rFVII for Pediatric Acute Intracranial Hemorrhage

To the Editor:

A recent interesting phase IIB randomized, double-blind, placebo-controlled, dose-ranging “proof-of-concept” trial on recombinant activated factor VII (rFVIIa) for acute intracranial hemorrhage in adult patients has been reported.1 A lacking of similar experience in the pediatric population is noted. rFVIIa has been anecdotally reported as effective for profound bleeding episodes in children. In the pediatric literature, case reports have been made with apparent clinical improvement seen after the use of rFVIIa for acute life-threatening bleeding; however, there are limited data regarding its use in infants younger than 4 months of age, regardless of whether it is a congenital or acquired condition.2–3

We report on a case of acute intracranial hemorrhage in a newborn with congenital factor VII deficiency treated with rFVIIa and given a prophylactic program during a follow-up of 36 months. A full-term newborn boy, the first child of nonrelated black parents, was born to his mother aged 29, and the father was 28 years old. The family history was unremarkable. The pregnancy was uneventful. Her birth weight was 2800 g, height was 47.0 cm, and cranial perimeter was 33 cm. Appgar scores were 5 and 6 at 1 and 5 minutes, respectively. Multifocal seizures occurred on the second day postpartum. The fontanelle was tense, and the cerebrospinal was bloody. Cranial CT did not reveal factor VII deficiency. rFVIIa was given 150 g/kg body weight are given every 4 to 6 hours, whereas higher doses of 150 to 200 μg/kg body weight are used in neonates.

We do not know exactly the doses for both treatment and prophylaxis. Nor do we know if doses for both congenital and acquired condition are the same. Effect was reached with all 3 doses that were tested (40, 80, and 160 μg/kg).1 A phase III trial comparing 20 and 80 μg/kg rFVIIa with placebo is now in progress. However, physiological differences in the hemostatic system between children and adults have been reported.6 The most commonly used dose is 90 μg/kg body weight rFVIIa as bolus, and, if necessary, followed by additional injections at intervals of 2 to 3 hours. In factor VII deficiency, lower dosages of 15 to 30 μg/kg body weight of rFVIIa are given every 4 to 6 hours, whereas higher doses of 150 to 200 μg/kg body weight are used in neonates.

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Third, the use of rFVIIa in hemorrhagic shock in neonates and preterm infants are increasing. For instance, neonates with massive postsurgical hemorrhage after ileostomy, with severe pulmonary hemorrhage in the course of mechanical ventilation for meconium aspiration syndrome, with congenital heart disease. Also, during postoperative resuscitation after cardiac surgery for congenital heart disease in which multiple administrations of rFVIIa (120 μg/kg per dose) and antifibrinolytic therapy, aminocaproic acid (100 mg/kg per dose), were successfully used.8

Prevention of intraventricular hemorrhage and its potential long-term sequelae remain one of the major challenges in the early management of preterm infants. rVIIa, a novel hemostatic agent with an ever-expanding list of potential applications, warrants consideration for use in this setting. The hypothesis that early prophylactic administration of rVIIa to extremely preterm infants (<28 weeks) would reduce the incidence of severe intraventricular hemorrhage needs to be tested.9

Finally, intracerebral hemorrhage causes severe disability and a staggering economic burden. Because rFVIIa is a very expensive therapy, possible strategies for optimizing its use in these settings in the pediatric population are particularly needed.10

Disclosures

None.

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