

Evaluation of topical application of platelet rich fibrin (PRF) in homeostasis of the bleeding after teeth extraction in patients taking warfarin

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Abstract

Purpose: Evaluation of topical application of platelet rich fibrin (PRF) in homeostasis of the bleeding after simple tooth extraction in patients taking warfarin.

Materials and Methods: Fifty patients, 34 males and 16 females with mean age of 63 years were included in this study. Inclusion criteria was patients on warfarin with an INR ≤ 3.5 who were referred to the Department of Oral and maxillofacial Surgery, faculty of Dentistry, Al Andalus University for Medical Science for simple single dental extraction. After tooth extraction the sockets in 25 patients were filled with a platelet rich fibrin (PRF) (group A) while the other were covered with dry gauze and served as control (group B). Bleeding from the extraction site was evaluated and it considered mild if it lasts less than ten minutes, moderate if it lasts between ten and twenty minutes and severe if it lasts more than twenty minutes. *P*-value of less than 0.05 was considered significant.

Results: 80% of patients in group A have moderate bleeding and 20% have mild bleeding, while 28% of patients in group B have moderate bleeding and 72% have severe bleeding.

Conclusion: According to the protocol of this study, the topical application of platelet rich fibrin (PRF) after teeth extraction in patients taking warfarin is effective in homeostasis of the bleeding.

Keywords: Dental extractions, INR, post-operative bleeding, platelet rich fibrin (PRF), Warfarin.

Introduction

Warfarin is one of the coumarin group of drugs used to prevent and treat thromboembolism. It blocks the formation of prothrombin and factors II, VII, IX, and X, which are involved in both the extrinsic and common coagulation pathways, and prevents the metabolism of vitamin K to its active form that is needed for the synthesis of these factors^[1]. The activity of warfarin is expressed as the International Normalised Ratio (INR), which is the standard introduced by the World Health Organization 20 years ago^[2]. The American College of Chest Physicians suggests that patients should stop warfarin 5 days before any surgical intervention, and that warfarin should be temporarily replaced with low molecular weight heparin as a bridge therapy^[3,4]. The American Heart Association, in contrast, suggests reducing the INR to a range between 2.0 and 2.5, with strict INR monitoring^[5]. Various local measurements to control bleeding in patients on warfarin treatment are available, including local hemostatic agents, suturing, and tranexamic acid^[6,7]. The initial process in reaction to tissue injury is the prevention of bleeding through platelet aggregation and activation of hemostasis cascade those results in the release of platelet growth factors, cytokines, and hemostatic factors^[8]. In the existence of thrombin and Ca²⁺, the coagulation cascade leads to conversion of soluble fibrinogen into a network of insoluble fibrin fibers, which stabilizes the platelet plug^[9,10]. The plasma-derived homologous and autologous fibrin adhesives that mimic the last step of coagulation cascade used in orthopedic, periodontal, oral, and maxillofacial surgeries to provide topical

hemostasis, tissue sealing, and enhanced wound healing. Autologous Fibrin adhesives considered more advantageous than homologous types because they decrease the risk for transmission of viral diseases^[11-13]. For this purpose, platelet concentrates, commonly referred to as platelet-rich plasma, introduced to replace fibrin adhesives^[14].

Platelet-rich fibrin (PRF) is a second-generation platelet concentrate, developed in France by Choukroun et al^[15,16]. This technique allows obtaining an autologous fibrin matrix charged in platelet and leucocyte growth factors^[15,17-21]. The aim of this study was to evaluate the topical application platelet rich fibrin (PRF) in homeostasis of the bleeding after simple tooth extraction in patients taking warfarin.

Materials and Methods

A prospective study was made of 50 patients (34 men and 16 women), their mean age was 63 years who had been referred to the Department of Oral and maxillofacial Surgery, faculty of Dentistry, Al-Andalus University for Medical Science for simple single dental extractions were included in the study. All patients had been receiving warfarin for at least three months, and were on stable oral anticoagulant therapy. Exclusion criteria included any patient with INR >3.5 , any history of liver disease, or any other coagulopathies, and any patient who refused to sign the consent or refused to participate in the study after discussing possible complications related to the procedure. The INR value measured within 24 hours before surgery. All patients were purely on warfarin treatment, and no patients taking

other anticoagulants of antiplatelet drugs such as aspirin were included in this study. The same oral surgeon performed dental extractions. After tooth extraction the sockets in 25 patients filled with a platelet rich fibrin (PRF) (group A) while the other covered with dry gauze for 30 minutes and served as control (group B). Bleeding from the extraction site was evaluated and it considered mild if it lasts less than ten minutes, moderate if it lasts between ten and twenty minutes and severe if it lasts more than twenty minutes. Patients strictly advised to contact the clinic at any time post-extraction in case of any complications related to the extraction.

All data entered into the Statistical Package for the Social Sciences version. SPSS program V.17 Categorical data analyzed using the **Phi** test and **Cramer's V** test. The results considered significant P values less than 0.05.

Results

The INR mean value was 2.4 (range 1.0-3.5). 80% of patients in-group A have moderate bleeding, and 20% have mild bleeding. While 28% of patients in group B have moderate bleeding, and 72% have severe bleeding (Table 1). One of them returned to the clinic where they received local measures to control bleeding. In this case, a local hemostatic agent (a resorbable gelatin sponge) was employed with suturing using 3/0 Vicryl.

The correlation between the use of PRF and duration of bleeding studied using PHI and CRAMER Correlation coefficient, which illustrate the strength and direction of the relationship between these two variables (Table 2). These tests showed that the value of each of the coefficients is close to the correct one, indicating the strength of correlation between these two variables as the value of these coefficients significant (Sig = 0.00.).

Table 1: The distribution of the duration of bleeding (BLE) in both groups

	less than 10 minute	from 10 to 20 minute	more than 20 minute	
Group A	5	20	0	25
Group B	0	7	18	25
Total	5	27	18	50

Table 2: The correlation coefficients between the duration of bleeding and use of PRF

	Value	Approx. Sig.
Phi	.880	.000
Cramer's V	.920	.000
N of Valid Cases	50	

Discussion

In recent years the conventional wisdom suggested that the dentist instruct the patient to stopping taking their oral anticoagulant medication 2 days before surgery and then continue with their regular oral anticoagulant

regiment immediately after the dental extraction has been changed^[22]. Aframian et al concluded that withholding warfarin before dental extractions could not be justified based on the devastating consequences of a thromboembolic event^[23]. Guidelines published in

The British Dental Journal recommend that oral anticoagulants should continue in the majority of patients requiring dental extraction^[24]. These recommendations made despite the fact that there has been no reported case of a dental extraction causing a cardiovascular accident (CVA) in a patient whose warfarin temporarily discontinued. Although these authors' conclusion may intuitively make sense based on the precautionary principle, their recommendations consider neither the quantitative risks nor the patient.

Subjective preferences of the consequences for each treatment option. Postoperative bleeding after dental procedures can usually be controlled using one or more of the following local hemostatic methods: Compression of the surgical site with gauze pads, Administration of a local anesthetic with a vasoconstrictor and Placement of an absorbable hemostatic agent such as oxidized regenerated cellulose, a resorbable gelatin sponge, collagen (synthetic, microcrystalline, or porcine) cyanoacrylate, or fibrin glues in the extraction site^[25,26]. The aim of this study was to evaluate the topical application platelet rich fibrin (PRF) in homeostasis of the bleeding after simple tooth extraction in patients taking warfarin. The results of the present study suggests that is the topical application of PRF has positive effect on bleeding after simple extraction of the teeth, the results showed that most of the patients of control group had duration of bleeding more than 20 minutes, while it ranged between 10 to 20 in most of the patients of test group. Pereira et al,^[27] indicated that is not necessary to stop anticoagulant therapy prior teeth extractions and the using of Local hemostasis techniques, such as sutures alone are sufficient to prevent hemorrhagic complications. Perini et al published a study with 400 patients that treated with warfarin for at least six months submitted to dental extractions without modifying the anticoagulant therapy. All patients treated with suture, positioning of oxidized cellulose and topic tranexamic acid. The level of INR appraised immediately before surgery, ranged from 1.8 to 4. There only were 7 cases of late bleeding^[28]. Blinder et al. studied three management regimens in 150 patients undergoing 359 extractions with INR values ranging from 1.5-4.0. Thirteen patients (9%) bled postoperatively but local hemostasis with gelatin sponge and sutures alone were as effective as adjunctive treatment including tranexamic acid mouth-rinse and fibrin glue^[29]. In a controlled case series of 109 patients, 52 were allocated to a control group (warfarin stopped 2 days before extraction) and 57 were allocated to the intervention group (warfarin continued)^[4]. The incidence of bleeding in the intervention group was higher (15/57, 26%) than in the control group (7/52, 14%) as recorded in logbook entries

or by telephone, but this difference was not significant and all patients were managed at home by application of pressure. The authors concluded that continuation of warfarin with an INR up to 4.0 might lead to an increase in bleeding after extraction but that it was manageable and not clinically important^[30]. Carter et al,^[31] noted that there was no statistical difference in the risk of postoperative bleeding when patients rinsed with tranexamic acid for 2 days versus 5 days. The drug used for rinsing or as a solution to soak gauze used for compression postoperative. The use of gauze soaked in a tranexamic acid solution for compression is an alternative for preventing a postoperative bleeding. Al-Mubarak et al^[32] investigated postoperative bleeding in 214 patients in relation to INR value and the role of suturing. Only non-surgical extractions performed. Suturing resulted in a higher incidence of postoperative bleeding compared to when not suturing.

Conclusion

According to the protocol of this study topical application of platelet rich fibrin (PRF) after teeth extraction in patients, taking warfarin is effective in homeostasis of the bleeding.

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