Clinical Considerations in the Use of Antidote Agents to Non-Vitamin K Oral Anticoagulants: The Emergency Department Perspective

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CSRC
February 3, 2015

Oral Anticoagulants and the ED

- Often a toxic mix
- We see complications from both under- and over-anticoagulation
- We manage anticoagulated patients with all severities of bleeding and anticoagulated patients who need emergent “sharp” procedures
- We have relatively standardized approaches to warfarin-related bleeding* and no consistent approach to NOAC management

* *sans* comfort with PCCs

NOACs and the ED

- Generally, a great deal of insecurity
- Lack of familiarity with agents
- Most emergency physicians have a higher level of comfort with NOACs for VTE than for SPAF
  - Unfortunately, NVAF patients have a higher comorbidity burden, are older, and are more likely to have serious complications
- Significant concern over inability to measure effect
- Without assay, NOAC-related bleeding cannot be managed by a protocol similar to that for warfarin

Managing Bleeding and Bleeding Concerns with NOACs in the ED

- No correlate to INR in warfarin-treated patients
- For bleeding concerns (e.g., pre-surgery), education needed re half-lives, knowing time of last dose, renal function, available assays and their interpretation, etc
- For frank bleeding, same information is helpful, but even when it is used appropriately, how is therapy escalated?
  - Decontamination
  - Vitamin K (RE-LY experience)
  - FFP
  - PCCs and specific factor concentrates
  - Will specific antidotes be overutilized?

What Are Examples of Post-Marketing Data That Are Most Appropriate to the NOAC Antidotes?

- Pharmacovigilance on lytics (NRMI)
- CRUSADE: captured data on use of ACS therapies and compared to evidence basis
- Pharmacovigilance on Xygris
- Single institution evaluations of pertinent assays and dosing data vs practice, i.e., manual chart review
- Must combat emergency physician's perspective of addressing the most immediate life threat

What Indications Should be Tracked and What Information is Needed for these Indications?

- Two indications: Bleeding and Bleeding Concern
- Both should be tracked
- Emergency physicians and neurosurgeons will be most common decision makers for bleeding, whereas surgeons and IR will be most common decision makers for bleeding concerns
- Compare decision to treat with dosing and renal function parameters, coag assays
- Compare outcomes for similar patients who are managed without antidotes

How Strong Does the Level of Evidence Have to Be to Support Safety?

- No evidence of thrombin generation
- No (or extremely rare) hypersensitivity reactions, hypotension, etc
- No signals of poorer outcomes than with current (non-antidote) management
- Need to see consistency of effect

How Strong Does the Level of Evidence Have to Be to Rule Out Inappropriate Use?

- Will be a significant challenge
- Once emergency physicians or surgeons cross the Rubicon . . .
  - to state that there is a life threat that is due to a specific drug . . .
  - and now I can take that drug's effect away? . . .
  - hard to stop that momentum
- Price and resulting formulary controls will doubtless impact use
  - Have to be very careful about putting up roadblocks to potentially life-saving therapy