Complications and Management of Patients with Inherited Bleeding Disorders During Dental Extractions: a Systematic Literature Review

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ABSTRACT

Objectives: The systematic literature review aims to assess patients' dental extraction with inherited bleeding disorders, to understand the type, dosage, and modality of administration of the haemostatic agents for safe intra- and postoperational results.
Material and Methods: The search was undertaken in MEDLINE (PubMed) databases and Cochrane library for articles published in English from 1 January, 2010 till 31 October, 2020. Before the full-text articles were considered, titles and abstracts were screened.
Results: A total of 78 articles were screened, from which 3 met the necessary criteria and were used for the review. Minor complications, such as postoperative bleedings from the socket and epistaxis, were observed, but they were resolved with proper medical care. No major fatal complications were reported. Generally, all the articles provided evidence of successful extractions with correct treatment plans made by haematologists and surgeons.
Conclusions: Available clinical trials demonstrate that local and systemic haemostatic therapies in combination are effective in preventing bleeding during dental extractions in patients with coagulopathies.

Keywords: hemophilia A; hemophilia B; hemorrhage; postoperative hemorrhage; surgical hemostasis; tooth extraction.

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INTRODUCTION

Inherited bleeding disorders such as haemophilia or von Willebrand disease (vWD) are characterized by spontaneous bleeding, impaired haemostasis, a high risk of intra- or postoperative bleeding, and excessive bleeding after haemostatic challenges as trauma and invasive procedures [1,2]. The extent and severity of bleeding are very individual to each patient [2]. Various factors are influencing bleeding. Some of the followings are local and systemic factors such as periodontitis, vasculopathy, type and number of extracted teeth, wound size, platelet dysfunction, and haemophilia severity [2].

vWD and haemophilia are the most common congenital bleeding disorders [2]. Worldwide over 400,000 people are affected by haemophilia, with a prevalence of 1 in 5,000 males [3,4]. However, the most common is vWD, with 1% of the population being affected but clinically significant vWD is much lower due to mild symptoms and undiagnosed cases [1,2,5].

Haemophilia is an X-linked inherited recessive bleeding disorder. Type A is characterized by a deficiency of factor VIII (FVIII), while haemophilia B (Christmas disease) is due to factor IX (FIX) deficiency [1-7]. Factors VIII, IX, XI, along with others, and also vWF, are coagulation proteins that play a vital role in the successful completion of primary (vWF) and secondary haemostasis (VIII) and formation of blood clot eventually [2]. The variation in haemophilia severity depends on the different genetic mutations that might occur. Women affected by haemophilia are mostly asymptomatic, while men are expressing the disease. Type A affects approximately 1 : 5,000 males compared to type B, which is not so often occurring, and it affects 1 : 30,000 males [3].

VWD is characterized by a deficiency in vWF. Von Willebrand factor is a blood glycoprotein that is essential for primary haemostasis to occur normally. During vascular injury, this factor's primary role is to guide platelet adhesion to the sub-endothelial wall. Another important function is that FVIII is bound to vWF during circulation when it is inactive. Therefore, in moderate or severe vWD, there will also be a deficiency in FVIII, which will lead to additional impairment in secondary haemostasis [2]. There are three subtypes of vWD: type 1 is mild and is characterized by vWF > 30 %. It is also considered the most common type; type 2 is moderate, and the factor amount is 10% to 30%, and type 3 is severe with a factor level < 10% [2,6].

Inherited autosomal recessive disorders are among the least common congenital bleeding disorders, and they are characterized by deficiencies of other coagulation factors such as factor II (fibrinogen), factors V, VII, X, XII, enzymes, or other components responsible for platelet function and proteins that regulate the biosynthesis or expression of the factors. Their prevalence is approximately 1 : 500,000 to 1 : 2,000,000 births. These numbers are higher in populations where marriage between family members is common [1].

Haemophilia A and B can be mild, moderate, and severe, according to the residual plasmatic concentration of the missing protein (FVIII or FIX). Severe - less than 0.01 units per millilitre (u/ml), moderate - from 0.01 to < 0.05 u/ml and mild - bigger than 0.05 to 0.4 u/ml.

Dental extractions and dentoalveolar surgery in patients with haemophilia can lead to severe intra- and postoperational bleeding. The surgeon and haematologist should strictly manage any dental management for such patients with a proper treatment plan to avoid fatal complications [1-7].

An important aspect that has to be planned for haemophilia patients is local anaesthesia. In case the patient needs an inferior alveolar nerve (IAN) block, then systemic replacement therapy of the missing or insufficient factors is necessary. Because of the abundance of blood vessels in the area, there is an 80% risk of hematoma development into adjacent muscle tissue that can be very dangerous if it forms in the pterygoid or retromolar spaces and obstructs the airway. Infiltration anaesthesia on the lingual aspect of mandibular teeth is also associated with a higher risk of hematoma development. However, buccal infiltration, intraligamental, intrapulpal, and intraosseous techniques, as well as a mental nerve block, are considered safe and do not require systemic preoperative treatment. Therefore, IAN can be replaced by a combination of these anaesthetic techniques [6,7].

The systematic literature review aims to assess patients' dental extraction with inherited bleeding disorders, to understand the type, dosage, and modality of administering the haemostatic agents for safe intra- and postoperative results.

MATERIAL AND METHODS

Protocol and registration

The review was conducted according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) [8].

Focus question

The focus question was developed according to the Patient, Intervention, Comparison, Outcome, and Study design (PICOS) framework, as described in Table 1.
What is the preferred treatment plan for patients with inherited bleeding disorders and is local therapy enough to perform teeth extractions or systemic therapy is mandatory?

Types of publication

The review included studies on humans published in English. Abstracts, case-control studies, PhD thesis and literature reviews were excluded.

Types of studies

The review included controlled clinical trials and cohort sudies from 13th of March 2013 till 13th of April 2015.

Information sources

Search was undertaken in MEDLINE (PubMed) and Cochrane library for studies related to treatment of patients with haemophilia A and B and vWD with various local or systemic medications. The time frame for the published articles was from 1 January, 2010 till 31 October, 2020.

Search

The primary search inquiries used were: "Hemorrhage "[Mesh] AND "Hemophilia A"[Mesh], AND "Tooth Extraction"[Mesh], AND "Hemophilia B", AND "Hemostasis, Surgical"[Mesh], AND "Postoperative Hemorrhage" and secondary keywords were "von Willebrand Diseases" and "Antifibrinolytic Agents".

Type of population

Males and females of any age that suffered from inherited coagulation disorders and required a dental extraction.

Inclusion criteria

Studies were included if they fulfil the following criteria as follows:
- Studies on patients with inherited bleeding disorders (haemophilia A, B, vWD, factor V/XI deficiency) in need of various dentoalveolar surgeries, including teeth extraction;
- Haemophilia (all severities) with or without inhibitors;
- Publications including comparison of outcomes in treatment between systemic and local administration of haemostatic agents;
- Studies that include more than 15 patients;
- Studies in English language.

Exclusion criteria

If articles presented any of the following, they were excluded from the current review:
- Studies on animals;
- Only abstracts;
- Studies that include acquired bleeding disorders;
- Case reports;
- Studies on patients that take anticoagulative drugs.

Data extraction

Data extracted from the included articles for this review is listed below:
- "Author and publication year" - discloses the author and year of study.
- "Type of study" - designates the type of study.
- "Groups" - the patients that received either local or systemic therapy or a combination.
- "Age" - indicates the age intervals of the patients involved in each study.
- "Female/male ratio" - the number of females and males included in each study.
- "Total amount of patients treated" - the total amount of patients from all the studies.

Table 1. PICOS framework of the framed clinical question

Patients (P)	Patients suffering from haemophilia A, B, von Willebrand disease
Intervention (I)	Antifibrinolytic therapy and clotting factor replacement therapy
Comparison (C)	Between outcomes of local and systemic administration
Outcome (O)	Presence or absence of secondary haemorrhage
Study design (S)	Randomized and Non- Randomized controlled trials
Focus question	What is the preferred treatment plan for patients with inherited bleeding disorders and is local therapy enough to perform teeth extractions or systemic therapy is mandatory?

- "Total amount of extractions performed" - the sum up of all the extractions.
- "Systemic medicaments" - types of haemostatic medications administered orally or intravenously before or after the surgery.
- "Local medicaments" - types of haemostatic medications administered locally after the teeth extractions to prevent bleeding.
- "Secondary bleeding" - total number of patients that suffered postoperative haemorrhage and required additional treatment.
- "Other complication" - any postoperative complication other than secondary bleeding.
- "Number of patients that did not suffer any complications".
- "Inhibitors" - any patients that are diagnosed with antibodies to FVIII or FIX.
- "Follow up" - indicates the postoperative visits to the dental surgeon for assessment of any potential complication.

Risk of bias

The risk of bias was assessed with the use of Joanna Briggs Institute (JBI) Critical Appraisal Checklist for randomised controlled trials (RCT) and non-randomised controlled trials (non-RCT) [9]. Thirteen questions were answered for RCT and 9 for non-RCT. Every question was answered with "yes ", "no", "unclear", and "not applicable" according to the data extracted from the studies (Table 2). The presented tools are indicating if the quality of studies is low, moderate or high, but it does not present if they have a high or low risk of bias. The purpose of this appraisal in the systematic literature review is to analyse the studies and include only those with high quality and respectively exclude the studies with poor quality.

Synthesis of results

Relevant data of interest on the previously stated variables were collected and organised into 3 tables, divided according to the selected parameters. Table 3 summarises data about the total number of patients, total of extractions performed and treatment methods. Table 4 presents the division of patients according to the gender, the types of pathologies, and the local and systemic haemostatic agents used in every study. Table 5 provides information about the complications outcomes as well as presence or absence of inhibitors.

Statistical analysis

Meta-analysis was not performed due to heterogeneity between the studies. There are different study designs and control groups.

RESULTS

Study selection

The extraction of the selected articles for this review was performed using PRISMA flow diagram guidelines. A total of 78 publications were screened. After the duplicates were excluded, 59 articles remained. In the next step, after the titles and abstracts were screened, 54 articles were excluded, and 5 full texts were assessed for eligibility. Two articles were excluded because they did not meet the inclusion criteria, aim and focus question of this review. As a result, only 3 articles were selected in the systematic review (Figure 1).

Table 2. Joanna Briggs Institute risk of bias table for randomised non-randomised controlled trials

Study	Year of publication	Study design	Checklist												
			Q1	Q2	Q3	Q4	Q5	Q6	Q7	Q8	Q9	Q10	Q11	Q12	Q13
Peisker et al. [3]	2014	Non-RCT	+	?	+	-	N/A	+	+	?	-				
Cocero et al. [5]	2015	RCT	+	+	+	-	?	?	+	+	?	+	+	+	+
Kazancıoğlu et al. [12]	2013	RCT	+	+	+	-	?	+	+	+	?	+	+	+	+

"+" = yes; "- " = no; "?" = unclear; "N/A" = not applicable; RCT= randomised clinical trial.

Table 3. Characteristics of studies included in the systematic review, treatment methods and extractions

Study	Number of patients	Treatment methods	Number of extractions
Peisker et al. [3]	15	Combined, systemic and local	58
Cocero et al. [5]	120	Combined systemic and local	204
Kazancıoğlu et al. [12]	27	Combined systemic and local	57

Table 4. Characteristics of studies included in systematic review, age, gender ratio, pathology and local and systemic agents used in each clinical trial

Study	Mean age (years)	Gender ratio	Pathology	Systemic agents	Local agents
Peisker et al. [3]	32 (SD 22.5)	14 males; 1 female	H.A = 11; H.B = 4	Tranexamic acid; recombinant and plasma derived replacement therapy; desmopressin	Collagen vlies; oxycellulose; fibrin glue; sutures; compressive splints
Cocero et al. [5]	6 - 78	83 males; 37 females	H.A = 47; vWD = 53; H.B = 11; F V/XI = 9	Tranexamic acid; ugurol; desmopressin; plasma derived/recombinant replacement therapy	Fibrin glue; plasma rich growth factor
Kazancıoğlu et al. [12]	20.3 (SD 11.4)	27 males	H. A = 27	Tranexamic acid; FVIII or FIX; rFVIIa (when inhibitors)	Ankaferd blood stopper; direct packing with gauze

H.A = haemophilia A; H.B = haemophilia B; vWD = von Willebrand disease; F V/XI = factor V/XI deficiency; FVIII = factor VIII deficiency; FIX = factor IX deficiency; rFVIIa = recombinant activated factor VII; SD = standard deviation.

Table 5. Characteristics of studies included in systematic review, secondary bleeding, other complications and inhibitors

Study	Secondary bleeding and additional therapy	Other complications	Presence of inhibitors
Peisker et al. [3]	1 patient	1	0
Cocero et al. [5]	5 patients	0	2
Kazancıoğlu et al. [12]	2 patients	0	2

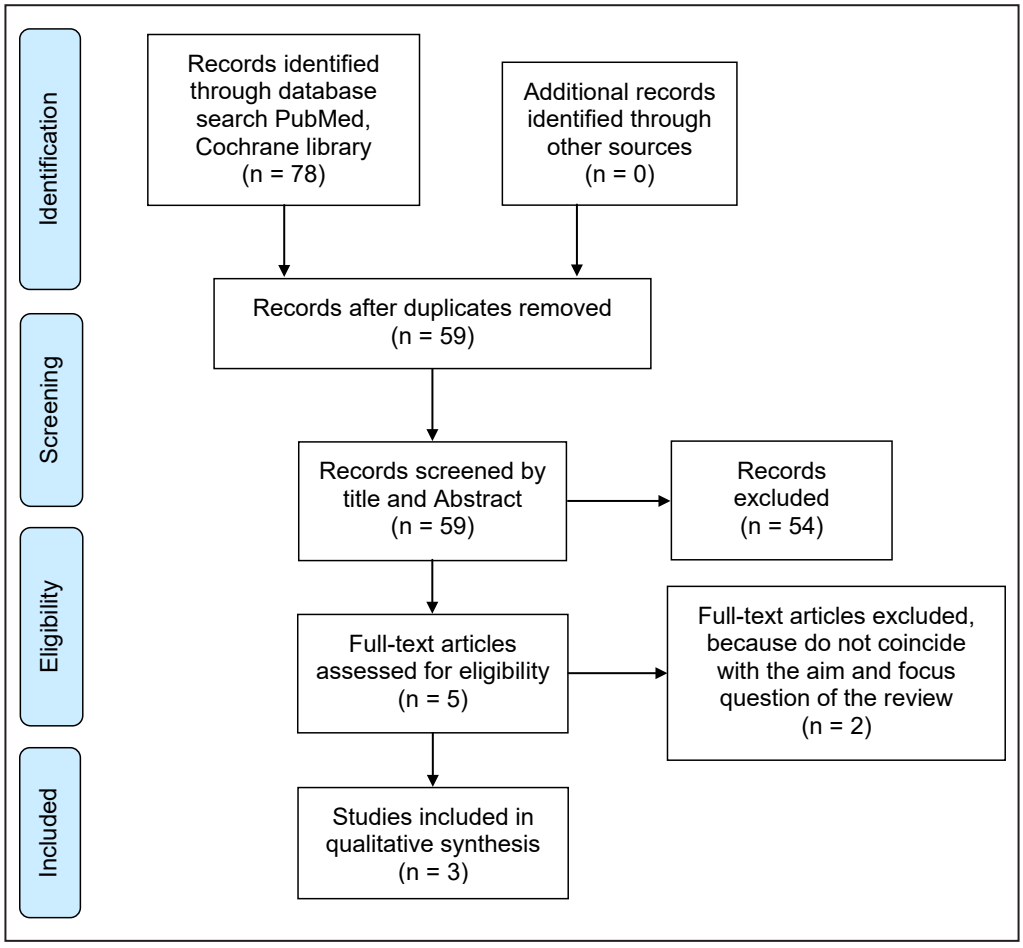

Figure 1. Flow diagram of studies selection according PRISMA guidelines.

Exclusion of studies

One article was excluded because it also involved patients with acquired bleeding disorders [10]. The other article was excluded because it is not based on patients with inherited bleeding disorders but on healthy individuals who need more extensive surgery and therefore are exposed to an increased risk of haemorrhage [11].

Quality assessment of the included studies

JBI tools for RCT and non-RCT were used to assess the included studies' quality [9] (Table 2). RCT [5,12], included in this review, represented relatively a low risk of bias, having high quality; however, the blinding of participants was not possible. Due to their severe conditions, they were informed about the whole procedure and the systemic and local haemostatic agents that they were going to receive. They had to agree to be included in the study. Some aspects of the study remained unclear. A survey by Peisker et al. [3] revealed an unclear risk of bias and moderate quality of studies.

Study characteristics

Two studies included in the review are RCT [5,12], and one article is a non-RCT [3] published from 2013 to 2015 [3,5,12].

A total of 162 haemophilia patients with 319 extractions were included in this systematic review. Three patients with cardiovascular diseases were reported in the first article [3]. The second study excluded the patients that suffer from hepatitis B or C, but systemic conditions such as diabetes, kidney failure, and liver diseases were accepted in the trial [5]. In the third study, patients with systemic diseases such as diabetes mellitus or hypertension and any psychological diseases were excluded. All studies used a combined treatment method made up of systemic and local haemostatic agents in order to prevent bleeding. Details are summarized in Table 3.

Patients of all ages were included, from 4 to 78 years. In total, 38 females and 124 males are included in this review. Of the whole number of patients, 85 are affected by haemophilia A (H.A), 15 by haemophilia B (H.B), 53 by vWD, and 9 patients by factor V/XI deficiency. All three articles presented data about H.A while, H.B was assessed by two papers [3,5], and only 1 article included the other two pathologies [5]. According to a specific protocol, the patients of all the clinical trials received systemic treatment with tranexamic acid (TXA) and factor replacement therapy. Local, postoperative haemostatic agents were administered obligatorily after all the extractions [3,5,12]. In each study, the authors used different local haemostatic agents. Several studies [5,12] tried to identify if some new local haemostatic agents are more efficacious and have better properties than older and conventional ones.

Secondary bleeding was reported in all clinical trials [3,5,12]. In total, eight patients were recorded to have suffered from secondary bleeding from the extraction site [3,5,12], while one patient had epistaxis [3]. Four patients were diagnosed with inhibitors to FVIII, and recombinant activated factor VII (rFVIIa) was administered to them [5,12].

DISCUSSION

The objective of this systematic review was to assess the dental extraction procedure in patients with inherited bleeding disorders and to understand the type, dosage and modality of administration of haemostatic agents for safe intra- and postoperative results. One article that was included was non-RCT with moderate quality [3], while the other two articles that were included were RCT and had high quality. These studies corresponded well to the systematic review because it matched the inclusion criteria.

Patients with congenital bleeding disorders live every day with the fear of bleeding due to possible trauma or injury to the mucous membrane [13]. This leads to bad oral hygiene practices, such as inadequate brushing and avoidance of interdental brushes or dental floss, increasing the risk of caries, gingival inflammation, and periodontal problems [7,13,14]. The literature provides studies demonstrating a higher decayed, missing due to caries and filled teeth (DMFT) in patients who have haemophilia compared to healthy patients [15,16]. However, some studies prove the opposite results. In a survey carried out in Northern Ireland, children with haemophilia had a significantly lower amount of caries and DMFT than healthy children. This can be explained due to a serious approach of the parents and children to the importance of disease and its complications and the importance of preventing them with good oral hygiene and regular appointments [7,17]. Due to insufficient data, it is not possible to conclude whether the oral status is worse or better in haemophiliacs compared to the healthy population. Nevertheless, it is very important for this patient group to maintain excellent oral hygiene and prevent any inflammatory processes that will lead to bleeding [4,18].

Haemophilia and vWD are inherited bleeding disorders that place the patients that undergo dental extractions at a very high risk of either intra- or postoperative bleeding complications [2,3]. Treatment of such patients is not direct, and it requires cooperation between the oral surgeon and the haematologist before any intervention can be performed [3,6]. The World Federation of Haemophilia (WFH) provides protocols regarding the management of such patients [3]. It advises the administration of clotting factor concentrates directly into the bloodstream to improve the blood's ability to clot along with local haemostatic techniques such as suturing and local therapy with fibrin glue (FG), TXA, or oxidized cellulose [1,12].

The process of haemostasis occurs when at the site of vascular injury, the bleeding is arrested [19]. Haemostasis is a highly complex process that consists of several important factors, such as platelets, plasma proteins, coagulation, and fibrinolytic pathways and the interaction between them [8]. This process is divided into primary and secondary haemostasis. During primary haemostasis, a blot clot is formed, but secondary haemostasis assures the maintenance of this blot clot. At this stage of coagulation, specific plasma proteins interact to form a cross-linked fibrin bridge that prevents the initial platelet plug from falling apart. Factors VIII and IX are inactive circulating in the bloodstream. When a blood vessel injury is detected, they get activated as a part of secondary haemostasis, and as a result, they activate factor X (FX).

The cascade continues with the generation of thrombin and fibrin, which have a crucial role in stabilizing blood clots. So, in haemophilia patients, the inability of factors VIII and IX to activate FX is the reason for uncontrolled bleeding and is characterized as a secondary haemostatic defect. Disorders of vWF are associated with primary haemostasis, as this protein is insufficient or does not work as it should, the platelets cannot adhere properly to each other or the sub-endothelium, and the primary clot fails to form [19,20].

There are two groups of factors VIII and IX concentrates: plasma-derived factor and recombinant (non-human derived) but, WFH does not specify the type of factors mostly preferred [3]. There is still a risk that plasma-derived factors can transmit infections and viruses, despite the viral inactivation technique introduced in the mid-1980s [2,13]. Recombinant FVIII is developed without animal or human protein to overcome the danger of disease transmission. However, there is not yet a recombinant factor developed for vWF [6,14].

Another problem related to factor replacement therapy is the development of antibodies or inhibitors to factors VIII or IX [13,14]. This therapy is indicated for moderate to severe forms of haemophilia A, B, and vWD [6]. Inhibitors develop primarily in patients with severe H.A, 25 to 40% lifetime risk compared to 5 to 15% lifetime risk for patients with mild or moderate H.A [21]. For patients that develop inhibitors, the treatment is more problematic as conventional therapy is not effective, and special care should be taken to perform good local haemostasis [15]. Besides that, an activated prothrombin complex concentrates or a rFVIIa concentrate is suitable for these patients [3].

So, in order to reduce the risk of infections and immunization, desmopressin (DDAVP) can be used as an alternative to factor replacement therapy in patients with mild or moderate H.A and mild type 1 vWD [3,6]. A single dose of 0.3 micrograms administered before surgery raises vWF and FVIII level three to six-fold in patients with good response [3,20].

Besides systemic agents mentioned above, TXA is also a famous systemic antifibrinolytic agent for haemophilia patients because it reduces fibrinolysis by inhibiting the action of plasmin [12]. Peisker et al. [3] used it intravenously and orally at a dose of 20 mg/kg every 8 hours for seven days before surgery in 16 interventions. Kazancıoğlu et al. [12] used TXA additional for patients with inhibitors to FVIII. Cocero et al. [5] used TXA in combination with DDAVP for mild/moderate H.A and type 1 vWD.

In the studies by Forbes et al. [22] and Walsh et al. [23], antifibrinolytic agents TXA [22] and aminocaproic acid (EACA) [23] were administered systemically and compared with placebo to assess if they can replace or decrease the amount of clotting factor concentrates. Both trials showed the significant effectiveness of antifibrinolytic agents [2]. According to the WFH, TXA and EACA are used to reduce the necessity of factor replacement after a dental procedure [18].

Proper preparation of the patients for surgical treatment is a critical point in order to avoid excessive bleeding. In all clinical trials included in this review, haemophilia patients underwent systemic preoperative treatment with factor replacement therapy [3,5,12]. Data regarding the pre- and postoperative systemic treatment was given in articles [3,12], but no data was exposed in the paper [3]. Local haemostatic treatment is mandatory in these patients and was performed in all the studies. The detailed data about the local agents used are given in Table 4. Several studies [5,12] tried to identify possible better and safer local haemostatics agents, and the result proved that indeed these new agents have excellent properties.

Cocero et al. [5] tried to prove the benefit of autologous plasma rich in growth factors (PRGF) over FG. FG is a famous local haemostatic agent used to prevent bleeding in haemophilia patients; however, it has a disadvantage that it is plasma-derived, so it carries the risk of disease spreading. On the other hand, PRGF is a gel made out of highly concentrated autologous platelets, so it is safe for the patient. The study results proved that it is not less effective than FG. In addition, tissue repair and wound healing were accelerated in patients treated with PRGF.

Kazancıoğlu et al. [12] examined the effect of a new local haemostatic agent ankaferd blood stopper (ABS), for the first time in haemophilia patients and proved to be effective, safe, and easy to use. Also, they found that out that the duration of postoperative bleeding was significantly reduced in the treatment group with ABS compared to the control group (P = 0.002). The median duration of bleeding in patients that were administered ABS was 70 seconds compared to 101 seconds for the group treated with direct gauze packing.

Besides, ABS can be used for patients with both primary and secondary haemostasis disorders since it does not affect the coagulation factor level, but it only interacts with fibrinogen and other blood proteins. Some studies were done to see the effectiveness of ABS as a local haemostatic agent without factor replacement therapy, and the results were successful without bleeding complications [24,25].

Secondary bleedings were reported by all the publications, as previously mentioned in Table 5. Peisker et al. [3] reported two complications that occurred in two patients suffering from mild H.A. One patient had epistaxis on the seventh day after the operation and was managed with a nasal tamponade for two days. The second patient that suffered from bleeding on the fifth day needed additional clotting factor therapy to stop the bleeding as well as compression with gauzes saturated with TXA.

Cocero et al. [5] reported five patients with secondary bleeding, and 4 out of 5 patients suffered from H.A. Two of the bleedings appeared in patients treated with PRGF on the 1st day after surgery, and three bleedings in the group treated with FG were reported on the 3rd day after surgery, and in one case, the bleeding happened on the seventh day. There was no need for additional systemic therapy in the PRGF group. Bleedings were arrested with an additional application of PRGF. However, in the FG group, all 3 cases required additional systemic therapy plus reapplication of FG. For the case that presented bleeding on the seventh day, the third administration of systemic clotting factor was performed as well as additional FG application.

Kazancıoğlu et al. [12] reported 1 postoperative bleeding in a patient suffering from severe H.A and had inhibitors against FVIII. However, another patient in this study had as well severe H.A with inhibitors but did not present postoperative bleeding. Thus, the authors believe that blood clot destruction for this patient was due to poor oral hygiene and multiple extractions (3 teeth at the same time) [12]. The bleeding was managed with additional ABS application as well as systemic rFVIIa after 3 and 6 hours.

The second postoperative bleeding and impaired wound healing occurred in a patient suffering as well from severe H.A, and it happened because he didn't follow the study protocol.

After the surgery, patients with coagulative disorders should avoid nonsteroidal anti-inflammatory drugs and aspirin due to their effect on platelets and blood coagulation [3,6,7,18]. A safe painkiller is paracetamol, and it can be taken every 6 hours for 2 to 3 days after the surgery [3-5,13,18].

They require postoperative surveillance in order to avoid episodes of excessive bleeding, as well as very detailed and understandable instructions that they must follow [3]. According to the WFH [13], after dental extractions, patients must not rinse their mouth for 24 hours to avoid smoking, eat soft food for 24 hours, strictly follow the prescribed medications and immediately call the emergency if any complications appear.

In addition, starting with the following day after surgery, patients must use saltwater mouthwashes (a teaspoon of salt dissolved in a glass with warm water) 4 times a day for seven days; antibacterial mouthwashes can be used as well [13,18]. Cocero et al. [5] and Kazancıoğlu et al. [12] performed the follow-up on the 1, 3, and 7 day after surgery to assess the healing, if possible, hematoma or bleeding occurred.

Before any dental intervention exposes the patient to bleeding, a laboratory diagnosis is required in order to evaluate the blood parameters and administer adequate factor therapy for a safe procedure [27]. Such tests include BT, platelet count, PT, and prolonged activated partial thromboplastin time (APTT). APTT is an essential test since it determines the time necessary for blood clot formation and, therefore, a problem with factors VIII and IX. However, in mild cases, some of these tests may not detect abnormalities [4,18,27].

Any postoperative bleeding episodes must be immediately managed by the surgeon and haematologist together. Every case is individual, and the management depends on factors such as

the disease's type and severity. In the literature, secondary bleeding is usually managed with additional clotting factor therapy and local haemostasis [1-3,5,28].

Consultation with a haematologist for the dental treatment of patients with inherited bleeding disorders is an indispensable part of the overall treatment. These are severe conditions, which can cause life-threatening bleeding complications if the exact treatment protocol is not properly planned.

CONCLUSIONS

In the result of this systematic literature review, the following aspects can be concluded:

1. Dental extractions in patients with inherited bleeding disorders always require systemic and local therapies. Local therapy alone is not sufficient. Factor replacement therapy is indicated for all patients with moderate to severe haemophilia A, B, and type 2 and 3 von Willebrand disorder. Mild cases can be managed with systemic haemostatic treatment. Dosages depend on the type and severity of the disease.
2. New local haemostatic agents discussed in this review are very effective and helpful in bleeding management. Moreover, they have better properties than conventional local haemostatic agents. However, more clinical trials are required to conclude the possibility of treating these patients only with local agents without factor replacement therapy.
3. If the haemostatic protocol is properly followed, dental extractions for these patients are safe and do not cause uncontrolled bleeding. However, complications are all the time a risk, especially in severe cases. Management should be already planned and prepared. Additional factor replacement therapy and local haemostasis is the treatment of choice.

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The authors have not encountered any conflict of interests.

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