CHOLECYSTECTOMY IN A MAN WITH HEMOPHILIA A AND INHIBITOR ON EMICIZUMAB PROPHYLAXIS: A CASE REPORT

PC Giacometto [a,b], MT Bavaresco [c,d,e], RCM Molina [b], J Alvares-Teodoro [f], RM Camelo [g]

[a] *Department of Clinics, Hospital Regional Universitário de Maringá (HUM), Universidade Estadual de Maringá (UEM), Maringá, PR, Brazil*
[b] *Bleeding Disorders Outpatient Clinic, Centro de Hematologia e Hemoterapia do Paraná (HEMEPAR), Maringá, PR, Brazil*
[c] *Department of Surgery, Hospital Regional Universitário de Maringá (HUM), Universidade Estadual de Maringá (UEM), Maringá, PR, Brazil*
[d] *Department of Surgery, Hospital Santa Casa de Maringá, Maringá, PR, Brazil*
[e] *Faculty of Medicine, UniCesumar, Maringá, PR, Brazil*
[f] *Department of Social Pharmacy, Faculty of Pharmacy, Universidade Federal de Minas Gerais (UFMG), Belo Horizonte, MG, Brazil*
[g] *Departament of Clinics, Faculdade de Medicina, Universidade Federal de Minas Gerais (UFMG), Belo Horizonte, MG, Brazil*

There are few reports about the hemostatic effectiveness and safety of emicizumab on major surgeries, especially non-orthopedic ones. We described a man with severe hemophilia A and high-responding inhibitor under emicizumab prophylaxis who was submitted to an open cholecystectomy due to acute-on-chronic calculous cholecystitis. A 32-year-old man first visited the Emergency Department complaining severe diffuse abdominal colic unresponsive to oral analgesics, in the last 7h. He denied fever, nausea, or diarrhea. He had severe hemophilia A with high-response inhibitor, receiving prophylaxis with emicizumab (1.5 mg/kg weekly). He also had been submitted to several abdominal surgeries (appendicectomy, midgut volvulus, and abdominal trauma). Physical examination was unremarkable. Aspartate and alanine aminotransferases were mildly elevated (56 and 83 U/L, respectively). He was discharged home after ameliorating with dipyrone, tramadol, and bromopride. He came back 4 days later, with the same complaints. He had a positive Murphy's sign and a negative Blumberg's sign. Blood tests were unremarkable. The gallbladder had a normal wall thickness (0.6 cm) with several mobile calculi (from 0.9 to 1.8 cm) by abdominal ultrasound, without dilation of the biliary tract, alteration of the pancreas/pancreatic duct, or lymphadenomegaly. He declined hospitalization and returned 5 days later, after having discussed with his Hematologist about the surgical procedure. Emicizumab was maintained throughout the described period. Before the procedure, he received intravenous rFVIIa 93 μg/kg and tranexamic acid (TxA) 1 g. rFVIIa was maintained each 2h, during the first 24h. The procedure was performed under general anesthesia. Videolaparoscopic cholecystectomy was withheld, due to adhesions precluding peritoneal inflation. Upon a right subcostal incision, a hydropic gallbladder was removed (anatomopathological analysis confirmed acute-on-chronic calculous cholecystitis). A purified pigskin sterile absorbable gelatin sponge was placed on his hepatic bed, before closing the surgical wound. The surgeon reported an above-the-usual bleeding during the procedure (estimated blood loss of 500 mL against usually minimal blood loss). Ceftriaxone and metronidazole were prescribed throughout the hospitalization. rFVIIa 77 μg/kg was scattered on a daily base: every 2h until every 12h along 1 week (total 2,400 μg/kg). TxA 1 g every 8h was prescribed during the same period. He had mild hematic drainage (less than 30 mL on the post-operatory day and decreasing in the following days). This was judged as good hemostasis by the surgeon. The drain was removed in the 4th post-operative day. Hemoglobin decreased from 13.7 g/dL at the day of the procedure until 9.4 g/dL the day before discharge (lowest 8.9 g/dL). No blood transfusion was required throughout the hospitalization. He was discharged home 1 week after surgery. No bleeding event was reported during the outpatient follow-up within 3 weeks. No symptoms nor signs of thrombosis were reported. In conclusion, we would like to reinforce the importance for the surgeons (a) to know that people with hemophilia A, with or without inhibitors, are susceptible to the same risks of developing gastrointestinal diseases as individuals without hemophilia; (b) in such cases, an interdisciplinary approach is always the best option; and (c) there is a biopharmaceutical which may effective and safely reduce the bleeding risk in the periprocedural period.

https://doi.org/10.1016/j.htct.2021.10.375

DEFICIÊNCIA COMBINADA DE FATOR V DE LEIDEN + FATOR VIII: RELATO DE CASO

FM Aguiar, G Cattani, AB Florian, EW Silva, MFL Pezzi, MS Machado, AL Cauduro, TS Hahn, CT Burtet, GR Bosi

Universidade de Caxias do Sul (UCS), Caxias do Sul, RS, Brasil

Introdução: A deficiência combinada de fator V e de fator VIII é um distúrbio hemorrágico genético autossômico recessivo, que cursa com reduções simultâneas dos níveis plasmáticos de ambos fatores de coagulação. A prevalência estimada é de um caso por milhão, sendo extremamente raro. **Objetivo:** Relatar caso de uma paciente que apresentou deficiência combinada de fator V e fator VIII. Relato de caso: Paciente feminina, 21 anos, previamente hígida, com histórico de menarca aos 12 anos e colocação de dispositivo intrauterino com levonorgestrel aos 16 anos. Encaminhada ao hematologista para avaliação de menometrorragia com até 20 dias de duração por ciclo menstrual. Refere ainda quadro de equimoses frequentes e sangramento gengival por 36 horas depois de um procedimento dentário. Foram realizados exames para investigação que evidenciaram hemograma e provas de coagulação normais, mas com alteração nos fatores de coagulação V (62,7%) e VIII (60,9%). O diagnóstico final foi de deficiência combinada do fator V e do fator VIII, e a conduta instituída foi de orientações e transfusão de plasma fresco congelado em caso de sangramento, de trauma ou de necessidade de cirurgia. **Discussão:** A deficiência combinada de fator V e fator VIII

é um distúrbio autossômico recessivo extremamente raro, mais comum em países mediterrâneos e asiáticos, sendo a consanguinidade um dos principais fatores para a ocorrência da doença. Sua fisiopatogenia está relacionada com mutações nos genes LMAN1 e MCFD2 que fazem parte da cascata intracelular na formação destes fatores. O diagnóstico se firma com a confirmação da deficiência através da aferição dos fatores V e VIII, sendo geralmente 10 a 20% do valor normal. Os sintomas geralmente são leves e incluem frequentemente sangramento excessivo durante ou após trauma, cirurgia e trabalho de parto, além de epistaxe, sangramento gengival, hematomas e menorragia. O tratamento depende da gravidade do sangramento, podendo utilizar plasma fresco congelado e concentrado de FVIII ou desmopressina. **Conclusão:** Assim, mesmo se tratando de um distúrbio muito incomum, a deficiência combinada de fator V e fator VIII deve ser um dos diagnósticos diferenciais em pacientes com histórico de sangramento, principalmente em mulheres jovens com metrorragia. Ademais, é de suma importância o acompanhamento e a orientação destes casos, a fim de evitar grandes sangramentos e de agregar uma maior qualidade de vida aos pacientes.

https://doi.org/10.1016/j.htct.2021.10.376

DRAWBACKS OF PERSONALIZATION OF PROPHYLAXIS AMONG ADULT MEN WITH HEMOPHILIA A

PC Giacometto [a,b], L Hirle [b], J Alvares-Teodoro [c], LL Jardim [d], RM Camelo [d,e]

[a] *Department of Clinics, Hospital Regional Universitário de Maringá (HUM), Universidade Estadual de Maringá (UEM), Maringá, PR, Brazil*
[b] *Bleeding Disorders Outpatient Clinic, Centro de Hematologia e Hemoterapia do Paraná (HEMEPAR), Maringá, PR, Brazil*
[c] *Department of Social Pharmacy, Faculty of Pharmacy, Universidade Federal de Minas Gerais (UFMG), Belo Horizonte, MG, Brazil*
[d] *Department of Clinical Epidemiology, Leiden University Medical Centre, Leiden, The Netherlands*
[e] *Department of Clinics, Faculdade de Medicina, Universidade Federal de Minas Gerais (UFMG), Belo Horizonte, MG, Brazil*

Personalization of prophylaxis applying population pharmacokinetic (PK) tools has recently rendered fewer bleeding episodes for people with hemophilia A (PwHA). However, despite PK data (e.g., terminal half-life – t– and clearance), many other variables should be considered when proposing an individualized replacement therapy, such as bleeding phenotype, arthropathy, physical exercise, and adherence to treatment. All these should be considered, especially among adult PwHA who have lived for many years with exclusive episodic treatment. We evaluated factor VIII (FVIII) consumption among adult PwHA who had been treated with exclusive episodic therapy and had changed to prophylaxis, when personalization was provided. Men with severe (FVIII < 1%) or moderate (FVIII 1%-5%) HA and inhibitor negative who were treated at the Universidade Estadual de Maringá (Maringá/Brazil) signed the Consent Form to participate in the study. Anthropometric and hemophilia-related data were obtained using a standardized form. PK analysis was performed according to the WAPPS-Hemo tool, based on two blood samples (3 and 24 h after infusion and one-step coagulometric test). After PK analysis, PwHA were approached to adjust their regimen (time, dose, and frequency of infusion) according to bleeding phenotype, arthropathy, physical exercise, and adherence to treatment. Bleeding episodes, regimen, and FVIII disposal (from now called consumption) were assessed 12 months before and after treatment adjustment. The estimated FVIII consumption was calculated by multiplying the daily dose by the number of infusions in a month, based on the prescription. The percentage of the quotient between the actual FVIII consumption per the estimated FVIII consumption for prophylaxis was considered a proxy for adherence to treatment. Plasma-derived FVIII (Beriate®, CSL Behring, and Fahndi®, Grifols) were prescribed during the 2-year analysis. Five men with HA (2 receiving Beriate®, 1 moderate and 1 severe; and 3 receiving Fanhdi®, 2 moderate and 1 severe) were included. All PwHA received exclusive on-demand infusions for at least 30 years and tertiary prophylaxis was started in the last 10 years. They presented hemophiliac arthropathy, ranging from 1 to 6 affected joints. None practiced physical exercise. None had HIV and 3 had HCV. PK analysis was performed at ages ranging from 38 to 61 years and twere 10.3 and 16.5 h for those receiving Beriate®and 8.8 to 13.5 h for those receiving Fanhdi®. All PwHA were advised about the best time to infuse FVIII, but only 2 PwHA had an increment of their regimens. Pre-adjustment PK-estimated trough levels varied 0.0 to 1.2 IU/dL from baseline which we had access. During this period, the monthly actual FVIII consumption for prophylaxis ranged from 12.8% to 74.5% of the estimated FVIII consumption. During the year following the adjustment, this relation increased from 28.0% to 93.8%. However, the total annual bleedings did not change between these moments. We believe personalization of therapy is important to guarantee joint health and quality of life of PwHA. However, based on the analyses of the individual cases we reported, adherence to treatment may be an important impacting factor to consider among adult PwHA.

https://doi.org/10.1016/j.htct.2021.10.377

ELECTROCARDIOGRAPHIC ALTERATIONS AMONG ASYMPTOMATIC ADULTS WITH HAEMOPHILIA

CGP Roncal [a], BP Duarte [a], MCB Moura [a], NCM Costa [a], IM Costa [a], AM Vanderlei [a], TMR Guimaraes [a,b], RM Camelo [c]

[a] *Fundação de Hematologia e Hemoterapia de Pernambuco (Hemope), Recife, PE, Brazil*
[b] *Faculdade de Enfermagem Nossa Senhora das Gracas, Universidade de Pernambuco (UPE), Recife, PE, Brazil*
[c] *Faculdade de Medicina, Universidade Federal de Minas Gerais (UFMG), Belo Horizonte, MG, Brazil*