J. Maxillofac. Oral Surg. (Oct–Dec 2019) 18(4):579–583
https://doi.org/10.1007/s12663-018-1156-6

ORIGINAL ARTICLE

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

**Sachin Rai**[1] · **Vidya Rattan**[1]

Received: 20 September 2018 / Accepted: 25 September 2018 / Published online: 27 September 2018


**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

✉ Sachin Rai
drraisachin@gmail.com

Vidya Rattan
drvidyarattan@gmail.com

[1] Unit of Oral and Maxillofacial Surgery, Oral Health Sciences Centre, Postgraduate Institute of Medical Education and Research, Chandigarh 160012, India

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 ± 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 ± 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 ± 0.93 mg (*RR: 2–5*), and the mean INR was 2.83 ± 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 | *p* 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-acrilic 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 anticoagulant 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.

**Funding** The study did not receive any funding from any private or government institution.

**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.

## References

1. Kahn SR, Morrison DR, Cohen JM, Emed J, Tagalakis V, Roussin A, Geerts W (2013) Interventions for implementation of thromboprophylaxis in hospitalized medical and surgical patients at risk for venous thromboembolism. Cochrane Database Syst Rev 7:CD008201
2. Broekema FI, van Minnen B, Jansma J, Bos RR (2014) Risk of bleeding after dentoalveolar surgery in patients taking anticoagulants. Br J Oral Maxillofac Surg 52:15–19
3. Jaffer AK (2009) Perioperative management of warfarin and antiplatelet therapy. Clevel Clin J Med 76(Suppl 4):37–44
4. Jaffer AK, Ahmed M, Brotman DJ, Bragg L, Seshadri N, Qadeer MA et al (2005) Low-molecular-weight-heparins as periprocedural anticoagulation for patients on long-term warfarin therapy: a standardized bridging therapy protocol. J Thromb Thrombolysis 20:11–16
5. Al-Mubarak S, Rass MA, Alsuwyed A, Alabdulaaly A, Ciancio S (2006) Thromboembolic risk and bleeding in patients maintaining or stopping oral anticoagulant therapy during dental extraction. J Thromb Haemost 4:689–691
6. Souto JC, Oliver A, Zuazu-Jausoro I, Vives A, Fontcuberta J (1996) Oral surgery in anticoagulated patients without reducing the dose of oral anticoagulant: a prospective randomized study. J Oral Maxillofac Surg 54:27–32
7. Soares EC, Costa FW, Bezerra TP, Nogueira CB, de Barros Silva PG, Batista SH et al (2015) Postoperative hemostatic efficacy of

gauze soaked in tranexamic acid, fibrin sponge, and dry gauze compression following dental extractions in anticoagulated patients with cardiovascular disease: a prospective, randomized study. Oral Maxillofac Surg 19(2):209–216
8. Svensson R, Hallmer F, Englesson CS, Svensson PJ, Becktor JP (2013) Treatment with local hemostatic agents and primary closure after tooth extraction in warfarin treated patients. Swed Dent J 37(2):71–77
9. Caliskan M, Tükel HC, Benlidayi ME, Deniz A (2017) Is it necessary to alter anticoagulation therapy for tooth extraction in patients taking direct oral anticoagulants? Med Oral Patol Oral Cir Bucal 22(6):767–773
10. Blinder D, Manor Y, Martinowitz U, Taicher S, Hashomer T (1999) Dental extractions in patients maintained on continued oral anticoagulant: comparison of local hemostatic modalities. Oral Surg Oral Med Oral Pathol Oral Radiol Endod 88:137–140
11. Surg Steinberg MJ, Moores JF (1995) Use of INR to assess the degree of anticoagulation in patients who have dental procedures. Oral Med Oral Pathol Oral Radiol Endod 80:175–177
12. Lahoti BK, Aggarwal G, Diwaker A, Sharma SS, Laddha A (2010) Hemostasis during hypospadias surgery via topical application of Feracrylum citrate: a randomized prospective study. J Indian Assoc Pediatr Surg 15(3):87–89
13. Bhagwat AM, Save S, Burli S, Karki SG (2001) A study to evaluate the antimicrobial activity of Feracrylum and its comparison with povidone-iodine. Indian J Pathol Microbiol 44(4):431–433
14. Bernardoni-Socorro C, Arteaga-Vizcaino M, Villamizar Y, Diez-Ewald M, Vizcaino-Salazar G, Torres-Guerra E et al (1998) Mouth-washing with tranexamic acid in patients treated with oral anticoagulants subjected to oral surgery procedures. Invest Clin 39:77–83
15. Gaspar R, Brenner B, Ardekian L, Peled M, Laufer D (1997) Use of tranexamic acid mouthwash to prevent postoperative bleeding in oral surgery patients on oral anticoagulant medication. Quintessence Int 28:375–379
16. Borea G, Montebugnoli L, Capuzzi P, Magelli C (1993) Tranexamic acid as a mouthwash in anticoagulant-treated patients undergoing oral surgery. An alternative method to discontinuing anticoagulant therapy. Oral Surg Oral Med Oral Pathol 75:29–31
17. Ramstrom G, Sindet-Pedersen S, Hall G, Blomback M, Alander U (1993) Prevention of postsurgical bleeding in oral surgery using tranexamic acid without dose modification of oral anticoagulants. J Oral Maxillofac Surg 51:1211–1216