DENTAL MANAGEMENT OF PATIENTS WITH INHIBITORS TO FACTOR VIII OR FACTOR IX

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# Table of Contents

Introduction ................................. 1
Prevention ................................. 1
Routine Dental Care ......................... 1

Dental Procedures .......................... 1
   Endodontics ............................ 1
   Local anesthesia ....................... 1
   Dental extractions ..................... 1

Complications ............................. 3
   Uncontrolled bleeding following a dental extraction .................. 3
   Infection ................................ 4

Conclusion .................................. 4
Acknowledgements ......................... 4
References .................................. 4
Dental Management of Patients with Inhibitors to Factor VIII or Factor IX

Andrew Brewer

Introduction

The dental management of patients with inherited bleeding disorders is described in the Guidelines for Dental Treatment of Patients with Inherited Bleeding Disorders [1]. The principles described therein are still appropriate for the management of patients with inhibitors to either factor VIII or factor IX. Such patients should always be managed in the setting of specialized units with appropriate clinical expertise and laboratory support. The very high cost of certain treatment products also needs to be kept in mind when planning dental work in such cases. The aim of this monograph is to suggest management strategies that reduce the need for dental intervention or allow treatment without the need for prophylactic coagulation factor cover. In cases where coagulation factor concentrates may be required, appropriate regimens will be suggested.

Prevention

Prevention is the primary aim of dental care. Prevention strategies are discussed in detail in the Guidelines for Dental Treatment of Patients with Inherited Bleeding Disorders, but the following measures are of particular importance:

1. **Tooth brushing**
   This is probably the most important element in the prevention of dental problems. Patients must be taught about the importance of regular cleaning and the proper technique. The use of plaque disclosing tablets in the clinic is of value, as they will show the areas that are not being cleaned properly.

2. **Diet**
   The patient and their parents should be advised to restrict the intake of sugary foods and drinks to mealtimes.

3. **Regular dental care**
   Regular dental check-ups will allow early diagnosis and prompt treatment of dental problems.

Routine Dental Care

It is very unlikely that a routine scale and polish, including the using of ultrasonic scalers, will cause significant bleeding. If the gingival condition is poor and there is a worry about bleeding, a 5-day course of metronidazole (200 mg 3 times a day), along with a chlorhexidine mouthwash used twice a day, will help. This will often reduce the inflammation to a level where a routine scale and polish can be carried out. The procedure may need to be carried out over several visits, as each treatment will further reduce inflammation and the possibility of bleeding.

Dental Procedures

Removable prosthodontics are unlikely to cause any problems in patients with inhibitors. Similarly, fixed and removable orthodontic appliances may be used along with regular prevention and hygiene therapy. Restorative dentistry, including the provision of crowns and bridges, can be carried out safely provided the local anesthetic guidelines are followed.

Endodontics

Endodontic treatment should not cause problems, although there is sometimes bleeding at the apical foramen where vital pulp is present. This may continue to bleed for some time and would cause pain if the canal were obturated with a final restoration at the first visit. The use of sodium hypochlorite for irrigation and calcium hydroxide paste as a canal medicament appears to reduce this problem. It is advisable that instrumentation should not proceed beyond the apex and that working length should be estimated up to the apical foramen.

Local anesthesia

Intravenous coagulation factor treatments are usually only required when an inferior dental nerve block or a lingual infiltration is required. Local anesthetic techniques do not require the prophylactic use of factor.
The following techniques, often used in combination, may be used to anesthetize any tooth for either restorative treatment or extraction.

**Buccal infiltration**
A standard agent such as lidocaine with adrenaline can be used for anesthetizing all the upper teeth and the lower premolars, canines, and incisors. The buccal bone surrounding the lower molar teeth is denser and does not allow the local anesthetic to infiltrate adequately. Articaine, an amide anesthetic, has the ability to penetrate the buccal bone using a standard infiltration technique. It is important that the patient be left for 5-10 minutes before carrying out any treatment in order to achieve adequate anesthesia.

**Intrapapillary injections**
This can be used for anesthetizing the palatal or lingual mucosa of any teeth, as an adjunct to a palatal or lingual infiltration for dental extraction.

**Intraligamentary injections**
These injections should not cause any problems, although they are not commonly used. There is a slight risk of bleeding into the periodontal ligament. It is an ideal method for anesthetizing a tooth prior to extraction. It can also be used to anesthetize the lower molar teeth, in addition to buccal infiltration, in situations where articaine is not readily available.

**Dental extractions**
As discussed in Guidelines for Dental Treatment of Patients with Inherited Bleeding Disorders, careful treatment planning is essential. If several extractions are needed, it would be advisable to perform them one at a time. The following technique is suggested:

- The patient should be observed for 24 hours following the extraction.
- A dental impression should be taken prior to the extraction and cast in the laboratory. The tooth being extracted is removed from the model and a soft vacuum-formed splint is constructed to cover the socket completely.
- The hemophilia unit should arrange for appropriate cover to be given. Desmopressin (DDAVP) may be of use in some patients with low-affinity antibodies and residual factor VIII to increase the circulating level of factor. This may not be sufficient for hemostasis alone but, if used in conjunction with the local measures (and oral tranexamic acid), it may be beneficial. It is advisable to test the individual patient response to DDAVP before the procedure is started.

- The tooth should be extracted as atraumatically as possible and the socket filled with fibrin glue [2]. If fibrin glue is not available, the socket may be packed with a resorbable gelatine sponge (Gelfoam®) rolled in thrombin powder (Thrombostat®) [3]. It may be possible to substitute oxidized cellulose (Surgicel®) for the gelatine sponge, as they work in a similar manner.

- The splint should then be fitted and left in situ for at least 48 hours.

- The patient should be instructed not to wash the mouth vigorously while wearing the splint, although he may eat and drink normally.

- Tranexamic acid tablets (1 g, or 15 mg/kg, every 8 hours) should ideally be started the day before treatment for a total of 7 days. If this is not possible, it may be taken immediately before the extraction. Tranexamic acid should not be given in combination with activated prothrombin complex concentrate (see “Recurrent bleeds”, next page).

- After 48 hours, the splint should be removed and the socket checked. If a good clot has formed, the splint may be removed and standard mouth care protocol should be followed. The splint may be cleaned and replaced if necessary.

- The use of antibiotics following a dental extraction is controversial. In this group of patients, it may be useful to prescribe them prophylactically to reduce the risk of a secondary infection.

If there are problems achieving hemostasis, the following strategies may be helpful:

- Topical thrombin may be used either as a mouthwash or by direct application to the socket. It is important that the splint be replaced immediately after treatment and left undisturbed. This treatment may be repeated if bleeding persists.
• Tranexamic acid 10% solution has been used as a mouthwash and shown to reduce bleeding. The splint should be removed and the patient asked to rinse the mouth for 1 minute. The splint should be replaced immediately. This may be repeated every 2-3 hours if there is a reduction in bleeding.

• The patient’s blood pressure may increase due to worry and pain and should be monitored. If the patient has pain, a suitable analgesic should be prescribed. If there is no pain, a small dose of a benzodiazepine or similar medication will help to minimize anxiety and reduce blood pressure.

• The patient should be instructed not to play with the splint or remove it, and should be monitored carefully.

Complications

Uncontrolled bleeding following a dental extraction

**Early bleeds – within 24 hours of extraction**
The splint should be removed and the area inspected to ensure that there are no mucosal tears. If there is mucosal damage, it should be sutured to prevent further problems. If the bleeding appears to be from the socket, it may be necessary to remove the blood clot and fibrin plug, irrigate the socket, and examine the area to ensure that there are no foreign bodies causing the problem. The socket should be packed as described above and the splint fitted. Oral antibiotics should be prescribed if any foreign body has been located, as there may be some remaining infection.

**Late bleeds**
These usually occur between 2 and 5 days after the extraction and are commonly thought to be due to infection, although there is no evidence available in the recent literature to support this theory. If the bleeding is from the socket, the clot should be removed and the socket irrigated and re-packed as above. The splint should be replaced and left in situ for at least 2 days. Oral antibiotics should be prescribed.

**Recurrent bleeds**
If all the above regimens have failed, the use of coagulation factors should be considered [4].

• The infusion of a high dose of factor VIII or factor IX may be used in a patient with inhibitor levels below 5 BU/mL [5]. However, this approach may not be suitable for patients with high-responding inhibitors, as the antibody level can rise very dramatically after the infusion.

• Recombinant factor VIIa (rVIIA, NovoSeven®) is commonly given as a series of bolus injections because the half-life is only 2-3 hours. Various regimes have been described in the literature. In all cases the study size was small, but it appears that the infusion of rVIIa at a dose of 90 µg/kg, immediately followed by further doses every 2-3 hours, if needed, is the most beneficial [3,6]. Once hemostasis is achieved, the splint should be left in situ for 48 hours and the patient monitored carefully. Sometimes, rVIIa is ineffective in treating bleeding following a dental extraction [7]. In these cases, a change to a different product may be warranted. Combining rVIIa with tranexamic acid helps to enhance clot stability.

• Activated prothrombin complex concentrate (e.g. FEIBA®) is a plasma-derived product licensed for the management of bleeding in patients with inhibitors to factors VIII or IX. It is typically given as twice-daily doses of 50-100 U/kg, with the maximum daily dose not exceeding 200 U/kg. It should not be given in combination with tranexamic acid, as this can provoke thromboembolism.

• A combination of lower doses of rVIIa and FEIBA®, administered simultaneously or sequentially, has been used successfully in some patients who were resistant to each of the treatments separately.

• Porcine factor VIII has been used in the past for the treatment of patients with a low level of inhibitor [8]. However, this product, which was derived from porcine plasma, is no longer available. It was withdrawn in 1996 because of concerns about the possible transmission of porcine viruses. A recombinant version is now under development and may become available in the next few years.
Infection

**Minimal facial swelling**
Dental problems that cause minimal swelling can often be treated first with high dose antibiotics, usually given intravenously. The patient should be monitored and if the swelling worsens, surgical intervention may be required. The cause of the infection, usually a decayed tooth, needs to be removed as soon as possible using the local measures previously described.

**Marked facial swelling**
Dental sepsis, which causes significant facial swelling, can become life-threatening. The patient should be treated with intravenous antibiotics and, if there is any risk of airway compromise, urgent surgical drainage should be performed. If the airway is not at risk, the patient should be closely monitored and, if the swelling worsens, surgical drainage should be performed. If the swelling reduces with antibiotics, the patient should be treated as for minor swelling.

Patients requiring surgical drainage will require factor concentrates. The regimens already available for the management of surgery in this group of patients should be followed.

Conclusion

This monograph was written to help healthcare professionals establish local guidelines for the management of patients who have developed inhibitors to factor VIII and IX and should be used in conjunction with the WFH’s Guidelines for Dental Treatment of Patients with Inherited Bleeding Disorders. The WFH’s Oral Care for People with Hemophilia or a Hereditary Bleeding Tendency [9] will also be useful.

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References:


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