EDITORIAL

What´s New in Orthopedic Surgery for People with Hemophilia

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Hemophilia is a congenital bleeding disorder due to a clotting factor VIII (FVIII - hemophilia) or factor IX (FIX - hemophilia B) deficiency. The current gold standard in hemophilia treatment is called primary hematologic prophylaxis (intravenous infusion of the deficient coagulation factor) from early childhood. The goal is to achieve no hemarthroses. In people with hemophilia (PWH), the most affected joints are the knees, the ankles and the elbows. Unfortunately, primary prophylaxis is not 100% effective, and musculoskeletal complications still occur. Moreover, 25%–30% of the global population with hemophilia has no primary prophylaxis available due to its tremendous cost (1).

PWH must be treated by a well-coordinated multidisciplinary team, including hematologists, orthopedic surgeons, physical medicine and rehabilitation physicians, physiotherapists and specialized nurses. If this is achieved, orthopedic surgical procedures in PWH are usually safe, even for patients with inhibitors (acquired antibodies against the deficient coagulation factor), human immunodeficiency virus (HIV) and hepatitis C virus (HCV) (2). All orthopedic surgical procedures must be performed with adequate clotting factor coverage. This means that the hematologist in charge must perform the intravenous infusion of the deficient factor, plasma-derived or recombinant, at the right dose and during the right period of time, to achieve appropriate hemostasis during the entire perioperative period (2).

A novel recombinant FVIII produced in a human cell line has been proven to maintain perioperative hemostasis in patients with hemophilia A. Zozulya et al have used simoctocog alfa with excellent results in terms of hemostasis (3). In a series of 52 surgical procedures, neither adverse events nor inhibitors were observed. In hemophilia B, another new product (long-acting recombinant glycoPEGylated factor IX) has allowed the achievement of excellent hemostasis with less factor consumption compared with the standard FIX. In a series of 13 surgical procedures, neither adverse events nor inhibitors were observed (4). For patients with inhibitors there are two drugs (bypassing agents) available: aPCCs (activated prothrombin complex concentrates) and rFVIIa (recombinant activated FVII) (5-9).

Radiosynovectomy (RS) has been noted as a first-line therapy, with arthroscopic synovectomy the second-line therapy after failure of three consecutive RSs (10, 11). Other surgical procedures performed in PWH are arthroscopic synovectomy, hamstring release, arthroscopic debridement, alignment osteotomy, and total knee arthroplasty (TKA). Intra-articular tranexamic acid (TXA) has been used, with satisfactory results, to control bleeding and reduce the rate of blood transfusions after TKA (12). An intra-articular injection of 35 mL of a combination of TXA (25 mL, 2500 mg) and sodium chloride (10 mL, 18 mg) is used. Moreover, local infiltration analgesia (LIA) is also recommended during TKA in PWH (12, 13). A major problem in PWH is that TKA is associated with a high risk of bleeding and infection (7% on average).

A recent meta-anaysis of TKA in PWH found a rate of complications of 31.5% (14). A study by Ernstbrunner et al showed a rate of infection of 12% and a rate of revision of 30% (15). The survival rate was 59% for any complication as the end point and 82% for infection as the end point. In bilateral advanced hemophilic

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arthropathy of the knee in PWH, coincident bilateral TKA is feasible. In addition to cost savings, the biomechanical result (gait) will be better. However, we cannot underestimate the potential risks of bilateral TKA in the same surgical procedure (16). The manner in which the deficient factor should be infused during the postoperative period of a TKA is also a matter of debate. We can perform bolus infusions or continuous infusion by means of a pump. Park et al recently concluded that continuous infusion is more effective and tolerable than bolus infusion (17). Regarding the need of suction drainage in patients with hemophilic arthropathy undergoing TKA, Mortazavi et al have recently reported that there is no rationale for the use of drain after primary TKA (18).

For ankle problems, RS (first-line therapy) or arthroscopic synovectomy (second-line therapy) for synovitis can be performed. Later, in the initial phases of joint degeneration, arthroscopic ankle debridement is indicated (8, 19). When joint degeneration is advanced, the options available are ankle distraction (arthrodiastasis), ankle arthrodesis or total ankle replacement (8, 20-23). Regarding ankle arthrodesis in children and adolescents with hemophilia, de l'Escalopier et al obtained good long-term results, with a low rate of complications (22). In adult patients, ankle arthrodesis is a good option (21). The rate of nonunion is 10%, the rate of infection 2.5%. Regarding total ankle arthroplasty, Preis et al reported promising results in a series of 14 PWH, with a mean follow-up of 6 years (23).

Total hip arthroplasty (THA) is uncommon in PWH. In a recent report, 49 THAs (43 PWH) were analyzed. The mean follow-up was 11 years. The infection rate was 6% and the rate of aseptic loosening was 10% (24). Regarding total elbow replacement, the rate of complications in PWH was 62%. In this series, 13 arthroplasties were performed on 9 PWH. The mean follow-up was 8 years and the mean age of the patients was 55 years (25).

Hemophilic pseudotumors are the consequence of unsolved muscle hematomas in hemophilia. It is paramount to prevent them by means of continuous hematologic treatment, even surgical evacuation, until their total disappearance. Their status must be confirmed by imaging, such as ultrasonography, computed tomography scan or magnetic resonance imaging (2). Zhai et al recently reported a 13% rate of infection and a 9% rate of recurrence in a series of 23 hemophilic pseudotumors (26).

During surgery, local fibrin glue is not absolutely necessary because intravenous infusion of the deficient coagulation factor is usually sufficient to achieve adequate perioperative hemostasis. However, in cases of pseudotumors and patients with inhibitors, it is advisable to have local fibrin glue in the surgical room, just in case (27).

The need for venous thromboembolic pharmacological prophylaxis in PWH is a matter of debate. In a recent report, Ahmed et al did not recommended routine postoperative use of pharmacological thromboprophylaxis (28). Orthopedic procedures that are usually necessary in PWH include surgical synovectomy (open or arthroscopic), arthroscopic joint debridement, tibiotalar fusion (arthrodesis of the ankle), total joint arthroplasty (knees, hips, elbows, ankles), and removal of pseudotumors. Routine postoperative use of pharmacological thromboprophylaxis for venous thromboembolism is not recommended. Local fibrin glue must be considered in patients with inhibitors and removal of pseudotumors (in case of excessive bleeding despite adequate infusion of the deficient coagulation factor).

Orthopedic surgery should always be the last resort in hemophilic arthropathy. In cases of synovitis, it is recommended to use RS as the first therapeutic line. The alternative is arthroscopic synovectomy. In cases of painful and disabling severe joint degeneration of the knee or hip it will be necessary to think of a total knee or hip arthroplasty. The survival of elbow and ankle arthroplasties is not as long as in the hip and knee. In the ankle, the alternative is arthrodesis.

In developed countries, the use of primary prophylaxis will make orthopedic surgery less and less necessary. However, in developing countries, due to the lack of primary prophylaxis, the orthopedic problems of hemophilia will last and make surgical interventions necessary (29). Hopefully, primary prophylaxis can be used worldwide in the next five years, so orthopedic surgery will be less and less necessary. Surgical procedures in PWH are usually safe; however, this is not always the case in patients with inhibitors. In TKA, intraarticular TXA and local infiltration analgesia (LIA) are recommended. However, the average rate of periprosthetic infection following TKA is 7%.

In conclusion, modern orthopedic surgery can improve the musculoskeletal problems of people with hemophilia. The most commonly affected joints are the knees, the ankles and the elbows. The most common orthopedic procedures that PWH undergo are the following: RS, arthroscopic synovectomy, arthroscopic joint debridement, ankle arthrodesis, total joint arthroplasty and removal of pseudotumors. Every surgical procedure must be performed with adequate clotting factor coverage, following the indications of the hematologist in charge. For PWH, routine pharmacological thromboprophylaxis is not indicated. In patients with inhibitors (acquired antibodies against the deficient coagulation factor) and for the surgical removal of pseudotumors, local fibrin glue is advised. The mean infection rate with TKA in PWH is 7%. Intraarticular TXA is advised to control surgical bleeding. LIA is also recommended to control postoperative pain after TKA.

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