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# Efficacy of Feracrylum as Topical Hemostatic Agent in Therapeutically Anticoagulated Patients Undergoing Dental Extraction: A Comparative Study

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## Abstract

**Aims and Objective** To compare the efficacy of feracrylum with tranexamic acid (TXA), following dental extraction in patients who are therapeutically anticoagulated with warfarin.

**Study Design** Sixty patients on warfarin were randomly divided into three groups. Groups 1 and 2 patients were given feracrylum (1%), and TXA (5%) solution pressure pack and a control group (Group 3) was given normal saline (NS) pressure pack after extraction. Postoperative bleeding was assessed and graded numerically and periodically (0, 1, 2, 5 and 7 days). The values were statistically analyzed.

**Results** Sixty patients (M:F::37:23) with a mean age of 56 years who were therapeutically anticoagulated for different medical conditions were included. The mean warfarin dosage was 3.5 mg, and the mean INR was 2.83. Out of 27 patients who showed bleeding on day of extraction, eight, ten and nine patients belonged to groups I, II and III, respectively, and the difference was nonsignificant. Out of 15 patients who showed bleeding on post-extraction day 1, one, five and nine patients belonged to groups I, II and III, respectively. The difference was statistically significant on day 1 and nonsignificant in the next follow-ups.

**Conclusion** Local hemostatic agents like TXA and feracrylum arrest bleeding without having any systemic action

and without the necessity of altering the anticoagulant regimen. Feracrylum has an added advantage of a single application, formation of a mechanical barrier and an additional antimicrobial effect. These agents should be incorporated in the protocol for managing patients on oral anticoagulants.

**Keywords** Feracrylum · Tranexamic acid · Warfarin · Anticoagulant therapy · INR

## Introduction

The therapeutic use of anticoagulants has increased many folds over the last few decades. These are usually prescribed to treat many cardiac or vascular disorders, which include atrial fibrillation, ischemic cardiac disease, cardiac valvular disease, prosthetic cardiac valves, postmyocardial infarction, deep venous thrombosis (DVT), pulmonary embolism, rheumatoid heart diseases (RHD) and cerebrovascular accident [1]. Oral warfarin is the most common drug prescribed for therapeutic anticoagulation. Patients receiving warfarin that undergo tooth/teeth extraction or minor oral surgical procedure may encounter prolonged and excessive hemorrhage [2]. Over the years, many protocols have been suggested for treating these patients. Preoperative substitution with heparin before any major surgical procedure is a universally excepted protocol [3, 4]. For any minor surgical procedure like a tooth extraction or intraoral surgery, decreasing or temporarily withholding the warfarin dosage is a common practice [5]. Temporarily withholding or decreasing the dosage of the anticoagulant exposes the patient to the risk of venous thromboembolism and potential systemic emboli [6]. In recent years, continuation of anticoagulant therapy in oral surgical procedures

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has gained more attention due to increased emphasis on the role of local hemostatic agents like tranexamic acid (TXA), ethamsylate, styptochrome and viper venom [7, 8]. This prospective study was conducted to evaluate and compare the efficacy of a relatively newer oral hemostatic agent 1% feracrylum with the standard 5% TXA.

## Materials and Methods

Sixty patients who were on oral anticoagulants requiring dental extraction were randomly divided into three equal groups ( $n = 20$ ). International normalized ratio (INR) was evaluated on the day of extraction, and those patients with an INR ranging from 2.5 to 4 were included in the study. The Institute's ethics committee approved the study, and a written informed consent was obtained from each patient. Each group would receive a different solution for post-extraction pressure pack after dental extraction.

### Group I

After extraction, the socket was irrigated with 1% feracrylum (*Sepgard Solution 100 ml, Themis Medicare Ltd. Mumbai, India*) followed by a sterile gauge pressure pack soaked in 1% feracrylum solution for 30 min. A single application is indicated with no repetition of the procedure.

### Group II

An active 5% TXA solution was produced prior to extraction by dissolving a 500-mg tablet (*Trenaxa 500 mg, Macleods Pharmaceuticals Ltd., Mumbai, India*) in 20 ml of sterile water and stirring until the tablet was completely disintegrated to form a fine particular suspension. Immediately after extraction, a gauze pack soaked in the solution was placed on the socket for 30 min. The procedure was repeated thrice daily for the next 2 days. The 5 ml solution was also used as a mouthwash thrice daily for the next 5 days.

### Group III

After extraction, a normal saline (NS) gauze pack was used as a pressure pack for 30 min. The procedure was repeated thrice daily for the next 2 days.

All patients were prescribed paracetamol and 0.2% chlorhexidine mouthwash. Patients were recalled the next day and at the end of 1 week, and in-between they were followed by making telephonic conversation by a single person (PI). Postoperative bleeding was numerically graded at regular intervals of 0, 1, 2, 5 and 7 days. Grading for hemorrhage was as follows: no bleeding—0, persistent

ooze—1, persistent flow—2. Patients who presented with post-extraction bleeding socket were managed by suturing and gelfoam (oxidized cellulose) packing, and the intervention was noted.

## Statistical Analysis

Data were entered in Microsoft Excel, and statistical analysis was performed using SPSS version 18.0 (Chicago Inc.). Categorical values were expressed in the form of frequencies and percentages, whereas continuous variables were expressed as mean  $\pm$  SD. Association between different study groups at different time interval was assessed using Chi-square/Fisher's exact test.  $p$  value was kept at  $\leq 0.05$  to establish statistical significance.

## Results

Thirty-seven (62%) males and 23 (38%) females with a mean age of  $56 \pm 12.10$  years (*Ref. Range: 23–80*) were included in the study. Table 1 depicts the systemic conditions with which the patients presented themselves. The common conditions were valvular replacements (35%), pacemakers (13%), DVTs (13%) and RHDs (11%). The mean warfarin dosage was  $3.5 \pm 0.93$  mg (*RR: 2–5*), and the mean INR was  $2.83 \pm 0.55$  (*RR: 2.5–4*). Thirty patients (50%) had a history of the previous extraction, and 12 out of these 30 (40%) had encountered postoperative bleeding. Six out of these 12 were managed with TXA impregnated pressure packs, and the rest six were managed with either gelfoam, suturing or repeated NS pressure packs. Table 2 depicts the numerical grading of post-extraction bleeding in all the three groups comprising 60 patients in all. On the day of extraction (0 days), 33 patients had no bleeding (0), 23 patients had mild persistent ooze (1) and four patients

**Table 1** Systemic conditions for which the patients were therapeutically anticoagulated

Serial no.	Medical condition	$n = 60$	Percentage
1.	Valve replacement	21	35.0
2.	Distal venous syndrome	8	13.3
3.	Pacemaker	8	13.3
4.	Rheumatoid heart disease	7	11.7
5.	Atrial fibrillation	5	8.3
6.	Atrioventricular regurgitation	4	6.7
7.	Open heart surgery	3	5.0
8.	BudChiary syndrome	3	5.0
9.	Alcoholic liver disease	1	1.7

**Table 2** Numerical grading of bleeding episodes in all the three groups at different time intervals

Days	Bleeding Score	Group I 1% Feracrylum	Group II 5% Tranexamic acid	Group III Normal saline	<i>p</i> value
0 Day	0: No bleeding	12	10	11	0.307
	1: Persistent ooze	7	10	6	
	2: Persistent flow	1	0	3	
1st Day	0: No bleeding	19	15	11	0.020*
	1: Persistent ooze	1	5	6	
	2: Persistent flow	0	0	3	
2nd Day	0: No bleeding	20	20	18	0.126
	1: Persistent ooze	0	0	2	
	2: Persistent flow	0	0	0	

Fifth and seventh days were uneventful with no bleeding in any of the 60 patients

\*Statistically significant

showed persistent flow (2). On first post-extraction day (*first day*), 45 patients has no bleeding (0), 12 patients had mild persistent ooze (1) and three patients showed persistent flow (2). On second post-extraction day (*second day*), 58 patients have no bleeding (0), two patients had mild persistent ooze (1), whereas no patients showed persistent flow (2). On fifth and the seventh days, none of the patients presented with bleeding in any form.

Out of 27 patients who showed bleeding on the day of extraction (*Day 0*), eight patients belonged to the feracrylum group, ten patients belonged to the TXA group and nine patients belonged to the NS group. The difference on day 0 was nonsignificant (*p* value = 0.307). On the first post-extraction day (*Day 1*), 15 patients showed some form of bleeding. One patient belonged to the feracrylum group, five patients belonged to the TXA group and nine patients belonged to the NS group. The difference in bleeding score on day 1 was statistically significant (*p* value = 0.020). On the second post-extraction day (*Day 2*), only two patients in the NS group showed mild persistent ooze. None of the patients from the TXA and feracrylum group showed any further bleeding. The difference on day 2 was nonsignificant (*p* value = 0.126). The fifth and seventh days were uneventful for all the patients.

The correlation was done between the age of the patients, dosage of warfarin and INR with bleeding at different intervals, and no correlation was found. The dose of warfarin was found to be negatively correlated with INR, and strength was weak ( $r = -0.111$ ). Age was found to be positively correlating with bleeding on 0 days ( $r = 0.035$ ). Higher INR was resulting in higher bleeding incidences, but the correlation was nonsignificant.

## Discussion

In recent years, a continuation of anticoagulant therapy in oral surgical procedures has gained more attention in the international literature and hence there has been an increased emphasis on the role of local hemostasis [9]. Local methods such as resorbable gelfoam packing or/and suturing with/without local hemostatic agents like TXA, ethamsylate, styptochrome and Viper venom have given variable but satisfactory hemostasis [10]. International normalized ratio (INR) remains the main parameter for such patients, and a level of < 4 is advocated to be safe for minor oral surgical procedures. An INR of 2–3 is the usual therapeutic range for deep vein thrombosis, and an INR of up to 3.5 is required for patients with prosthetic heart valves [11].

The present comparative study showed the importance of an adjunctive procedure in these patients who can have prolonged bleeding from the extractions socket if managed with the conventional NS pressure pack. In this study, nine out of 20 patients (45%) in the control group showed either persistent ooze (*grade 1: 6 patients*) or persistent flow (*grade 2: 3 patients*) on the day of extraction (*day 0*), and the same patients continued to bleed on *day 1* despite repeated pressure packs. On *day 2*, two out of these nine patients still showed mild continuous ooze (*grade 1*) and had to be managed with gelfoam and suturing.

1% Feracrylum solution is an aqueous solution of the iron salt of poly-acrylic acid with hemostatic, antibacterial and hygroscopic properties [12]. It also possesses antimicrobial properties and decreases the postoperative infection [13]. Its mode of action is via activation of thrombin, which subsequently causes conversion of fibrinogen to fibrin and thus clots formation. Also, on coming in contact with serum proteins, it forms a thin film, thus acting as a mechanical barrier and preventing exogenous contamination. In this study, eight out of 20 patients (40%) in the

feracrylum group showed persistent ooze (*grade 1*) on the day of extraction (*day 0*), and one patient (5%) continued to ooze on day 1. None of the patients showed any bleeding henceforth on *day 2–day 7*. Formation of a mechanical barrier prevents exogenous contamination and dislodgement of the fragile clot, and hence single application is indicated. No repetition of the procedure improves patient compliance.

TXA is a synthetic derivative of the amino acid lysine, which exerts an antifibrinolytic effect through the reversible blockade of lysine-binding sites on plasminogen molecules [14]. It impedes the proteolytic degradation of fibrin by plasmin. TXA is used topically as 5% weight/volume solution in the form of a mouthwash or preferably in sterile gauge pressure packs. The solution has to be used multiple times for the next 5–7 days [15–17]. In this study, ten out of 20 patients (50%) in the TXA group showed persistent ooze (*grade 1*) on the day of extraction (*day 0*), and five patients (25%) continued to ooze on day 1. None of the patients showed any bleeding henceforth on *day 2–day 7*. We attributed this to varying compliance of patients regarding the application of pressure packs or TXA mouthwash. The necessity of a repetition of the procedure can be a drawback for TXA.

When comparing all the three groups, no difference could be noted on the day of extraction wherein eight, ten and nine patients showed bleeding in groups I, II and III, respectively. Three out of these 27 patients showing persistent flow (*grade 2*) belonged to the control (*NS*) group. Rest of the 24 patients showed persistent ooze (*grade 1*). The statistically significant difference ( $p$  value < 0.05) was noted on post-extraction day 1 when one, five and nine patients showed bleeding in groups I, II and III, respectively. All the nine patients in control (*NS*) group showed no improvement in achieving hemostasis on *day 1*, and two out of these nine patients persisted with mild ooze on day 2 also. None of the patients in groups I and II (*feracrylum* and TXA) bled on *day 2–day 7*.

Age of the patients was significantly correlating with higher bleeding on the day of extraction (*0 day*). Other medical problems like hypertension and diabetes can add to the already slowed or altered physiological healing in this age group [7]. Elderly patients with warfarin therapy should be managed with precaution.

## Conclusion

Dental extraction in patients who are therapeutically anticoagulated with warfarin has the potential to cause complication of post-extraction bleeding. The application of local hemostatic agents like TXA and feracrylum should be incorporated in the management of these patients. This

eliminates the need for interference with regimen of anti-coagulant drugs, thus minimizing the risk of venous thromboembolism and systemic emboli from a potential source. It also decreases hospital admission along with associated physical and social inconveniences. The local intervention is simple, effective and lacks any side effects. Feracrylum has an added advantage of a single application, formation of a mechanical barrier and an additional antimicrobial effect in the socket. Patient awareness about the potential complication, an atraumatic extraction technique, adjunctive procedures like suturing, gelfoam packing and use of local hemostatic agents can minimize the chances of post-extraction bleeding.

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## Compliance with Ethical Standards

**Conflict of interest** Both the authors, Sachin Rai and Vidya Rattan, declare that they have no conflict of interest.

**Ethical Approval** All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards.

**Informed Consent (In Case Humans are Involved)** Informed consent was obtained from all individual participants included in the study.

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