Protocol for Oral Implant Rehabilitation in a Hemophilic HIV-Positive Patient With Type C Hepatitis

Lizett Castellanos-Cosano, DDS,* Ramiro-José Núñez-Vázquez, MD, PhD,† Juan-José Segura-Egea, MD, DDS, PhD,‡ Daniel Torres-Lagares, DDS, PhD,‡ José-Ramón Corcuera-Flores, DDS, PhD,* and Guillermo Machuca-Portillo, MD, DDS, PhD§

Hemophilia is an inherited X-linked bleeding disorder caused by deficiencies of clotting factors VIII (hemophilia A) or IX (hemophilia B). Mutations in the factor VIII or IX genes manifest as hemophilia in males and as the carrier state in females. In carrier females, levels of factors VIII and IX vary widely and may sometimes be low enough to result in clinical bleeding problems. Factors VIII and IX are both essential for the formation of a fibrin clot. The pivotal role played by these 2 factors is underlined by the significant hemorrhagic diathesis caused by deficiency of either protein. 

Hemophilia A and B are clinically indistinguishable; they are characterized by easy bruising, spontaneous muscle and joint hemorrhage, and excessive bleeding after trauma and surgical procedures. Diagnosis must be confirmed by specific laboratory assay. The severity of bleeding is related to the measured residual factor concentration and is classified as mild, moderate, or severe. Severe hemophilia is normally defined as a plasma level of coagulation factor activity less than 1% of that in healthy individuals. Moderate disease is between 1% and 5%, and mild disease is more than 5% to 40% of normal activity.

Since the 1960s, hemophilia patients have received intravenous factor VIII and IX replacement therapy. In the years that followed, it became apparent that viruses like HIV and hepatitis C virus (HCV) were transmitted due to transfusion of infected plasma products. The 2011 global survey of the World Federation of Hemophilia showed that 2.4% of hemophiliacs were infected by HIV, and 8.2% were infected by HCV. HCV infection in a hemophiliac could aggravate the bleeding tendency due to thrombocytopenia and the effects of drugs such as protease inhibitors. Untreated HCV infection may progress to liver fibrosis, cirrhosis, or hepatocellular carcinoma. Liver disease caused by HCV is now recognized as an important cause of morbidity in hemophilia patients.

To the best of our knowledge, implant surgery has not been described previously in these patients. This article reports implant-supported prosthesis
treatment in a hemophiliac with HIV and hepatitis C infection, and the development of a protocol agreed with the Hemophilia Unit of Virgen del Rocio Hospital, Seville, for managing these cases.

**Case Report**

The patient, a 46-year-old man with severe hemophilia A (factor VIII = 0.7 U/dL), stage A2 HIV infection (HIV RNA 400 [2.6]; CD4: 489 cells per microliter [30.93%]) and chronic hepatitis C genotype 1A, was on highly active antiretroviral therapy with efavirenz-emtricitabine-tenofovir. The patient received routine dental care at the Dentistry Unit of Virgen del Rocio University Hospital, Seville since the discovery of his hereditary coagulation disorder. His principle request was to replace his missing teeth with a fixed-prosthesis dental treatment.

Oral examination revealed 2 mandibular edentulous sections and poor oral hygiene (Figs. 1–3). A digital panoramic radiograph of the jaws was performed to evaluate bone support for implant placement in the edentulous zone and to rule out other underlying conditions (Fig. 4). This was followed by a computerized tomography. Treatment objectives were to improve oral hygiene and to achieve adequate oral masticatory function.

**Protocol Design**

After consultation with the patient’s hematologist, a protocol (Table 1) was followed to avoid complications caused by bleeding into the surgical sites that would have compromised the osseointegration of the implants.

**Surgical Treatment**

Surgical treatment was performed under local infiltrative anesthesia with vasoconstrictor (articaine plus 1:100,000 epinephrine) by periapical injection. A mucoperiosteal flap was made along the crestal bone of the edentulous space. The previous drug therapy regimen for treatment, performed before each of 2 surgical procedures, along with local hemostasis, effectively controlled the bleeding. The right edentulous mandibular section was fitted with 3 Straumann
Standard Plus Regular Neck implants (Ø 4.1 mm, length 10 mm) in the right first mandibular premolar, the right first mandibular molar, and the right second mandibular molar. Eight months later, 2 implants of the same characteristics were placed in the left second mandibular premolar (Ø 4.1 mm, length 8 mm) and left first mandibular molar (Ø 4.1 mm, length 10 mm). Postoperatively, administration of factor VIII clotting factor, antibiotic and analgesic treatment was prescribed for both surgical procedures, as described in the protocol (Table 1). The patient showed no postoperative complications and no additional need for factor VIII concentrate or other blood products, and there was no bleeding once the course of tranexamic acid was completed. The patient never required blood transfusions.

**Prosthetic Treatment**

After implant placement, the patient attended scheduled review appointments. After a 3-month period of osseointegration, the rehabilitative prosthesis was fitted. The patient was reviewed every 6 months for 2 years. Figures 5–8 show his clinical and radiological treatment status at the end of 2 years.

**DISCUSSION**

Establishing a medical protocol to control bleeding represented a significant challenge. Hemostasis had to be optimal because any bleeding would have compromised the osseointegration of the implants. The factor VIII dose needed for replacement therapy is calculated as body weight (66 kg) × factor VIII increase (80%–100%) (IU/dL) × 0.5. Guidelines tailored to the individual diagnosis depend on the severity of bleeding and the type of surgery planned. This patient was prescribed 45 U/kg. The planned replacement dose of 3000 units was calculated to raise his factor VIII level to approximately 80% to 100%, ensuring the best hemostasis possible. A presurgical test for factor VIII inhibitors (antibodies) was negative. This allowed factor VIII concentrates to be used, at regular doses. In the absence of inhibitors, factor VIII has a half-life of 8 to 12 hours. This meant that the second dose could

<table>
<thead>
<tr>
<th>Drug Therapy</th>
<th>Treatment Regimen</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tranexamic acid 1 g (OR)</td>
<td>1 tablet every 6 h, from the night before the procedure during 5–7 d</td>
</tr>
<tr>
<td>Factor VIII 3000 UI (IV)</td>
<td>15 min previous the procedure</td>
</tr>
<tr>
<td>Factor VIII 2000 UI (IV)</td>
<td>12 h after surgery</td>
</tr>
<tr>
<td>Factor VIII 3000 UI (IV)</td>
<td>24 h after surgery</td>
</tr>
<tr>
<td>Factor VIII 2000 UI (IV)</td>
<td>48 and 72 h after surgery</td>
</tr>
<tr>
<td>Paracetamol 500 mg</td>
<td>Alternate every 4 h</td>
</tr>
<tr>
<td>Metamizole 575 mg (OR)</td>
<td>1 tablet every 8 h during 7 d</td>
</tr>
<tr>
<td>Amoxicilin clavulanic acid 875/125 mg (OR)</td>
<td></td>
</tr>
</tbody>
</table>

Hospital admission is recommended with observation for the first 12 to 24 hours at the discretion of the hematologist. IU indicates international units; IV, intravenous; OR, oral.
be administered 12 hours later, while the patient was in hospital. An observation period is essential to control possible hemorrhagic complications in the event of damage to important arteries during dental implant surgery, potentially leading to compromise of the airway. Once the patient had successfully had this second dose at the hospital, he was able to continue the treatment at home. The objective was to maintain the factor VIII level at 80% constantly during the 24 hours after surgery.

Tranexamic acid was prescribed to keep weak blood clots intact for longer and to prevent bleeding in plasmin-rich areas such as the oral cavity. Tranexamic acid significantly reduces blood losses after oral surgery in patients with hemophilia and can be used topically or systemically. It was used systematically at a dose of 1 g (30 mg/kg) orally, 4 times daily, starting 24 hours preoperatively for surgical procedures for 5 to 7 days. Initial factor VIII replacement allowed clots to form, and tranexamic acid enabled them to remain hemostatically effective for a long time. This combination resulted in outstanding bleeding control in the surgical field.

It has been suggested that HIV-positive patients are more likely to develop both early and late postoperative complications, such as sepsis. In HIV-negative patients, even those with a CD4 count of 200/µL, sepsis has occurred. This risk is increased in patients with CD4 counts below 500/µL. Infection also seems to induce fibrinolysis, so antimicrobials such as oral amoxicillin/clavulanic acid, 875/125 mg 3 times daily, were given postoperatively for a full 7-day course to reduce the risk of secondary infections.

**CONCLUSIONS**

Only one article has described implant placement in a hemophilic patient with successful implant osseointegration after a hemostasis protocol (Gornistky et al, 2005). The results presented in our case show that even in a hemophilic with HIV and hepatitis C infection, with a correct hemostasis protocol and special management, complications after oral surgery can be controlled and masticatory function improved.

**DISCLOSURE**

The authors claim to have no financial interest, either directly or indirectly, in the products or information listed in the article.

**REFERENCES**