Evaluation of direct oral anticoagulant (DOAC) prescribing habits at a VA Health Care System

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Abstract #2
IRB Approved

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Disclosure

- Hanifah Davis
- Protection conflicts of interests: none
- Sponsorship: none
- Proprietary information or results of ongoing research may be subject to different interpretations
- Speaker's presentation is educational in nature and indicates agreement to abide by the non-commercialism guidelines provided

Objectives

- Identify the current need to evaluate DOAC prescribing habits at the Oklahoma City VA
- Discuss common patient and medication factors that contribute to inappropriate prescribing

Pre-assessment

1. Which of the following ordering methods are utilized to encourage safe prescribing?
   a) Non-formulary
   b) Prior authorization
   c) Criteria for use
   d) Restricted consult
   e) All of the above
2. Which of the following patient factors exclude a patient from receiving a direct oral anticoagulant?
   a) Creatinine clearance of 36 ml/min
   b) Acute viral hepatitis
   c) Past medical history of non-small cell lung cancer
   d) Tricuspid regurgitation

Introduction

- Thrombotic events are amongst the leading causes of morbidity and mortality in the US
- Atrial fibrillation increases stroke risk by 5-fold
- 600,000 suffering annually from deep vein thrombosis (DVT) or pulmonary embolism (PE)
- 100,000 die from venous thromboembolism (VTE) related causes

Kirley K, et al. *Circ Cardiovasc Qual Outcomes*. 2012;5(5):615-21
Hellwig T, et al. *Am J Health Syst Pharm*. 2013;70(2):113-25.

Warfarin

- Previous gold standard
- Challenges:
  - Narrow therapeutic index
  - Frequent monitoring
  - Complex dose adjustments
  - Significant drug-drug interactions
  - Dietary considerations

Direct Oral Anticoagulants

- Dabigatran, apixaban, rivaroxaban, edoxaban
- Offer solutions to many challenges associated with warfarin
  - Fixed dosing
  - No drug monitoring
  - Fewer drug interactions
  - Not effected by vitamin K foods
- FDA approved as alternative first line agents
  - VTE treatment/prophylaxis
  - Non-valvular atrial fibrillation

Review of the Literature

- Larock et al:
  - Evaluated use of dabigatran and rivaroxaban in NVAF
  - 34 of 69 (49%) patients: ≥1 inappropriate criteria, 23% clinically important
    - Choice → patients >110kg
    - Dosage
    - Administration
  - Bleeding and thrombosis occurred more often with ≥1 inappropriate criteria

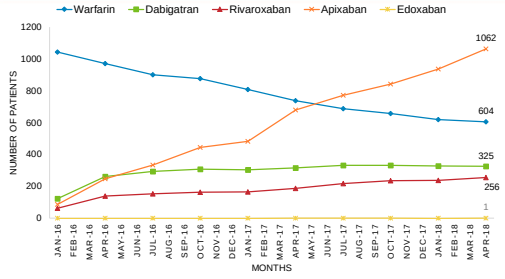
Larock AS, et al. *Ann Pharmacother*. 2015:48(10):1258-68.

Review of the Literature, cont.

- Whitworth et al:
  - Evaluated use of all DOAC's in NVAF and VTE
  - 60% patients with ≥1 inappropriate criteria
    - Duration, Administration, Dosage
  - Significant predictor of bleeding
- Post marketing registry data:
  - Underdosing/Overdosing
  - Dosing discrepancies: Age, female, CHA_2DS_2-VASc ≥2, bleeding risk

Whitworth MM, et al. *Int J Gen Med*. 2017;10:87-94.
YoaX, et al. *J Am Coll Cardiol*. 2017;69(23):27779-2790.
Steinberg BA, et al. *J Am Coll Cardiol*. 2016;68(24):2597-2604

Anticoagulant Trends at the OKC VA



Oklahoma City VA Ordering Methods

- Formulary
- Non-formulary
  - Prior authorization/restricted consult
- Criteria for use (CFU)

Criteria-for-use Process

- Recommendations provided by VA Pharmacy Benefits Management Services
- Outlines:
  - Exclusion criteria
  - Inclusion criteria
  - Dosing
  - Clinical considerations

1. Create new note
2. Select indication
3. Select drug
4. Select dose
5. Order generated

DOAC CFU

EXCLUSION CRITERIA

- Severe renal impairment
  - CrCl <25ml/min or Scr >2.5mg/dL (if apixaban)
  - CrCl <30ml/min all other DOACS
- Indication other than VTE or NVAF
- Comorbidities
  - Significant liver disease
  - Prosthetic heart valve or significant valvular disease
  - Active bleeding or endocarditis
- Drug interactions
  - Strong P-gp/CYP3A4 inhibitors or inducers

Study Objective

- To evaluate the effectiveness of the CFU process for guiding safe and appropriate prescribing of a DOAC at the Oklahoma City VA Health Care System
- To identify patient factors that may influence inappropriate prescribing

Study Design

- Retrospective chart review
- January 2017 – March 2017
- Institution:
  - Oklahoma City VA Health Care System
  - 192-bed, tertiary care facility
  - Community Based Outpatient Clinics (CBOCs)
    - Ada, Altus, Ardmore, Blackwell, Enid, Lawton, Oklahoma City, Stillwater and Wichita Falls
  - Provides ≥630,000 encounters to ≥225,000 patients annually

Patient Population

Inclusion Criteria

- Active prescription for rivaroxaban, apixaban, dabigatran or edoxaban
- Ordered through CFU note specified for VTE treatment or stroke prevention in NVAF

Exclusion Criteria

- Ordered using non-formulary review process
- Initiated by non-VA physician
- Inadequate documentation in medical record to meet inclusion

Outcome Measures

- Primary outcome:
  - Prevalence of inappropriate prescribing
- Secondary outcome:
  - Description of categories of inappropriate prescribing
  - Thrombotic events within 3 months of CFU
  - Bleeding events within 3 months of CFU
  - Subgroup analysis
    - Indication, prescriber type, agent, weight, age

Data Collection

- Patients identified through the Veterans Information Systems and Technology Architecture (VISTA)
  - Active DOAC prescription
  - January – March 2017
- Clinical Patient Record System (CPRS) to collect patient information
- CFU guide to determine appropriateness of medication

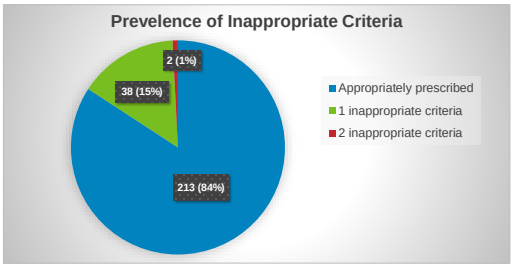
Statistical Analysis

- Descriptive statistics
  - Percentage, mean, range, standard deviation
- Subgroup analysis
  - Chi-square – categorical data
  - T-tests – continuous data
  - ANOVA – multiple groups
- Alpha value set at 0.05

Baseline Demographics

Variable	Statistic; n=253
Age (years; mean)	70
Gender	
Male	96.4%
Female	3.6%
Indications	
Atrial Fibrillation	69.2%
VTE treatment	30.8%
Both	4%
Orthopedic prophylaxis	0.4%
DOAC prescribed	
Apixaban	64%
Rivaroxaban	19.8%
Dabigatran	15%
CHA2DS2-VASc Score (mean)	3.5%
CHF	28.6
Hypertension	85.9%
Age ≥75	41.1%
Diabetes	42.7%
Stroke/TIA	9.2%
Vascular disease	50.8%
CrCl (mean)	73.6 ml/min

Primary Endpoint



Secondary endpoints

- Description of inappropriate criteria

Description	Number of patients
Dose	19
Indication	10
Renal impairment	7
Drug-disease exclusion	4
Drug-drug interaction	2

- Prevalence of adverse events with 3 months of CFU

Adverse event	Number of patients
Thrombosis	3
Bleeding	10*

*Only 2 patients with bleeds had ≥1 inappropriate criteria

Subgroup analysis

Category	Event rates - n (%)	P-value
Indication		
PE	1 (3.3)	0.04
DVT	10 (20.4)	
AFIB	33 (19)	
DOAC		
Apixaban	28 (17.1)	0.53
Dabigatran	9 (23.1)	
Rivaroxaban	7 (14)	
Weight		
≥120 kg	8 (22.2)	0.42
<120 kg	36 (16.6)	
Age		
≥75 years	13 (20.3)	0.48
<75 years	31 (16.4)	

Conclusion

- CFU process was effective in guiding appropriate DOAC prescribing 84% of the time
- The most commonly identified inappropriate prescribing criteria include dose, indication and renal impairment
- Each of the listed criteria are clearly outlined and displayed in the CFU note template while ordering a DOAC
- Patient characteristics within the subgroups did not play a role in inappropriate prescribing
- Contrary to current literature, our findings do not indicate a correlation with prevalence of inappropriate criteria and adverse safety outcomes

Discussion

- Based on the results, there is no need to return to non-formulary/restricted consult as an ordering method
- National DOAC monitoring system recently initiated at VA
  - Flags patient profiles with inappropriate prescribing criteria
- Education to the physicians based on trends
- CFU note improvement
  - Hard stops/flags when patients do not meet criteria
  - Incorporate pulled lab values

Post-assessment

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2. Which of the following patient factors exclude a patient from receiving a direct oral anticoagulant?
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Reference

1. Kirley K, Qato DM, Kornfield R, Stafford RS, Alexander GC. National trends in oral anticoagulant use in the United States, 2007 to 2011. *Circ Cardiovasc Qual Outcomes*. 2012;5(5):615-21
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