Commentary on Pilot Trial of a Novel Two-Step Therapy Protocol Using Nebulized Tranexamic Acid and Recombinant Factor VIIa in Children with Intractable Diffuse Alveolar Haemorrhage

Hind Bafaqih* and Farah Thabet

Pediatric Intensive Care, Prince Sultan Military Medical City, Riyadh, KSA, Saudi Arabia

The cases presented here is an initiative trial in the management of diffuse alveolar hemorrhage (DAH) in a noninvasive method [1]. In the evaluation and treatment of a pediatric patient with pulmonary hemorrhage, a three step approach may be the straightest forward. The physician must prevent asphyxiation, stop the bleeding, and treat the underlying cause [2]. This study aimed at exploring the feasibility and efficacy of nebulized tranexamic acid (n-TXA) and a nebulized recombinant factor VIIa (n-rFVIIa) when used in a two-step therapy protocol in children with intractable DAH in a pediatric intensive care unit. In this prospective trial, n-TXA (250 mg/dose for children < 25 kg and 500 mg/dose for children ≥ 25 kg) was administered to 18 children (median age 24.0 months [11.3, 58.5]) with intractable DAH. n-rFVIIa (35 µg/kg/dose for children < 25 kg, and 50 µg/kg/dose for children ≥ 25 kg) was added if no or minimal response was seen after 3 to 4 doses (18 to 24 hours) of n-TXA. DAH was stopped in 18 (55.6%) children with n-TXA alone within 24 hours of therapy. In the other 8 (44.4%) children, n-rFVIIa was added due to n-TXA failure. Six (75.0%) showed complete cessation of DAH, while two children failed to respond with the addition of n-rFVIIa (25.0%). None of the children who responded to therapy showed recurrence of DAH after therapy termination. Documented concomitant respiratory infection showed a significant negative association with response to n-TXA in a stepwise regression analysis (OR=0.06; 95% CI=0.01–0.74). No complications related to therapy were recorded [3-6].

Tranexamic acid (TXA), a synthetic derivative of the amino acid lysine, is an anti-fibrinolytic agent that exerts its action through binding to plasminogen preventing its binding to fibrin and hence its activation to plasmin [7]. TXA was also successful in controlling bleeding when directly administered intrapleurally [8] and into the pericardial cavity [9].

Recombinant factor VIIa (rFVIIa) is a hemostatic agent that achieves hemostasis by one of two mechanisms:

1) Activating factors X and IX at sites of tissue injury through binding to tissue factor (TF) and activated platelets resulting in thrombin generation;

2) TF-independent mechanism, in which rFVIIa directly activates factor X on the surface of activated platelets [10]. There is an increasing interest in off-label use of intravenous rFVIIa in children with clinical bleeding due to non-hemophilic reasons [11], including DAH in newborns [12] and children [13].

Recently, two case reports were published in which DAH was treated by direct intrabronchial rFVIIa instillation in children [14,15]. Several cases reported the successful use of rFVIIa locally administered through bronchoscope to adults with DAH. One case in was given rFVIIa through nebulization after failure of intravenous rFVIIa [16]. Direct intrabronchial instillation was the primary method of drug delivery in all reports [17-19].

This preliminary clinical trial confirmed the feasibility of n-TXA and n-rFVIIa when used in a two-step therapy protocol to control intractable DAH in PICU settings. The two drugs as used in this study showed an excellent risk/benefit profile that warrants further exploration through a larger multicenter prospective double blind randomized clinical trial which we are currently planning to start.

References

*Corresponding author: Hind Bafaqih, Pediatric Intensive Care, Prince Sultan Military Medical City, Riyadh, KSA, Saudi Arabia. Tel: 966555582218; E-mail: hbaqahf13@gmail.com

Received December 17, 2015; Accepted December 22, 2015; Published December 28, 2015

Copyright: © 2015 Bafaqih H, et al. This is an open-access article distributed under the terms of the Creative Commons Attribution License, which permits unrestricted use, distribution, and reproduction in any medium, provided the original author and source are credited.


