Literature review

Pre-operative management of periodontal procedures for bleeding disorders

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In general

Gingival health is critically important as one of the protective factors for patients with bleeding disorders, so regular dental visits and proper oral hygiene maintenance are advised.[1] Dental flossing should be avoided when platelet count is low.[1] Work-up on underlying medical conditions and review of current medications should be conducted. In the absence of a personal or family history of bleeding disorder, pre-operative hemostatic tests are little or of no value in predicting surgical bleeding, and should; therefore, be avoided.[2] However, suspicious clues should lead to screening using blood tests such as complete blood count (CBC), bleeding time/ platelet function analyzer (PFA), prothrombin time (PT) and activated partial thromboplastin time (APTT). There should be communication between the dentist and hematologist[1] regarding the purpose of the intervention and the management plan. Assessment should consider the type of procedure, deep scaling, number of dental extractions and type of anesthesia.

Intervention techniques

Anesthesia: Nerve block should be avoided due to risk of hematoma formation. For example, the inferior alveolar nerve block injection at the mouth or lingual floor in hemophilia without factor replacement carries an 80% chance of bleeding and may be fatal if the accumulated blood passes through the mediastinum and compromises the airway.[3,4] Whenever possible, local infiltration is preferred especially with vasoconstrictor use though vasoconstrictor may also cause delayed bleeding due to rebound vasodilatation.

Less-invasive surgical procedures: All less-invasive procedures can be performed similarly as healthy among individuals without increasing the risk of bleeding and replacement therapy before procedure is rarely needed. When debridement is required at the inflamed area, chlorhexidine mouthwash solution should initially be applied to reduce inflammation[6]. Less invasive procedures include those listed below.[2,5,6]

- Gingival probing
- Supragingival scaling
- Ultrasonic instrumentation
- Crown fitting
- Fixed partial dentures fitting
- Removable prostheses fitting
- Polishing
- Buccal infiltration and intrapapillary injection
- Endodontics procedures
- Orthodontics procedure (except for severe bleeding disorders damaging gingival tissue)

Invasive surgical procedures: Dental extraction should be performed the least traumatic as possible, and suturing the socket is not performed routinely. The risk of postextraction hemorrhage is also not increased when the wound was good and left unsutured[6]. Resorbable or nonresorbable sutures may be used depending on the dentist's decision. However, with nonresorbable sutures, bleeding becomes a concern when the sutures are removed.

Local control of bleeding: Several methods are available to control bleeding locally. Some options are local hemostatic agents (Gelfoam, Bleed-X®), Surgicel®, fibrin sealant, Fibrin glue, Lyostpt®, ankaferd Blood stopper[7] and electrocautery. The wetted-gauze biting for at least 30 min or suturing may also be beneficial. Periodontal packs and stents can stop active bleeding immediately and provide protection from further injury. Packing

should be left for 4 to 7 days[8]. The sitting position may also help reduce acute immediate hemorrhage. The same goes with using soft vacuum-formed splints for at least 48 hours.[6]

Timing

Ideally, all surgical interventions among patients with bleeding disorders should be performed as elective procedures with careful pre- peri- and postoperative planning. A hematologist should be consulted. In addition, available replacement therapy should be prepared before the procedure.

Elective procedures should be scheduled at the beginning of the week (Monday or Tuesday) when all supportive units are available rather than at the end of the week.[9]

Emergency surgical intervention in dentistry is rarely needed as pain can often be controlled. However, when necessary, all treatment plans should be discussed with a hematologist before implementing.

Medications

Antifibrinolytic agents such as oral tranexamic acid or epsilon-aminocaproic acid (EACA) serve important roles in both primary and secondary hemostatic disorders and should be prescribed in nearly all cases. For most mild hemostatic disorders and with less invasive procedures, local antifibrinolytic agents with a dose of 15 to 25 mg/kg/dose (approximately 1 g for adults), three to four times daily, may be sufficient. Oral tranexamic acid can reversibly block plasminogen and prevent degradation of the existing fibrin clot. The oral form is far more effective than the intravenous form because a large amount of plasminogen is present in the saliva. The drug should be administered from 2 hours before an intervention until 7 to 10 days postoperatively.[10] For the local preparation, tranexamic acid should be diluted to 5% concentration which can be prepared by dissolving one 500 mg tablet in 10 mL of water.[11] Whenever possible, especially among adolescents and adults, they should gently rinse inside the mouth for 2 to 3 mins before swallowing or spitting out.

Desmopressin acetate (DDAVP) is a hemostatic agent promoting platelet adhesion to the vessel wall and enhancing clot formation by stimulating the release of von Willebrand factor (vWF) from the Weibel palade body at the subendothelium.[12] The recommendation is to give the agent 1 hour (30-90 mins) before the operation intravenously at a dose of 0.3 μg/kg using 4 μg/mL concentration or subcutaneously 0.3 μg/kg using 15 μg/mL concentration or intranasally at dose 150 μg.[10] Desmopressin acetate is the treatment of choice for some mild forms of von Willebrand disease (vWD) type 1 and mild hemophilia A and also may play a role in some platelet disorders. At present, only the intravenous form is available in Thailand.

For pain control, aspirin and NSAIDs should be avoided because these can increase bleeding risks.[13] Acetaminophen or selective COX-2 inhibitor is preferred.[14]

Antibiotics can be used in some dental procedures. In general, some infections of dental origin are managed by dental extraction or endodontic treatment without antibiotics. However, for bleeding disorders, antibiotics are often used upfront and should be considered initially because surgical interventions are to be avoided when possible, in the first place. Drug selection should be based on normal oral pathogens: Streptococcus viridans, anaerobic gram-positive cocci and anaerobic gram-negative rods.[15] Penicillin, the first-line drug, and metronidazole are extremely effective against anaerobic organisms when given for 5 to 7 days.

Hospitalization

Regarding platelet disorders, when the platelet count is below the target level as noted in Tables 1 and 2 below, platelet transfusion may be required and is usually transfused 30 mins before surgery. Furthermore, other bleeding prevention preparations as above should be planned and hospitalization may be needed.

Table 1 American Academy of Pediatric Dentistry recommendations for minimum platelet values for performing invasive dental procedures among patients with thrombocytopenia.[16]

Platelet count (/μL)	Dental treatment
> 75,000	No additional support is required.
40,000-75,000	Platelet transfusion may be considered within 24 hours pre- and postoperatively.
< 40,000	Invasive dental treatment is to be avoided. In case of dental emergency, the patient's physician is to be contacted before dental treatment to discuss supportive measures, such as platelet transfusion, control of bleeding and need for hospitalization.

Table 2 Recommendations for acceptable platelet counts for dental procedures.

Procedure	Platelet count (/μL)
Simple dental elective procedures	≥ 20,000
Tooth extraction, simple	≥ 30,000
Tooth extraction, complex	≥ 50,000
Local anesthesia	≥ 30,000
Minor surgery	≥ 50,000
Major surgery	≥ 80,000

Patients with mild hemophilia and vWD may be treated at a primary care setting after consulting the hematologists. For moderate to severe hemophilia, in addition to hematologists' consultation, replacement therapy should be planned, especially in high risk or surgical procedures. Patients should be admitted after the procedure to be observed for any bleeding problem. Preparation and post-operative observation should be readied in the hospital due to the severity and risk of delayed bleeding.[5]

Safety laboratory monitoring

Concerning platelet disorders, the procedures' safety depends on the required platelet counts which are shown in Table 2.[17] As for patients with immune thrombocytopenia, despite a poor correlation in platelet count and clinical presentation, the platelet count remains important. For platelet function disorders, not requiring laboratory postoperative monitoring, clinical monitoring is mandatory.

Regarding secondary homeostatic disorders, the safety level that has good correlation with the bleeding phenotype, is only seen in deficiency of factors VIII, IX, X, XIII, vWD and fibrinogen[18]. The others will not necessarily correlate with the level of factor deficiency. For hemophilia, factor level monitoring is important and should be raised from 50 to 75% before general periodontal surgery and 75 to 100% before maxillofacial surgery.[19]

Post-extraction hemorrhage

Performing tooth extraction the least traumatic as possible is mandatory. When any evidence is found of a gingival tear, local bleeding control should be employed. Administering factor concentrates/blood components may benefit in specific circumstances.

Special consideration in immune thrombocytopenia (ITP)

Oral corticosteroid may increase the platelet to target level if prescribed 7 to 10 days before intervention without the need of platelet transfusion and is the first line drug before nonurgent procedures in most hospitals. For individuals presenting a history of apparent response with oral corticosteroid for other methods, a repeat of that dose should be considered.

Special consideration in hemophilia

Mild form of hemophilia A

Desmopressin acetate can raise factor VIII by three to five fold at 30 to 90 minutes after administering and should be the hemostatic agent of choice. However, a minority of patients may respond poorly. Therefore, a trial to demonstrate good response of DDAVP should be conducted before the operation. Desmopressin's half-life to release factor VIII is 8 to 12 hours, the same as normal circulating proteins. Once daily administration is usually sufficient, but sometimes a repeat dose after 12 hours may be needed. Tachyphylaxis may develop after just three to five doses of DDAVP and should be of concern when bleeding occurs.

Mild form of hemophilia B

In contrast to factor VIII, the factor IX level does not respond to DDAVP and factor replacement therapy is needed.

Moderate to severe form of hemophilia A and B

Pre-operative inhibitor screening should be performed within one week of the invasive procedure. Factor replacement therapy is required. Giving 30 to 60 minutes or less[10] before intervention is recommended. Specific factor concentrates should be available intra-operatively and sufficiently throughout the postoperative period.

Target factor level monitoring is mandatory for hemophilia and should be kept from 50 to 75% before periodontal surgery and from 75 to 100% before maxillofacial surgery.[19] The trough factor level can be tapered following Table 3. The monitoring frequency is discussed below.

- Pre-operative factor level measurement after administration should not routinely be performed. However, in some circumstances such as a very low level of inhibitor or when pharmacokinetic data are unavailable, a blood sample is usually taken 10 to 15 minutes postinfusion to ensure that the target factor level is reached.
- Peri-operative factor level measurement is unnecessary.
- Post-operative factor level measurement is highly recommended and should be tested immediately after the intervention. Inadequate levels should prompt additional factor replacement before clinical bleeding occurs.

The response of hemophilia with inhibitor to factor concentrates is of much concern but is not discussed in this review.

Special consideration in von Willebrand disease

Type 1 and some type 2A, 2M, 2N vWD

Desmopressin is the treatment of choice with complete and partial response of over 90% of patients in type 1 vWD[21] when the baseline vWF level is > 10 IU/dL.[22] Some patients with vWD type 2A, 2M, and 2N may respond to DDAVP; therefore, a DDAVP challenge test should be performed to determine the response. The doses and timing are the same as in hemophilia. However, vWF is acute phase reactant; hence the hemostasis level may be sustained for several days due to inflammation without need for further DDAVP. The vWF level should be checked postoperatively and DDAVP doses should be adjusted to meet the requirement in Table 4. The interval is 12 to 24 hours for major surgery until healing has occurred.[23]

Table 3 Coagulation factor target trough levels and tapered steps (when initial loading target 80-100%)[20]

	Bolus dosing			
	Trough factor level (%)		Interval frequency (hour)*	
Day	Factor VIII	Factor IX	Factor VIII	Factor IX
1-3	80-100	80-100	8-12	12
4-6	60-80	60-80	8-12	12
> 7	40-60	40-60	12	24

*Regular half-life of factor VIII concentrate is 8-12 hour and factor IX concentrate is 18-24 hour

Table 4 Target vWF levels and duration according to several types of intervention[20]

Procedures	Recommendations
Major surgery	100% vWF pre-operatively and trough daily levels of 50% until wound healing (5-10 days)
Minor surgery	60% vWF level pre-operatively and trough daily levels of 30% until wound healing (2-4 days)
Dental extractions	60% vWF level pre-operatively (single dose)

Table 5 Hemostasis in rare coagulation disorders with therapeutic options[24]

Factor deficiency	Hemostatic trough level	Approximate half-life of factor transfused (hours)	Therapeutic options
I	1-2 g/L	96	Plasma-derived fibrinogen concentrate, cryoprecipitate*
II	20-30 IU/dL	72	PCC, FFP
V	15-20 IU/dL	40-80	FFP, platelet transfusion
VII	15-20 IU/dL	4-6	Recombinant factor VIIa, FFP, PCC
X	15-20 IU/dL	48	PCC
XI	15-20 IU/dL	48	Factor XI concentrate, FFP
XIII	70 IU/dL if using dose 35 IU/kg	150-160	Factor XIII concentrate, recombinant factor XIII*

PCC, prothrombin complex concentrate; FFP, fresh frozen plasma; *Available in some countries

Most type 2 and all type 3 vWD

Administering von Willebrand rich factor concentrate or cryoprecipitate 30 to 60 minutes or less before intervention is recommended. Postoperative levels should be checked and recommendations in Table 4 should be followed until wound healing has been achieved.

Special consideration in rare coagulation disorders.

As previously noted, good correlation of levels and bleeding phenotype are only observed in deficiency of factors VIII, IX, X, XIII, vWD and fibrinogen.[18]. The hemostatic trough levels in Table 5 should be followed.

Special consideration in platelet function disorders

For minor procedures, local or systemic tranexamic acid is often the only medication required. More invasive procedures may require DDAVP and some may need platelet transfusion. Benefit of platelet transfusion should be weighed against developing antibodies against human leukocyte antigens (HLA) or human platelet antigens (HPA)[25] which would make future transfusion unresponsive. Administration of HLA-matched platelets is advised whenever possible.

Conclusion

No absolute contraindication exists for dental care when good pre-operative management of periodontal procedures is planned. Each pre-, peri- and postoperative step is very important. Two-way communication between dentist and hematologist is necessary to achieve successful treatment plans.

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