Saint Barnabas Medical Center

RWJBarnabas HEALTH

Retrospective review of andexanet alfa prescribing and outcomes at a community teaching medical center

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Background

- In May 2018, the FDA approved Andexxa (andexanet alfa) as a specific reversal agent for rivaroxavan and apixaban – treated patients presenting with life-threatening or uncontrolled bleeding.
- At this community teaching medical center, this medication was added to formulary with specific restrictions for safety and efficacy, as listed below:

a) Life threatening hemorrhage when a Xa inhibitor medication was administered within the last 18 hours
b) In intracranial hemorrhage patients with Glasgow Coma Score of >5
c) Ordering will be restricted to critical care units, emergency department, cardiology, and/or hematology attending physicians or their direct designee

- The ANNEXA-4 study lacked correlation to improved patient outcomes or comparison to standard of care therapy. The study noted that no significant relationship existed between hemostatic efficacy and reduction in anti-factor Xa activity during treatment.
- Rates of thrombosis and mortality in ANNEX-4 were 18% and 15% respectively.

Objective

- The objective of this study was to evaluate the prescribing patterns for andexanet and determine efficacy and safety for patients in which andexanet alfa was administered in life threatening hemorrhage

Methods

- IRB approved retrospective chart review
- Inclusion: patients who received andexanet alfa or for whom andexanet alfa was requested from a pharmacist by a prescriber and not ultimately administered
- The clinical outcomes evaluated: time to administration and verification, length of hospital stay, use of blood products, vital signs, complete blood counts, coagulation studies, past medical history, medication history, evidence of thrombosis including of arterial and venous thromboembolic events, ischemic events including stroke and heart attack, cardiac arrest, and sudden death, and mortality at hospital discharge
- Statistical analysis entailed descriptive statistics only

Results

N (%)	Administered (N=9)	Inquiry rejected (N=7)
Indications		
ICH	5 (55.5)	1 (14)
GI Bleed	2 (22.2)	2 (28)
Emergent Surgery	2 (22.2)	4 (57)
Other	----	1 (14)
Anticoagulants		
Apixaban	6 (66.6)	5 (71)
Rivaroxaban	3 (33.3)	2 (28)
Other	0 (0)	1 (14)
Hospitalization		
ICU Admission	9 (100)	6 (85.7)
ICU LOS (Avg. days)	5.6	3.2
Hospital LOS (Avg. days)	8.6	5.5
Inpatient Mortality	4 (44.4)	1 (14)
Thrombotic Event, total	3 (33.3)	1 (14)
Ischemic stroke	2 (22.2)	0
Cardiac	1 (11)	0
DVT	0	1 (14)
Other treatments		
PRBC's	2 (22.2)	3 (42.9)
FFP	0	2 (28)
Cryo	0	1 (14)
Platelets	0	2 (28)
DDAVP	0	1 (14)
PCC	2 (22.2)	3 (42.9)
Time to treatment min -Mean (SD)		
Presentation to order	144.7 (±188.9)	---
Order to verification	16.6 (±5.26)	---
Verification to admin.	93.75 (±81.62)	---
Approving Prescriber		
Critical Care	7 (77.7%)	---
Cardiology	0 (0)	---
Emergency	2 (22.2)	---
Restriction Criteria Met	6 (66.6)	0 (0)
Medication Cost November 2018 to November 2019	Drug Spending from $319,000	Estimated Drug cost avoided from $203,280

Patient Cases in which Andexanet Alfa Administered

Bleed Type	Concomitant therapy	Patient Outcome
Intracranial hemorrhage per verbal communication GCS 8 per all documentation GCS 3T	PCC prior to transfer to SBMC, neurosurgical intervention	Death within 24 hours
Intracranial hemorrhage ICH score 3 with poor prognosis noted	Extra ventricular drain inserted	Death within 24 hours
Intraventricular hemorrhage with "greater than 90% mortality" GCS of 3T	N/A	Death within 24 hours
Subarachnoid hemorrhage GCS 14	N/A	MCA infarct identified 9 days post administration
GI bleed from apixaban and unknown last ingestion. Blood pressures maintained SBP >90, HBG drop from 8.5 to 6.5 within 4 hours	Andexanet alfa ordered prior to standard of care therapies such as blood products. Blood products where subsequently hung with additional fluids after andexanet alfa.	MCA ischemic stroke within 24hrs of andexanet alfa administration, Death within 30 days
Right sided thalamic intracranial hemorrhage, GCS of 15	N/A	Survived
Emergent spinal surgery for cord compression on apixiban	Bolus andexanet given only	No significant blood loss
ICH with intraventricular extension, GCS 14,	Decompressive craniotomy, neurosurgery 4PCC intraoperatively also	TEE with left atrial appendage thrombus 3 days after surgery, expired after 14 days
Jehovah's witness patient, refused transfusions, received andexanet alfa	N/A	Survived

Discussion

- Primary reason for non- adherence to restriction criteria was GCS < 5, followed by surgical use
- Concomitant treatment with PCC occurred due to transfer from outside institution and intraoperative use
- The restriction process and pharmacist intervention lead to a significant number of cases of avoided use and potentially thrombosis without a greater rate of mortality
- Ongoing review of PCC use will be necessary
- A formalized escalation process for cases which did no meet criteria would be beneficial in the future

Limitations

- Single center
- Retrospective study analysis
- No formal process for statistical analysis
- Severity of illness scales were not reported

Conclusion

After 1 year of use at a community medical teaching institution there was a larger rate of adverse effect and mortality with the use of andexanet alfa than illustrated in clinical trials This is potentially due to the use in a more severely ill population and lack of adherence to restriction criteria

This represents a single center experience and minimal conclusions can be drawn until more institutions provide clinical use data or a randomized controlled trial comparing to the previous standard of care, prothrombin complex concentrate is available.

References

1. Andexanet alfa (Andexxa®) Package Insert. Portola Pharmaceuticals, Inc. December 2018.
2. Connolly SJ, Crowther M, Eikelboom JW, et al. Full Study Report of Andexanet Alfa for Bleeding Associated with Factor Xa Inhibitors. N Engl J Med. 2019;380(14):1326-1335..

Disclosure

The authors have nothing to disclose.