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CASO CLÍNICO

Perioperative Management of a Girl with Hemophilia B Undergoing Dorsolumbar Spine Posterior Instrumentation

Abordagem Perioperatória de uma Adolescente com Hemofilia B Submetida a Instrumentação Posterior da Coluna Dorsolombar

Liliana Martinho[1,*], Luísa da Câmara[1], Sara Batalha[2], Joana Rodrigues[1], Filipa Carioca[1], Joana Marques[1]

Afiliação
[1] Serviço de Anestesiologia, Centro Hospitalar Universitário Lisboa Central, Lisboa, Portugal.
[2] Serviço de Hematologia Pediátrica, Centro Hospitalar Universitário Lisboa Central, Lisboa, Portugal.

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ABSTRACT

Hemophilia B is a coagulation disorder characterized by a deficiency of clotting factor IX. Women are often heterozygous carriers of the disease, however if their clotting factor levels are less than 60%, they may have an increased bleeding tendency. This is even higher if levels are under 40%. We present a case of a 14-year-old female, with mild hemophilia B (hemophilia B carrier with factor IX level < 40%) who underwent a major surgery: a posterior spinal instrumentation from D6 to L1. The perioperative management was discussed, including the perioperative administration of blood products and coagulation adjuncts. This was coordinated by a multidisciplinary team (orthopedists, anesthesiologists, hematologists and nurses) to provide the best perioperative care and follow-up. Close collaboration and communication among/with the team members and the patient/family was vital throughout.

RESUMO

Hemofilia B é um distúrbio da coagulação caracterizado por uma deficiência do fator IX da coagulação. As mulheres são frequentemente portadoras heterozigóticas da doença, contudo se estas apresentarem níveis de fator inferiores a 60% podem ter uma maior tendência para fenómenos hemorrágicos. Esta tendência é particularmente acentuada se os níveis de fator IX forem inferiores a 40%. Apresentamos o caso de uma rapariga de 14 anos com hemofilia B ligeira (portadora de hemofilia B com nível de fator IX < 40%) que foi submetida a uma cirurgia hemorrágica (instrumentação posterior da coluna de D6 a L1). Discutimos a abordagem perioperatória, incluindo a administração perioperatória de hemoderivados. Para providenciar os melhores cuidados perioperatórios, uma equipa multidisciplinar coordenada (ortopedistas, anestesiologistas, hematologistas, enfermeiros e serviço de Imunohemoterapia) e uma boa comunicação entre os membros da equipa e o doente/família foram fundamentais.

Autor Correspondente/Corresponding Author*:
Liliana Martinho
Morada: Rua de Santa Marta 50, 1169-024 Lisboa, Portugal.
E-mail: lilianamartinho8@gmail.com

INTRODUCTION

Hemophilia B, also known as Christmas disease, is a coagulation disorder characterized by a deficiency of clotting factor IX (FIX). Typically, it results from an inherited mutation in the FIX gene, but can also be acquired.[1] According to the World Federation of Hemophilia (WFH), there are 195 263 patients worldwide with hemophilia, with up to 20% having type B hemophilia, most of them males.[2] Women are most often heterozygous carriers of the disease.[3] Bleeding tendency depends on disease severity.

Hemophilia B bleeding phenotype is typically categorized according to FIX levels: FIX levels between 5%-40% represent mild disease; 1%-5% levels a moderate form; and severe hemophilia if levels are under 1%.[4]

The expected mean clotting factor levels in carriers of hemophilia is 50% of the concentration found in the healthy population. However due to lyonization, a wide range in clotting factor levels is found in carriers. Levels less than 60% may have an increased bleeding tendency, which is higher for levels less than 40%.[3] Invasive procedures, such as major surgery, may be associated with significant blood loss, warranting a careful preoperative evaluation and specific care for these patients. Since this is a rare disease, current literature about the anesthetic management of these patients is scarce.

CASE REPORT

We present the case of a 14-year-old female, 58 kg, ASA II, who was proposed for a posterior spinal instrumentation from D6 to L1.

She had a personal history of idiopathic scoliosis and mild hemophilia B (hemophilia B carrier with factor IX level < 40%).[5] She had no history of bleeding diathesis episodes and denied prior surgeries, allergies, and any regular medication. Physical examination was unremarkable. Regarding laboratory analysis, she presented a hemoglobin level of 12.8 g/dL, a platelet count of $212x10^9$ and normal coagulation tests (PTT, PT and INR) despite mild FIX deficiency (38%).

Pediatric hematology accessed the patient and recommended administration of recombinant FIX (BeneFIX® - nonacog alfa) and tranexamic acid, with close monitoring of FIX levels perioperatively. After obtaining informed consent from the legal guardian, blood was crossmatched and four units of red blood cells were prepared.

Recombinant FIX (bolus of 4000 IU ~70 U/kg – target FIX level of 95%) and tranexamic acid (1 g ~20 mg/kg) were administrated 30 minutes before surgery. In the operating room, in addition to standard ASA monitoring, neuromuscular blockade and anesthesia depth were monitored. Following induction of general anesthesia and tracheal intubation, a second peripheral intravenous catheter and an arterial line were placed. Anesthesia was maintained intravenously with propofol and remifentanil target-controlled infusions to facilitate somatosensory and motor evoked potential monitoring.

The patient was positioned prone for the procedure for 4.5 hours. Blood loss was estimated in 650 mL. No blood products were transfused intra-operatively. Postoperative analgesia was accomplished with a fentanyl patient-controlled analgesia device and intravenous acetaminophen and metamizole.

In the immediate postoperative period, she was surveilled in a level 1 Intensive Care Unit. After surgery, she had a FIX level of 88% and a hemoglobin level of 10.6 g/dL (2 g/dL decrease from the preoperative value). Following hematology's recommendation, recombinant FIX (with gradual dose reduction) and tranexamic acid (1 g every 8 hours) were administered during the first five days postoperatively. Blood analysis were performed daily to evaluate FIX levels, with daily adjustment of FIX dose by the hematologist.

On the first two postoperative days, quantitative FIX levels were 67.2% and 67.9% (pre-FIX administration) and 3000 UI (~53 UI/kg) were administered each day. 1500 UI (~26.5 UI/kg) were administered on postoperative days 3 and 4. On postoperative day 5, FIX dose was reduced to 1000 UI (17.5 UI/kg), with a FIX level of 86% 2 hours after administration.

The postoperative course was uneventful. She was transferred to the ward on postoperative day 2 and discharged home after a week. In the hematologic follow-up, one month after surgery, she had a FIX level of 40% and a negative inhibitor screening (< 0.5 U Bethesda).

DISCUSSION

Hemophilia B is a rare hematologic disorder that presents several challenges in the perioperative setting. Despite carriers not having the disease itself, they presented increased bleeding tendency and therefore should not be devalued. Carriers with factor levels of 5% to 40% have bleeding tendencies similar to males with mild hemophilia. Those with factor levels lower than 4% have bleeding tendencies similar to males with moderate to severe hemophilia. Carriers of hemophilia with low factor levels should be evaluated, treated and managed as males with hemophilia.[4] Past medical history, namely prior history of bleeding, and family history of bleeding disorders may help us understand the evolution and severity of the disease.

According to WFH guidelines, specific preoperative care is indicated for hemophilia patients and carriers who require surgical interventions. These include consultation with hematologists, quantification of factor basal level, targeted FIX replacement, use of antifibrinolytics and warranting the availability of blood products.[4] These issues are crucial during major surgical procedures such as spine surgery, which may be associated with significant hemorrhage, even in patients with mild disease. As such, multidisciplinary assessment and planning are the cornerstones of preoperative care in hemophilia patients and carriers. Medications that may impact coagulation function, such as non-steroidal anti-inflammatory drugs (NSAIDs), synthetic colloids, antiplatelet and anticoagulants, should be avoided perioperatively.[4] Therefore, a multimodal analgesia avoiding NSAIDs is recommended by WFH.

Viscoelastic point-of care coagulation tests are useful in the perioperative management of hemophilia patients and carriers, especially if FIX inhibitors are present, or when approaching massive perioperative bleeding. These devices can provide multilateral information about coagulation properties that cannot be evaluated by the usual clotting times.[4,6]

Despite WFH recommendations on pharmacokinetic FIX monitoring (at least 8 blood samplings taken over a period of 72 hours) for hemophiliac patient or carriers receiving FIX concentrates prophylactically, this approach is not used routinely for dose tailoring, due to the burden of sampling requirements on clinicians and patients.[4,7] In our case, FIX monitoring was done with limited sampling in combination with population pharmacokinetic estimates.

Postoperative follow-up of these patients is important to exclude any complication, particularly the development of inhibitors. Inhibitors are IgG alloantibodies to exogenous clotting factor that neutralize the factor's activity. The

development of an FIX inhibitor is considered the most serious complication in patients with hemophilia B due, not only to loss of response to FIX replacement, but also to the associated risks of anaphylaxis and nephrotic syndrome.[4] Inhibitors are associated with a higher disease burden, including increased risk of musculoskeletal complications, pain, physical limitations, and treatment challenges, all of which may impact a patient's physical functioning and quality of life. Coordinated delivery of comprehensive care by a multidisciplinary team of healthcare professionals (orthopedists, anesthesiologists, hematologists, nurses) is recommended to provide the best perioperative care and follow-up.[4,8] Close collaboration and communication among the team members and the patient/family is vital throughout.

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