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(REVIEW ARTICLE)

The effectiveness of antifibrinolytic drugs as anti-Haemorrhage treatment for patients with anticoagulant during tooth extraction procedure: A review

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Abstract

Significant increases in major bleeding have been reported in patients receiving antithrombotic therapy who are undergoing dental extractions. To manage this risk, local hemostatic agents are commonly used, either to enhance the blood's natural clotting process or to mechanically limit external bleeding. These agents work by reducing the proteolytic activity of plasminogen activators, which prevents the formation of plasmin and inhibits clot dissolution. Among the various local hemostatic agents available, such as gelatin sponge, collagen sponge, oxidized cellulose, fibrin sealant, and tannic acid, tranexamic acid (TA) is the most frequently utilized. TA is widely employed both topically and as a mouthwash due to its proven efficacy in controlling bleeding. It can be administered in various forms, including as a dressing with gauze, local irrigation (250 mg/5mL solution), or as an oral suspension using crushed tablets (250 mg) mixed with saline or local anesthetic. Furthermore, it can be applied directly to the wound site for localized effect. The most common and effective approach involves using TA as a mouthwash before the extraction and continuing its application for 3-7 days post-extraction to minimize bleeding risk and promote hemostasis. The findings suggest that the localized application of antifibrinolytic agents can play a crucial role in ensuring safe dental extractions for anticoagulated patients.

Keywords: Tranexamic Acid; Anticoagulant; Dental Extraction; Antifibrinolytic; Hemostasis

1. Introduction

Oral anticoagulants are widely prescribed drugs in preventing cerebrovascular diseases or thromboembolism in patients with cardiac vascular prostheses, venous thrombosis, and pulmonary embolism (Queiroz et al., 2018). These drugs work by counteracting the effects of vitamin K. In order to bind Ca2+, which is crucial for the synthesis of coagulation factors, and to carry out the carboxylation process of coagulation factors, vitamin K is required. A coagulative cascade is ineffective in the absence of vitamin K (Isola, et al., 2015). Oral anticoagulants antagonize the regeneration of vitamin K thus inducing a condition of functional deficiency. Therefore, significant increases of major bleeding have been reported in patients receiving antithrombotic therapy that are undergoing invasive procedures which are common in the dentistry field (Rocha, et al., 2017).

Dental extraction is one of the more invasive dental procedures and also frequently done. Anticoagulant therapy has previously been advised to be discontinued or reduced for a few days prior to a dental extraction because research suggests that patients taking antithrombotic medications, especially anticoagulants, have a higher risk of bleeding than those who do not. Research conducted by Ockerman et al. (2021) stated that oral bleeding is a frequent complication after dental extraction in anticoagulated patients and might occur in up to 25% of these patients. However, some researchers now advise performing extractions without pausing or reducing anticoagulant therapy in order to prevent

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further, potentially fatal thrombotic events (Soares et al., 2015). Therefore, hemostatic management to reduce bleeding after dental extraction in these patients is needed.

There are many methods available in order to reduce post-extraction bleeding including socket suturing material or gluconic polymer-based sterile knitted fabric. Other effective techniques include the use of gelatin foam, topical bovine thrombin, a local hemostatic agent, and microfibrillar collagen. Better hemostasis is achieved by using biological tissue adhesives made of beriplast composite that simulate the final stages of blood coagulation. Hemostasis is further aided by fibrin glue, human fibrinogen concentrate, absorbable collagen paste, and calcium alginate (Jaiswal et al., 2021). One of the more common methods for limiting intraoperative hemorrhage is the administration of a local hemostatic medication (Larik et al., 2020). Local hemostatic agents either reduce or reduce the blood's natural clotting process, or they limit external bleeding mechanically (Bajkin et al., 2015). These medications work by inhibiting fibrinolysis. It is able to reduce the proteolytic activity of plasminogen activators to form plasmin, thereby inhibiting the dissolution of clots (Queiroz et al., 2018).

Based on the background, the author aims to verify the effectiveness of using local hemostatic in preventing hemorrhage reactions on patients with anticoagulant therapy undergoing dental extractions without the need for altering the anticoagulant therapy.

2. Methods

This systematic review selects previous clinical or randomized clinical trials dating back the past 10 years. This review also featured the PICO framework. The data used was sourced through secondary research online. This review only includes individuals who are undergoing anticoagulant therapy or are under the influence of anticoagulant, that are treated using antifibrinolytics such as tranexamic acid or aminocaproic acid for hemorrhage control during one's tooth extraction procedure. Age and gender restrictions were not applied. For inclusivity, anticoagulants referred to are not limited to only a selection of drugs. Dental extraction discussed refers to any kind of tooth removal procedure that may involve the loss of blood.

Databases used in this review include Pubmed, Science Direct, and Scopus. The following keywords were used in combination; tranexamic acid, aminocaproic acid, antifibrinolytics, anticoagulant, and tooth extraction. Items included should follow the PICO framework as follows: i. Population: Patients under the influence of anticoagulants undergoing teeth extraction of any tooth; ii. Intervention: The usage of tranexamic acid or aminocaproic acid as an antifibrinolytic agent in any kind of administration route, dose, frequency, and duration of administration; iii. Comparison: the lack of antifibrinolytic usage or any other kind of intervention iv. Outcome: Hemorrhages, post-operative bleeding, or any kind of conflicting result. The sourcing was conducted until late April 2023 and the language was restricted to English.

3. Results

Using the keywords combination of 'tranexamic acid', 'anticoagulant', and 'tooth extraction' with the filter clinical trial, randomized control trial, in the last 10 years applied on PubMed has resulted in 5 journals shown. Only 3 journals fulfilled the PICO framework desired and were taken for review. Duplicates of the 3 journals are also found when using the keyword combination of 'aminocaproic acid', 'anticoagulant', and 'tooth extraction' with the same filter.

No.	Title of Journal	Population Used	Method Used	Result of Trial
1.	Tranexamic acid and bleeding in patients treated with non-vitamin K oral anticoagulants undergoing dental extraction: The EXTRACT-NOAC randomized clinical trial. (Ockerman et al., 2021)	222 randomized patients that are treated with NOACs. Patients are taken from 4 different hospitals in Belgium, that over the age of 18 years old with a mean age of s 74.8 (±8.8) years,	Patients are anonymously assigned to either 10% TXA or placebo mouthwash, used once before dental extraction, followed within the next 3 days, each day administered 3 times. Patients with post-extraction oral bleeding of any kind within the next 7 days were noted.	When it comes to general bleeding and delayed oral bleeding occurrence, the TXA group has less occurrence compared to the placebo group. Oral bleeding found in the TXA group includes up to 3 bleeds compared to the 10 the placebo group has.

2.	Managing Anticoagulant Patients Undergoing Dental Extraction by using Hemostatic Agent: Tranexamic Acid Mouth Rinse. (Jaiswal, et al., 2021)	100 subjects over the age of 18 years old are taken under the influence of anticoagulants and antiplatelets. Patients with bleeding disorders or liver failure are excluded.	This trial uses two methods of TXA administration; pressure pad followed by TXA mouthwash. The socket from the extracted tooth was irrigated with 10% tranexamic acid using a pressure pad soaked in tranexamic acid prior. Subjects are prescribed postextraction antibiotics, and analgesics, followed by post-treatment INR on the fourth day. Dissolved 500 mg tranexamic acid was used as mouthwash 4 times a day for 7 days.	The tranexamic pressure pad has managed to handle 84 out of the 100 subjects' post-operative bleeding. The topical use of tranexamic acid as mouthwash is also found to be a way of reducing the possibility of postextraction bleeding in patients with anticoagulant therapy.
3.	Tranexamic acid as a local hemostasis method after dental extraction in patients on warfarin: a randomized controlled clinical study. (Queiroz et al., 2018).	37 patients on anticoagulant therapy for both males and females, with a mean age of 45. 20 are placed in the control group, and the remaining 17 are in the TXA group.	Two groups were formed; one treated with saline gauze and suture as the control group, the other with TXA gauze each kept for 5 minutes and sutured. 2 mL gauze of the corresponding solvent was also kept in place for 3 minutes. Patients' conditions are monitored within the first 12 hours, 24 hours, and 7 days. Any kind of postoperative complications was noted. Analgesics were also prescribed taken every 6 hours for 2 days.	On the first 12 hours, only little bleeding occurred in 70% if the study group population, while moderate bleeding occur in 95% of the control group. The number of bleeding does decrease at 24 hours with 85% of the study group having no any bleeds while 85% of the control group only experienced litte bleeds. By day 7, each group experienced no bleeding of any form at all.
4.	Control of Post Extraction Haemorrhage by Tranexamic Acid Pressure Pack in Patients on Anticoagulant and Antiplatelet Therapy: A Prospective Clinical Study. (Mithiborwala et al., 2020).	Ten adult patients with no age restriction underoing anticoagulant/antiplatelet therapy. TXA	TXA are applied via pressure pack for 10 minutes post extraction. Duration of bleeds are kept track of using stopwatch. Patients are observed for the foloowing week, checked up on the third and seventh day.	There are one case of aemorrhage control failure found post-extraction, with the remaining 4 are successfully dealt with the TXA. No tertiary hemorrhage oare found, and only 1 case of secondary hemorrhage found.
5.	Hemostatic Effect Of Platelet Rich Fibrin Versus Tranexamic Acid After Tooth Extraction In Patients Under Anticoagulant Therapy (Larik, 2020).	84 total patients with age ranging between 30-70 years old that are on anticoagulant medication for upwards of 4 days continuously prior to tooth extraction. No gender restrictions are applied.	Patients are divided into 2 groups. One group are treated with tranexamic dressing applied followed by tranexamic acid mouthwash for the following 3 days administered 3 times a day post-extraction. Another group treated with platelet rich fibrin of the corresponding patients.	Both group performs well on showing hemostatic effect with no greater difference. Group treated with platelet rich fibrin shows a 97.61% efficacy compared to the tranexamic acid at 92.86%.

4. Discussion

The literature that has been studied mentions a number of drugs that have local hemostatic effects. These include tranexamic acid (TA), gelatin sponge, collagen sponge, oxidized cellulose, fibrin sealant, and tannic acid. Of those drugs, tranexamic acid is the most frequently used both locally for topical treatment and as a mouthwash (Shastry et al., 2014). The usage of tranexamic acid as an antifibrinolytic counters the effect of anticoagulants, thus decreasing the chance of hemorrhage (Abed et al., 2017). However, the working mechanism of each item does not directly affect each other like how an antifibrinolytic counters the effect of TPA.

Antifibrinolytics such as tranexamic acid disturb fibrinolysis dissolution (Michalets and Harris, 2018). The plasminogen, which functions to dissolve blood clots through plasmin, has its lysin receptor blocked by tranexamic acid (Chauncey and Wieters, 2022). The slowing down of blood clots or fibrin formation by plasmin is no longer occurring due to the tranexamic acid.

Anticoagulants such as heparin, on the other hand, inactivates thrombin, preventing the formation of blood clots that should have occurred. Another anticoagulant such as coumarin, shaped like vitamin K but without having the same effect, produces defective clotting factors that are unable to bind. Notice how antifibrinolytics such as tranexamic acid and anticoagulants affect different items that are not correlated with each other. Antifibrinolytics such as tranexamic acid are able to successfully counter anticoagulant's effects while each having its own independent mechanism unchanged (Ullah et al., 2022).

Tranexamic acid prevents the breakdown of blood clots while an anticoagulant keeps the blood from forming the clot. Those two items do not directly intervene in each other's process, yet, affect each other's end product (Liras et al., 2019). Even though in the trials, tranexamic acid relies on the less usual chance of fibrin formation occurring while being under the influence of anticoagulants, the tranexamic acid is still able to do its job, heavily shown by the trial conducted by Larik, (2020), where anticoagulant was used extensively prior to the tooth extraction

The dosage and duration of tranexamic acid used within the reviewed articles vary as it can be administered in many forms with different dosages. Research conducted by Queiroz et al. (2018) has stated that the manner of use in TA does not seem to affect its effectiveness. It can be administered orally or topically. It may be used in dressings with gauze, local irrigation (250 mg/5mL solution), and as an oral suspension in tablet form (250 mg) crushed with saline or local anesthetic. It can even be used directly on the wound. The most popular amongst them is the usage of mouthwash prior to extraction and over the course of three days as conducted by Ockerman et al., (2021), or seven days as done by Jaiswal, et al., (2021), with both having similar rates of success.

5. Conclusion

Various literature has reported that the use of local hemostatic agents may be sufficient in managing the bleeding risk in patients with anticoagulant therapy undergoing dental extractions without the need for altering the anticoagulant therapy. The major local hemostatic used currently is tranexamic acid (TA) which has been shown to have major success. Further research is advised to provide more evidence regarding the effectiveness of other local hemostatic agents as it appears to be still limited.

Compliance with ethical standards

Disclosure of conflict of interest

No conflict of interest to be disclosed.

References

[1] Abed, H and Abdalrahman, A. (2017). Dental management of patients with inherited bleeding disorders: a multidisciplinary approach. General Dentistry, 413(61): 56-60.

[2] Bajkin, B.V., Sanja, B.V., Bojana, R.M., Biljana, A.V. (2015). Risk factors for bleeding after oral surgery in patients who continued using oral anticoagulant therapy. J. Am Dent Assoc, 146(6):375-381.

[3] Chauncey, J.M. and Wieters, J.S. (2022). Tranexamic Acid. StatPearls Publishing, In: StatPearls Publishing [Internet].

[4] Galen, K., Eveline, T.E., Evelien, P.M.B., Robert, J.J., Roger, E.G.S. (2019). Antifibrinolytic therapy for preventing oral bleeding in patients with haemophilia or Von Willebrand disease undergoing minor oral surgery or dental extractions. Cochrane Database of Systematic Review, 4(CD011385):1-32.

[5] Isola, G., Giancarlo, C., Giovanni, M. (2015). Anticoagulant therapy in patients undergoing dental interventions: A critical review of the literature and current perspectives. Minerva Stomatologica, 64: 21-46.

[6] Jaiswal, P., Raghav, A., Aniruddh, G., Arvind, J., Abhishek, K., Rathi, R. (2021). Managing Anticoagulant Patients Undergoing Dental Extraction by using Hemostatic Agent: Tranexamic Acid Mouthrinse. J. pHarm Bioallied Sci, 13(1): 469-472.

[7] Larik, M.D., Syed, G.H., Sajid, A.M., Wajid, A.R., Waqas, W.W., Babar, A., Salman, S. (2020). Hemostatic Effect of Platelet Rich Fibrin Versus Tranexamic Acid After Tooth Extraction in Patients under Anticoagulant Therapy. Biomedical Sciences, 2(4): 404-407.

[8] Liras, A. and Luis, R. (2019). Dental management of patients with haemophilia in the era of recombinant treatments: increased efficacy and decreased clinical risk. BMJ case rep, 12(e227974):1-6.

[9] Michalets, E. & Lindsay, H. (2018). Antifibrinolytics: Pharmacologic Profile and Clinical Utilization. Cardiovasculat Throumbus, 44: 615-649.

[10] Mithiborwala, A., Navin, S., Amit, M., Isha, K.B., Dipen, D., Darshan, S. (2016). Control of Post Extraction Haemorrhage by Tranexamic Acid Pressure Pack in Patients on Anticoagulant and Antiplatelet Therapy: A Prospective Clinical Study. J. Craniofacial Res, 1(1):6-10.

[11] Ockerman A, Miclotte I, Vanhaverbeke M, Vanassche T, Belmans A, Vanhove J, et al. (2021) Tranexamic acid and bleeding in patients treated with non-vitamin K oral anticoagulants undergoing dental extraction: The EXTRACT-NOAC randomized clinical trial. PLoS Med, 18(5): e1003601

[12] Rocha, A.L., Alessandra, F.S., Maria, A.P.M., Marina, G.F., Denise, V.T., Ana, C.B.O., Daniel, D.R., Tarcilia, A.S. (2018). Oral surgery in patients under antithrombotic therapy: perioperative bleeding as a significant risk factor for postoperative hemorrhage. Blood Coagul Fibrinolysis, 29(1):97-103.

[13] Shastry, P.S., Rachna, K., Kusai, B., Dilshad, U. (2014). Hemophilia A: Dental considerations and management. J. International Society of Preventive and Community Dentistry, 4(3):147-152.

[14] Soares, ECS., Fabio, W.G.C., Tacio, P.B., Carlos, B.P.N, Paulo, G.B.S., Saulo, H.B.B., Fabricio, B.S., Cristiane, S.R.F. (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 Maxilloofac Surg, 19:209-216.

[15] Ullah, K., Humzah, M., Ushna, K., Zouina, S., Azza, S. (2022). Is Antifibrinolytic Therapy Effective for Preventing Hemorrhage in Patients with Hemophilia Undergoing Dental Extractions? A Systematic Review and Meta-Analysis. Clinical and Applied Thrombosis/Hemostasis, 28:1-9.

[16] Queiroz, S.I.M.L., Valeria, D.S., Renata, M.S., Giordano, B.P.C., Adriano, R.G., Jose, S.P.S. (2018). Tranexamic acid as a local hemostasis method after dental extraction in patients on warfarin: a randomized controlled clinical study. Clin. Oral Investigations, 22:2281-2289.