Evaluation of Safety and Efficacy of Currently Used Reversal Strategies for Factor Xa Inhibitor Associated Bleeding Events: A Retrospective Study

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BACKGROUND

- Around 2.9 million people in the U.S. are on factor Xa inhibitor therapy and from those patients, nearly 85,000 of them are hospitalized due to a bleeding event per year. [1]
- There are multiple reversal strategies that are currently used in the U.S. for factor Xa inhibitor associated bleeding events including activated and non-activated prothrombin complex concentrate (PCC), factor VII, activated charcoal, blood transfusion and a factor Xa inhibitor reversal agent.[2,3]
- Even though Andexxa (andexanet alfa) is the only current factor Xa inhibitor reversal agent, it has multiple barriers that restrain it from becoming a viable option for reversal.
- Additionally, although there have been studies in regards to some of these reversal strategies, they were either specific to one strategy alone and/or discussed limited data.[4,5,6,7,8,9]

OBJECTIVE

- To evaluate the safety and efficacy of currently used reversal strategies for factor Xa inhibitor associated bleeding events.

METHODS

Study Design
- Retrospective, patient chart review

Inclusion Criteria
- Adults of at least 18 years of age
- Must be on factor Xa inhibitor therapy such as Xarelto (rivaroxaban), Eliquis (apixaban), Savaysa (betrixaban), or Bevyxxa (betrixaban)
- Admitted to St. Elizabeth's hospital for a bleeding event within 11/2017 to 11/2019
- Received a reversal strategy

Study Measures
- Safety: documented complication(s) including ischemic event, cardiac event, or sudden death
- Efficacy: whether or not hemostasis was achieved and time to hemostasis

LIMITATIONS

- Not all documented factor Xa inhibitor reversal strategies were used at this hospital
- The completeness of the data collected was dependent on the quality of the documentation that was completed for each patient chart
- The sample size was smaller than anticipated

RESULTS

Table 1. Personal Demographic Information

Characteristic	n=8 (%)
Sex	
Male	2 (25%)
Female	6 (75%)

RESULTS

Table 1. Personal Demographic Information Continued

Characteristic	n=8 (%) or average (range)
Age	
60-69	1 (12.5%)
70-79	2 (25%)
80-89	5 (62.5%)
Weight (kg)	
<60	0 (0%)
60-69	1 (12.5%)
70-79	3 (37.5%)
80-89	2 (25%)
90-99	2 (25%)
Serum Creatinine (mg/dL)	1.59 (0.84-3.03)
Creatinine Clearance (mL/min)	
<30	2 (25%)
30-60	3 (37.5%)
>60	3 (37.5%)

Table 2. Factor Xa Inhibitor

Characteristic	n=8 (%)
Factor Xa Inhibitor	
Eliquis (apixaban)	8 (100%)
Xarelto (rivaroxaban)	0 (0%)
Savaysa (edoxaban)	0 (0%)
Bevyxxa (betrixaban)	0 (0%)
Indication	
Atrial Fibrillation	8 (100%)
Deep Vein Thrombosis (DVT)	0 (0%)
DVT Prophylaxis	0 (0%)
Pulmonary Embolism (PE)	0 (0%)
Dose & Frequency	
2.5 mg BID	1 (12.5%)
5 mg BID	7 (87.5%)

Table 3. Bleeding Event

Characteristic	n=8 (%)
Type	
Subdural Hematoma	1 (12.5%)
Soft Tissue Hematoma	1 (12.5%)
Upper Gastrointestinal	1 (12.5%)
Lower Gastrointestinal	2 (25%)
Hematemesis	2 (25%)
Intracranial Hemorrhage	1 (12.5%)
Cause(s)	
Unknown/Undocumented	4 (50%)
Dose double up	1 (12.5%)
Drug interaction	2 (25%)
Trauma	1 (12.5%)

Table 4. Reversal

Characteristic	n=8 (%)
Reversal Strategy	
Non-activated Prothrombin Concentrate Complex (nAPCC)	8 (100%)
Blood transfusion	7 (87.5%)
Activated Prothrombin Concentrate Complex (APCC)	0 (0%)
Activated Charcoal	0 (0%)
Factor VII	0 (0%)
Andexxa (andexanet alpha)	0 (0%)
Non-activated Prothrombin Concentrate Complex (nAPCC)	
Dose (units/kg)	
20-26	1 (37.5%)
40-54	5 (62.5%)

RESULTS

Table 4. Reversal Continued

Characteristic	n=8 (%)
Blood transfusion	
Dose (units)	
1	5 (71.4%)
2	1 (14.3%)
7	1 (14.3%)

Table 5. Safety

Characteristic	n=8 (%)
Complications	
Non-documented	8 (100%)
Ischemic Event	0 (0%)
Cardiac Event	0 (0%)
Sudden Death	0 (0%)

Table 6. Efficacy

Characteristic	Overall n=8 (%) or average (range)
Achieved Hemostasis*	
Yes	4 (50%)
No	2 (25%)
Undocumented/ Transferred	2 (25%)
Hb Level Before Reversal Strategy (g/dL)	8.8 (4.4-12.7)
Hb Level After Reversal Strategy (g/dL)	9.8 (7.7-12.9)
Approximate time to hemostasis (days)	
Non-applicable	2 (25%)
Non-documented	2 (25%)
1	2 (25%)
2	1 (12.5%)
3	1 (12.5%)

*Defined as improvement of signs/symptoms of bleeding or resolution of bleeding

CONCLUSION

- Although the sample size of this study was small, it shows us that factor Xa inhibitors seem to be dosed appropriately. However, they may have caused or contributed to bleeding events despite appropriate dosage.
- No documentation of a thromboembolic event, ischemic event, cardiac event or sudden death. Does not necessarily imply safety of these reversal strategies.
- This reversal strategy does not seem to be efficacious for factor Xa inhibitor associated bleeding events.
- More studies should be completed including multiple hospitals to maximize data collection that includes multiple reversal strategies and has a larger sample size.

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