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Short-term efficacy of recombinant porcine factor VIII in patients with acquired factor VIII inhibitors

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Abstract

Introduction: Acquired hemophilia A (AHA) is a rare, often severe, bleeding disorder caused by autoantibodies against factor VIII (FVIII) 1 . Current first-line treatment includes bypass agents (BPA), which are challenging to dose due to inability to measure activity levels and response to therapy. Furthermore, high dose BPA can be associated with thrombotic events especially in the elderly 2 . Recombinant porcine sequence FVIII (rpFVIII) was developed as an alternative to BPA 3 . Available data as to its efficacy, safety, and durability of its use has been limited due to the rarity of these patients. One series of seven patients reported good hemostatic efficacy 4 . De novo development of anti-porcine FVIII (anti-pFVIII) has been observed in a small subset of patients in another study 5 . We describe our institutional experience with rpFVIII in 5 treated patients. Methods: In a retrospective cohort, we reviewed the medical charts of 5 patients treated with rpVIII at our institution between 2016 and 2018. Results: We identified 5 patients treated with rpFVIII at our facility, 4 of which had AHA and 1 had congenital hemophilia with acquired high-titer inhibitor. All 5 patients received rpFVIII for indications of acute bleeding, dosed at 100 U/kg daily, or initially every 12 hours tapered to daily. The treatment was well-tolerated in all patients, with no adverse events upon infusion. Initially, all 5 patients exhibited an effective response evidenced by increase in FVIII levels from baseline <1% to 81-170% (peak value obtained within 1 h of infusion), with normalization of the activated partial thromboplastin time (aPTT) and resolution of bleeding symptoms. However, in 4 out of 5 patients (including the congenital hemophilia patient), continued treatment was associated with decreased efficacy of the drug as demonstrated by a lowered peak FVIII value upon infusion and reversion to a prolonged aPTT. The total number of doses given per patient within one treatment course ranged from 3 to 27 doses. Decreased efficacy was noted after an average of 14 doses. Anti-pFVIII levels were measured in 3 patients and found to be elevated (11-20 Bethesda units), consistent with the development of an inhibitor to rpFVIII. Baseline anti-pFVIII were not measured prior to treatment, and it was assumed that none of the patients had pre-treatment porcine inhibitors based on the robust treatment effect observed. Our results are summarized in Table 1. Conclusion: At our institution, rpFVIII was safe and initially effective in all patients. However, our clinical experience demonstrates rapid and early development of an inhibitor to rpFVIII, which decreases its efficacy and limits its use. Neverthless, its initial ability to control bleeding remains extremely valuable when embarking on the care of this disorder. A larger study is necessary to appropriately assess the incidence of anti-pFVIII antibody development in this patient population.