Comparison and Evaluation of The Pain Experience between Vitamin D and Injectable Platelet Rich Fibrin - A Randomised Controlled Trial

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ABSTRACT
Introduction Orthodontic discomfort is a major barrier to treatment compliance, with pain being a common reason for patients to discontinue. Pain often originates from the periodontal ligament due to pressure, ischemia, and swelling, and is influenced by individual factors like age, gender, and stress. Vitamin D and Platelet-Rich Fibrin (PRF) have emerged as non-invasive methods to accelerate orthodontic tooth movement while potentially reducing treatment pain. Materials and Methods This split-mouth, randomized control trial involved 20 adult patients undergoing canine retraction post-premolar extraction. PRF and Vitamin D were administered in different quadrants, with saline serving as the control. PRF was prepared using the double centrifugation technique and injected into the periodontal ligament. Vitamin D was prepared as a 50 pg dose and administered similarly. Canine retraction forces were applied using 150 grams of elastomeric chains, and pain was assessed using a Visual Analog Scale (VAS) immediately, after 24 hours, and at one week. Results PRF showed significantly higher pain scores than the control group after 24 hours and one week. In contrast, no significant difference in pain perception was observed between Vitamin D and control groups. Additionally, there was no significant difference in pain between PRF and Vitamin D groups at any time point.

1. Introduction

Orthodontic discomfort is a significant barrier to seeking treatment and is one of the most common causes for patients to halt their treatment.[1] Since patients and orthodontists may not always align in their assessments of treatment outcomes, it's reasonable to assume that a gap also exists between patients' pain experiences and the way orthodontists perceive that pain.[21] Of the various orthodontic procedures examined, the activation of T-loops during tooth retraction was reported to result in the most intense pain.[3] It's believed that orthodontic pain originates in the periodontal ligament due to the combined effects of pressure, ischemia, and swelling. Inflammatory agents such as histamine, substance P, prostaglandin, and serotonin are found to increase in the periodontal ligament during orthodontic treatment.[4] Since pain is subjective, individuals exhibit wide variability in their responses. Pain sensitivity may be influenced by a range of factors including age, gender, personal pain tolerance, the force applied during treatment, emotional state, stress levels, cultural background, and prior pain experiences.[5]

Accelerated Orthodontics takes advantage of localized interventional inflammation known as the "Regional Acceleratory Phenomenon" [6] inorder to reduce treatment time to prevent or reduce the incidence of white spot lesions or root resorption among other iatrogenic effects. [7,8910] Non-Invasive pharmacological methods of achieving this include Vitamin D and Platelet Rich Fibrin. Vitamin D's significance in dentistry goes well beyond its conventional role in calcium metabolism and bone integrity, playing a pivotal part in orthodontic tooth movement. When specific forces are exerted during orthodontic procedures, they trigger dual responses: bone resorption on the pressure side via osteoclast activity and bone formation on the tension side through osteoblast stimulation. These processes can be accelerated when paired with mechanical, chemical, or electrical triggers.[11] Research on both animal and human subjects suggests vitamin D may enhance tooth movement, with studies on rats showing heightened alveolar bone formation and mineral apposition following 1.25(OH)2D3 injections during orthodontic treatment.[11,1213] Human clinical trials also reported increased maxillary canine retraction with localized vitamin D3 applications, though some studies

found no statistically significant differences compared to control groups.[14,15] Simultaneously, Platelet-Rich Derivatives (PRDs), including Platelet-Rich Fibrin (PRF), are emerging as influential tools in various spheres of dentistry as well as modern orthodontics.[16] These autologous products, derived from a patient's blood, offer a concentrated mix of platelets loaded with growth factors that promote osteoclast and osteoblast activity, aiding in alveolar bone remodeling.[17] PRF, classified as a second-generation PRD, demonstrates exceptional potential in tissue regeneration and wound healing, primarily due to its fibrin matrix, which houses a robust collection of cytokines and growth factors like PDGF, TGF-β1, and VEGF.[18,19]

There are no documented clinical trials in the existing literature that directly compare the efficacy of injectable Platelet-Rich Fibrin and Vitamin D in accelerating orthodontic tooth movement. This study seeks to address this gap. This study therefore aims to compare the pain experience of localized Calcitriol injections with injectable Platelet-Rich Fibrin during canine retraction.

2. Material and Methods

The study was conducted with consent. Adult patients undergoing fixed appliance therapy with MBT prescription, post-extraction of maxillary first premolars, were included. Ethical clearance was granted by the Institutional Review Board (SRB/SDC/ORTHO-2005/21/TH-052), and the trial was registered with the Clinical Trials Registry-India (CTRI/2024/04/066280). This split-mouth, randomized control trial involved a sample size calculation based on Erdur et al. (2021), yielding 10 quadrants per group (n=10/group) to account for attrition and bias. Participants were recruited following strict inclusion criteria (adults aged 18–35 years, with good oral hygiene, no systemic illness, and requiring mini-implant-assisted canine retraction). Patients were informed about the study, signed consent was obtained, and they were assured of their right to withdraw. Randomization of intervention and control quadrants was performed using a coin toss.

Exclusion criteria included patients with a history of smoking, anemia, vascular diseases, or long-term use of steroids, bisphosphonates, or NSAIDs, as well as those unwilling to participate. The study ensured transparency in patient involvement and informed consent procedures. This split-mouth randomized clinical trial involved patients who required extraction of the maxillary first premolars. Extractions were performed at least a month before the study commenced to minimize interference from the regional acceleratory phenomenon (RAP). Participants were in the final stages of fixed appliance therapy using 0.22 MBT metal brackets (AO mini master, USA), with canine retraction conducted on 0.019 x 0.025 stainless steel archwires.

I-PRF Preparation and Administration Following the collection of 5-10 ml of venous blood from each participant, the double centrifugation technique, as described by Marx et al. (2005) and Rashid et al. (2017), was employed. A 0.2 ml intraligamentary injection of injectable Platelet-Rich Fibrin (iPRF) was administered to the disto-buccal, middle, and disto-palatal areas of the maxillary canine. In the control quadrant, 0.2 ml of saline was injected. This protocol was repeated every 30 days for 3 months. Vitamin D Preparation and Injection

Sachets of Vitamin D3 (Calcitriol, Mibe, Germany) were used to create a 50 pg dose of 1,25-dihydroxyvitamin D3, diluted in 0.2 ml of dimethylsulfoxide (DMSO, Bisolve B.V., Netherlands). This solution was administered intraligamentary to the maxillary canine, while the contralateral canine received only saline. Injections were repeated every 30 days for 3 months. Force Application Canine retraction was initiated with elastomeric power chains exerting 150 grams of force, calibrated using a Dontrix gauge at each appointment. Forces were applied bilaterally to mini-implants.

Pain Perception Pain was assessed using a Visual Analog Scale (VAS) immediately post-intervention, after 24 hours, and again after one week on both the control and intervention sides. Patients were instructed to avoid analgesics during the evaluation period. Inter-group and intra-group differences in pain perception were studied using Mann-Whitney U test and Wilcoxon signed rank test respectively. A p value of less than 0.05 was considered as significant.

3. Results and Discussion

In the I-PRF group, At 0 hours from the point of administration of I-PRF and saline control the difference in pain scores between the two groups was found to be insignificant (p=0.018). However after 24 hours, a statistically significant (p=0.007) higher pain score rating was reported in the I-PRF group. In the 1 week assessment, where the intervention reported a lower pain score, which was statistically significant.

Table 1: Comparison of mean pain perception scores between I-PRF and control (* denotes significance)

Parameter	N	Mean	Std. Deviation	Std. Error Mean	*Z* value	P value
Immediately after Intervention	10	1.70	.483	.153	-1.342	0.18
Immediately after Control	10	1.40	.516	.163		
24 hrs after Intervention	10	6.40	.516	.163	-2.714	0.007*
24 hrs after Control	10	5.50	.527	.167		
1 week after Intervention	10	2.10	.316	.100	-2.121	0.011*
1 week after Control	10	2.30	.483	.152		

There was no statistically significant difference in pain experience between the groups immediately after administration of Vitamin D and saline nor after 24 hours(Table 1). Pain experience reduced after 1 week of administration, and was noted to be higher on the intervention side (p=0.063).

Table 2: Comparison of mean pain perception scores between Calcitriol and control

Parameter	N	Mean	Std. Deviation	Std. Error Mean	*Z* value	P value
Immediately after Intervention	10	1.40	.516	.163	-1.63	0.102
Immediately after Control	10	1.80	.422	.133		
24 hrs after Intervention	10	6.30	.675	.213	-2.71	0.190
24 hrs after Control	10	5.90	.316	.100		
1 week after Intervention	10	2.1	.567	.179	-2.131	0.063
1 week after Control	10	1.5	.527	.166		

On comparing both interventions(Figure 1), it was noted that while I-PRF was associated with higher pain scores, the difference between both groups was not statistically significant (Table 2).

Table 2: Comparison of mean pain perception scores between the I-PRF and Calcitriol groups at various time points

Time	Group	N	Mean	Std. Deviation	Std. Error Mean	P value
Immediate	I-PRF	10	1.70	.483	.153	0.189
	Calcitriol	10	1.40	.516	.163	
24 hours	I-PRF	10	6.40	.516	.163	0.853
	Calcitriol	10	6.30	.675	.213	
1 week	I-PRF	10	2.10	.316	.100	0.529
	Calcitriol	10	2.1	.567	.179	

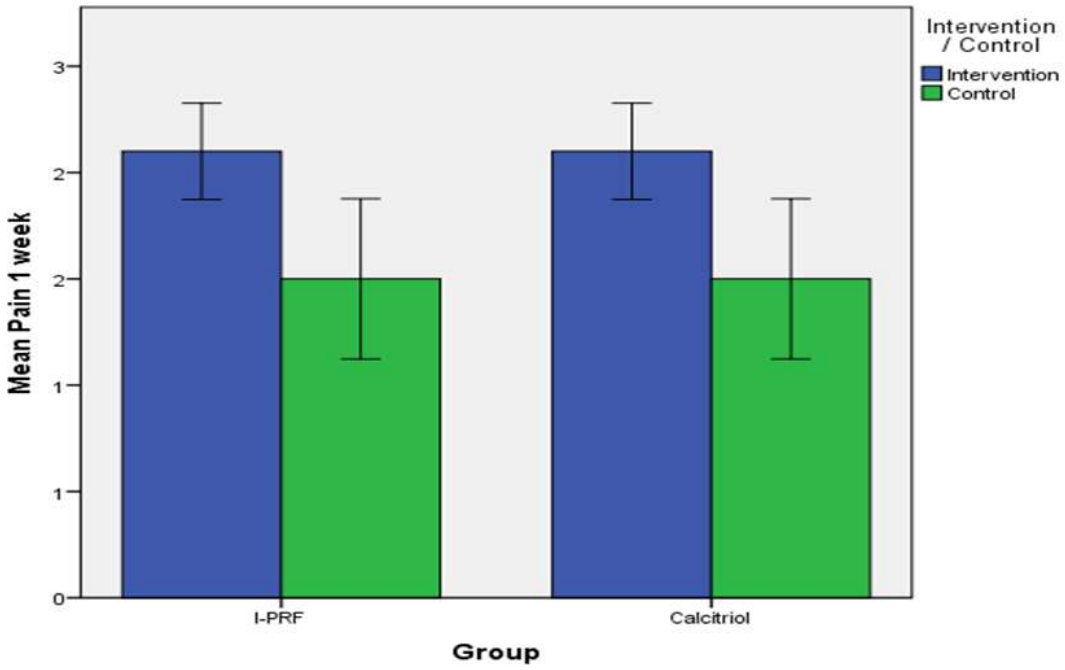

Figure 1: Comparison of mean 1 week pain perception score between each of the interventions and control.

The I-PRF group reported higher pain scores compared to the control group at 24 hours and 1 week post-intervention, with statistically significant differences noted at both time points. No statistically significant differences in pain perception between the Calcitriol and control groups at any time point. No statistically significant differences in pain perception between the I-PRF and Calcitriol groups at any time point. Overall, the administration of I-PRF was associated with higher pain scores compared to the control group, with statistically significant differences observed at 24 hours and 1 week post-intervention. However, no significant differences in pain perception were observed between the Calcitriol and control groups or between the I-PRF and Calcitriol groups at any time point. Vitamin D, particularly its active form 1,25-dihydroxyvitamin D3 (calcitriol), plays a role in bone remodeling during orthodontic tooth movement by enhancing osteoclastic activity on the pressure side and osteoblastic activity on the tension side.[20,21] Localized injections of Vitamin D have been shown to accelerate tooth movement, but the pain associated with its application tends to be more pronounced, especially in the hours following the intervention.[22] This may be due to its direct effect on bone

remodeling, leading to heightened sensitivity in the periodontal ligament and surrounding tissues, as reported by patients in studies. The inflammatory response triggered by Vitamin D can lead to discomfort, which typically peaks within 24-48 hours after the injection but subsides over time.[23]

On the other hand, PRF, an autologous derivative rich in platelets and growth factors, is primarily utilized for its regenerative properties. It promotes both osteoblastic and osteoclastic activity, facilitating bone remodeling while also enhancing tissue healing.[24] When used in orthodontics, PRF injections have been associated with less pain compared to Vitamin D, largely due to its wound healing properties.[25] PRF's fibrin matrix slowly releases growth factors, reducing inflammation and accelerating tissue recovery. [26] Consequently, patients typically report lower levels of pain post-injection, and discomfort is generally minimal. The gradual release of healing factors helps mitigate the discomfort that is often experienced with other bone-stimulating agents.Future investigations should aim to evaluate the efficacy of PRF in expediting orthodontic tooth movement by incorporating larger sample sizes and extending follow-up durations, while factoring in variables such as individual bone density, which could offer more definitive insights. Moreover, future research might explore the impact of modifying the frequency, location, and dosage of iPRF and Vitamin D applications to better understand how these variations influence both the speed and mechanics of tooth movement. Expanding the scope of forthcoming studies could involve a deeper examination of the total treatment duration and additional clinical parameters—such as changes in canine angulation, trajectory, and overall tooth movement dynamics—providing a more comprehensive understanding of the therapeutic potential of iPRF and Vitamin D in orthodontic contexts.

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