

Complex dental extractions in a patient with severe haemophilia A and inhibitors treated with activated prothrombin complex concentrate

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Introduction

Inhibitors that neutralise the function of clotting factor VIII occur in up to 30% of patients with severe haemophilia A¹. The development of these allo-antibodies is one of the most serious complications of haemophilia and bleeding episodes become refractory to standard treatment. Among patients whose inhibitor titre is greater than 5 Bethesda units (BU), factor VIII (FVIII) replacement, even at very high doses, is generally ineffective at stopping the bleeding. Consequently, alternative therapeutic approaches are necessary: these consist primarily of using inhibitor bypassing agents.

Two bypassing products are currently available on the market: factor eight inhibitor bypassing activity (FEIBA; Baxter Healthcare Corporation, Vienna, Austria), which is an activated prothrombin complex concentrate (aPCC), and recombinant activated factor VII (rFVIIa; Novoseven Novo Nordisk A/S Bagsvaerd, Denmark). The two bypassing agents achieve haemostasis through different mechanisms, bypassing the FVIII-dependent step in the coagulation cascade and promoting haemostasis by enhancing the generation of thrombin. Both products are used for controlling bleeding during surgery in haemophilic patients with inhibitors, though their efficacy may differ. As each bleeding episode is unique to each patient, each surgical operation and site of bleeding, clear guidelines on the treatment of patients are lacking and indications come from suggestions of experts in the field².

With reference to dental surgery in haemophilic patients with high inhibitor titre treated with FEIBA, few case reports have been published in the literature^{3,4}.

We proposed a treatment protocol consisting in anaesthesia without vasoconstriction, sutures associated with local haemostatic measures, such as

oxidised cellulose sponges and tranexamic acid, and administration of factor replacement, which proved extremely effective in non-haemophilic patients undergoing tooth extractions⁵. The same protocol, modified by the use of a bypassing agent instead of FVIII replacement therapy, was applied in the patient described below.

Case report

We documented the case of a 45-year old patient suffering from severe haemophilia A (FVIII <1%), whose diagnosis was made at the age of 3, following the appearance of haemarthrosis of the right knee. At the age of 5, while the patient was being treated with plasma and cryoprecipitate, a high-level inhibitor (80 BU) was found. Since the age of 6 the patient had also undergone several orthopaedic surgical operations: bilateral synovectomy of the knees and elbows, and right hip replacement, the last operation with incapacitating results. As a consequence of transfusions, the patient tested positive for hepatitis C virus (HCV) infection at the age of 25.

In October 2009, the patient was seen by his dentist, who reported the presence of periodontal disease along with a number of destructive caries. Total dental extraction surgery was suggested. The patient had already been examined by different dentists in the past, but had not given consent to dental extraction surgery.

Coagulation tests carried out preoperatively showed an activated partial thromboplastin times (aPTT) of 94.3 seconds (normal 30 to 40 seconds), FVIII: C of 0.9 IU/dL, and antibodies to FVIII at a level of 16 BU/mL. The patient's blood count, transaminase level and kidney function were normal. He was positive for HCV-RNA.

Prophylactic therapy with FEIBA was started so as to prevent bleeding. The choice to use this bypassing

agent rather than another was based on the fact that we have more experience with FEIBA, gained by performing dental extractions in haemophilic patients with inhibitor.

An hour before the surgical operation, the patient was given FEIBA at a dose of 85 IU/kg i.v. After administration of a local anaesthetic, mepivacaine 3% without a vasoconstrictor, the following teeth or radicular remains were extracted: 18, 14, 13, 11, 21, 23, 24, 25, 28, 45, 38 (Figure 1). Local haemostatic measures were used: the sockets were stitched with non-absorbable sutures and oxidised cellulose sponges and topical tranexamic acid (a gauze saturated with tranexamic acid) were applied to the tooth sockets.

On the first day, FEIBA was administered 8 and 16 hours after the surgical procedure at a dose of 50 IU/kg. Over the following 5 days, the patient was treated with 65 IU/kg of FEIBA every 12 hours. The post-operative course was regular and without haemorrhage, thrombotic or further complications; the sutures were removed after 7 days.

At home, because of the large number of bleeding episodes, especially muscle-related, and low quality of life, preventive treatment using FEIBA at a dose of 30 IU/kg three times a week was started.

Discussion

This is the first described case of bi-maxillary multiple dental extractions, during a single sitting, in a patient suffering from haemophilia A with a high-level inhibitor.

In the last decade both the availability and safety of bypassing products have made it possible to perform surgical operations in haemophilia patients with a high-level inhibitor⁶⁻¹⁰. With the exception of orthopaedic surgery, very few cases of major or minor surgery have been described in the literature. There are two case reports of dental surgery in haemophiliacs with inhibitors^{3,4} treated with FEIBA, alongside a few works⁶⁻⁸ providing incomplete data on the type of dental extraction, dosage and outcome outlined in some tables of minor surgery operations.

In the case reported by Heiland³, the patient had two teeth removed (upper right second molar and upper left second premolar); FVIII prophylaxis was performed prior to dental extraction and FEIBA was used to treat a serious bleeding complication on the



Figure 1 - Panoramic X-ray showing teeth and radicular remains needing extraction.

third day postoperatively. The case presented by Sacripanti at the ISTH Meeting⁴ reported on simple multiple dental extractions of six contiguous teeth from the same side of the mandible and distant from probable sites of bleeding. In contrast, our patient successfully underwent dental extraction of teeth, even multi-rooted ones, in all four quadrants of the oral cavity including some which were distant from each other and some in the posterior sectors of the oral cavity and, therefore, notably subject to a major risk of bleeding.

Mucosal bleeding is one of the most difficult haemorrhages to manage with bypassing agents, and is very often aggravated by the need to administer a bypassing agent several times over a short period.

The dose of FEIBA suggested by our protocol associated with sutures with local haemostatic measures, such as oxidised cellulose sponges and tranexamic acid, proved highly effective in preventing bleeding following complex multiple dental extractions. The drug was particularly practical and safe in view of the absence of haemorrhage and thrombotic complications during and after treatment. Finally, the treatment costs, at the suggested dosage, were satisfactory.

Keywords: haemophilia, inhibitor FVIII, aPCC (FEIBA), dental extraction.

The Authors declare no conflicts of interest.

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Arrived: 30 June 2011 - Revision accepted: 22 September 2011

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