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Hemophilia and its dental consideration and management

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Abstract

Hemophilia is a medical condition that can cause medical emergency for dentist. Hemophilia patients have high risk of bleeding during various dental procedures. Manage Ment of bleeding in these patients during & after surgery is the biggest challenge for dental surgeons. Here we present a review on management of Hemophilia in dentistry for which literature obtained from published articles, books and manual.

Keywords: Hemophilia, Dentistry, Management.

Introduction

Bleeding disorders are the disorders of blood in which blood doses not clot properly because of any defects present in the blood vessels, coagulation mechanism, and/or blood platelets.

Person affected with bleeding disorder may bleed spontaneously or for longer than a healthy person without bleeding disorder [1]. The most common and frequently occurring congenital plasmatic hemorrhagic diathesis is Hemophilia. Worldwide it affects more than 400,00 people. It is X-linked recessive chromosomal bleeding disorder which is caused by a variety of mutations in clotting factor VIII (Hemophilia A) and/or factor IX (Hemophilia B). Hemophilia A is the most common than Hemophilia B. It affects male more, than female, which is approximately 1:5,000 [2].

Hemophilia A is caused by deficiency of factor VIII and Hemophilia B (also known as Christmas disease) is caused by a deficiency of factor IX. Hemophilia is considered normal when ranges between 50-100, moderate if it ranges between 2 and 5 IU/dL, and mild if it is between 6 and 40 IU/dL and severe when plasma activity is < 1 1 IU/dL [1].

The treatment of the patients with bleeding disorder Hemophilia A and/or Hemophilia B includes the replacement of the deficient clotting factors via intravenous infusion to control or prevent bleeding [2] and become life threatening.

This article includes different dental procedure which can lead to profuse bleeding in hemophilic patient and different method which can prevent it from become life threatening procedure.

In a WFH monograph by Harrington [3], lower doses (30% of normal) of clotting factor concentrates are recommended for infiltration anesthesia of the lower jaw and periodontal curettage.

For more invasive surgical interventions, the recom mendation is to increase the factor level from 50-100 IU/dL of normal pre-operatively and use an oral antifibrinolytic agent pre- and post-operatively.

Sindet-Pedersen [4, 5] suggests that the dose of factor replacement therapy can be significantly reduced if used with an oral rinse of an antifibrinolytic agent (tranexamic acid) is used following a dental extraction. He recommends a single dose of factor, in cases of severe hemophilia A elevating the factor VIII level to 10IU/dL. Desmopressin, a synthetic derivative of the hormone vasopressin, has been shown to increase factor VIII level in some patients with mild or moderate forms of hemo philia A or type 1 von Wille brand disease.

Un fortunately, not all patients respond so this should be checked before performing any surgical procedure. Its use is well documented in cases of mild and moderate hemophilia A [6,7,8]. DDAVP releases bound factor VIII and is therefore not used to treat patients with hemophilia B. A report by Ehl et al. [9] showing a clinical response to desmopressin in four patients with hemophilia B with baseline factor IX levels of 1.4 to 5% for oral surgery. They report a reduction in the use for plasma products following treatment. Fibrin glue is used as a local hemostatic measure in some centers for achieving hemostasis and reducing the needs for clotting factor replacement therapy.

Diagnosis of hemophilia

1. Prenatal testing: it is performed during pregnancy for gene detection. For gene test, a sample of placenta removes from the uterus and chorionic villus sampling (CVS) test perform.

2. Blood test: If a child has hemophilia, a blood test can determine whether the patient or child has hemophilia A or B. Blood tests can perform anytime from the time of birth onwards life.

Oral manifestation of hemophilia

Hemophilia characterized by excessive bleeding from gingival and/or extraction socket and/or oral mucosa due to trauma, and/or any inflammatory condition and/or post dental procedures.

Patients may or may not have history of multiple bleeding events over their lifetime. Bleeding episodes may differ, it may be more in severe hemophilia, which may or may not be followed by moderate and mild hemophilia.

A study by Sonis and Musselman found an average of 29.1% bleeding events per year in hemophilia patients out of which 9% involved oral structures (labial frenum, 60%; tongue, 23%; buccal mucosa, 17%; gingiva and palate, 0.5%) [10]. Therefore, for dental consideration through history is mandatory for proper diagnosis and management of hemophilia.

Table 1: Local anesthetic techniques with requirement of factor replacement.

No Hemostatic coverage required	Hemostatic coverage required
• Buccal infiltration • Intra- papillary injections • Intra-ligmentary injections	• Inferior alveolar nerve block • Lingual nerve block

Prevention

The prevention of dental problems is an essential component of oral care. A successful regimen will reduce the need for treatment and should reduce the number of emergency visits. Dental prevention depends on a number of different factors. Some of these may not be available in developing countries but are included to demonstrate the ideal situation.

• Brushing twice daily with a fluoride toothpaste. - 1,000-ppm fluoride toothpaste for children under 7 years of age. 1,400-ppm fluoride toothpaste for people over 7 years of age. The use of fluoride toothpaste depends on the fluoride concentration in the water supply as well as the use of additional fluoride supplements. It should not be used if fluoride supplements are taken or if the water supply has a fluoride content of 1 ppm or more.

• The toothbrush should have medium texture bristles because hard bristles can cause abrasion of the teeth and soft bristles are inadequate to remove plaque.

• Interdental cleaning aids, such as floss, tape, and interdental brushes, should be used to prevent the formation of dental caries and periodontal disease.

• Fluoride supplements may be used but are not recommended if the water supply has a fluoride content of 1 ppm or more. Supplements include: - Fluoride drops - Fluoride tablets - Topical application of fluoride using trays - Fluoride mouth rinses which can be used on either a daily or a weekly basis.

• The consumption of foods and drinks with a high sugar or acid content should be limited to mealtimes. Three exposures per day is the recommended maximum. The aim is to ensure that the intake of food and drink does not cause the pH of the oral cavity to fall below the critical level of pH 5.5.

• Artificial sweeteners can be used as an alternative to sugars in food and drinks. Examples are aspartame, sorbitol, ace sulfamate, etc.

• Regular dental visits, usually every 6 months, will help identify problems early, reinforce prevention, and emphasize the importance of reducing the intake of food and drink containing high levels of sugar or acid.

The Scottish Intercollegiate Guideline Network has published Preventing Dental Caries in Children at High Risk, which includes a quick reference guide, may also be a useful resource [11].

Dental treatment

It is essential to prevent accidental damage to the oral mucosa when carrying out any procedure in the mouth. Injury can be avoided by: Careful use of saliva ejectors; Careful removal of impressions; Care in the placement of X-ray films, particularly in the sublingual region; Protection of soft tissues during restorative treatment by using a rubber dam or applying soft yellow paraffin (Vaseline®).

Periodontal treatment

Healthy periodontal tissue is essential to prevent bleeding and tooth loss. If oral hygiene is poor treatment must start as soon as possible after the patient has had a dental examination and treatment plan formulated to prevent additional damage to the periodontal tissues. In cases of severe periodontal disease, it may be necessary to carry out supragingival scaling initially along with oral hygiene education. Subgingival scaling can start as soon as the inflammation has decreased. The treatment

may need to be carried out over several visits to prevent excessive blood loss.

In addition, chlorhexidine gluconate mouthwash can be used to control periodontal problems. Antibiotics may be required to help reduce the initial inflammation. Blood loss of all kinds can be controlled locally with direct pressure or periodontal dressings with or without topical antifibrinolytic agents. Periodontal surgery in patients with bleeding disorders must always be regarded as a high-risk procedure with a significant risk of blood loss. It should only be considered were' conservative treatment has failed and oral hygiene is good. Periodontal surgery can be a greater challenge to hemostasis than a simple extraction. The procedure must be carefully planned and the risks fully explained to the patient.

Removable prosthodontics

Patients with bleeding disorders can be given dentures as long as they are comfortable. If a partial denture is provided it is important that the periodontal health of the remaining teeth is maintained.

Orthodontic treatment

Fixed and removable orthodontic appliances may be used along with regular preventive advice and hygiene therapy.

Special care should be taken when treating patients with a severe bleeding disorder to ensure that the gingiva is not damaged when fitting the appliance.

Restorative procedures

Restorative treatment can be undertaken routinely providing care is taken to protect the mucosa. There is a risk of bleeding with the use of matrix bands or wooden wedges. This can be controlled by local means or the application of topical agents.

The risks of using local anesthetics and the requirement for prophylaxis are discussed in a later section.

Endodontics

Endodontic treatment is generally low risk for patients with bleeding disorders. If a pulpectomy is indicated, the possibility of the tooth requiring conventional endo dontic treatment must also be considered.

It is important that the procedure be carried out carefully with the working length of the root canal calculated to ensure that the instruments do not pass through the apex of the root canal. The presence of bleeding in the canal is indicative of pulp tissue remaining in the canal. Sodium hypochlorite should be used for irrigation in all cases, followed by the use of calcium hydroxide paste to control the bleeding. Formaldehyde derived substances may also be used in cases where there is persistent bleeding or even before the pulpectomy.

Anesthesia and pain management

Dental pain can usually be controlled with a minor analgesic such as paracetamol (acetaminophen). Aspirin should not be used due to its inhibitory affect on platelet aggregation. The use of any non-steroidal anti-inflammatory drug (NSAID) must be discussed beforehand with the patient's haematologist because of their effect on platelet aggregation. There are no restrictions regarding the type of local anesthetic agent used although those with vasoconstrictors may provide additional local hemostasis. It is important to advise patients and parents of children about the risks of local oral trauma before the anesthetic wears off. A buccal infiltration can be used without any factor replacement. It will anesthetize all the upper teeth and lower anterior and premolar teeth. The mandibular molar teeth are usually treated using the inferior alveolar nerve block. This should only be given after raising clotting factor levels by appropriate replacement therapy, as there is a risk of bleeding into the muscles along with potential airway compromise due to a hematoma in the retromolar

or pterygoid space. The intra-ligamental technique or interosseous technique should be considered instead of the mandibular block. Articaine® has been used as a buccal infiltration to anesthetize the lower molar teeth. A lingual infiltration also requires appropriate factor replacement since the injection is into an area with a rich plexus of blood vessels and the needle is not adjacent to bone. There is a risk of a significant airway obstruction in the event a bleed [12].

Surgery

Surgical treatment, including a simple dental extraction, must be planned to minimize the risk of bleeding, excessive bruising, or hematoma formation. The following points will help prevent problems: Emergency surgical intervention in dentistry is rarely required as pain can often be controlled without resorting to an unplanned treatment.

All treatment plans must be discussed with the hemophilia unit if they involve the use of prophylactic cover. Treatment plan The treatment plan should be formulated using the following guidelines

• Conduct a thorough clinical and radiographic examination.

• Identify which treatment may require prophylactic cover. If multiple extractions are required, only one or two teeth should be extracted at the first appointment to ensure that hemostasis can be achieved.

Note - It is important to remember the patient's social circumstances (Do they live alone? What are their preferences for treatment) as well as the clinical condition when making this decision.

• Observe all patients for a prolonged period after a dental extraction.

This may be for a few tendency whilst those with more severe conditions or a history of prolonged bleeding despite hemostatic cover may require supervision overnight in hospital. [13]

• Discuss treatment requiring the administration of coagulation factor or desmopressin (DDAVP) with the hemophilia unit and they will be arranging the administration and monitoring of treatment products.

• Discuss the use of local hemostatic agents. This could include the use of oxidized cellulose (Surgical®) or fibrin glue. Fibrin glue should not normally be used in patients who have never received human-derived blood products or those who are receiving treatment with recombinant factor VIII or IX because of the potential risks of human viral transmission.

• Consider whether to use antibiotics following a dental extraction. This is controversial, but there are a number of anecdotal reports suggesting that their use may prevent a late bleed, which is thought to be due to infection. However, if a patient has an infection before treatment, it should be treated with antibiotics.

• Always carry out treatment as a traumatically as possible.

Pre-operative period

• Ensure that the oral cavity is as healthy as possible before any surgical procedure. This can be achieved by arranging treatment with a hygienist to remove as much calculus and plaque as possible. The regular use of an antibacterial mouthwash, for example chlorhexidine, may also help.

• Consider using an antifibrinolytic agent. It may be helpful to start the treatment the day before the surgery. Tranexamic acid (usual adult dose 1 g three times a day) and epsilon aminocaproic acid (EACA) (50 mg/kg four times a day), are the most commonly used drugs. They should be continued for a total of 7 days.

Peri-operative period

• Have the patient rinse with chlorhexidine mouthwash for 2 minutes before the administration of the local anesthetic.

• Carry out the extraction out as a traumatically as possible.

• Suture the socket if the gingival margins do not oppose well. Brewer [14] reports a small series where sutures were not used routinely and there was no significant increase in post extraction hemorrhage. Resorbable and non-resorbable sutures may be used at the operator's discretion.

The only problem with non-resorbable sutures is the need for a post-operative visit and the possibility of bleeding when the suture is removed.

• Use local hemostatic measures if indicated. These include the use of oxidized cellulose or fibrin glue (see notes on the use of fibrin glue).

• Use a soft vacuum formed splint to protect the socket if needed.

Post-operative

period The patient must be given detailed post-operative instructions:

• No mouth rinsing for 24 hours

• No smoking for 24 hours

• Soft diet for 24 hours

• No strenuous activities for 24 hours

• Prescribed medication must be taken as instructed

• Analgesia should be prescribed for use if required

• Salt-water mouthwashes (1 teaspoon of salt in a glass of warm water) should be used four times a day starting the day after the extraction for 7 days [15]

• Antibacterial mouthwash may be used

• Emergency contact details must be given to the patient in case of problems.

Post-extraction hemorrhage

Careful pre-operative planning and the use of antifibrinolytic agents will prevent many post-operative problems [16]. However, post-extraction bleeding will occur on occasion. If post-extraction hemorrhage occurs: Contact the hemophilia unit and consider using additional factor concentrate.

Inspect the site of the bleed. If there is any evidence of a tear in the gingiva or other obvious bleeding point this should be treated using local measures as previously described. Instruct the patient to sit up and bite on a damp gauze swab for at least 10 minutes. Use a 10% solution of tranexamic acid or EACA to dampen the swab or as a mouthwash if the bleeding is difficult to stop. Monitor the patient's blood pressure as it may increase due to worry and pain. If the patient has pain, a suitable analgesic should be prescribed whilst if there is no pain a small dose of a benzo diazepine or similar will help to reduce the worry and reduce the blood pressure.

Fibrin glue

In some hemophilia centres, fibrin glue is used as a local hemostatic measure, along with an oral antifibrinolytic agent, to achieve hemostasis and reduce the need for clotting factor replacement therapy.

All fibrin glue contains human or animal components, which has made a number of physicians and patients being hesitant to use this treatment particularly for patients who are receiving recombinant factor concentrates or have never received blood products derived from humans. Fibrin glue mimics the final pathway of coagulation cascade at the point where fibrinogen is converted into fibrin in the presence of thrombin, factor XIII, fibronectin, and ionized calcium.

The cascade reaction provokes the cleavage of fibrinogen through thrombin, forming fibrin peptides A

and B from each molecule of fibrinogen resulting in the formation of the fibrin monomers.

Thrombin itself also activates factor XIII, which in the presence of calcium permits the stabilization of the clot. Fibronectin takes part in the process as well and its inclusion in the adhesive system appears to promote cellular migration and the activation of fibroblasts in the area where the fibrin glue was applied [17- 20].

Splints

Soft vacuum-formed splints can be used to provide local protection following a dental extraction or prolonged post-extraction bleed. The following technique is used to construct the splint pre-operatively:

• Take a dental impression before the extraction and cast a model in the laboratory.

• Remove the tooth being extracted from the model.

• Construct a soft vacuum-formed splint to cover the socket completely.

• Keep the splint in place for at least 48 hours before checking the socket. If there is any sign of bleeding it should be replaced and checked every 24 hours. If the splint is to be used to stop a post-extraction hemorrhage, the impression must be thoroughly cleaned and dis infected before it is transported to the laboratory.

Management of oral infections

Dental infections Many patients with infections of dental origin are managed without the use of antibiotics but instead by dental extraction or endodontic treatment, for example [21]. Antibiotics are often used to treat an acute bacterial infection. This should be considered for all patients with inherited bleeding disorders since surgical intervention should be avoided if possible.

The initial treatment usually starts based on the normal oral pathogens, Streptococcus viridans, anaerobic gram-positive cocci and anaerobic gram-negative rods. Anti-biotic regimes should cover all of these groups of organisms [22]. Penicillin is a first-line antibiotic used to treat dental infections. It can be taken orally in the form of penicillin V.

Metronidazole is extremely effective in treating anaerobes and is often used in combination with penicillin to give good coverage of both the aerobic and anaerobic bacteria present in the oral cavity. The doses of the drugs may vary depending on the availability in different countries but the treatment should continue for 5–7 days.

A number of different formulations of peni cillin are available with a broader spectrum of activity. These can be used either alone or in conjunction with metronidazole.

However, it is important to remember that if these drugs are ineffective treatment of the infection will become more complicated. Erythromycin and clindamycin have been prescribed to patients who are allergic to penicillin [21]. These drugs can be used in conjunction with metronidazole. Erythromycin may be effective in people with penicillin allergies, but it may not be suitable for more severe infections [22]

Clindamycin produces high alveolar concentrations [23], and bactericidal activity is reached with the usual recommended oral dose of 150 mg every 6 hours. In more severe cases it can be given intravenously. It has been reported that clindamycin can cause antibiotic-associated colitis and therefore is often reserved for the treatment of the more serious infections or when penicillin has failed.

Periodontal infection

Periodontal pockets host a variety of different bacteria, the majority of them being anaerobic. Regular oral hygiene prevents these bacteria from causing gingival inflammation.

In patients with severe gingival inflammation, in particular those who are immune compromised, the use of an antimicrobial agent may be indicated. Metronidazole is considered the drug of choice due to its action against anaerobic organisms.

It may be used in conjunction with either penicillin or erythromycin. However, antimicrobial therapy is no substitute for oral hygiene treatment.

Topical treatment

Most common forms of topical treatment involve the use of an antibacterial mouthwash. These have value as an adjunct to hygiene phase treatment. The most common treatments are

• Chlorhexidine gluconate: Chlorhexidine is available as a mouthwash, spray, and tooth gel. It is most commonly used as a twice a day mouthwash with the patient rinsing their mouth with the solution for 30–60 seconds. The tooth gel may be used in addition to the mouthwash. chlorhexidine has a tendency to stain teeth so the length of each course of treatment should be limited.

• Povidine-iodine: povidine-iodine is available as a mouthwash and can be used for the treatment of acute periodontal problems. In addition, it may be useful to irrigate the periodontal pockets. It must be used with caution during pregnancy.

Dental emergencies

Dental emergencies can occur at any time; however, it is important to remember that no treatment should be carried out without prior planning as this could result in additional problems. The most common dental problems are pain due to caries and bleeding from the periodontal tissues. Pain related to caries can usually be treated with either antibiotics or pulpectomy in order to allow time for the planning of the extraction. Bleeding from the periodontal tissues can usually be controlled with anti-biotics until an appointment with a hygienist can be arranged. The management of dental trauma is more complex as it usually involves both the gingiva and the teeth.

Local measures will usually control gingival bleeding and temporary splinting can be used for fractured or loose teeth. With dental trauma, it is important to remember that we are part of the comprehensive hemophilia care team treating these patients. Treatment planning for an emergency requires input from the whole team to reduce the risk of further problems.

An assortment of techniques available to control bleeding

Local Measures

Local haemostatic measures are obligatory following dental extraction in hemophilia patients. Local haemostatic agents are sutures, collagen vlies, oxy cellulose, gelatin, a fibrin glue and cyanoacrylate. A study conducted by Peisker A et al to prevent late bleeding; absorbable sutures used and for pain control, non-steroidal anti-inflammatory drugs and aspirin avoided [24]. Wagner et al. compared use of topical haemostatic agents in terms of their ability to mediate platelet aggregation, deposition and activation in a series of in vitro tests. An overall activity ranking of the materials sed was collagen > gelatin > oxidized regenerated cellulose [25]. List of different local hemostatic agents is given in table 2.

List of local haemostatic agents [26]

Brand name	Generic name or Description
Gelfoam	Absorbent gelatin sponge
Bleed – X	Microporous polysaccharide
Surgicel	Oxidized cellulose
Tisseel	Fibrin sealant
Thrombostat	Topical thrombin
Cyklokapron	Tranexamic acid
Amicar	Epsilon amino – caproic acid

Principal agents for systemic management of patients with bleeding disorders [27]

Table 1:

Agent	Description	Indications
Platelets	1 unit = 50 ml; may raise count by 6,000	Platelet count < 10,000 in non-bleeding individuals < 50,000 pre-surgical level < 50,000 in actively bleeding individuals Non-destructive thrombocytopenia
Fresh frozen plasma	1 unit = 150–250 ml 1 hour to thaw Contains factors II, VII, IX, X, XI, XII, XIII and heat-labile V and VII	Undiagnosed bleeding disorder with active bleeding Severe liver disease When transfusing > 10 units of blood Immune globulin deficiency
Cryoprecipitate	1 unit = 10–15 ml	Hemophilia A, Von-Willebrand's disease, when factor concentrates and DDAVP are unavailable and Fibrinogen deficiency
Factor VIII concentrate	1 unit raises factor VIII level 2% Heat-treated contains von Willebrand's factor Recombinant and monoclonal technologies are pure factor VIII	Hemophilia A with active bleeding or Pre-surgery; some cases of Von- Willebrand's disease
Factor IX concentrate	1 unit raises factor IX level 1–1.5% Contains factors II, VII, IX and X Monoclonal formulation contains only factor IX	Hemophilia B, with active bleeding or Pre-surgery Prothrombin complex concentrates used for hemophilia A with inhibitor
Desmopressin	Synthetic analogue of anti-diuretic hormone 0.3µg/kg IV or SC Intranasal application	Active bleeding or pre-surgery for some patients with von Willebrand's disease, uremic bleeding of liver disease, bleeding esophageal varices
Epsilon-aminocaproic acid	Antifibrinolytic: 25% oral solution Systemic: 75 mg/kg/6 h	Adjunct to support clot formation for any bleeding disorder
Tranexamic acid	Antifibrinolytic: 4.8% mouth rinse Systemic: 25mg/kg every 8 hours	Adjunct to support clot formation for any bleeding disorder

Systemic Measures

The World Federation of Hemophilia (WFH) advises the use of factor concentrates to cryoprecipitate or fresh frozen plasma for the replacement therapy in patients with Hemophilia. Doses and indication of different therapeutic agents used in the systemic management of the bleeding disorders are summarized in table 3. If coagulopathies are reported transfusion of appropriate factors to 50% to 100% of normal levels recommended. Recommended plasma factor levels and duration of factor replacement therapy vary according to the type of surgery as given in table 4. In hemophilia patients, additional postoperative factor maintenance requires after extensive surgeries. This can be done by infusion of desmopressin, cryoprecipitate or fresh frozen plasma depending on the patient's condition. Before planning any treatment with hemophilic patients always, consult with their haematologist

Plasma factor level and duration of the replacement therapy needed for surgical interventions in patients with Hemophilia [9]

Table 2:

	Hemophilia A		Hemophilia B	
Type of surgery	Desired factor level	Duration days	Desired factor level	Duration days
Major Surgery				
Pre – op	80 – 100 %		60 – 80%	
Post – op	60 – 80%	1 – 3	40 – 60 %	1 – 3
	40 – 60 %	4 – 6	30 – 50 %	4 – 6
	30 – 40 %	7 – 14	20 – 40 %	7 – 14
Minor surgery				
Pre – op	50 – 80 %		50 – 80 %	
Post – op	30 – 80 %	1 – 5	30 – 80 %	1 – 5

Conclusion The monograph has been written to help healthcare workers develop local guidelines for the management of patients with inherited bleeding disorders. They should be studied in conjunction with the two previously published WFH monographs Primary Dental Care of Patients with Hemophilia and Oral Care for People with Hemophilia or a Hereditary Bleeding Tendency. We should like to thank the members of the dental committee for their help and support in the development of these guidelines and hope that they help hemophilia healthcare workers throughout the world improve dental care for their patients

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