment
- T2: Eighth week of treatment
- T3: Twelfth week of treatment

The measurements will be taken to determine the anterior-posterior canine or molar movements between the medial end of the third palatal rugae and the tip of the upper canine [8]. The third rugae are considered relatively stable reference points for evaluating tooth movement [8].

Safety Evaluation

Any adverse events, such as inflammatory apical root resorption, bone hyalinisation and necrosis, dehiscence and fenestration, and non-vitalisation of teeth, will be noted by a research assistant in the case report form for safety assessment. The Institutional Ethics Committee will be notified of any major adverse occurrences within 24 hours.

STATISTICAL ANALYSIS

The data will be analysed using statistical software, including the Chi-square test and Student t-test. The software used for statistics will be GraphPad Prism 7.00 and Statistical Package for Social Sciences (SPSS) 27.00. Approximately, a sample size of 10 patients will be used for this study.

Trial status:

Recruitment for this clinical study will begin in September 2022 and is expected to be completed by March 1, 2024.

Acknowledgement

The authors would like to acknowledge the publishers of the journals and books that were used to review the literature for this study. The authors would also like to thank the Honourable Vice-Chancellor of DMIMS (DU), the teaching and non-teaching personnel of the Department of Orthodontics and Dentofacial Orthopaedics, and colleagues for their assistance in this study.

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PARTICULARS OF CONTRIBUTORS:
1. Postgraduate Student, Department of Orthodontics and Dentofacial Orthopaedics, Sharad Pawar Dental College, Wardha, Maharashtra, India.
2. Associate Professor, Department of Orthodontics and Dentofacial Orthopaedics, Sharad Pawar Dental College, Wardha, Maharashtra, India.

NAME, ADDRESS, E-MAIL ID OF THE CORRESPONDING AUTHOR:
Kushal Taori,
Postgraduate Student, Department of Orthodontics and Dentofacial Orthopaedics,
Sharad Pawar Dental College, Wardha-442004, Maharashtra, India.
E-mail: kushaltaori97@gmail.com

PLAGIARISM CHECKING METHODS: [Jain H et al.]
- Plagiarism X-checker: Dec 12, 2022
- Manual Googling: Mar 15, 2023
- iThenticate Software: Apr 05, 2023 (21%)

ETYMOLOGY: Author Origin

EMENDATIONS: 7

AUTHOR DECLARATION:
- Financial or Other Competing Interests: None
- Was Ethics Committee Approval obtained for this study? Yes
- Was informed consent obtained from the subjects involved in the study? NA
- For any images presented appropriate consent has been obtained from the subjects. NA

Date of Submission: **Dec 05, 2022**
Date of Peer Review: **Jan 13, 2023**
Date of Acceptance: **Apr 06, 2023**
Date of Publishing: **Jul 01, 2023**