Journal of Research in Medical and Dental Science
2022, Volume 10, Issue 11, Page No: 115-122

Available Online at: www.jrmds.in
eISSN No. 2347-2367: pISSN No. 2347-2545

Efficacy of Various Hemostatic Agents in Controlling Bleeding During Dental Procedures: A Systematic Review

Marwa Salman Al Awad[1], Hanan Ahmed Alghamdi[2], Hend Abdrahman Ahmad[3], Khadijah Ali Almomen[3], Leena Faisal Al Jaafar[1], Suhael Ahmed[1*]

[1]Department of Oral and Maxillofacial surgery, Riyadh Elm University, Riyadh, Saudi Arabia
[2]Ministry of Defense, Saudi Arabia
[3]Ministry of Health, Saudi Arabia

ABSTRACT

One of the common complications that occur in patients with hemostatic disorders after oral surgery is excessive bleeding. This study systematically reviews the available literature on evaluating the efficacy of various hemostatic agents used in dentistry in different dental procedures.

This systematic review was done following the criteria of Cochrane Handbook for Systematic Reviews of Interventions Handbook. Authors also followed the recommendations of Preferred Reporting Items for Systematic Reviews and Metaanalysis (PRISMA) to conduct this systematic review.

Various hemostatic agents have been investigated to accomplish hemostasis by the different mechanisms to limit bleeding and encourage coagulation. Studies confirmed that application of pressure with gauze containing tranexamic acid would be the management of choice. Chitosan proved superiority compared to Platelet Rich Fibrin in achieving hemostasis. Feracrylum and HemCon Dental Dressing have also resulted in positive association with coagulation especially in patients undergoing antiplatelet therapy. Haemocoagulase was correlated with paediatric patients, while Ankaferd Blood Stopper in hemophilic patients in hemostasis. Further studies are needed to support results.

Key words: Haemocoagulase, Ankaferd blood stopper, Hemophilic patients

HOW TO CITE THIS ARTICLE: Marwa Salman Al Awad, Hanan Ahmed Alghamdi, Hend Abdrahman Ahmad, Khadijah Ali Almomen, Leena Faisal Al Jaafar, Suhael Ahmed, Efficacy of Various Hemostatic Agents in Controlling Bleeding During Dental Procedures: A ystematic Review, J Res Med Dent Sci, 2022, 10 (11): 115-122.

Corresponding author: Suhael Ahmed

e-mail✉**:** drsuhael@riyadh.edu.sa

Received: 10-October-2022, Manuscript No. jrmds-22-76795;

Editor assigned: 12-October-2022, PreQC No. jrmds-22-76795(PQ);

Reviewed: 26-October-2022, QC No. jrmds-22-76795(Q);

Revised: 31-October-2022, Manuscript No. jrmds-22-76795(R);

Published: 07-November-2022

INTRODUCTION

In dentistry multiple complications can arise during or after performing several procedures, so dentists should be prepared pre-operatively to know how to act when it happens to prevent further problems. One of the common complications that occur in patients with hemostatic disorders after oral surgery is excessive bleeding. Prevention is the best approach to avoid bleeding complications in procedures involving the oral cavity. There should be well documented detailed medical history of the patient in the patients file and dentists require comprehensive understanding of the hemostasis physiology. Medical history will highlight previous bleeding events due to procedures, and any personal and family predilection that may influence bleeding and alter effective hemostasis [1]. Coagulopathies are diseases that cause tendency of bleeding and hemorrhage, and they are a consequence of alterations in plasma proteins that are involved the phases of blood coagulation [2]. Anticoagulation drugs are used frequently to prevent arterial and venous thrombosis in individuals with diseases such as ischemic cardiopathy, and who are with carriers of prosthetic heart valves and whom are with high risk for ischemic stroke [3]. Patients that follow anticoagulation drugs treatments would have a higher tendency to experience general bleeding, as the mechanism include in the inhibition of platelets [4]. The most commonly used oral anticoagulants these days are warfarin and acenocoumarol. They require a precise motorization of International Normalized Ratio (INR) to correct the medication dose and achieve the desired therapeutic results [5]. The aim is to reduce the likelihood of any adverse effects as a consequence of excess of anticoagulation producing more bleeding or

not having the minimum level requirement to achieve thrombosis [6]. This is of high importance when patients are undergoing surgical procedures like tooth extractions, and must follow the available guidelines to proceed and minimize complications [7].

Hemostasis is the mechanism that terminates bleeding occurring from blood vessels. It involves several interconnected steps. These steps collectively aid in the formation of a blood clot that will control bleeding by closing the damaged wound site. Hemostasis promotes a series of enzymatic initiations that aid in the formation of a plug by platelets and fibrin. There are two pathways the influence clot formation, intrinsic and extrinsic pathways [8]. The intrinsic pathway respond to endothelial damage and is composed of factors I, II, IX, X, XI, and XII that play a role in this process. The extrinsic pathway responds secondary to trauma. Both of these pathways will have an influence on the common hemostasis pathway, which will aid in the transformation of prothrombin to thrombin, thus activating the transformation of fibrinogen to fibrin and aid in clot formation [9]. It will close the injured area, thus controlling bleeding and preventing followed consequences, as tissue rehabilitations occur. When healing of the injury start, the blood clot will slowly remodel and dissolve to restore the normal tissue at damaged site. This occurs first by the formation of a provisional plug, then the activation of the coagulation will occur finally by the formation of fibrin plug [2]. This study systematically reviews the available literature on evaluating the efficacy of various hemostatic agents used in dentistry on different dental procedures.

MATERIALS AND METHOD

This systematic review was done following the criteria of Cochrane Handbook for Systematic Reviews of Interventions Handbook. Authors also followed the recommendations of Preferred Reporting Items for Systematic Reviews and Metaanalysis (PRISMA) to conduct this systematic review. Analyses were based on the population, intervention, comparison, and outcome (PICO) index: those undergoing different dental procedures (population), those receiving hemostatic agents to control bleeding (intervention), patients that use conventional way to achieve hemostasis as by pressure application (comparison), and studies evaluating the efficiency of various hemostatic agents in the control of bleeding on patients undergoing different dental procedures (outcome).

Studies were selected according to the search strategy with respect to 4 inclusion criteria: Studies should be a clinical trial, cohort or case control study; Patients needed to undergo a dental procedure; In the study group, patients were treated by one or more hemostatic agent and comparison was done between them; Study outcomes included accuracy and efficiency of the various hemostatic agents discussed.

Case reports; Case series; Systematic reviews; Meta-analysis; Literature reviews; Full text not available; Papers that are not related to our topic either due to different treatment approach or methods were excluded from this review.

The databases used included PubMed, Medline, Cochrane Library and Web of Science. Searches were conducted for articles published from January 2000 to July 30, 2022. An electronic search was done to answer this reviews' focus question, "Is the various used hemostatic agents effective in bleeding control in the different dental procedures?". The following keywords were used to search the selected databases "Hemostatic agents", "Hemostasis", "Coagulation", "Bleeding", "Dental procedures", "Dentistry", "Efficacy" and "Accuracy". As well as manual search of no published studies was conducted.

Prisma 2020 flow diagram was followed during the multiple exclusion phases until selecting the included high evidence studies. Articles were first screened based on articles title and abstract, then afterward full texts were reviewed to confirm its eligibility. Studies were excluded during the title screening stage according to the following criteria: Titles not in English language and irrelevant titles. Studies that were included at the abstract level were according to the following criteria: English language; Full text available; Randomized clinical trials studies; retrospective and prospective clinical studies; cross-sectional studies and cohort studies. Studies that were excluded during abstract screening stage were based on the following criteria: Irrelevant topics that are not related to this review and studies that are not in English language. A total of 10 articles were identified in the search after duplicates was removed; full-text articles were selected based on inclusion and exclusion.

RESULTS

Flow diagram

Figure 1 demonstrates the PRISMA 2020 flow diagram followed in this review. A total of 936 articles were found in the initial search with 325 articles from medline, 232 articles from Scopus2, 167 articles from web of science3 and 212 from other databases. Any articles duplicated between the various databases were removed. Further elimination was done by correlating the resulted articles from the titles and abstract summaries, a total of 10 articles remained. Additional elimination was done after reading the articles and correlating them with the inclusion and exclusion criteria's. Exclusion criteria included by literature reviews, systematic reviews and meta-analysis, case reports, case series, irrelevant, article not in English or full text was not available. A total of 10 articles remained and was selected to be included in this systematic review, and were all assessed in the quantitative and qualitative analysis.

Study characteristics

Most clinical trials included in this systematic review had a sample size ranged from as low as 27 in the study

by [10] to as high as 100 in Jaiswal's study in 2021. However, most of the case control studies have included 20-60 patients, while one included a sample size of 300 patients (Table 1) [11]. As for randomized control trials which comprise the majority of studies included in this review had a mean of 30 participants, but it ranged to as high as 90 in a study done by Bajkin, et al. [12]. Table 1 demonstrates the summarized characteristics data of included articles. Within the included ten studies, most studies constituted of a control group and compared with other groups with different hemostatic measures, and the number of participants between study and control groups was comparable. Two studies compared different agents to another without a control group [11,13]. While one clinical trial had no comparisons, and only studied the outcomes of one regiment [14]. As for sex inclusions, male and female participants were comparable in seven studies. One study only included males [10]. While in two studies no information was reported regarding males and females [11,15]. The mean age of participants was similar about 50 years old between patients in the included studies, but it ranged between 21 years old [10] and 70 years old [16]. While Swamy et al. conducted their study on children ranged from 5-9 years old [15].

The selected studies all investigated various hemostatic agents in oral and maxillofacial surgery, specifically teeth extraction. Jaiswal et al and Queiroz, et al. investigated tranexamic acid use on ant coagulated patients [14,17]. Rajendra, et al. and Sarkar, et al. compared use of platelet-rich fibrin versus chitosan-based Axiostat as hemostatic agents on patients whom are under antiplatelet therapy [11,13]. Bajkin, et al. and Halfpenny, et al. investigated the use of different hemostatic modalities on ant coagulated patients [12,18]. Rai, et al. studied the efficacy of Feracrylum on anticoagulated patients [19]. Pippi, et al. investigated the use of an extra-alveolar hemostatic agent on ant coagulated elderly patients [16]. Kazancıoğlu, et al. investigated the use of (Ankaferd Blood Stopper) in hemophilia patients [10]. Lastly Swamy, et al. correlated the use of topical Haemocoagulase on children undergoing teeth extraction [15].

Quality and risk of bias assessment of selected studies

Risk of bias and quality assessment was done using Cochrane ROB 2 risk of bias assessment tool for the selected articles. Domains assessed included: bias arising from randomization process, bias due to

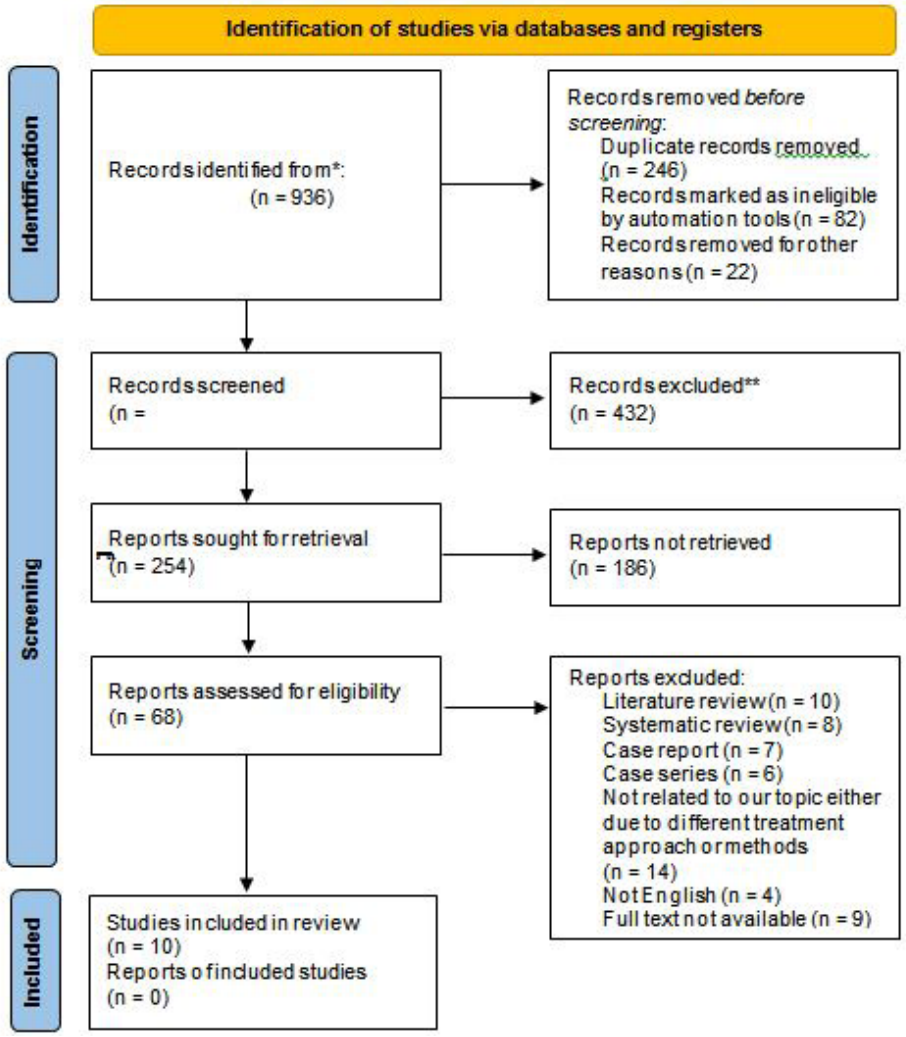

Figure 1: PRISMA flowchart.

deviations from the intended interventions, bias due to missing outcome data, bias in measurement of the outcome and bias in selection of the reported results. According to the risk of bias tool used, included studies could receive a maximum score of nine which indicates the methodological quality, thus indicates the risk of bias. Studies scored 7–9 points were considered being a low risk of bias article; 5–6 points were considered medium-level risk of bias article and those scored less than five points were considered high risk of bias. Of the included 10 articles in this review, 3 were of high risk, none had some concerns and 6 had low risk of bias. The randomized control trials, retrospective studies, methodological quality assessment was conducted using the modified Newcastle-Ottawa scale, which covered 3 aspects, patient selection, comparability between study groups and assessment of the outcome (Table 2).

DISCUSSION

There are multiple articles discussing the different hemostatic agents in various areas of dentistry. In this review, the efficacy was the major concern. Most high evidence studies were focusing in oral and maxillofacial specialty, specifically teeth extractions, as it will be further discussed.

Two of the articles included in this review studied the efficacy of Tranexamic Acid hemostatic agent on patients under anticoagulants whom are undergoing dental extraction. Tranexamic acid inhibits fibrinolysis, the binding of plasminogen to fibrin and the converting plasminogen to plasmin, by stabilizing hemostatic clots thus bleeding [20]. Jaiswal, et al. evaluated the efficacy of tranexamic acid on anticoagulated patients after teeth extraction. Study reported that 16 patients experienced bleeding after 1 and 2 days of the extraction and was managed by tranexamic acid. The study concluded that the use of tranexamic acid post teeth extraction is an effective and secure way to manage bleeding on anticoagulated patients at a therapeutic INR level [14]. Queiroz, et al. it evaluated hemostatic modalities to the control hemorrhage that occur after tooth extraction in ant coagulated patients with warfarin. Tranexamic acid was significantly associated with hemostasis, principally in the first 24 hours post extraction. The study concluded with that tranexamic acid in conjunction with compression and irrigation was more effective in reducing and preventing immediate bleeding, especially

Table 1: Summarized data of the 10 included studies.

Literature	Research Design	Research Purpose	Subject	Result	Conclusions
Jaiswal, et al.[14]	Clinical Trial	To manage anticoagulated patient who will undergo dental extraction by using hemostatic agent and the ability to rule out potential risk factor that may initiate bleeding.	100 (55 males, 45 females) participants. Mean age 50 years 10% tranexamic acid solution and pressure pad with intranexamic acid solution for 10 min.	16 reported postextraction bleeding controlled by tranexamic acid pressure pack. 10 reported postextraction bleeding controlled by gelatin foam.	Tranexamic acid mouthrinse after extraction is effective in controling bleeding on patients who are under antiplatelet therapy.
Queiroz, et al. [17]	Randomized Controlled Trial	To compare hemostatic measures in controlling post extraction hemorrhage in patients on anticoagulation therapy with warfarin.	37 (14 males, 23 females) participants. Mean age of 45.5 years Two groups: Study group; local tranexamic acid. (n=17) Control group; conventional hemostasis measures. (n=20)	The study group this was much faster than control group in achieving cessation of bleeding. The use of tranexamic acid was more significantly associated with the absence of bleeding.	Tranexamic acid with gauze compression was more effective in reducing the time to attain immediate hemostasis, and in preventing intermediate hemorrhage.
Rajendra, et al. [11]	Case Control	To evaluate the effect of PRF and Axiostat hemostatic activity after tooth extraction among cardiac patients on antiplatelet medication.	300 participants. Two groups: Group I; PRF dressing. (n=150) Group II; Axiostat dressing. (n=150)	Hemostasis was achieved faster when using Axiostat compared to PRF dressing.	Chitosan is a superior wound dressing material in achieving hemostasis in cardiac patients on antiplatelet medication after tooth extraction.
Sarkar, et al [13]	Randomized Controlled Trial	To compare the effectiveness of Platelet Rich Fibrin gel and Chitosan gel dressing in providing hemostasis in patients receiving Oral Antiplatelet Therapy after dental extractions.	60 (29 males, 31 females) participants. Mean age 58 years. Two groups: Group A; PRF gel. (n=30) Group B; Chitosan hydrogel. (n=30)	All extraction sockets with chitosan hydrogel achieved hemostasis faster than Platelet-rich fibrin.	Chitosan hydrogel dressing proved to be a superior hemostatic agent compared to PRF gel, that significantly shortens the clotting time following dental extraction in patients under antiplatelet therapy.
Bajkin, et al.[12]	Randomized Controlled Trial	To compare different local hemostatic modalities after tooth extraction in patients receiving chronic Vitamin-K antagonist therapy.	90 (55 males, 35 females) participants. Mean age of 65 years. Three groups: Group A; suturing without any local hemostatic agent. (n=30) Group B; local hemostatic agent without suturing. (n=30) Group C; only local pressure. (n=30)	All cases of hemorrhage were easily solved with local hemostatic measures. A difference between the groups was not statistically significant.	In therapeutically anticoagulated patients tooth extractions can be safely performed without altering the dose of anticoagulant medication if efficient local hemostasis is provided.

Halfpenny, et al.[18]	Clinical Trial	To compare the use of a resorbable oxycellulose dressing with a fibrin adhesive in preventing postextraction hemorrhage in patients on anticoagulants.	46 (30 males, 16 females) participants. Mean age of 65 years. Two groups: Study group; fibrin adhesive dressing. (n=20) Control group; resorbable oxycellulose dressing and suturing (n=26)	No discernible difference in the postoperative outcome with regard to hemorrhage was noted. Only 1 patient had significant postoperative bleeding.	Patients receiving warfarin whose INR is within the therapeutic range, the fibrin adhesive is as effective as the resorbable oxycellulose dressing in preventing postextraction hemorrhage.
Swamy, et al. [15]	Randomized Controlled Trial	To assess the effectiveness of topically-administered haemocoagulase (batroxobin) after teeth extractions in children.	30 participants. Age group of 5–9 years. Two groups: Study group; with haemocoagulase. (n = 30) Control group; without haemocoagulase. (n = 30)	Time to bleeding cessation was lower in haemocoagulase group than control group.	Topical haemocoagulase produced significant reductions in time for haemostasis from extraction wounds in children.
Rai, et al. [19]	Case Control	To compare the efficacy of feracrylum with tranexamic acid after extraction in patients who are therapeutically anticoagulated with warfarin.	60 (37 males, 23 females) participants. Mean age 56 years. Three groups: Group 1; given feracrylum (1%) (n=17), Group 2; TXA solution pressure pack (5%) (n=33) Group 3; control (n=10).	Age was found to be positively correlating with bleeding on 0 days. Higher INR was resulting in higher bleeding incidences, but the correlation was nonsignificant.	Tranexamic acid and feracrylum can arrest bleeding without having any systemic action and without the necessity of altering the anticoagulant regimen.
Pippi, et al. [16]	Case Control	To evaluate the effectiveness of HemCon Dental Dressing in patients receiving oral anticoagulant treatment and undergoing tooth extractions compared with common local hemostatic agent.	20 (15 males, 5 females) participants. Mean age of 70. Two teeth on same participant: Study tooth; HemCon Dental Dressing applied, Control site; hemostatic sponge (CollaPlug, Zimmer Dental) used	The mean application time was significantly lower in the test group than in the control group.	Tooth extraction in patients receiving anticoagulant treatment and have an INR lower than 3.5 is a safe procedure without discontinuation of the regimen. The HemCon Dental Dressing obtain rapid soft tissue healing.
Kazancıoğlu, et al.[10]	Clinical Trial	To assess the hemostatic efficacy of Ankaferd Blood Stopper following tooth extraction in hemophiliacs.	27 male participants. Mean age 21 years. Two groups: Study group; application of ABS (n=17) Control group; local packing with gauze. (n=10)	The most significant clinical difference between the groups was associated with the use of Ankaferd Blood Stopper; those in the treatment group had significantly shorter duration of bleeding.	Ankaferd Blood Stopper can be considered an alternative local hemostatic agent for reducing clotting factor concentrates in hemophilia patients.

Table 2: Risk of bias assessment with the recommended approach of cochrane ROB 2.

Authors	D1	D2	D3	D4	D5	Overall
Jaiswal, et al.	Description: Badge Follow with solid fill	Description: Badge Follow with solid fill	Description: Badge Unfollow with solid fill	Description: Badge Follow with solid fill	Description: Badge Follow with solid fill	Description: Badge Follow with solid fill
Queiroz, et al.	Description: Badge Follow with solid fill	Description: Badge Unfollow with solid fill	Description: Badge Question Mark with solid fill	Description: Badge Follow with solid fill	Description: Badge Question Mark with solid fill	Description: Badge Question Mark with solid fill
Rajendra, et al.	Description: Badge Follow with solid fill	Description: Badge Follow with solid fill	Description: Badge Unfollow with solid fill	Description: Badge Unfollow with solid fill	Description: Badge Follow with solid fill	Description: Badge Follow with solid fill
Sarkar, et al.	Description: Badge Follow with solid fill	Description: Badge Question Mark with solid fill	Description: Badge Follow with solid fill	Description: Badge Unfollow with solid fill	Description: Badge Follow with solid fill	Description: Badge Follow with solid fill
Bajkin, et al.	Description: Badge Follow with solid fill	Description: Badge Question Mark with solid fill	Description: Badge Follow with solid fill	Description: Badge Follow with solid fill	Description: Badge Follow with solid fill	Description: Badge Unfollow with solid fill
Halfpenny, et al.	Description: Badge Question Mark with solid fill	Description: Badge Follow with solid fill	Description: Badge Unfollow with solid fill	Description: Badge Follow with solid fill	Description: Badge Unfollow with solid fill	Description: Badge Follow with solid fill
Swamy, et al.	Description: Badge Unfollow with solid fill	Description: Badge Follow with solid fill	Description: Badge Follow with solid fill	Description: Badge Unfollow with solid fill	Description: Badge Question Mark with solid fill	Description: Badge Unfollow with solid fill
Rai, et al.	Description: Badge Unfollow with solid fill	Description: Badge Unfollow with solid fill	Description: Badge Unfollow with solid fill	Description: Badge Follow with solid fill	Description: Badge Follow with solid fill	Description: Badge Unfollow with solid fill
Pippi, et al.	Description: Badge Follow with solid fill	Description: Badge Follow with solid fill	Description: Badge Follow with solid fill	Description: Badge Unfollow with solid fill	Description: Badge Follow with solid fill	Description: Badge Follow with solid fill
Kazancıoğl, et al.	Description: Badge Question Mark with solid fill	Description: Badge Unfollow with solid fill	Description: Badge Follow with solid fill	Description: Badge Unfollow with solid fill	Description: Badge Follow with solid fill	Description: Badge Follow with solid fill

in patients who take anticoagulant medications such as warfarin [18]. For stabilizing intraoral bleeding, for treatment options, dentists should always start from least invasive to more technical. Pressure application with gauze contained tranexamic acid would be an ideal start, more surgical approaches can be considered if bleeding continues. Prevention of such bleeding would be better than any other post-bleeding measures, it needs excellent recognition of possible risk factors and planning before surgical procedure [21].

Two articles investigated the effect of platelet-rich fibrin and chitosan-based Axiostat hemostatic agents on hemostasis compromised patients. Platelet-rich fibrin is a biomaterial, while chitosan is a natural material derived from chitin. They have demonstrated several properties including acceleration in wound coagulation, healing, bleeding control and improving immune responses. Minor oral surgical procedures such as teeth extractions performed in patients with cardiac surgeries require prophylactic anti-coagulant therapy, so as a consecounce they will be prone to high risk of complications postoperatively due to hemorrhage. The most common used anti-coagulants are warfarin and acetylsalicylic acid, so they must be addressed during surgical planning before operation [22]. Rajendra, et al. evaluated the hemostatic effect of Platelet-rich fibrin and chitosan-based Axiostat after tooth extraction on cardiac patients taking antiplatelet medicament. Axiostat dressing demonstrated minor pain postoperatively. Hemostasis in Axiostat group was attained faster compared to Platelet-rich fibrin group. The study concluded that chitosan-based Axiostat is an excellent hemostatic agent to control bleeding after tooth extraction in cardiac patients on anticoagulant therapy [12]. Sarkar, et al. evaluated the effectincy of Platelet Rich Fibrin and Chitosan in achieving hemostasis in anticoagulated and socket healing capacity post extraction. Sockets attained hemostasis when treated by platelet rich fibrin in 2.64 minutes while chitosan in 1.182 min. The study concluded that chitosan demonstrated superiority in controlling bleeding compared to Platelet Rich Fibrin, by decreasing the clotting time after extraction in patients on anticoagulation therapy. While Platelet Rich Fibrin showed superiority in wound healing with less pain after minor oral surgical procedures when compared to Chitosan [13]. Studies collectively concluded with that Chitosan is an effective haemostatic agent in controlling bleeding post extraction and is of great help used on cardiac patients taking anticoagulants.

Two articles investigated the effect of multiple different hemostatic agents on anticoagulated patients undergoing teeth extraction. Bajkin, et al. evaluated various local ways to achieve hemostasis after tooth extraction in patients taking Vitamin-K antagonist medicaments. Results showed that 1 patient treated with nonresorbable suture, 2 patients treated with absorbable gelatin sponge and whom were treated with pressure only have experienced bleeding post-extraction. The study concluded that when effective hemostatic agents provided, tooth extractions can be conducted without any change in the anticoagulant therapy. In most cases; when INR level is equal to or less than 3.0 after tooth extraction, local pressure can control the postoperative bleeding without the need of additional hemostatic agents [12].

Halfpenny, et al. evaluated the use of a resorbable oxycellulose dressing and fibrin adhesive in minimizing hemorrhage after teeth extraction in anticoagulated patients. No significant difference between the two modalities was viewed in regard to hemorrhage. 1 patient had significant bleeding postoperatively. The study concluded that patients taking anticoagulant and INR level within the acceptable range, the both modalities, oxycellulose dressing and fibrin adhesive, are equally effective in reducing hemorrhage and aid in faster coagulation. These studies supports that dental extractions can be accomplished without the need to modify the anticoagulant therapy. Several studies agree that hemostasis can occur with absorbable oxidized cellulose, tranexamic acid and suture. If patient is unable to use mouthwash then autologous fibrin glue would be more effective.

Swamy, et al. evaluated the efficacy of Haemocoagulase (batroxobin) after teeth extractions in children. Hemostasis was faster and bleeding time was less in the group that used haemocoagulase compared to control. The study concluded that haemocoagulase resulted in significant speed for haemostasis and was effective in bleeding control within empty sockets after teeth extraction in children. Haemocoagulase is effective and efficient to be used by paediatric dentists, with cooperative or special needs patients, thus enhancing patient care [15].

Rai et al. evaluated the effectiveness of feracrylum compared to tranexamic acid, after teeth extraction in anticoagulated patients by warfarin. The study concluded that hemostatic agents such as tranexamic acid and feracrylum would stop bleeding without the need to alter the anticoagulant therapy. Feracrylum have also added multiple benifits such as single application, mechanical barrier formation and antibacterial and antifungal effect, cost effective and better handling characteristics. Such agents should be added when managing patients on oral anticoagulants [19].

Pippi et al. evaluated the efficacy of HemCon Dental Dressing, which is a new agent used to control bleeding, in patients taking anticoagulant regiments and who are undergoing teeth extractions without any modification in anticoagulant therapy compared to other common hemostatic agents. The study concluded that teeth extraction done on patients who take anticoagulants and have INR level less than 3.5, it is considered a safe procedure without any change. The postoperative side effects and wound healing by using HemCon Dental Dressing was sufficient and effective [16].

Kazancıoğlu, et al. evaluated the efficacy to control bleeding after tooth extraction in hemophilia patients by

using a new hemostatic agent, Ankaferd Blood Stopper. Patients that have used Ankaferd Blood Stopper to control bleeding demonstrated a significant shorter bleeding time. The study concluded that Ankaferd Blood Stopper can be used as an alternative hemostatic agent for minimizing the clotting factor concentration in hemophilic patients [10].

The presented systematic review had some limitations including, there was a limited number of available clinical studies on this subject fitting the inclusion criteria. Almost all studies included was related to oral and maxillofacial surgery specialty of dentistry, were as all dental procedures of all available specialties was supposed to be considered, but due to the limited available literature with high evidence it they were excluded. Participant's randomization and sample size calculations were not considered. In the selected studies there were major differences in sample characteristics which altered comparisons, Thus Age, Sex, Hemostatic agent used and health status of the participants should be controlled and unified as much as possible to confirm review results. Most studies considered participants with a bleeding disorder or who are talking medications the increase bleeding risk and not healthy participants, this it may affect this study results. Differences among sample and methodologies would prevent the possibility to do meta-analysis for this review. Most included articles were non-controlled studies which increase the possibility of bias thus altering the outcomes and conclusions of the studies. Only four articles in this systematic review were identified as randomized controlled trials. Future studies with higher quality, larger populations and randomization needed.

CONCLUSION

Various hemostatic agents have been investigated to accomplish hemostasis by the different mechanisms to limit bleeding and encourage coagulation. Studies confirmed that application of pressure with gauze containing tranexamic acid would be the management of choice. Chitosan proved superiority compared to platelet rich fibrin in achieving hemostasis. Feracrylum and HemCon Dental Dressing have also resulted in positive association with coagulation especially in patients undergoing antiplatelet therapy. Haemocoagulase was correlated with paediatric patients, while Ankaferd Blood Stopper in hemophilic patients in hemostasis. Further studies are needed to support results.

REFERENCES

1. Haas DA. Management of medical emergencies in the dental office: Conditions in each country, the extent of treatment by the dentist. Anesth Prog 2006; 53:20-24.
2. Palta S, Saroa R, Palta A. Overview of the coagulation system. Indian J Anaesth 2014; 58:515.
3. Harter K, Levine M, Henderson SO. Anticoagulation drug therapy: A review. Western J Emerg Med 2015; 16:11.
4. Swieringa F, Spronk HM, Heemskerk JW, et al. Integrating platelet and coagulation activation in fibrin clot formation. Res Pract Thromb Haemost 2018; 2:450-60.
5. Kuruvilla M, Gurk-Turner C. A review of warfarin dosing and monitoring. In Baylor University Medical Center Proceedings 2001; 14:305-306.
6. Shoeb M, Fang MC. Assessing bleeding risk in patients taking anticoagulants. J Thromb Thrombolysis 2013; 35:312-319.
7. Verma G. Dental extraction can be performed safely in patients on aspirin therapy: A timely reminder. Int Scholar Res Notices 2014; 2014.
8. Smith SA, Travers RJ, Morrissey JH. How it all starts: Initiation of the clotting cascade. Crit Rev Biochem Mol Biol 2015; 50:326-336.
9. Robertson S, Miller MR. Ambient air pollution and thrombosis. Part Fibre Toxicol 2018; 15:1-6.
10. Kazancıoğlu HO, Çakır O, Ak G, et al. The effectiveness of a new hemostatic agent (Ankaferd Blood Stopper) for the control of bleeding following tooth extraction in hemophilia: A controlled clinical trial. Turk J Haematol 2013; 30:19.
11. Rajendra K, Vempalli S, Kadiyala M, et al. Effect of platelet-rich fibrin versus chitosan-based Axiostat hemostatic agent following dental extraction in cardiac patients on antiplatelet therapy: A comparative study. Natl J Maxillofac Surg 2021; 12:361.
12. Bajkin BV, Selaković SD, Mirković SM, et al. Comparison of efficacy of local hemostatic modalities in anticoagulated patients undergoing tooth extractions. Military Med Examin 2014; 71:1097-1101.
13. Sarkar S, Prashanth NT, Shobha ES, et al. Efficacy of platelet rich fibrin versus chitosan as a hemostatic agent following dental extraction in patients on antiplatelet therapy. J Oral Biol Craniofac Res 2019; 9:336-339.
14. Jaiswal P, Agrawal R, Gandhi A, et al. Managing anticoagulant patients undergoing dental extraction by using hemostatic agent: Tranexamic acid mouthrinse. J Pharm Bioallied Sci 2021; 13:S469.
15. Swamy DF, Barretto ES, Rodrigues JS. Effectiveness of topical haemocoagulase as a haemostatic agent in children undergoing extraction of primary teeth: a split-mouth, randomised, double-blind, clinical trial. Eur Arch Paediatr Dent 2019; 20:311-317.
16. Pippi R, Santoro M, Cafolla A. The effectiveness of a new method using an extra-alveolar hemostatic agent after dental extractions in older patients on oral anticoagulation treatment: An intrapatient study. Oral Surg Oral Med Oral Pathol Oral Radiol Endod 2015; 120:15-21.
17. Queiroz SI, Silvestre VD, Soares RM, et al. Tranexamic acid as a local hemostasis method after dental extraction in patients on warfarin: A randomized controlled clinical study. Clin Oral Investig 2018; 22:2281-2289.
18. Halfpenny W, Fraser JS, Adlam DM. Comparison of 2 hemostatic agents for the prevention of postextraction hemorrhage in patients on anticoagulants. Oral Surg Oral

Med Oral Pathol Oral Radiol Endod 2001; 92:257-259.

19. Rai S, Rattan V. Efficacy of feracrylum as topical hemostatic agent in therapeutically anticoagulated patients undergoing dental extraction: a comparative study. J Maxillofac Oral Surg 2019; 18:579-583.
20. Boccardo P, Galbusera M, Remuzzi G. Prevention and therapeutic management of bleeding in dialysis patients. Handbook of Dialysis Therapy E-Book 2007; 445.
21. Zirk M, Zinser M, Buller J, et al. Supportive topical tranexamic acid application for hemostasis in oral bleeding events–Retrospective cohort study of 542 patients. J Craniomaxillofac Surg 2018; 46:932-936.
22. Eldibany RM. Platelet rich fibrin versus Hemcon dental dressing following dental extraction in patients under anticoagulant therapy. Tanta Dent J 2014; 11:75-84.