Comparison of antithrombin III products in patients on extracorporeal membrane oxygenation in a children's hospital: a pilot study of recombinant antithrombin III versus human antithrombin III

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Background

- Extracorporeal membrane oxygenation (ECMO) therapy is indicated in pediatric patients with acute severe respiratory or cardiac failure with life-threatening illness that is unresponsive to conventional medical therapy
- A major challenge of ECMO therapy is the balance between the prevention of thrombosis due to the body's hypercoagulable response to foreign material and drug-induced hemorrhage
- Unfractionated heparin (UFH) is the mainstay of anticoagulation therapy in pediatric patients on EMCO to prevent thrombosis of the circuit
- Pediatric patients have developmentally low levels of Antithrombin III (ATIII), which is an endogenous glycoprotein that irreversibly inhibits coagulation factors and as such tend to have higher heparin requirements because UFH requires ATIII to exert its anticoagulant effects
- In patients with escalating heparin requirements or clinically subtherapeutic anticoagulation, ATIII supplementation my be warranted but this practice has yet to be validated by prospective clinical trials
- There are two products currently available in the United State, one recombinant and one human
- ATIII levels are measured as a percent of normal and the goal range is 80-120% and at our institution, ACT values are the backbone of monitoring degree of anticoagulation

Objectives

- Compare the pre-ATIII heparin rates to post-ATIII heparin rates for pooled data to determine if there is a benefit of ATIII supplementation
- Compare the two current ATIII products with regard to safety, efficacy, and cost in pediatric patients requiring ATIII supplementation during ECMO
- *Primary*: reduction of heparin infusion rates from pre-ATIII to post-ATIII supplementation and length of ECMO circuit life
- *Secondary*:
  - ACT levels achieved post-supplementation
  - Goal ATIII levels post-supplementation
  - Quantity of transfusion requirements
  - Cost of ATIII supplementation

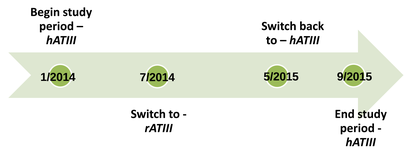
Disclosure

The authors have nothing to disclose.

Methods

- Retrospective chart review for pediatric patients receiving ECMO
- Including approximately 30 patients and 100 orders of either human of recombinant ATIII
- Study period of January 1st, 2014 to September 30th, 2015
- Evaluated ATIII supplementation on the order level

Inclusion Criteria
Pediatric patients < 18 years old
Venoarterial (VA) or venovenous (VV) ECMO
Received at least one dose of ATIII from the period of January 1st, 2013 to September 30th, 2015
Exclusion Criteria
None



Results

Baseline Characteristics

Characteristic	rATIII (N=10)*	hATIII (N=11)	Total ATIII (N=20)
Male – no. (%)	7 (70)	8 (73)	14 (70)
Age – yrs.	0.1	2.2	1.2
Neonate (0 – 30 days) – no. (%)	8 (80)	5 (45)	13 (65)
ECMO length - hrs.	109.9	183.5	150.4
Venovenous ECMO – no. (%)	10 (100)	11 (100)	20 (100)
Baseline ATIII level (%)	35.7	34.9	35.3
Doses of ATIII – no.	37	49	86
Doses per patient – no.	5.5	3.2	4.5
ATIII dose (units)	98.8	338.6	334.5

*One patient received both products
Data presented as mean unless otherwise noted

Figure 1. Mean ATIII levels before and after ATIII supplementation

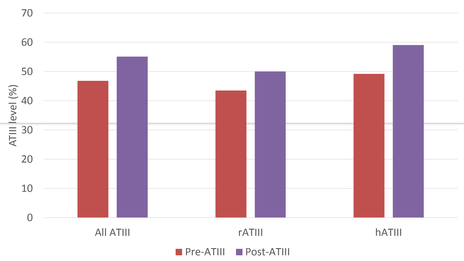


Figure 2. Mean heparin infusion rates before and after ATIII supplementation

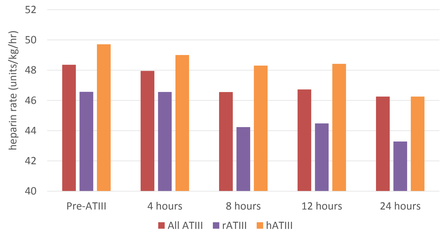
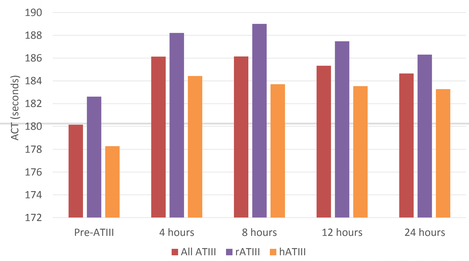


Figure 3. Mean ACT value before and after ATIII supplementation



Results

Figure 4. Cost of ATIII supplementation for the pooled data

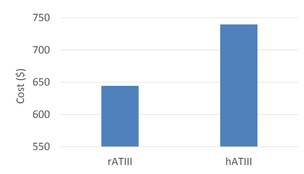
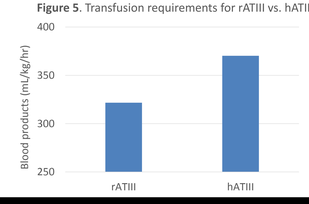


Figure 5. Transfusion requirements for rATIII vs. hATIII



Conclusions

- ATIII supplementation reduced heparin infusion rates and improved global anticoagulation
- Trend toward reduced need for transfusions and lower cost for the recombinant product
- Plan to analyze the data further for statistical differences between the products
- Limitations
  - Small patient population
  - Retrospective chart review
  - Results may be confounded by differences in pharmacokinetic characteristics
  - Redosing often occurred before the 24 hour time period

Bibliography

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